ANGEWANDTE
CHEMIE

Volume 20 · Number 1
January 1981
Pages 1–134

International Edition in English

# Condensed Metal Clusters

By Arndt Simon[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

The chemistry of metals in low valence states is marked by the frequent occurrence of metal clusters, which are easily recognizable when they occur as molecular units. Many metal-rich compounds of transition metals with p-elements (3rd to the 6th main groups) are closely related to the corresponding halides, since they are built up from metal clusters of the same type. The clusters are however, linked together (condensed) by metal-metal bonds. This principle of construction holds particularly well in the case of the novel reduced halides of the lanthanoids.

## 1. Introduction

The chemistry of compounds of transition metals in low oxidation states with main group elements is full of examples showing unusual compositions in terms of traditional valence rules. Above all, 4d- and 5d-elements are capable of using the remaining valence electrons to form metal-metal bonds. The occurrence of M—M bonds rationalizes the coincidental integer values of the oxidation state of many transition metals, and has resulted in the replacement of the old scheme of classification of simple compounds of these elements by oxidation numbers, by one involving structural elements.

M—M bonds can be restricted to a few directly coupled atoms, which leads to clearly defined bonded groups ("clusters"). Such clusters occur in discrete molecules or in quasi-molecular units joined by bridging ligands. Frequently, however, infinitely extended regions of bonded metal atoms result. The first group of cluster compounds have been the subject of numerous studies in the last twenty years and have been described in a series of review articles[1-15], which are already difficult to list completely; detailed descriptions are to be found in text books of inorganic chemistry. The following study is concerned with the structural relationship between cluster compounds of this sort and compounds containing extended regions of M—M bonding, which occur in the metal-rich binary compounds of transition metals as well as lanthanoids, with the elements of the seventh to the third main groups.

Conditions for the formation of metal clusters are particularly favorable when the non-metal involved, donates as many valence electrons as possible to the metal atoms on the one hand and, is present in a proportion which is sufficient to fully surround the cluster, on the other hand. As a result, the M—M bond has been most thoroughly studied in discrete clusters of the halides of the transition metals. In the case of compounds with elements of the 6th to the 3rd main groups the two above conditions cannot be readily met simultaneously. High valence electron concentration (VEC) for the metals normally demands a low non-metal content so that the resulting metal clusters do not show up as isolated (and easily recognizable) units. Metal-rich compounds of transition metals with the above elements are therefore as a rule, characterized by extended regions of M—M bonds, and the coordination of non-metal by metal atoms becomes the dominant structural feature. The structures of metal-rich compounds of the transition metals with elements of the 6th to

---

[*] Prof. Dr. A. Simon
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)

the 3rd main groups have therefore been repeatedly reviewed in terms of characteristic coordination polyhedra of non-metal atoms and the way in which they link together[16–18]. The interaction between the metal atoms, which in these compounds is also extremely important, has not received so much attention[18, 19], although its significance in the structural chemistry of the halides had been recognized much earlier. A detailed analysis in fact shows that the same atomic arrangements as in the halide clusters, play an important role in a vast number of metal-rich compounds of transition metals with multivalent non-metals. The basic principle is simple; when the number of non-metal atoms in a compound is not sufficient to completely surround the metal cluster, the latter link up *via* direct M—M bonds, *i. e.* they "condense".

Cluster-condensation closely corresponds to the stepwise transition from benzene to graphite *via* intermediate carbon-rich polycyclic compounds. A second analogy can be found in the structural chemistry of silicates, which is dominated by various arrangements of condensed $SiO_4$-tetrahedra. This comparison in particular, illustrates the main difficulty in applying the concept of condensed metal clusters. Because of the exclusive presence of $SiO_4$-tetrahedra and their linkage *via* vertices, the structural principles of silicates are relatively simple.

On the contrary, the large variety of existing isolated metal clusters is further extended in systems with condensed clusters. Furthermore, the kind of linkage between clusters is variable and, finally, the bond lengths in metal clusters may fluctuate within a large range. These difficulties explain the prolonged hesitation in presenting the still qualitative concept[20–24] in a comprehensive version. The encouragement to give a more extensive description has been provided by some of the most recent results; compounds containing two or three condensed $Mo_6S_8$ clusters have been recognized as intermediate species on the way to the infinite $Mo_3S_3$-chain (*cf.* Section 3.3) and it has become evident that the novel chemistry of metal-rich halides of the elements Sc, Y, and the lanthanoids can be readily explained by application of this concept (*cf.* 3.2.2).

This review article has two objectives; firstly an attempt is made to reach a unified description and an understanding of the underlying structural principles of a wide range of metal-rich compounds of the transition metals, by considering characteristic M—M contacts (together with M—X contacts). Secondly, it is desirable to demonstrate the essential unity of "molecular" and "solid state" inorganic chemistry. It is also hoped that a contribution will be made to the understandig of an important class of substances, which fall equally under the headings of molecular compounds and coordination compounds as well as intermetallic phases.

## 2. General Approach to the Concept of Condensed Clusters

What boundary conditions determine the existence of a particular isolated metal cluster? This question has been treated several times, particularly for carbonyls and organometallic compounds[25–27]. In the present discussion on halide cluster compounds, only qualitative aspects will be considered. For this purpose, the number of valence electrons on the metal atom (VEC) which are available for M—M bonding for some binary compounds and anions are plotted in Figure 1 against the halogen/metal ratios (X/M). In the ionic limit, the value of VEC for the compound can be obtained from the VEC of the appropriate free metal ($VEC_0$) according to:

$$VEC = VEC_0 - n \cdot (X/M)$$

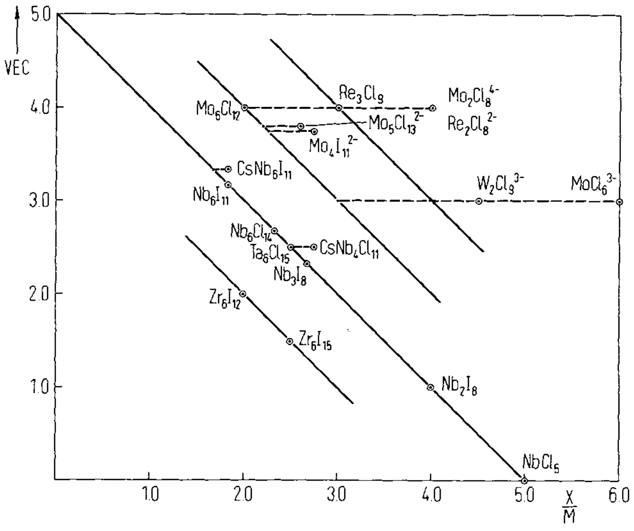


Fig. 1. Influence of valence electron concentration at the metal atom (VEC), and non-metal/metal ratio (X/M) on the size of a metal cluster in the halides of Zr, Nb, Ta, Mo, W, Re (see text).

This type of treatment is valid for the halides ($n = 1$) in general, and is still applicable with certain restrictions, for the chalcogenides ($n = 2$). Basic differences exist, however, from other procedures for "counting electrons"[28]. An extension of this approach to compounds of transition metals with elements of the 5th and 4th main groups is however not possible in this simple form. The X atom will certainly, however, remain the anionic counter-ion and it also behaves structurally much as a chalcogen, as will be seen from the comparisons discussed in the next chapter.

From the examples given in Figure 1, the following trivial conclusions can be drawn:

(a) Lowering the oxidation state of a transition metal (and with it an increase in VEC) in one of the halide compounds which lies on the line (solid) of gradient −1, leads to larger metal clusters; $NbCl_5$ contains isolated Nb atoms[29], $Nb_2$ pairs are present in ($\alpha$)-$Nb_2I_8$[30] and $Nb_3I_8$ contains $Nb_3$ clusters[31]. The $M_6X_{12}$ cluster is formed in the compounds $Nb_6F_{15}$[32] and $Ta_6Cl_{15}$[33], and is first retained as the oxidation number is lowered further in $Nb_6Cl_{14}$[34] but is finally replaced by the $M_6X_8$ cluster when the oxidation number is further lowered in $Nb_6I_{11}$[35] and $CsNb_6I_{11}$[36]. Interestingly enough, the $M_6X_8$ cluster only appears in a small area of Figure 1. It is not formed as an isolated cluster by Zr; the VEC is apparently too small. For Re halides, on the other hand, X/M (or VEC) is too large. As expected, however, the $Re_6S_8$ cluster exists[37]. In contrast to the $M_6X_8$ species, the $M_6X_{12}$ cluster turns out to be less sensitive to the VEC, occurring not only at very low values in the compounds $Zr_6I_{12}$ and $Zr_6Cl_{15}$[38], but also at extremely high values in $Pt_6Cl_{12}$[39] and corresponding Pd halides (M—M bonds absent). According to MO calculations[40,41], there may be 16 bonding electrons in this cluster (VEC = 2.67). A low X/M value is apparently more important in these species for the formation of the $M_6X_{12}$ cluster than special values of VEC. The influence of the VEC can be clearly seen in a comparison of the compounds $Nb_3Br_8$[39], $Nb_3Se_4$[50] and $Mo_6Se_8$[51]. In $Nb_3Br_8$, trigonal $Nb_3$ clusters are found; a trigonal $Nb_3$ grouping is also present in $Nb_3Se_4$ with the same VEC. In contrast, the compound $Mo_6Se_8$, with the same composition as the last compound but higher VEC, contains isolated $Mo_6Se_8$ clusters.

(b) The dominating effect of the X/M ratio on the cluster size can be seen from the examples in Figure 1, and is easily understood, since, with increasing cluster size, the number of non-metal atoms which can coordinate to metal atoms becomes smaller. The following examples demonstrate in an interesting way how the cluster shrinks through raising the X/M ratio. While the VEC is the same in $Nb_6F_{15}$, $Ta_6Cl_{15}$ and $CsNb_4Cl_{11}$[42] only $Nb_4$ clusters occur in the latter[42]. In the case of divalent molybdenum the dimeric anion $Mo_2X_8^{4-}$ forms, on raising the value of X/M[43], instead of the very stable $Mo_6X_8$ cluster. In this ion and in the isoelectronic $Re_2X_8^{2-}$ ion, the high VEC leads to a fourfold bond between the metal atoms[44]. The metal atoms in the $Mo_6X_8$- and $W_6X_8$-clusters can be oxidized up to the oxidation number +3[45,46], but the resulting compounds are thermodynamically unstable. In contrast, the stable compounds $[(C_4H_9)_4N]_2Mo_5Cl_{13}$[47] and $[(C_4H_9)_4N]_2Mo_4I_{11}$[48] contain clusters which result structurally from the removal of one or two Mo atoms from the $Mo_6X_8$ cluster. In the case of $K_3MoCl_6$, the "dilution" of the transition metal is so high that, despite the high value of VEC = 3, M—M bonding is no longer possible[49].

On studying the structures of $Nb_3Br_8$ and $Nb_3Se_4$, a problem becomes apparent which plays an important role in condensed metal cluster systems which will be treated later; the M—M distances inside a cluster are very variable. This is known for isolated clusters, but holds most strongly for clusters which can form bonds to M atoms of adjacent clusters. In the halide $Nb_3Br_8$, three $NbBr_6$ octahedra are joined by common *edges* (Fig. 2a). The M—M bond is recognizable by the shift of the Nb atoms towards the center of the cluster. Depending on the particular halogen atoms around the cluster, the Nb—Nb bond lengths are 281, 288 and 300 pm respectively in $Nb_3Cl_8$[52], $Nb_3Br_8$ and $Nb_3I_8$[31]. It is natural to attribute the variation in bond lengths to the matrix effect of the differently-sized halogen atoms.

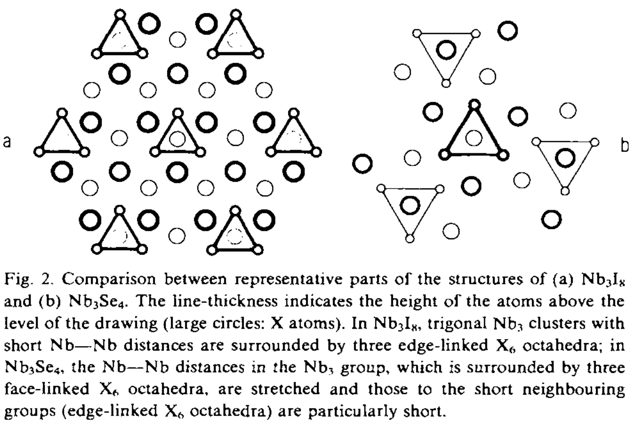


Fig. 2. Comparison between representative parts of the structures of (a) $Nb_3I_8$ and (b) $Nb_3Se_4$. The line-thickness indicates the height of the atoms above the level of the drawing (large circles: X atoms). In $Nb_3I_8$, trigonal $Nb_3$ clusters with short Nb—Nb distances are surrounded by three edge-linked $X_6$ octahedra; in $Nb_3Se_4$, the Nb—Nb distances in the $Nb_3$ group, which is surrounded by three face-linked $X_6$ octahedra, are stretched and those to the short neighbouring groups (edge-linked $X_6$ octahedra) are particularly short.

In the chalcogenide $Nb_3Se_4$, three $NbSe_6$ octahedra are joined by common *faces* to form trigonal $Nb_3$ groups (Fig. 2b). The resulting $Nb_3Se_{11}$ groups are, however, connected to each other *via* octahedral *edges* with bonds between similar surrounding groups, and the Nb atoms are shifted in the direction of the shared edges—as in the halides $Nb_3X_8$. For $Nb_3S_4$[53], $Nb_3Se_4$[50] and $Nb_3Te_4$[54], this interaction leads to an enlargement of the $Nb_3$ groups to 337, 347 and 365 pm, respectively, while particularly short Nb—Nb bonds form between atoms of the adjacent $Nb_3$ groups (288, 280 and 297 pm respectively). This can be explained by an improved orbital overlap for the Nb atoms *via* the edges of the coordination octahedra[55].

In summary, it can be stated that compounds with isolated $M_6X_8$ or $M_6X_{12}$ clusters form the boundary at low values of X/M in Figure 1. It was presumed therefore that clusters of the $M_6X_8$-type would maintain their importance as structural units on further reduction of the X/M ratio. This assumption has, in fact been confirmed in an impressive manner by the discovery of the stepwise condensation of $M_6X_8$ clusters (*cf.* Section 3.3).

The structure of $Nb_3Se_4$ makes it clear that the configurations of clusters should also be taken into account when analyzing the structural principles of metal-rich transition metal compounds, even if the M—M bond lengths within the cluster are not the shortest in the structure. There is of course a possible danger of setting up a scheme which ignores the core of the structure, namely the chemical bonds. On the other hand, it is a fact that every structural classification system is based on idealized structures. This is just as true for the "Frank-Kasper" concept[56] as for "lattice complexes"[57] or "chemical twinning"[58]. The ideal structure relaxes and only this relaxed structure is observed. A considerable amount of interpretation is already introduced when reconstructing the ideal arrangement. Two arguments speak in favour of considering the topology of a cluster even in the case of large M—M distances. On the one hand, it is only possible to describe the chemical bonding in an isolated cluster by taking the X atoms into account. Such multi-center bonds are also of importance in condensed bonding systems, as long as the geometry of the metal cluster is, in principle, retained. On the other hand, it should also be noted that no generally valid relationship exists between interatomic distance and bond order. Widely held concepts[59] are contradicted, *e.g.*, in the cases of metal-rich alkali metal oxides[60] and alkaline earth nitrides[61-63], as the bonding M—M distances are considerably larger than the non-bonding distances.

## 3. Principles of Cluster Condensation

The conclusion may be drawn from Section 2 that the $M_6X_8$ and $M_6X_{12}$ clusters, which tend to form isolated units down to X/M ratios of 1.33 and 2.00 respectively, will be retained as structural units on further reduction of X/M. The present study is chiefly concerned with those compounds which contain condensed octahedral $M_6$-groups, and concludes with compounds containing some further types of condensed clusters. Of course, only a certain proportion of the compounds with condensed clusters can be discussed.

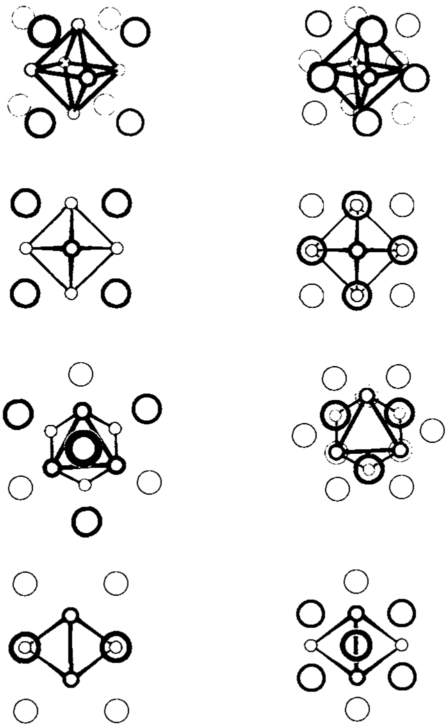


Fig. 3. $M_6X_8$ and $M_6X_{12}$ clusters shown three-dimensionally and as projections along the 4-, 3- and 2-fold axes.

The $M_6X_8$ and $M_6X_{12}$ clusters are shown three-dimensionally and in various projections in Figure 3, to explain the graphical representations which are used in a standardized way in this work. When such clusters are condensed, not only M atoms but also X atoms are shared by adjacent clusters. Positions which are occupied by X atoms in the isolated cluster can often, for steric reasons, no longer be occupied in the condensed cluster system[*]. Up to now, relatively few examples of condensed systems of $M_6X_{12}$ clusters are known. On the other hand, many structures exist in which $M_6X_8$ clusters (or fragments of these clusters) are present.

### 3.1. Vertex-Linked $M_6$ Clusters

The condensation of $M_6X_8$ clusters *via* opposite M atoms leads to a *one-dimensional* column with the composition $M_4M_{2/2}M_{8/2} = M_5X_4$ (Fig. 4a). A large number of transition metal compounds exist, which contain infinite one-dimensional structural elements of this type. The $Ti_5Te_4$-type structure[64] consists entirely of such columns arranged parallel to each other (Fig. 5a)[**]. This interpretation of the structure has already been mentioned[65,66]. On looking at further compounds of the same structural type, such as $V_5Sb_4$[67], $V_5S_4$[68], $V_5Se_4$[69], $Nb_5Sb_4$[70], $Ta_5Sb_4$[71], $Nb_5Se_4$[54], $Nb_5Te_4$[54] and $Mo_5As_4$[72], one is struck by the wide range of the values $2.4 \leq VEC \leq 3.6$. It may be concluded that the VEC is less important for the existence of this structure than the observance of certain size ratios between the atoms X and M, which have the same repeat distance along the c-direction. Band structure calculations show, however[73], that the stability is maximized at the values VEC = 2.6 and 3.4. The agreement with the experimental findings shows that the VEC also influences the choice of structure type.

In $Ti_5Te_4$, the chains are ordered in such a way relative to each other that the X atoms of one chain are close to the M atoms of a neighbouring chain. The marked compression of the M octahedra in the c-direction is certainly caused by additional bonding between the chains; in $Ti_5Te_4$, 8 octahedral edges are 284 pm long, while the 4 edges which form the base in the ac-plane, are 322 pm, and thus even longer than the Ti—Ti distances between neighbouring chains (294 pm). The other examples of this type exhibit the same geometrical details.

The structure of $Ti_5Te_4$ contains voids formed by the X atoms between neighbouring chains (Fig. 5a). By filling these voids, interesting structural variants result. In the simplest case the composition $M_5X_4 \cdot M \triangleq M_3X_2$ is obtained. Figure 5b shows the projection of the structure of $V_3As_2$, which corresponds to a "filled" $M_5X_4$-type. This relationship has already been established in the first discussion of the structure[74]. The function of the additional metal atoms in the structure is obviously to complete the (preferred trigonal prismatic) coordination of all X atoms by M atoms. Certainly, the tetragonal distortion of the M-octahedra remains, but the M—M distances in the octahedral bases are smaller or almost as long as the distances between the M atoms of neighbouring chains. The "expansion" of the $Ti_5Te_4$ structure discussed for $V_3As_2$ is continued with different stoichiometries. In this way, the atomic arrangement in $Nb_7P_4$ (*cf.* Fig. 5c)[75] is easily constructed from the $Ti_5Te_4$ structure by double occupation of the anionic voids according to $M_5X_4 \cdot M_2$. The additional M atoms again lead to the formation of trigonal prismatic coordination of the metal by the X atoms. Besides this, the intermediate M atoms arrange themselves in a very special way. This aspect will be treated in more detail in Section 3.4.3. A particularly striking form of an expanded $Ti_5Te_4$ structure is found in the compound $Nb_5Cu_4Si_4$[76]. As shown in Figure 5d, 4 M′ atoms (Cu) per formula unit occupy the spaces between the chains. Despite the resulting increase in volume, atomic distances can be found which are directly comparable with those in the basic $Ti_5Te_4$ structure; the octahedra in the $Nb_5Si_4$ chains are compressed, the Nb—Nb distances being 299 pm (vertex-base) and 338 pm (base). The Nb—Nb distances in the octahedron base are again slightly longer than those between neighbouring columns.

The fact that no binary compounds of the $Ti_5Te_4$-type exist with the elements of the 4th main group indicates that the VEC of the transition metal atoms is too small in such compounds; the role of the Cu atoms as electron donors in $Nb_5Cu_4Si_4$ becomes evident. This fact establishes a relationship with the intercalated cluster compounds $Mo_6X_8Cu_y$, in

---

[*] Although the X coordination is incomplete in this case, the use of the terms $M_6X_8$ and $M_6X_{12}$ cluster will be continued as long as the X atoms lie above the (remaining) faces and edges respectively.

[**] Except where otherwise noted, the following applies to the structural projections shown. The unit cell is indicated by broken lines; the shortest axis is the projection direction and the cluster atoms shown with differing line thickness lie at the heights 0 and 1/2. The lattice directions have not been entered in the drawing; the assignment is easy to make with the help of the collected crystal data at the end of the work (Table 3). From Figure 4 onwards, all drawings were made with the atomic parameters given in the references to Table 3 using the computer centre of the Max Planck Institutes in Stuttgart (ORTEP program), and completed with connecting lines to clarify the structural principles.

In preparing the graphical representations, I have deliberately avoided showing only those regions of the structure which can be described in terms of condensed clusters. The reproduction of the whole crystal structure is intended to put the reader in a position to follow the statements made in the text.

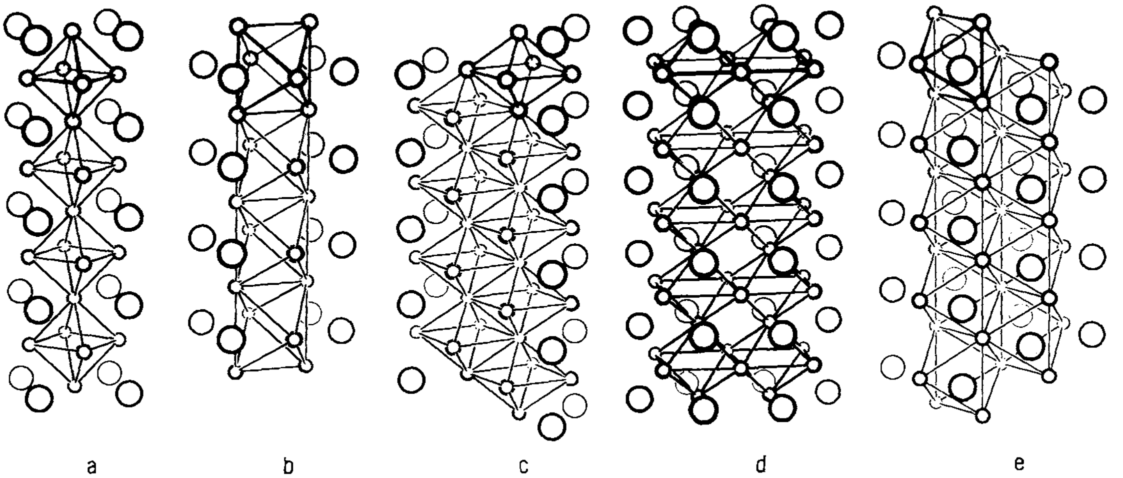


Fig. 4. Three-dimensional representations of the structural units present in compounds with condensed $M_6X_8$ clusters. (a) *trans* vertex-linked chain in $Ti_5TE_4$; (b) *trans* edge-linked chain in $Gd_2Cl_3$; (c) *cis* edge-linked chain or double chain of two edge-linked $M_5X_4$ units in $Nb_2Se$; (d) double chain of edge-linked $M_5X_4$ units in $Ti_2S$ ($Ta_2P$); (e) double chain of edge-linked $M_6X_8$ clusters in $Sc_7Cl_{10}$.

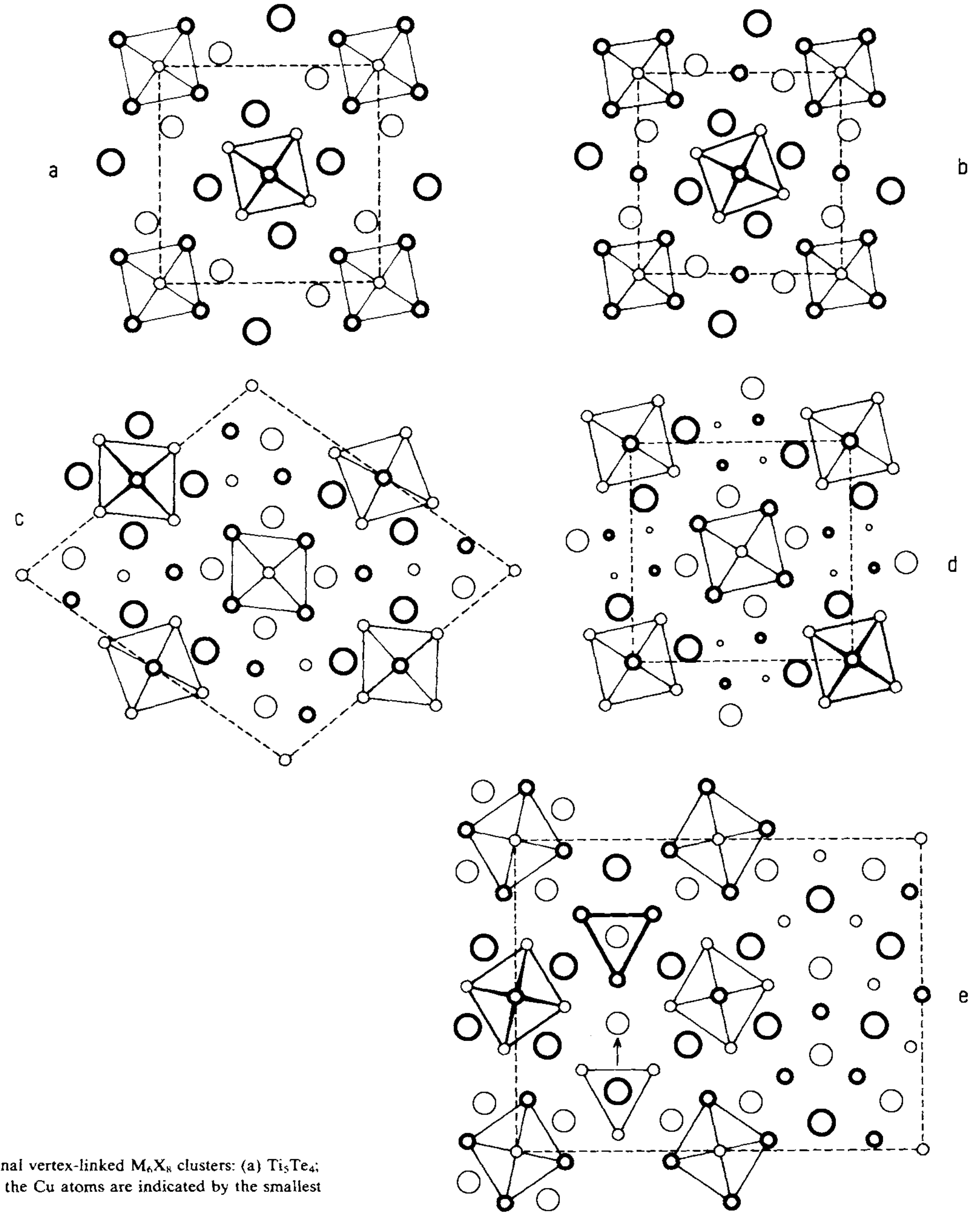


Fig. 5. Structures with one-dimensional vertex-linked $M_6X_8$ clusters: (a) $Ti_5Te_4$; (b) $V_3As$; (c) $Nb_7P_4$; (d) $Nb_5Cu_4Si_4$, the Cu atoms are indicated by the smallest circles; (e) $Nb_4As_3$.

which such electron transfer has been proved in detailed studies[77-79]. From these considerations a series of questions arises, which appear worthy of experimental investigation. Is it possible to stabilize $Ti_5Te_4$ variants by intercalation, *e.g.* $Ti_5As_4Cu_4$, $Ti_5Si_4Zn_4$? Are there phase widths in the sense of optimum VEC values? The existence of the recently discovered[80] compounds $Ta_5Ni_4P_4$ and $Nb_5Ni_4P_4$ points to an influence of the relative atomic sizes.

From the point if view of an "expansion" of the $Ti_5Te_4$ structure, only those compounds which have additional M atoms inserted, have been treated up to now. These compounds may be contrasted with others in which X atoms, as well as M atoms, have been introduced into the host lattice. A particularly interesting case of this type is given by the structure of $Nb_4As_3$[81] (cf. Fig. 5e), which is also adopted in the low-temperature form of $V_4As_3$[82] (α-form). The spaces between the $M_5As_4$ chains are occupied by $M_3$-groups, whose atoms contribute to the trigonal prismatic coordination of the As atoms around the chains, and in a similar way surround the As atoms which lie above the center of gravity of the $M_3$-groups. The coordination of the other As atom (indicated by an arrow in the drawing) is, however, very unusual, but can be understood by comparing Figures 2b and 5e. This As atom contributes to a coordination of the $Nb_3$ group as it is found in $Nb_3Se_4$. Thus, the characteristic structural elements of $Nb_5Se_4$ and $Nb_3Se_4$ alternate in a systematic way in the compound $Nb_4As_3$. The agreement holds right down to the details; in $Nb_4As_3$ the $Nb_3$ group is also considerably expanded. Further structural correlations of this type of chemically motivated "chemical intergrowth" will be treated in Section 3.4.3.

Starting from the $M_5X_4$ column as the simplest (infinitely extended) unit of vertex-linked $M_6X_8$ clusters, more complicated condensed structures can be built up by further condensing such columns. The condensation of $M_5X_4$ chains can be continued exclusively *via* further vertex-links or also include edge-linkage. The former case will be treated first.

Linkage *via* opposite vertices (as in the $M_5X_4$ chain itself) represents the simplest way of continuing the condensation, and leads to an assemblage whose composition is described by the general formula $M_{4n+1}X_{2n+2}$, where $n$ is the number of interconnected $M_5X_4$ chains. Intermediate members of this series are apparently unknown. The limiting case with an infinity of $M_5X_4$ chains is formed in the *two-dimensional* assemblage of the $Ti_2Bi$ structure[83], which is shown as a projection along the layers in Figure 6a. It is notable that the ordering of the $Ti_2Bi$ layers to each other, with regard to the M—M and M—X contacts, follows identical packing principles as in $Mo_6Se_8$ (for isolated clusters) and $Ti_5Te_4$ (for cluster-chains). The condensation of the $Ti_2Bi$ layers *via* the still unlinked *(trans)* octahedral vertices leads finally to a *three-dimensional* structure of linked $M_6X_8$-clusters, which is described by the formula $M_{6/2}X_{8/8} = M_3X$. An example within the range of elements chosen here is given by the structure of $U_3Si$ (Fig. 6b)[84,85], which has a tetragonally-distorted $Cu_3Au$ structure. The linkage of the $M_6X_8$ clusters *via* vertices in all three dimensions thus leads to a structure, which is observed in hundreds of intermetallic phases. This result is hardly surprising, since if X = M, the $M_6X_8$ cluster represents the unit cell of the cubic face-centered lattice. In the $Cu_3Au$-type structure the consequences of directed M—M or M—X bonds as well as the tendency to form a close-packed arrangement of atoms, when directed bonds are absent, must be borne in mind. It may be supposed that the specific distortions in representatives of the $Cu_3Au$ family give an indication of some specific type of chemical bonding[86]. In $U_3Si$, the Si atoms have an unusual coordination. The rotation of the columns relative to each other, as displayed by the structure of $U_3Si_2$ (Fig. 6c)[84], allows the Si atoms to have a trigonal prismatic coordination, and is in fact a type of coordination which is specially favored (*cf.* $V_3As_2$).

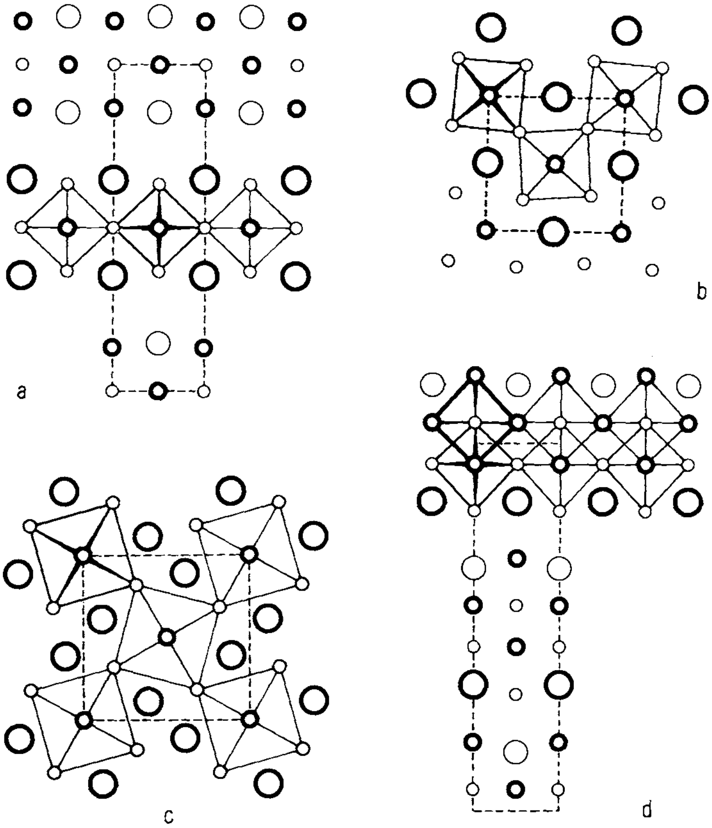


Fig. 6. Structures with two- and one-dimensional vertex-linked $M_6X_8$ clusters: (a) $Ti_2Bi$; (b) $U_3Si$, cell content shown up to z = 1/2, atomic positions z = 0 and 0.25; (c) $U_3Si_2$; (d) combined vertex- and edge-linkage in the structure of $Mn_3As$.

Compounds with condensed $M_6X_{12}$ clusters are, as mentioned in Section 3 comparatively rare, although NbO was recognized as such some time ago[1]. NbO crystallizes in a NaCl-type structure with ordered vacancies in the Nb and O sublattices. The specific order is understood in terms of a close packing of O-bridged "spherical" $Nb_6O_{12}$ clusters. The

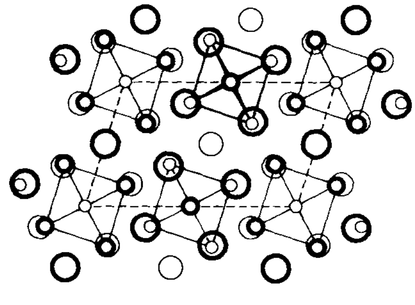


Fig. 7. Interpretation of the ordering of vacancies in the structure of TiO with the presence of *trans* vertex-linked $M_6X_{12}$ clusters (*cf.* Fig. 3, Table 3).

unusual thing about this point of view is that "spheres" and "vacancies" are geometrically identical in this packing; the compound can be described with the formula $Nb_{6/2}O_{12/4}$[1]. Both NbO and $U_3Si$ are, in principle, based on the same framework of three-dimensionally vertex-linked $M_6$ octahedra, which are edge-centered by X atoms ($M_6X_{12}$ cluster) in NbO, while in $U_3Si$ they are face-centered ($M_6X_8$ cluster).

Even under high pressure one observes practically no change in the concentration of vacancies or in their arrangement in NbO[87]; the clusters are very stable. Many other oxides, nitrides and carbides of transition metals with the composition MX, crystallize in NaCl defect-structures, without any recognizable ordering of the defects as in NbO. It may be supposed that an ordering of the defects in these high-melting compounds often does not take place for kinetic reasons. In this respect the structural studies on TiO are important. The homogeneous phase ranging from $TiO_{0.9}$ (O-vacancies) to $TiO_{1.25}$ (Ti vacancies) crystallizes in the NaCl structure. An ordering of both types of defects takes place for the composition TiO below 990 °C, forming the structure shown in Figure 7[88]. The analysis reveals chains of *trans* vertex-linked $Ti_6$ octahedra which are surrounded by O atoms in the same way as in the $M_6X_{12}$ cluster. An isolated chain of this sort (analogous to $M_5X_4$) has the composition $M_{2/2}M_4X_{8/2}X_4 = M_5X_8$. In the ordered TiO structure such chains are linked in a complicated way *via* shared O atoms; the composition can be described by the formula $Ti_{2/2}Ti_4O_{6/3}O_{6/2}$. The alteration of the linkage pattern leads to different compositions. It is possible that the homogeneous "TiO" phase splits into single phases with slightly different compositions upon ordering the defects, as found for the principally comparable oxide block structures[89].

Figure 6d shows the combination of vertice- and edge-coupling in the structure of $Mn_3As$ (see Section 3.2.1).

### 3.2. Edge-Linked $M_6$ Clusters

Edge-linkage differs from vertex-linkage in that not all the X positions around the $M_6$ cluster can be occupied. The missing X positions are partly occupied by M atoms of the neighboring cluster.

#### 3.2.1. Edge-Linked $M_5X_4$ Chains

There are two possible ways of connecting two $M_5X_4$ chains *via* edges: a) Each $M_6$ octahedron has one shared edge with a neighbouring octahedron. b) Each $M_6$ octahedron shares two *(cis)* edges with neighbouring octahedra. Case a) leads to an infinitely extended unit with the composition $M_{4/2}M_2X_{6/2} = M_4X_3$, case b) results in a unit with the composition $M_{3/3}M_3X_{4/2} \triangleq M_2X$. Both types of structural unit occur in a series of compounds. As an example for a), the structure of $Ta_2P$ is reproduced in Figure 8a[90]; the compounds $Ta_2As$[91], $Ti_2S$[92], $Ti_2Se$, $Zr_2S$, $Zr_2Se$[93], $Hf_2P$ and $Hf_2As$[94] are isostructural. The $M_4X_3$ chains run parallel; the regions between them are occupied by additional M atoms. The structure is directly comparable to that of $Nb_5Cu_4Si_4$, in so far as the single chains $M_5X_4$ (in the latter compound) are replaced by double chains. The structure of $Ti_2S$ ($Ta_2P$) can therefore be formulated as $M_8X_6 \cdot M_4$. This formulation raises the question of whether the M atoms which serve to complete the trigonal prismatic coordination of the X atoms could be replaced by suitable heteroatoms M′. The $M_6$ octahedra in the $Ta_2P$ structure type are strongly distorted, as in the $M_5X_4$ compounds; only the distances from the vertex atoms to the base atoms of the octahedra are shorter than 300 pm.

Figure 8b shows the structure of $Nb_2Se$[95], as an example of the structural unit b). This compound is at present the only known example which consists entirely of these type of *cis* edge-linked octahedral chains. In principle, the $M_6$ octahedra exhibit the same distortions as in the single chain $M_5X_4$ itself; all the distances within the octahedral base are more than 300 pm long (318 to 340 pm); the distances from base to vertex atoms are, in contrast, all short (282 to 294 pm). In particular, the edges shared by two octahedra are 286 pm long. The fact has already been mentioned that, because of the edge-linkage of the $M_6$ octahedra, the X-coordination remains incomplete, or is partly replaced by M atoms. This is quite evident in the $Nb_2Se$ structure; externally the $M_6$ octahedra are coordinated in the "normal" way by Se atoms at distances of 262 to 280 pm, while inside the chain the remaining X positions are occupied by M atoms at a distance of 290 pm. Short M—M distances are also found between adjacent double chains (297 to 311 pm). Besides regions of direct M—M contact between adjacent double chains, there are others which are only marked by van der Waals contacts between Se atoms. It should be possible to fill the resulting spaces with additional M atoms, as in the $Ti_5Te_4$ structure, which then leads to trigonal prismatic coordination of the Se atoms. In this context, the interesting question may be raised of whether the double chain could also be obtained with other elements (*e.g.* $Nb_8P_4 \cdot M_4$ by analogy with $Nb_5Si_4Cu_4$).

Apart from the short M—M distances between the double chains in $Nb_2Se$, the structural units are present in an unconnected form. The structure of $Mn_3As$[96] represents a particularly impressive example of vertex-linkage between units of this sort (Fig. 6d). With respect to the double chain, the structure forms the two-dimensional infinite case of (one kind of) *trans* vertex-linkage of these units. A similar approach applied to the simple $M_5X_4$ chain leads to the $Ti_2Bi$ structure (Fig. 6a, *cf.* Section 3.1). The structure of $Mn_3As$ can therefore also be discussed as the first step in the condensation of the simple octahedron layers in $Ti_2Bi$ *via cis* edges, which finally leads to the three-dimensional atomic arrangement of a cubic metal lattice.

Four possible ways of linking three $M_5X_4$ chains together *via* edges emerge. The linkage type a) for two chains ($Ta_2P$) can be extended linearly or at an angle of 90° and yields, if all X positions are filled, structural units with the compositions $M_{11}X_8$ and $M_{11}X_7$, respectively. The construction principle a) can, however, be combined with b) in two possible ways and then leads to chains with the compositions $M_{11}X_6$ and $M_2X$. The metal-rich niobium sulphide $Nb_{14}S_5$[97], whose structure is projected in Figure 8c, is an example of the last case. As indicated by the connecting lines, the network of condensed clusters contains not only the double chain with partially substituted X coordination known from the $Nb_2Se$ structure, but also the unit formed from three $M_5X_4$ chains. The units are linked to each other by vertex atoms with further M atoms occupying the spaces between the triple chains.

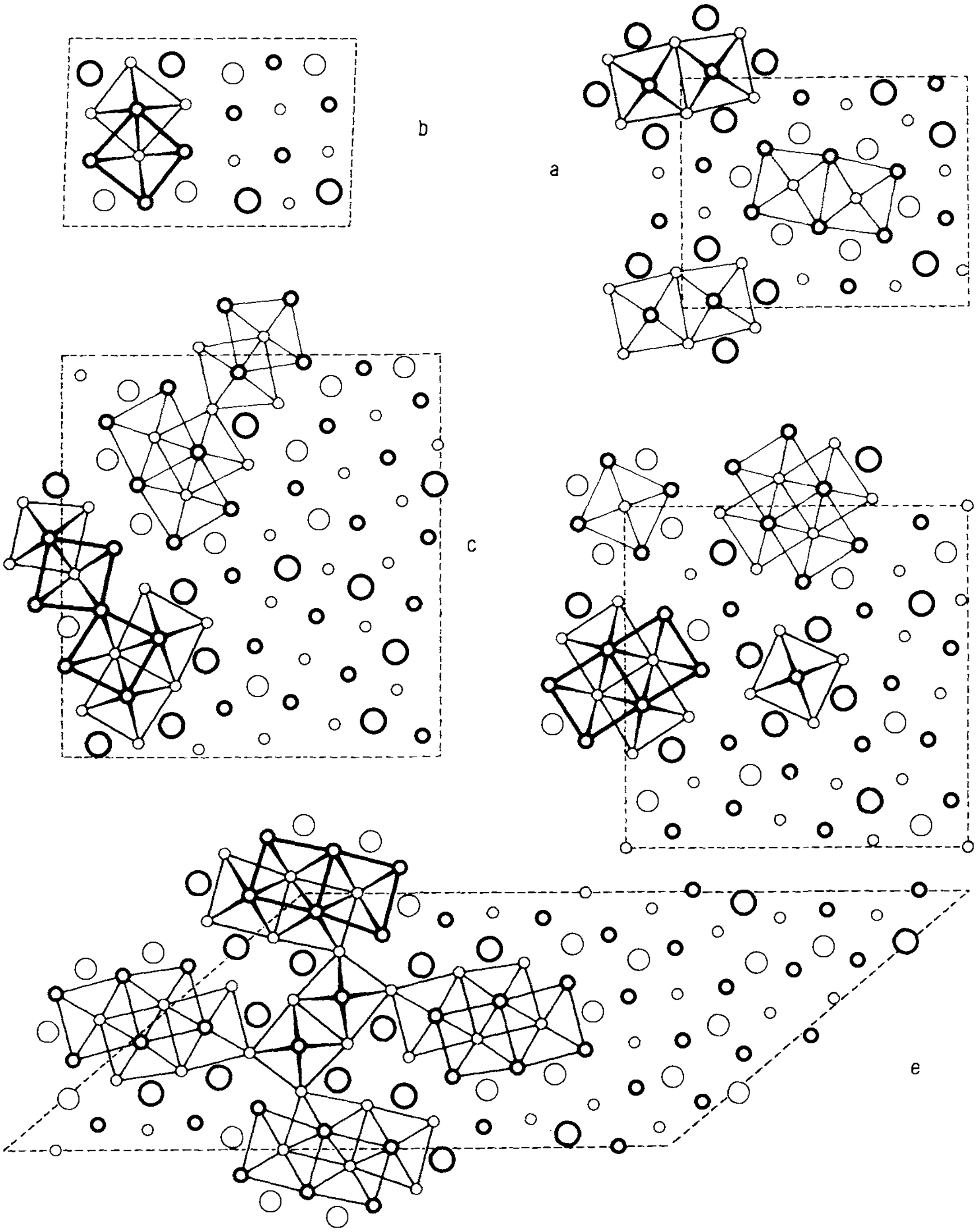


Fig. 8. Structures with edge-linked $M_5X_4$ chains: a) double chains in $Ti_2S$ ($Ta_2P$ type); b) double chains in $Nb_2Se$; c) triple chains in the structure of $Nb_{14}S_5$, linked with double chains as occurring in $Nb_2Se$; d) quadruple chains in $Nb_{21}S_8$ together with single $M_5X_4$ chains; e) quadruple chains in $Ti_8S_3$, linked to double chains in the manner of $Ti_2S$ (half the cell drawn up to $x = 1/2$).

The structure of $Nb_{21}S_8$[98] appears at first sight to be extraordinarily complicated, but from the point of view of condensed $M_6X_8$ clusters, it can be reduced to a simple pattern. It is obvious from Figure 8d that the compound consists of two kinds of building block, which are not mutually connected. On the one hand, $M_5X_4$ isolated chains occur, and on the other, units built up from four $M_5X_4$ chains which have the composition $M_{12/2}M_6X_{4/2}X_2 = M_{12}X_4 \hat{=} (M_3X)$. Additional M atoms fill the voids between these structural elements, and contribute once again to the trigonal prismatic coordination of all the S atoms. According to the structure, therefore, $Nb_{21}S_8$ can be described as $Nb_5S_4 \cdot Nb_{12}S_4 \cdot Nb_4$. The same construction principle is found in $Zr_{21}S_8$[99]. It is interesting that the octahedra in the $Nb_5S_4$ chain are considerably distorted, as they are in the compounds with the $Ti_5Te_4$ structure. The bond lengths within the quadruple chain are in accordance with expectation; the vertex-base distances in the octahedra are among the shortest in the structure (282 to 294 pm), while some of the atoms in the base are further apart (320 pm and more) from one another than they are from Nb atoms which do not belong to the same unit.

A variation of the unit formed from four $M_5X_4$ chains occurs in the structure of $Ti_8S_3$[100], which is shown in Figure 8e. The units containing two $M_5X_4$ chains are the same as in $Ta_2P$ (and $Ti_2S$). These are linked *via* vertices to form aggregates of four $M_5X_4$ chains, which are the condensation product of two double chains. Both kinds of double chain, a) and b), are contained in the quadruple chain. The same is true for the fourfold chain in $Nb_{21}S_8$.

Considering the many possible ways of varying both the number of chains which are condensed to form a unit, and the way in which different types of unit can be combined, the few known examples of compounds containing edge-linked $M_5X_4$ chains seem to be like the tip of an iceberg. Further studies are urgently needed to extend the classification scheme of this highly interesting class of compounds.

The condensed cluster concept reaches the field of intermetallic phases again with the structure of $Nb_{21}S_8$. The fourfold octahedron chains in the $U_6M$ structure (M = Ni, Co, Fe, Mn)[101] are the same as those which form the core of the $Nb_{12}S_4$ chains in $Nb_{21}S_8$. Curiously, the limit of the concept is also reached with sulphides. The structures of the compounds $Ta_6S$[102], $Ta_2S$[103] and $Zr_9S_2$[104] cannot yet be explained in terms of the known isolated clusters of these transition metals, but chains of interpenetrating metal icosahedra are present in the structures of these compounds. This amounts to a quasi one-dimensional variant of the Frank-Kasper principle[56], which has been realized in many intermetallic compounds.

### 3.2.2. *Trans* Edge-Linked $M_6$ Clusters

The attempt has been made in the previous sections to collect a fairly large number of known compounds and discuss them within the concept of condensed clusters. This approach has shown itself to be a useful aid to memory in treating a series of complicated structures as well as a scheme of classification for the structures of metal-rich transition metal compounds. The concept, however, also represents a useful starting point for opening up new groups of substances, as shown in the following, with the newly discovered metal-rich halides of Sc, Y and the lanthanoids. These metals occur in solid state compounds predominantly with the oxidation state +3; salt like dihalides are known, in particular for Eu and Yb where they have been understood for a long time on the basis of the particular stability of the $4f^7$ and $4f^{14}$ configurations[105], but also for Nd, Sm, Dy and Tm[106]. Oxidation states below +2 were however unknown until recently, although the existence of the metallic diiodides of La, Ce, Pr, Gd already demonstrated a way of obtaining low (formal) oxidation states; $Ln^{3+}$ ions are present, and the surplus valence electrons establish M—M bonds according to the formula $Ln^{3+}(I^-)_2e^-$[106]. In the metallic conducting $LaI_2$, all the La—La distances between neighbouring atoms are the same. In the case of $PrI_2$ (modification V), on the other hand, the M—M bonding produces discrete tetrahedral $M_4$ clusters[107], as have been recognized for some time in MoSBr[108].

$Gd_2Cl_3$ was the first lanthanoid compound to have an oxidation number less than +2. The structure[110-112] contains parallel chains of *trans* edge-linked $Gd_6$ octahedra, which on including the surrounding halogen atoms can be discussed in terms of condensed $M_6X_8$ clusters[20,21]. This structural principle, characteristic for such a wide variety of compounds of the d-metals, suggested the existence of a similar variety of reduced Ln halides. Investigations have led to the presently known compounds, summarized in Table 1; structurally, they correspond to the metal-rich halides of Sc and Y which have been discovered simultaneously. These results confirm the correctness of the original idea, which was based on the structure of $Gd_2Cl_3$ alone; a) all halides with $X/M \leq 1.6$ contain characteristic structural elements consisting of chains of *trans* edge-sharing $M_6$ octahedra, which are surrounded by halogen atoms centered over the edges of the octahedra faces as in the $M_6X_{12}$ or $M_6X_8$ cluster. The chains may be isolated or condensed with others. b) On the one hand, the compounds $NaMo_4O_6$[113] and $KMo_4O_6$[114] also contain chains of *trans* edge-linked $Mo_6O_{12}$ clusters; the cations $Na^+$ or $K^+$ are situated between the units formulated as $Mo_2Mo_{4/2}O_2O_{8/2}$ (*cf.* Fig. 9a). These compounds form a link from Sc, Y, and the lanthanoids, to the element Mo, whose structural chemistry is particularly strongly characterized by the presence of discrete octahedral clusters. c) On the other hand, compounds have also been isolated in the meantime which contain discrete $M_6X_{12}$ clusters of Sc and the lanthanides, which are the starting units of condensed systems. The structures of these compounds have also been discussed and reviewed elsewhere[115-117] in terms of condensed clusters.

The metals Sc, Y and the lanthanoids are distinguished by a particularly low VEC compared to the transition metals which have been treated up to now. Their distinct tendency to form M—M bonds is therefore all the more surprising. The "expansion" of the cluster structures by additional M atoms, which has already been discussed in detail, assumes special significance here due to their electron donor function. If one assumes that these M atoms are present as $M^{3+}$ ions in the anionic vacancies of the structures, the VEC in the cluster regions is raised correspondingly. The VEC values given in brackets in Table 1 have been calculated using this assumption. While the X/M ratio correlated only approximately with the degree of cluster condensation, the regions of M—M bonding become step by step larger as the VEC values increase—starting from the isolated cluster and proceeding *via* one-dimensional structures up to the two-dimensional layer structure. In complete contrast to the transition metal compounds with isolated $M_6X_8$ and $M_6X_{12}$ clusters, one finds that there is no particular preference for one or the other cluster type in the condensed structures because of the VEC.

The compounds with the formula $M_7X_{12}$, whose structural principle was first clarified for $Sc_7Cl_{12}$[38] and which in the meantime has been found in a series of Ln iodides, essentially play the role of a "missing link". The structure contains isolated $M_6X_{12}$ clusters, which are ordered according to a close-packing of "spheres" as in $Zr_6I_{12}$. Further M atoms occupy some of the octahedral voids formed by X atoms. The VEC is already extraordinarily low for $Zr_6I_{12}$ (12 electrons per cluster instead of 16); for the hypothetical $Sc_6I_{12}$ it would have the value 6. The gain of 3 additional electrons *per* cluster by inserting M atoms leads to a VEC identical to that found in the compound $Zr_6Cl_{15}$[38]. All representatives of the composition $M_7X_{12}$ contain considerable defects, so that to date only the principle of the structure is certain[119,120].

Chains of *trans* edge-linked octahedra form at the same value of VEC = 1.5, but with a lower X/M ratio. Figure 9b shows the projection of the structure of $Gd_2Cl_3$, which is found in the chlorides and bromides of yttrium, as well as a series of rare earth metals. The halogen atoms are centered

Table 1. Structurally characterized halides $MX_n$, with $n < 2$, of the metals Sc, Y and the lanthanoids; references in parentheses; further explanations *cf.* text.

| VEC | Formula | Cluster type | Linkage principle | X/M | Compounds |
|---|---|---|---|---|---|
| (1.50) | $M_6X_{12} \cdot M$ | $M_6X_{12}$ | discrete | 1.71 | $Sc_7Cl_{12}$ [38], $La_7I_{12}$, $Ce_7I_{12}$, $Pr_7I_{12}$, $Gd_7I_{12}$, $Tb_7I_{12}$, $Er_7I_{12}$, $Lu_7I_{12}$ [119, 120] |
| 1.50 | $M_2X_3$ | $M_6X_8$ | single chain | 1.50 | $Y_2Cl_3$, $Y_2Br_3$ [118, 122], $Gd_2Cl_3$ [110—112], $Gd_2Br_3$, $Tb_2Cl_3$, $Tb_2Br_3$, $Er_2Cl_3$, $Tm_2Cl_3$, $Lu_2Cl_3$ [121] |
| 1.50 | $(M_2X_3)$ | $(M_6X_{12})$ | single chain | 1.50 | $[Tb_2^{II}Br_3]$ [121] |
| (1.75) | $M_4X_8 \cdot M$ | $M_6X_{12}$ | single chain | 1.60 | $Sc_5Cl_8$ [116], $Gd_5Br_8$, $Tb_5Br_8$ [123] |
| 1.75 | $M_4X_5$ | $M_6X_{12}$ | single chain | 1.25 | $Er_4I_5$ [124] |
| (1.83) | $M_6X_{10} \cdot M$ | $M_6X_{12}$ | double chain | 1.43 | $Er_7I_{10}$ [124] |
| (1.83) | $M_6X_{10} \cdot M$ | $M_6X_8$ | double chain | 1.43 | $Sc_7Cl_{10}$ [115] |
| 1.83 | $M_6X_7$ | $M_6X_{12}$ | double chain | 1.17 | $Tb_6Br_7$, $Er_6I_7$ [125] |
| 2.00 | MX<br>ZrCl-Typ<br>[128, 129] | $M_6X_8$ | layers | 1.00 | YBr [122], LaBr, PrBr, GdBr, TbBr, HoBr, ErBr [127], CeBr, NdBr, DyBr, HoCl, ErCl, LuBr [121], t-GdCl, t-TbCl [21, 127] |
| | ZrBr-Typ [130] | | | | ScCl [126], YCl [122], LaCl, CeCl, PrCl [121], h-GdCl, h-TbCl [127] |

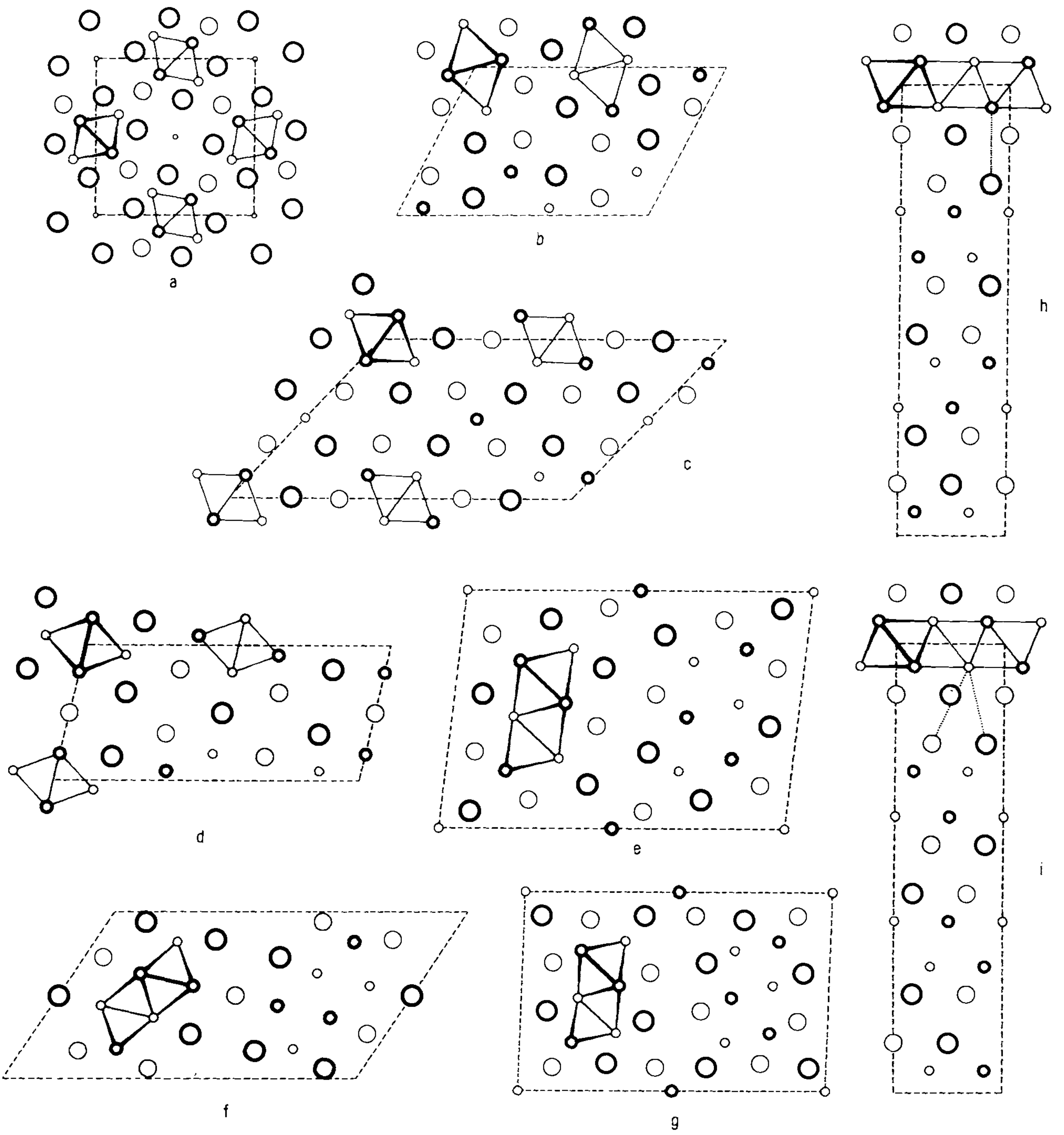


Fig. 9. *Trans* edge-linked chains of $M_6X_8$ and $M_6X_{12}$ clusters and structures derived from them (Table 1): a) chains of $M_6X_{12}$ clusters in $NaMo_4O_6$ (smallest circles correspond to Na positions); b) chains of $M_6X_8$ clusters in $Gd_2Cl_3$; c) chains of $M_6M_{12}$ clusters in $Tb_5Br_8$ and d) $Er_4I_5$; e) double chains of $M_6X_{12}$ clusters in $Er_7I_6$ and f) $Er_7I_{10}$; g) double chains of $M_6X_8$ clusters in $Sc_7Cl_{10}$; h) layers of linked $M_6X_8$ clusters in *h*-TbCl (ZrBr) and i) *t*-TbCl (ZrCe).

over the octahedral faces; however, only the outer faces are coordinated by X atoms, while the X atoms above the inner faces (between adjacent octahedra) are replaced by the M atoms of the next octahedron. Further X atoms lie approximately above the octahedral vertices. The composition is correspondingly $M_2M_{4/2}X_4X_2$. The M—M distances in the octahedron differ widely. Because of this, the bridging edges in $Gd_2Cl_3$ are, at 337 pm, shorter than the M—M bond lengths in the metal itself, while the distances in the chain direction are 389 pm. According to the Pauling relationship[59] $d_n = d_1 - 60\lg n$, the short distances correspond to single bonds, whereas the long distances indicate a bond order $n \approx 0.1$. These direct or indirect interactions are apparently also of critical importance to the entire structure (cf. Section 2).

Measurements made on the easily accessible compounds $Gd_2Cl_3$ and $Tb_2Cl_3$ allow first conclusions to be drawn about the character of the M—M bonding. Both are semi-conductors[131] in agreement with the results of a band structure calculation[132] and the findings of photoelectron spectroscopy[133]. Both the magnetic behaviour[134] and $^{155}$Gd-Mössbauer spectra[135] of $Gd_2Cl_3$ indicate the presence of a $4f^7$ core, as expected for $Gd^{3+}$. The additional 1.5e/Gd have (s,p)d-character. The lanthanoids behave therefore like d-metals with regard to the formation of M—M bonds in metal-rich halides.

Besides the normal form of $Tb_2Br_3$ which crystallizes in the $Gd_2Cl_3$ structure type, crystals have been obtained[121] with a structure very similar to that of $NaMo_4O_6$ (*cf.* Fig. 9a). The same framework of *trans* edge-linked $M_6X_{12}$ octahedra (composition $M_2M_{4/2}X_{8/2}X_2$) is probably present, without the large voids between the chains being filled. It is certainly a metastable form, because of the poor space-filling. But the structure of $NaMo_4O_6$ is of a "pathological" nature too, because the $Na^+$ ions possess extremely high Debye-Waller factors ($B \approx 24$ Å$^2$)[136]; $KMo_4O_6$ on the other hand behaves normally[114].

The compounds $M_5X_8$ also contain *trans* edge-linked $M_6X_{12}$ clusters (Fig. 9c). The halogen atoms which lie above the octahedral edges belong solely to one chain. Further X atoms lie exactly above the octahedral vertices. The chain structure can be described by the formula $M_2M_{4/2}X_{8/2}X_2X_2$; "expansion" by additional atoms in the octahedral sites between the X atoms yields $M_4X_8 \cdot M = M_5X_8$. The arrangement of the X atoms around the octahedron chain corresponds to that in $NaMo_4O_6$. The variation in bond length within the $M_6$ octahedra is nearly the same as in $Gd_2Cl_3$, with 333 pm for the shared edge, and 386 pm for the edge in the chain direction. It is interesting however, that the M—M distances of the atoms of the octahedral base to the vertex atoms in $Tb_5Br_8$ are equal within one standard deviation, while they differ significantly in $Gd_2Cl_3$ (373 and 378 pm). This difference in behavior is easily explained by the differing arrangements of X atoms around the octahedron chain, which only possess the chain symmetry in the case of $Tb_5Br_8$. This comparison gives clear evidence for the easy adaptation of the weak M—M bonds to their environment (*cf.* MX). The fact that distances between functionally very different pairs of M atoms are equal, is an important aspect of the $M_5X_8$ structure, especially when attempts to correlate atomic distances and bond orders are made. The distances between the isolated $M^{3+}$ ions are (for crystallographic reasons) just as large as the repeat distances within the cluster chain, whose (weak) bonding interaction is assumed in the concept of condensed clusters but, of course still has to be proved.

The structure of $Er_4I_5$ is, at first glance, surprising (*cf.* Fig. 9d). Despite the small ratio $X/M = 1.25$ only single chains of *trans* edge-linked octahedra are found, which are surrounded by X atoms in the manner of $M_6X_{12}$ clusters. If the VEC available for M—M bonds is taken into account, however, $Er_4I_5$ is found to be on a level with the $M_5X_8$ halides. The cluster chains, together with the entire arrangement of X atoms are, in fact, identical in the two compounds. The higher metal content in $Er_4I_5$ comes from sharing of I atoms (as $X^{i-i}$ or $X^{i-a}$)[1] between adjacent chains; $Er_4I_5 = Er_2Er_{4/2}I_{8/2}I_{2/2}$.

Further reduction of the X/M ratio to the value 1.17 leads to an increase in the degree of condensation. As shown in Figure 9e, the structure of $Er_6I_7$ contains units which are formed by the condensation of two *trans*-linked octahedron chains; the "fusion" takes place *via* two edges of each octahedron. X atoms lie above the remaining free edges as in the $M_6X_{12}$ cluster. The environment of the double chain corresponds exactly to that of the single chain, as for example in $Er_4I_5$. The agreement between the two structures is so marked that with $Er_6I_7$ some of the I atoms serve the same linking function ($I^{i-i}$ or $I^{i-a}$) as in $Er_4I_5$. The close relationship between the two structures will be discussed once more later.

The octahedra in $Er_6I_7$ (and $Tb_6Br_7$) are, as expected, considerably distorted, due to the differing environments of the individual M atoms. The shortest M—M distances are found for those edges which are shared between two octahedra (329 and 343 pm), while the distances parallel to the direction of the double chain are comparatively long (387 pm), as in the single chain. A comparison between the M—M distances in $Er_6I_7$ and $Tb_6Br_7$ leads to the same result as for $Gd_2Cl_3$ and $Gd_2Br_3$; although the matrix effect of the larger anions produces a lengthening of the M—M bonds affected, a shortening of other M—M bonds largely compensates for this, *i.e.* the average bond order in the M—M bonded part of the structure is maintained.

The compound $Er_7I_{10}$ (Fig. 9f) takes up the correct place in Table 1 regarding the degree of condensation, despite the high value of $X/M = 1.43$. As shown in the projection of the structure, double chains of condensed metal octahedra are present and besides these, single Er atoms with octahedral iodine coordination. Assuming that these are $Er^{3+}$ ions, one finds the same VEC for the M—M bonded regions as in $Er_6I_7$, and, correspondingly, the occurrence of the same structural element in both cases is not surprising. While the degree of condensation is apparently closely related to the VEC, there is no recognizable correlation between VEC and the environment around the halogen atoms. In the structure of $Er_7I_{10}$, the arrangement of the halogen atoms corresponds to that in the $M_6X_{12}$ cluster, while the double chains in the structure of the isoelectronic $Sc_7Cl_{10}$ (Fig. 9g) are surrounded as in the $M_6X_8$ cluster. The discovery that all the M—M distances in $Er_7I_{10}$ are on average *ca.* 45 pm longer than in $Er_6I_7$ has not yet however been explained.

The highest degree of condensation found up to now in the compounds of Sc, Y and the lanthanoids occurs in the layer structures of the monohalides MX. As can be seen in Figures 9h and 9i, the structure represents the final members in the series of (parallel) condensed *trans* edge-linked octahedron chains following the structure principle $M_{6/3}X_2$. The halogen atoms lie above the two remaining "free" octahedral faces *i.e.* their arrangement corresponds to that in the isolated $M_6X_8$ cluster. The remaining coordination sites of each octahedron are geometrically identical to that in the isolated cluster; six M atoms of the adjacent cluster occupy the sites which are otherwise occupied by X atoms.

As yet no evidence has been found for the existence of a form of the monohalides derived from the $M_6X_{12}$ cluster, in whose structure the halogen atoms lie above the unshared octahedral edges. Such hypothetical modifications are conceivable and appear in the final members of two series of compounds whose first members are already known; $M_5X_8$, $M_7X_{10}$ and $M_4X_5$, $M_6X_7$, respectively. These relationships are sketched in Figure 10[124]. The structure of $Er_4I_5$ shows a specific substitution of parallel rows of atoms in a cubic close-packed lattice of iodine atoms by *trans* edge-linked Er octahedra. Replacement of two adjacent rows of atoms by octahedron chains leads to the structure of $Er_6I_7$. The continuation of this structural principle, while maintaining the environment of the iodine atoms, leads to a series with the general formula $M_{2a+2}X_{2a+3}$; *a* is the number of interconnected octahedron chains. The structure of $Tb_5Br_8$ is derived in an analogous way from a hexagonal close-packed lattice of Br atoms, rows of which are substituted by *trans* edge-linked Tb octahedra in such a way that the remaining Br atoms coordinate only one octahedron chain; octahedral voids in the halogen packing are occupied by single Tb atoms. Raising the degree of condensation leads stepwise *via* the $Er_7I_{10}$ structure to hypothetical compounds with the general formula $M_{2a+3}X_{2a+6}$, whose structures, although predictable in detail

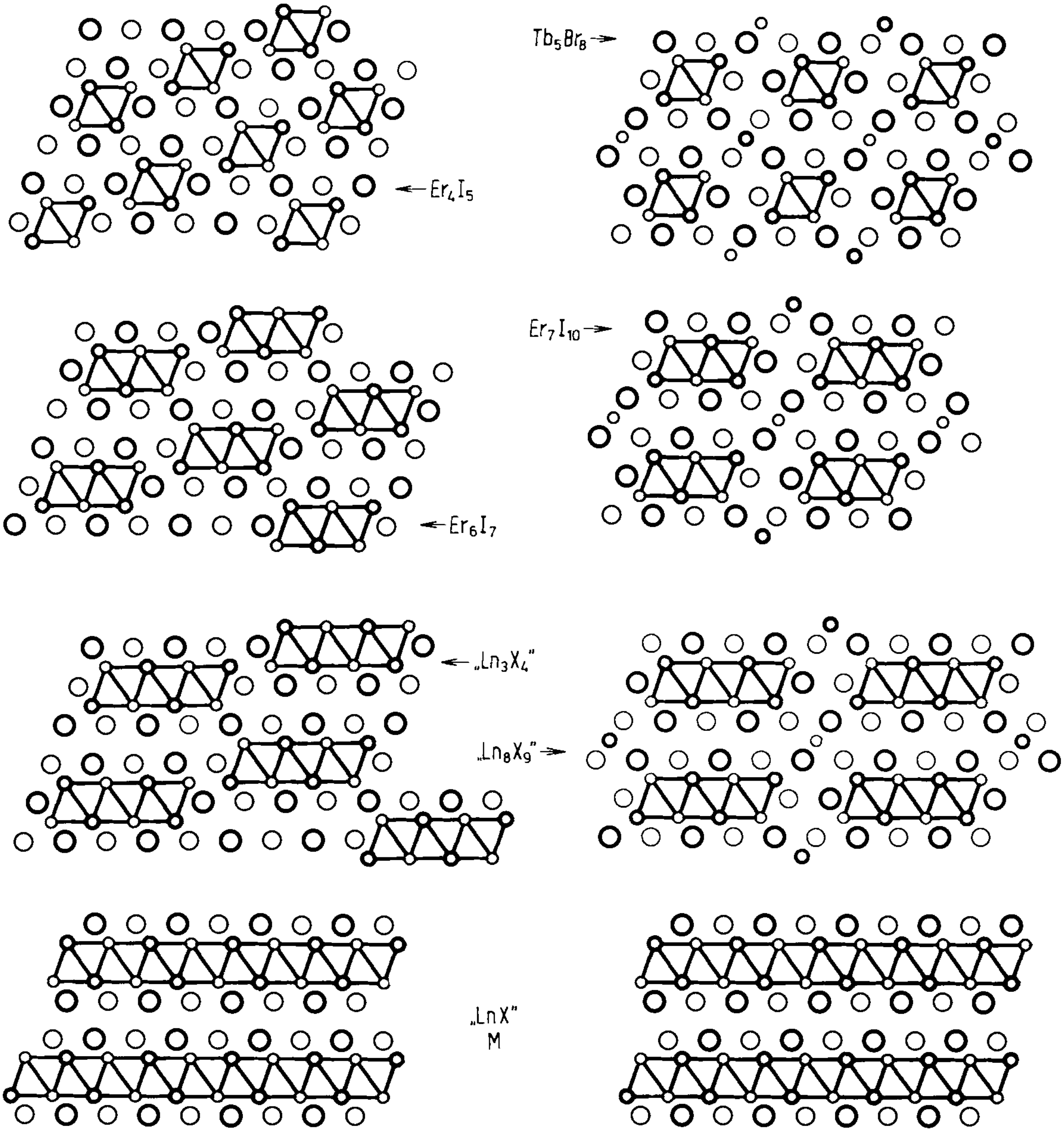


Fig. 10. Structural relationships between $Er_4I_5$, $Er_6I_7$ and $Tb_5Br_8$, $Er_7I_{10}$. The continuation of the structural principle leads to the series of compounds $M_{2a+2}X_{2a+3}$ and $M_{2a+3}X_{2a+6}$ respectively. Here "*a*" represents the number of linked octahedron chains in the structure. Hypothetical members of this series are shown in inverted commas.

have not yet been discovered. At the end of this series is, once again, a monohalide derived from the $M_6X_{12}$ cluster.

The layer structures of the monohalides of Sc, Y and the lanthanoids are closely related to a series of metal-rich compounds of the 4d and 5d metals; they are isostructural with ZrCl[129] or ZrBr[130] and, like these, they behave physically as two-dimensional metals[118]. A comparison of the bond lengths in various compounds which crystallize with these structures allows interesting conclusions to be drawn. a) As in the isolated chains of *trans* edge-linked $Ln_6$ octahedra, the shared edges are shorter (by about 7%) than the unshared edges. The Ln—Ln distances parallel to the octahedron layer become larger of course with increasing anion size (379 pm in TbCl, 384 pm in TbBr). The non-existence of corresponding monoiodides—the metals should form low oxidation states preferentially with iodine—may be attributed to the large size of the anion. The difference between the Zr—Zr distances in the structure of ZrCl is even more pronounced (about 11%). Of course, this effect can be expected because of the higher VEC, but can also be caused by the smaller interatomic distance arising from the size of the anions. b) ZrCl and ZrBr form layer structures, in which closely packed double layers of metal atoms are surrounded by halogen layers; such X—Zr—Zr—X layers are stacked in different ways[127]. The different mechanical properties of the crystals can be explained by assuming more pronounced interactions between Zr atoms and halogen atoms of the next layer but one, in ZrBr (*cf.* Fig. 9h and 9i)[130]. The M—M bond serves here as an indicator which clearly reveals the presence of such interactions; TbCl develops both stacking variants as temperature polymorphs. In the modification with ZrBr structure, in which additional interactions between Tb atoms and second-nearest Br atoms may be postulated, the distance between the Tb layers is significantly enlarged[127].

Further close relationships exist between the layer structures of the monohalides and those of other metal-rich compounds of d-metals. The MX structure represents the analogy (two-dimensional edge-linkage) to the structure of $Ti_2Bi$ (two-dimensional vertex-linkage of $M_6X_8$ clusters), which has been discussed in Section 3.1. The extension of the condensation *via* edges into three dimensions leads finally to the fcc lattice of a metal. An even more direct similarity exists between the MX structures and the structures which are formed by occupation of every second layer of octahedral sites in the close-packed metal lattice and which therefore correspond to the formula $M_2X$. Examples of this group are given by the metallic compounds; $Ti_2O$[137], $Ag_2F$[138], $Ta_2C$[139] (*anti* $CdI_2$-type) and the subcarbides $Y_2C$ and $Ln_2C$ (*anti* $CdCl_2$-type)[140, 141]. The behavior of $Y_2C$ is particularly interesting. Above 900 °C it exists with a wide range of homogeneity; the C atoms are statistically distributed in a rock salt structure. Below 900 °C it becomes ordered and the low temperature phase can be easily discussed in terms of condensed clusters. The compound thus resembles TiO (*cf.* Section 3.1, Fig. 7). The compounds listed above are formulated as $M_{6/3}X_{2/2}$ within the concept of condensed clusters, since the double layers of X atoms in the halides MX are replaced by single layers whose atoms function as bridges between neighboring layers of condensed M octahedra. It is noteworthy, in connection with the compound $Ag_2F$ mentioned above, that the isolated $Ag_6$ cluster is also known[142]. An interesting variant of the $M_2X$ layer structures is formed in $Hf_2S$. In this case, the condensed cluster layers are shifted relative to each other, in such a way as to give the S atoms a trigonal prismatic Hf atom coordination (*anti* $NbSe_2$ structure)[143]. A direct comparison of the bonding in $Hf_2S$ and in the MX layer structures is possible since the structure of the corresponding compound HfCl has been thoroughly studied[144]. For these two compounds, having the same VEC and containing anions almost equal in size, the M—M distances are identical within the accuracy of their determination.

The present section indicates that *trans* edge-shared $M_6$ octahedra occur above all in the halides of Sc, Y and the lanthanoids, producing a large number of compounds of almost unlimited variety. This may be caused by low VEC of these metals, which in particular with halogens as X atoms, allow the formation of M—M bonds. The comments made on discrete metal clusters in the introduction hold therefore for condensed aggregates as well. Such aggregates are easily recognizable because of the relatively high X content, and the halogen atoms tend to form markedly anisotropic bonds to the M atoms, which can be clearly seen in the substantial structural differences between isoelectronic pairs of compounds like TiO/ScCl or NbO/ZrCl.

The compounds $AMo_4O_6$ ($A = Na$, K) show how the specific properties of the halogens mentioned above can also be simulated by multivalent X atoms, through the formation of ternary compounds. These may be expected to be the first members of a whole family of ternary compounds containing low-dimensional regions of condensed clusters, in which, in addition to the transition metal in a low oxidation state, multivalent anions and large cations of the electropositive metals are to be found.

### 3.3. Face-Sharing $M_6$ Clusters

The *trans* face-linkage of an infinite number of octahedral $M_6$ clusters leads to a chain with the composition $M_{6/2}X_{6/2} \mathrel{\hat{=}} MX$ for $M_6X_8$ clusters and $M_{6/2}X_6 \mathrel{\hat{=}} MX_2$ for $M_6X_{12}$ clusters, respectively. With this kind of linkage the same restrictions hold as for edge-sharing; X positions which lie above those faces shared between two octahedra ($M_6X_8$ cluster) or above the shared edges ($M_6X_{12}$ cluster) must remain unoccupied for spatial reasons.

A large number of transition metal compounds with elements of the 4th to 6th main groups, especially intermetallic compounds, have been known for some time to contain MX chains as structural units derived from the $M_6X_8$ cluster[24]. A discussion of these units in terms of condensed clusters is, however, not without problems. The arrangement of the atoms in the MX chain corresponds to a section of the (hexagonal) close-packing, so that the occurrence of the structural unit, particularly in intermetallic phases, is hardly surprising. The same remarks hold as in the case of the $U_3Si$ structure (*cf.* Section 3.1, Fig. 6b). The recently discovered Mo cluster compounds, which will be discussed next, are therefore of special importance.

The approach sketched at the end of the previous section has, in principle, been adopted. Intercalation experiments with $Mo_6Se_8$ and In (see Fig. 11a), led to a compound with the approximate composition $In_3Mo_{15}S_{19}$. This compound produced the first evidence for a $M_9X_{11}$ cluster[145], shown in

Figure 11b, which consists of two face-linked $Mo_6$ octahedra, each surrounded by X atoms in the same way as the single $M_6X_8$ cluster. In the meantime, further compounds have been found containing this cluster (always together with $Mo_6X_8$ clusters)[146-150].

The $Mo_6X_8$ and $Mo_9X_{11}$ clusters are the first two members of a series which can be formulated as $M_{3n+3}X_{3n+5}$, where $n$ is the number of (linked) $M_6$ octahedra. The next member of the series, the $M_{12}X_{14}$ cluster, built up from three octahedra (Figure 11c), has been found in the compounds $K_2Mo_9S_{11}$[149] and $Tl_2Mo_9S_{11}$ together with the $M_6X_8$ cluster[151,152]. The final member, the infinite MX chain, was discovered in an independent investigation of the structure of $TlFe_3Te_3$[153,154]. The chain is shown in Figure 11d and the projection of the $TlFe_3Te_3$ structure in Figure 12a.

Meanwhile, isostructural ternary chalcogenides of molybdenum such as $KMo_3S_3$[149] have become known, together with the compounds $AMo_3X_3$ (A = In, Tl; X = Se, Te)[155]. Table 2 lists the known potassium compounds of the cluster series $M_{3n+3}X_{3n+5}$, whose structures in general show the expected relationship between X/M ratio and degree of condensation, but nevertheless cause surprise due to the joint occurrence of different types of cluster.

Table 2. Condensed $Mo_6S_8$ clusters in the ternary compounds $K_xMoS_y$ [149].

| Compounds | X/M | VEC | Structure |
|---|---|---|---|
| $K_{\approx 0.5}Mo_3S_4$ | 1.33 | ≈3.50 | $K_{\approx 1}[Mo_6S_8]$ |
| $K_2Mo_{15}S_{19}$ | 1.26 | 3.60 | $K_2[Mo_6S_8][Mo_9S_{11}]$ |
| $K_2Mo_9S_{11}$ | 1.22 | 3.78 | $K_4[Mo_6S_8][Mo_{12}S_{14}]$ |
| $KMo_3S_3$ | 1.00 | 4.33 | $K{}^1_\infty[Mo_3S_3]$ |

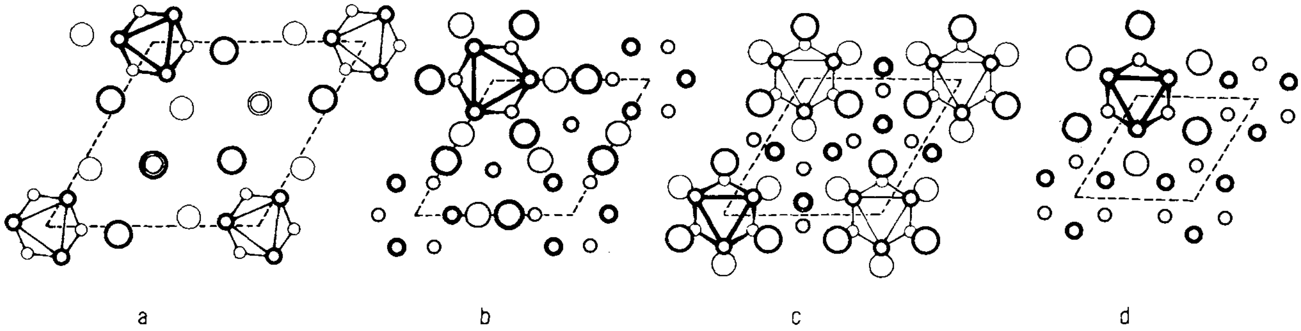


Fig. 12. *Trans* face-linked chains of $M_6X_8$ clusters: a) $TlFe_3Tl_3$, the Tl atoms are marked by double rings; b) $Mn_5Si_3$; c) $Ru_7B_3$ and d) $Ni_3Sn$.

General considerations[155] regarding the chemical bonding in the cluster structures $M_{3n+3}X_{3n+5}$ reveal that $6(n+1)$ bonding molecular orbitals or bands *per* cluster are available for M—M bonding; such cluster systems form preferentially about VEC = 4.0. The assumption signifies that the degree of condensation is, to a first approximation, independent of the VEC and therefore substantially controlled by the X/M ratio, or the cationic counterparts in the compounds. This proposal is in agreement with commonly accepted ideas about the single cluster[1,40] and leads to a quantitative understanding of the M—M distances in $TlFe_3Te_3$ (259 and 260 pm[154]) and $TlMo_3Te_3$ (275 and 262 pm[155]). In the limit of an ionic model, taking into account $Tl^+$, $Te^{2-}$, the values VEC = 6.33 and 4.33 respectively are obtained for the two compounds. This result explains the elongation of the Fe—Fe bonds (although in absolute terms shorter than in the Mo compound) with respect to the single bond lengths of Fe, by the occupation of anti-bonding states. Details of this approach, however, still require refinement. The assumption of an optimal value of VEC = 4 for all types of cluster $M_{3n+3}X_{3n+5}$ cannot explain the behavior of $In_xMo_{15}S_{19}$, which exhibits a range of homogeneity. As the content of In acting as a donor increases, the $Mo_6S_8$ clusters shrink, but the $M_9S_{11}$ clusters, which are also present, expand[148], although the average VEC (cf. Table 2) is still significantly below the value 4.0.

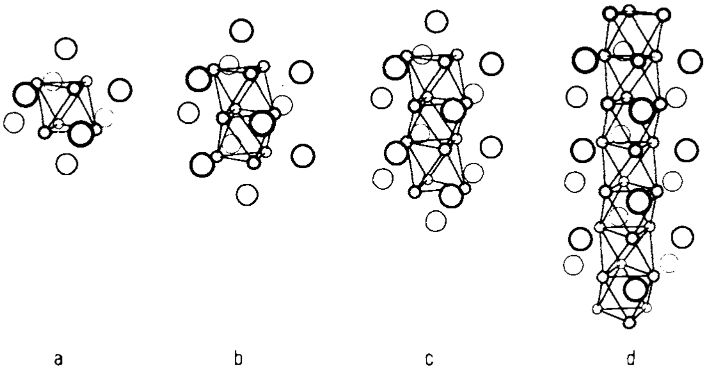


Fig. 11. Step by step condensation of a) $M_6X_8$ units *via* faces to b) double units $M_9X_{11}$, c) triple units $M_{12}X_{14}$ and d) to a one-dimensional infinite chain $M_3X_3$.

The $Fe_3Te_3$ chains are aligned parallel to each other in the structure of $TlFe_3Te_3$, as can be seen in Figure 12a; the $Tl^+$ ions occupy the channels formed by anions between the chains. The structure corresponds therefore to the "expanded" cluster structures[*], which have been treated before several times, and is closely related to a series of structures which can also be regarded as containing chains of face-sharing $M_6$ octahedra plus additional M atoms. The analogy with the $Mn_5Si_3$ structure type has already been referred to[154]. An extensive group of intermetallic phases crystallizes in this structure type[157]. Besides many silicides and germanides of transition metals and lanthanoids, the phosphide $Ti_5P_3$ should be mentioned too, as a representative of this structure

---

[*] The question arises as to why the basic MX structure without occupation of the voids does not occur, since the VEC in the cluster chain is not optimized by the additional M atoms.

type[158]. Figures 12a and 12b illustrate an extraordinary similarity between the structures of $TlFe_3Te_3$ and $Mn_5Si_3$. The second is derived from the first by substituting two Mn atoms for one Ti atom according to the formula $Mn_{6/2}Si_{6/2}Mn_2$. The topological changes involved are, however considerable. The $Fe_3Te_3$ chains are, in the presence of the large $Tl^+$ ions, separate structural units ($d_{Tl-Fe}=406$ pm) with almost undistorted $Fe_6$ octahedra ($d_{Fe-Fe}=260$ pm). In $Fe_5Si_3$ on the other hand, which forms a high temperature modification with the $Mn_5Si_3$ structure[159], strong interactions obviously exist between the Fe atoms belonging to the octahedron chain and those lying between the chains. The additional Fe atoms are 291 pm distant from the Fe atoms in the cluster chain and are extremely close together (236 pm). The $Fe_6$ octahedra themselves are expanded to 269 and 282 pm, the latter value holding for the distances in the chain direction.

The identical structural principle with *trans* face-linked $M_6X_8$ groups seems to be continued in the carbide $Mn_7C_3$[160,161]; the neighboring elements Cr and Fe form isostructural compounds[162,163]. The structure has not yet been solved quantitatively, but is similar to the structure of the boride $Ru_7B_3$ shown in Figure 12c[164], which corresponds to the formula $M_{6/2}X_{6/2}M_4$. All M atoms which are present in addition to the octahedron columns, form chains of $M_4$ tetrahedra. Further examples of this type will be briefly mentioned in Section 3.4.3. The special orientation of the octahedra and tetrahedra to each other, allows the X atoms in $Ru_7B_3$ to take up trigonal prismatic coordination once more.

One last example will show the extent of variation of possible structures on the basis of *trans* face-sharing $M_6X_8$ clusters. The MX chains of these clusters are as mentioned, sections of a hexagonal close-packing of spheres. Three-dimensional close-packing is obtained by linking the chains together *via* X atoms. The resulting composition, $M_{6/2}X_{6/6}=M_3X$, is realized in the compounds with the $Ni_3Sn$-type structure (Figure 12d), which appears in the low temperature modification of $Ni_3Sn$[165,166], as well as in a large number of other intermetallic compounds. The $Ni_3Sn$ structure is intimately related to the $Cu_3Au$ type; both are ordered $A_3B$ structures with hexagonal close-packing in the one case, and cubic close-packing[*] in the other. Thus, the same restrictions as were mentioned before when discussing the $U_3Si$ structure in terms of clusters hold for the $Ni_3Sn$ structure.

### 3.4. Linked Fragments of the $M_6X_8$ Cluster

Up to now, selected systems have been treated which can be discussed in terms of condensed octahedral $M_6$ clusters. This approach may give the false impression that the uniformity in the structures of metal-rich transition metal compounds is more pronounced than it really is. It was mentioned at the beginning that the variety of different $M_n$ clusters, which are known as isolated units, is retained in systems with condensed clusters. Some examples will be given in the following which can be derived by condensation of fragments ot the $M_6X_8$ cluster. Such "cluster fragments" occur frequently among the electron-rich d metals. A systematic treatment of the observed structures, as attempted for the $M_6$ cluster, cannot however be dealt with here.

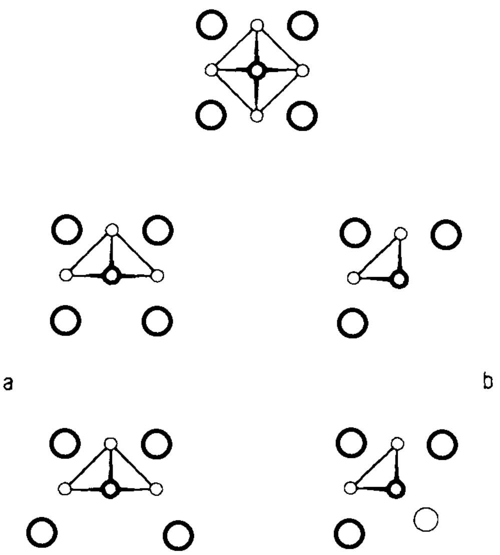


Fig. 13. Parts of the $M_6X_8$ cluster (*cf.* Fig. 3). a) The $M_5X_8$ grouping results from removal of one M atom. The atoms coordinated to the edges of the $M_5$ pyramid base ($X^{i'}$) can shift when the positions above the cluster vertex atoms ($X^a$) are not occupied. b) The cluster $M_4X_6$ results when two M and X atoms are removed in the indicated way. In the complex ion $Mo_4I_7^{2+}$, an additional I atom takes the place of the removed cluster fragment.

On removing one M atom from the $M_6X_8$ cluster, the $M_5X_8$ group remains, as shown in Figure 13a. This cluster has been prepared, as an isolated unit, in the compound $[(C_4H_9)_4N]_2Mo_5Cl_{13}$[47]. Cl atoms are bonded in several different ways in this unit; four atoms center the triangular faces of the square pyramid of M atoms ($X^i$), four lie above the edges of the pyramid base ($X^{i'}$) and five above the vertices ($X^a$). It may be imagined that the $X^{i'}$ atoms in the $Mo_5Cl_{13}^{2-}$ ion, in contrast to the $X^i$ atoms, are held in position by the $X^a$ atoms. In the case of unoccupied $X^a$ positions, an enlargement of the square formed by $X^{i'}$ atoms occurs in the way shown in Figure 13a.

There are two ways of removing two M atoms from an $M_6$ octahedron; the removal of two *trans* atoms leaves a square, the removal of two *cis* atoms a bent rhombus. Both groupings occur linked together in metal-rich compounds. The last named $M_4X_6$ cluster deserves mention as part of the $M_6X_8$ cluster since it was first identified as a linked structural unit in some transition metal compounds with elements of the 4th and 5th main groups, and was almost simultaneously synthesized as a discrete cluster in the compound $(C_4H_9)_4N_2Mo_4I_{11}$[48]. The cluster is coordinated by four additional I atoms in $X^a$ positions, and one further O atom above the centre of gravity of the bent rhombus. Some examples of condensed $M_5$ and $M_4$ clusters will now be given and discussed, followed by cases in which various cluster types occur together.

#### 3.4.1. $M_5$ Clusters

The linear structural element which results from the *trans* vertex-linkage of $M_5X_8$ clusters has the composition $M_{2/2}M_3X_{8/2}=M_4X_4$; it corresponds to the $M_5X_4$ chain formed from $M_6X_8$ clusters. This element stands out particu-

---

[*] It should be pointed out that $Fe_3Ge$ occurs in both forms [167, 168].

larly clearly in the structure of *o*-$Ni_4B_3$ (Fig. 14a)[169]. In this compound, discrete $M_4X_4$ chains are linked *via* $X^{i'}$ atoms, which are shifted considerably from their original positions in the isolated cluster. It is characteristic for this structure, as for all others with these chains, that the base of each $M_5$ pyramid is centered by an X atom. It may be assumed that the $Mo_5Cl_{13}^{2-}$ ion can bond additional ligands above the center of the pyramid base as well. The X atoms are surrounded by the M atoms in a trigonal prismatic manner. B—B bonds express themselves in the short distances (173 and 189 pm) between neighboring $X^{i'}$ atoms.

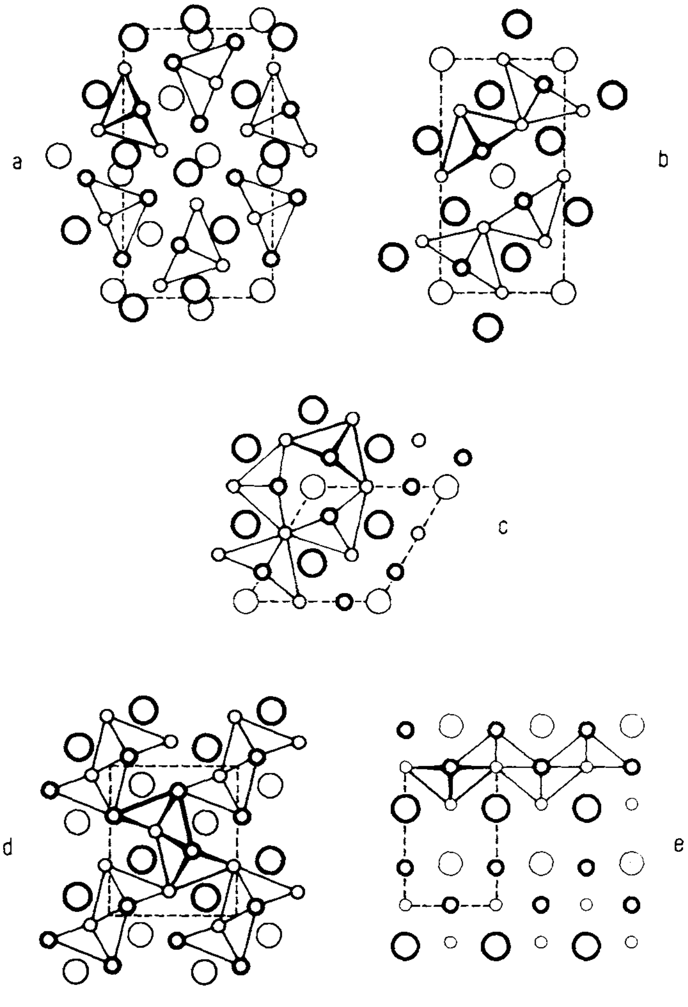


Fig. 14. Structures with condensed $M_5X_8$ clusters; a) *o*-$Ni_4B_3$; b) $Rh_5Ge_3$ and c) $Fe_2P$ with entirely vertex-linked $M_5$ clusters; d) $Co_2P$, whose structure contains (edge-linked) double chains of vertex-linked $M_5$ clusters and e) $Cu_2Sb$ with the corresponding two-dimensional infinite linkage.

The structure of $Rh_5Ge_3$ (Fig. 14b) offers an example of exclusive vertex-linkage between $M_5X_8$ clusters[170]. This structure constitutes an analogy to the $U_3Si$ type (Fig. 6b), but with the difference that the bases of the $M_5$ clusters are coordinated by additional X atoms. The structure corresponds to the formulation $M_{3/2}M_{2/2}X_{8/8}X_{1/2}$. $Cr_5As_3$ and the high temperature form of $V_5As_3$ crystallize in very similar structures[171].

The $M_5$ cluster plays a striking role in the $M_2X$ compounds of the electron-rich transition metals (in particular when X = Si, P, As). The structural principle extends from pure vertex-linkage to pure edge-linkage between the $M_4X_4$ chains formed by $M_5$ groups. In the $Fe_2P$ structure (Fig. 14c)[172], which is taken up by an extensive group of binary and ternary compounds, the chains are only bound *via* the free vertex atoms. The structure is described by the formula $M_{2/2}M_{3/3}X_{8/12}X_{1/3}$. By this is meant that the X atoms which surround every $M_5$ group occupy both $X^i$ and $X^{i'}$ positions in different clusters, and that additional X atoms coordinate the basal faces of neighboring $M_5$ groups (three in this case) as in the structure of $Rh_5Ge_3$. An interesting variant of the structure turns up for NiMoP (and other ternary compounds with the same composition)[173]. The atomic arrangement described in terms of trigonal $Ni_3$ and $Mo_3$ clusters, corresponds to the $Fe_2P$ structure; the Ni atoms taking the positions of the linking M atoms in the single $M_4X_4$ chain. $Co_2P$ crystallizes with the same structure at high temperature[174]; the structure of the low temperature form is shown in Figure 14d[175]. The atomic arrangement can be resolved into a single motif which contains two chains formed from $M_5$ clusters linked together *via* edges. As for the analogous double chain of $M_6X_8$ clusters in $Nb_2Se$ (*cf.* Fig. 8c), not all X positions are occupied. Double chains of this type are linked together *via* the free vertex atoms in the atomic arrangement of $Co_2P$ which is another important type of structure adopted by a number of binary and ternary compounds. The compound $V_2P$—in contrast to $Ta_2P$—also belongs to this type[176]. It is fascinating to compare the various compounds with structures related to $Co_2P$ (Fig. 14d) in the light of the present concept. The X coordination in the structure of $Co_2Si$[177] is considerably changed from that in $Co_2P$ but despite this the aggregation of M atoms can still be described as double chains of $M_5$ clusters. The disintegration of the cluster becomes recognizable in $Re_2P$[178]; the process is completed in the structure of $\theta$-$Ni_2Si$ ($Ni_2In$-type; *cf.* Fig. 15c)[179].

The first stage of the condensation of $M_4X_4$ chains *via* shared edges is completed in the $Co_2P$ structure. Continuing this type of condensation, a two-dimensional aggregate is obtained, and the final member of the series is reached with $Cu_2Sb$[180] whose structure is given in Figure 14e. Double layers of edge-linked $M_5$ groups are present. The X positions are (as for the edge-linked $M_6X_8$ cluster) partly occupied by the M atoms of adjacent clusters. Among many other compounds, $Mn_2As$ crystallizes with the $Cu_2Sb$ structure. The similarity to the structure of $Mn_3As$ is unmistakable; $Mn_3As$, $Cu_2Sb$ and $Ti_2Bi$ are in fact treated as stacking variants[181]. As for the structures with condensed $M_6$ clusters, there are a number of "expanded" structures with $M_5$ clusters, but these will not be dealt with here.

### 3.4.2. $M_4$ Clusters

If the $M_4X_6$ clusters shown in Figure 13b are linked together *via* the remote M atoms in the same way as the *trans* vertex-linkage of $M_6X_8$ clusters in the $M_5X_4$ chain, a linear unit with the composition $M_2M_{2/2}X_{6/2}$ results. Chains of this type, bound to each other by X atoms according to the formula $M_2M_{2/2}X_{2/2}X_{4/4}$, form the characteristic element in the structure of $Hf_3P_2$[182]. As shown in Figure 15a, this structure, which is also found for $Zr_3As_2$[183] consists entirely of such chains ordered parallel to each other. The structure of $Cr_3C_2$[184] is principally similar but the chains are oriented in a different way. $Sc_3P_2$ and $Sc_3As_2$ both have two modifica-

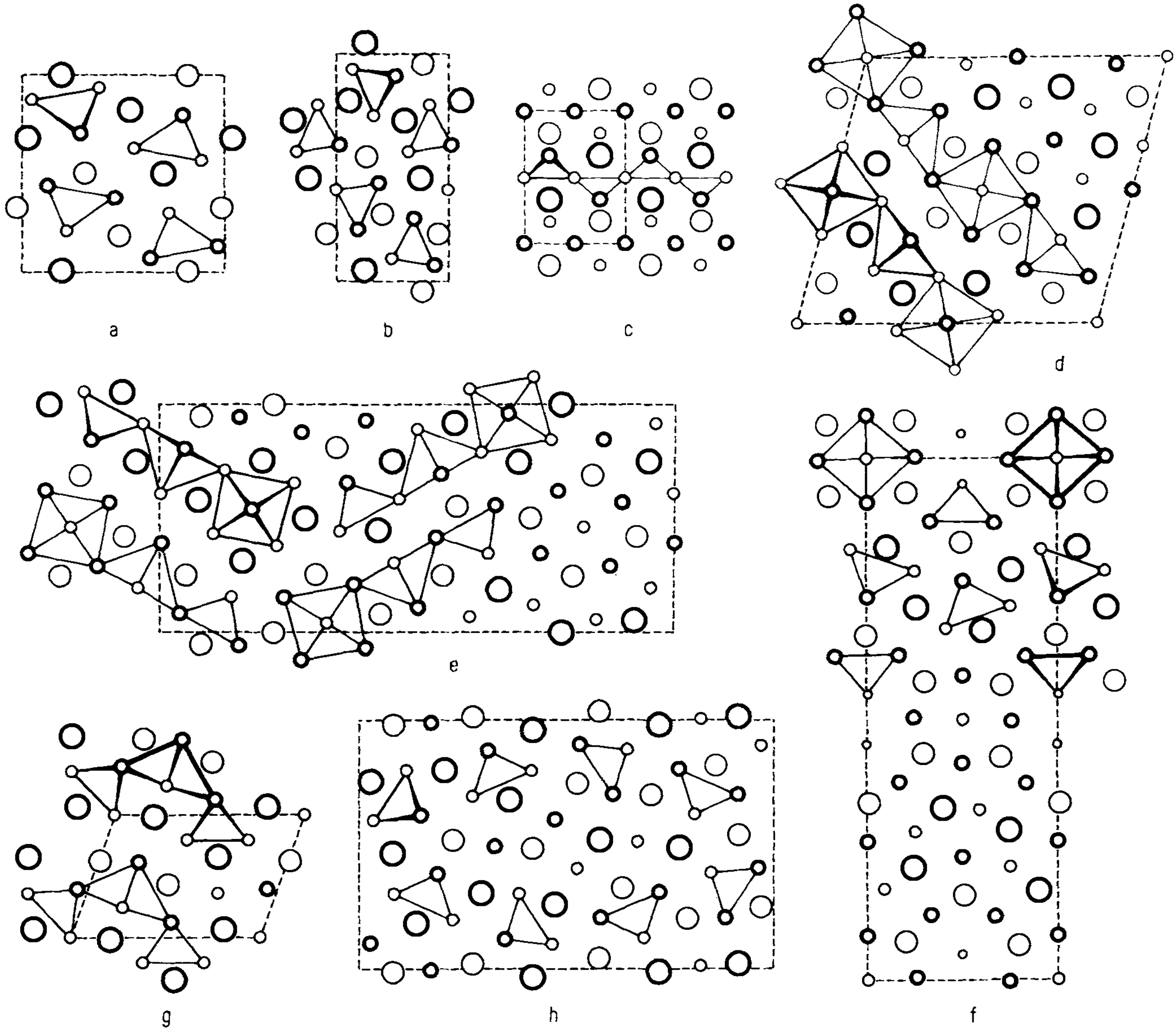


Fig. 15. Vertex-linked $M_4X_6$ clusters and structures which contain various types of condensed clusters together: a) $Hf_3P_2$ and b) $Cr_3C_2$ with isolated chains of vertex-linked $M_4X_6$ clusters; c) two-dimensional layers of vertex-linked $M_4X_6$ clusters in θ-$Ni_2Si$ (cf. $Co_2P$); projection of the structure onto the (110) plane; d) layer structure of alternating $M_5$ and $M_6$ clusters in $Nb_7P_4$ (cf. Fig. 5c); e) units of vertex-linked $M_6$, $M_5$ and $M_4$ clusters in $Nb_5P_3$; f) $Nb_8P_5$ contains isolated chains of vertex-linked $M_6$ and $M_4$ clusters; g) characteristic structural element of $Mo_8P_5$ built up from $M_5$ and $M_4$ clusters and h) structure of $Mo_4P_3$ formed of discrete chains of vertex-linked $M_4X_6$ units together with intermediate MX regions (cf. Fig. 5e).

tions with crystallize with the $Hf_3P_2$ and $Cr_3C_2$ structures[185]. Both the mixed-M carbide $Cr_2VC_2$[186] and the mixed-X boride-carbide and nitride-carbide, $Cr_3(BC)_2$ and $Cr_3(CN)_2$ respectively, exist with the $Cr_3C_2$-type arrangement[186, 187].

The $Hf_3P_2$ and $Cr_3C_2$ structures are crystallographically different but they are similar in that firstly, they both possess as characteristic elements the same chains formed from $M_4X_6$ clusters; secondly, the arrangement of the chains leads to directly comparable coordinations in which each $M_4$ group is surrounded by X atoms in much the same way as in the isolated $Mo_4I_7^{2+}$ cluster.

The structure of $Ni_2Si$ (θ-form) is shown in Figure 15c as an example of the three-dimensional linkage of the $M_4X_6$ cluster *via* vertex atoms[179]. This compound crystallizes with the $Ni_2In$ structure[188]. The layers of linked chains of $M_4X_6$ groups become evident in the chosen projection. The arrangement of the layers again leads to the characteristic coordination of each $M_4$ cluster by X atoms as in the isolated cluster $Mo_4I_7^{2+}$. The close relationship to the $Co_2P$ structure (Fig. 14d) has already been mentioned. In fact, the structure of θ-$Ni_2Si$ is converted into the $Co_2P$ structure by buckling the layers and simultaneously bringing them closer together. The bent $M_4$ rhombus seems to be an important structural unit in many further examples, some of which will be mentioned in the next section. Besides this arrangement of four M atoms, the square turns up frequently as an alternative octahedral fragment among metal-rich and intermetallic compounds of the elements under consideration. The many compounds which crystallize with the $W_5Si_3$- and $Al_2Cu$-type structures are possible examples[157, 189]. These will not be discussed in detail here, but for the sake of completeness one further $M_4$ cluster, which is well known as an isolated unit, must be mentioned; the tetrahedral $M_4$ cluster. One structure $Ru_7B_3$, which contains rows of such clusters has already been mentioned in Section 3.3. Further representatives exist in large numbers as "Tetraeder-Stern" structures[181]. One group of compounds with the composition $LnM_4B_4$, which has frequently been studied in recent times shows various possible modes in which tetrahedral $M_4$ clusters occur. In $YRu_4B_4$, isolated $Ru_4$ tetrahedra are present[190], whereas in $NdCo_4B_4$[191] and $LaRu_4B_4$[192] they are linked *via* edges to form one-dimensional chains. The present great interest in these compounds is related to their high superconducting transition temperatures[193] and, above all, to the discovery of competing superconductivity and ferromagnetism in $ErRh_4B_4$[194]. It may be noted in this context that the structures of the A15 phases, to which $Nb_3Ge$ belongs, with the highest superconducting transition temperature known, are also composed of networks of linked tetrahedra. Superconductivity and metal clusters may be related in a way that is not yet understood[195].

### 3.4.3. Structures with Several Types of Clusters

One example of the occurrence of various types of cluster in one compound ($M_6$, $M_3$) has already been given in Section 3.1 with the structure of $Nb_4As_3$. A few structures will now be discussed which can be completely resolved into mixed arrangements of linked $M_6$, $M_5$ and $M_4$ clusters. The niobium phosphides $Nb_7P_4$, $Nb_5P_3$ and $Nb_8P_5$, whose X/M ratios are very similar, are shown together, in Figures 15d, e, f. The structure of $Nb_7P_4$ has already been discussed in Section 3.1 as an "expanded" $M_5X_4$ variant according to the formula $M_5X_4 \cdot M_2$. It is interesting that the additional M atoms inserted between the $M_5X_4$ chains arrange themselves in such a way with the adjacent vertex atoms of the $M_5X_4$ chains that they form rows of linked $M_5$ clusters. This is indicated in Figure 15d. Thus, the $Nb_7P_4$ structure can also be regarded as a series of identical layers, each of which consists of alternating vertex-linked $M_6$ and $M_5$ cluster chains. A slight increase in the X/M ratio from 0.57 to 0.60 leads in $Nb_5P_3$[196] to a growth of the proportion of "partial-clusters". As indicated in Figure 15e, the entire atomic arrangement in this compound can be represented by linear units of vertex-linked parallel rows of $M_6$, $M_5$ and $M_4$ clusters. This type of structure was first found in $Hf_5As_3$[197]. A comparison with the $Hf_3P_2$ structure is interesting here since it shows that the atomic arrangements around the $M_4$ groups are to a large extent equivalent. Finally the structure of $Nb_8P_5$[198], which is also formed by $Zr_8As_5$[183], contains rows of vertex-linked $M_4$ clusters which surround single $M_5X_4$ chains. The Nb arsenides possess the same structures as the phosphides described above[91].

Interestingly enough, the compound $Mo_8P_5$[199] only contains structural elements formed from fragments of the $M_6X_8$ cluster even though it has the larger VEC. As illustrated in Figure 15g, each chain of $M_5$ clusters is linked *via* vertices to two chains of $M_4$ clusters. The structure is built up entirely by the repetition of such combined units. The arrangement of X atoms around each $M_4$ group is the same as in the isolated $Mo_4I_7^{2+}$ cluster. Around the $M_5$ group, neighboring M atoms occupy those positions, which are occupied by the Cl atoms in the isolated $Mo_5Cl_8^{3+}$ ion. In principle, the $M_4$ clusters can be completed in the structure of $Mo_8P_5$ to form distorted $M_5$ clusters by taking into account neighboring M atoms. In this way a network of such (vertex-sharing) clusters results. Close relationships can therefore be found to the structures treated in Section 3.4.1.

The phosphide $Mo_4P_3$[200] (Fig. 15h), which contains less Mo, provides another example of a compound whose structure demonstrates the possibility of an "expansion" of the cluster structure to a higher X content; additional M and X atoms are inserted in equal numbers between parallel chains of $M_4$ clusters, resulting in an overall composition $M_2M_{2/2}X_{2/2}X_{4/4} \cdot MK$. The situation corresponds to that in $Nb_4As_3$ and $V_4As_3$, which have already been mentioned and which can be described analogously as $M_4M_{2/2}X_{8/8} \cdot M_3X_2$. In $Nb_4As_3$ and the low temperature form of $V_4As_3$ however, the intermediate M atoms are arranged in trigonal $M_3$ groups with the X coordination as in $Nb_3Se_4$. The arrangement of the additional atoms in the high temperature form of $V_4As_3$ on the other hand, is very similar to that in $Mo_4P_3$.

### 3.5. Occupation of the Cluster Centers

One special aspect of the chemistry of metal clusters, which has increased in importance for molecular compounds should not be neglected. It was first demonstrated in the compounds $HNb_6I_{11}$[201] and $CRu_6(CO)_{17}$[202], in 1967, that the center of a transition metal cluster can be occupied by single atoms (H or C resp.). Since then an impressive number of comparable compounds with "interstitial" atoms has become known. These are of great interest because of their possible importance in catalytic processes, and have been summarized in several reviews[203-207].

It may be conjectured that the cluster centers can be occupied by single atoms in systems with condensed clusters as well. The first indication of the correctness of this supposition is given by the reversible $H_2$ absorption by the compounds ZrCl and ZrBr (*cf.* Section 3.2.2), which leads to the almost stoichiometric compounds ZrXH and $ZrXH_{0.5}$[208]; the position of the H atoms is still uncertain in these compounds. Apart from this, there are cases among the metal-rich transition metal compounds within the scope of this work, whose structures contain metal clusters, the centers of which are occupied by additional atoms. Such "filled" structures have already been mentioned in another context[209]. In conclusion, a few particularly striking examples of octahedral $M_6$ clusters will be discussed.

Three-dimensional vertex-linkage of $M_6X_8$ clusters leads to the structure of $U_3Si$ ($Cu_3Au$) (see Fig. 6b). If $M_6X_{12}$ clusters are linked in the same way, the NbO structure results (see Section 3.1). For the first arrangement, occupation of the octahedral centers leads to the perovskite structure. Indeed, many "perovskite" carbides and nitrides exist[210,211]; from these $Mn_3GeC$ and $Fe_3GeN$ may be cited here since they fall into the chosen range of element combinations. It is remarkable in this connection that the structure shows the same deviation as $U_3Si$ from cubic symmetry with increasing occupation of all centers. A fascinating example of the filled NbO structure is the nitride $W_3N_4$ ($N \cdot W_{6/2}N_{12/4}$)[212] whose structure however, still has to be verified; interestingly, NbO and $W_3N_4$ are isoelectronic!

The $Mn_5Si_3$ structure is particularly accommodating as far as the insertion of atoms into the octahedral centers is concerned[211,213,214]. Besides boron (*e.g.* $Nb_5Ge_3B$[215]), carbon above all is easily inserted, and the ferromagnetic compound $Mn_5Si_3C_x$[216] can be obtained by reaction of $Mn_5Si_3$ with C. For the compound $Ti_5P_3$, which has already been mentioned (Section 3.3), the composition $Ti_5P_3O_x$ is assumed[217,218]. The insertion of metal atoms is also possible, such as in the compound $Hf_5Sn_3Cu$[215]. Binary phases represent a special case. The complete occupation of all octahedral centers as for example in $Hf_5Sn_4$ ($=Sn{\cdot}Hf_5Sn_3$)[219], leads to the $Ti_5Ga_4$-type structure[220].

The ordered partial occupation of the centers of the $M_6$ octahedra is also known. For example, the structure of $Mn_{10}Ge_7$ corresponds to a half-filled $Mn_5Si_3$ structure[221]. In this case, it is interesting to see that the ordered semi-occupation resolves the *trans* face-linked octahedron chain into single $M_6X_8$ clusters, which are connected according to the formula $Mn_6Ge_6Ge_{2/2}$. This final example leads right back to the starting point of this work.

## 4. Final Remarks

The search for the smallest bonded units in the structures of metal-rich compounds of the transition metals and lanthanoids with p-elements leads to the following result—known for some time—that preferred coordination polyhedra occur for the non-metal atoms X. In addition the linkage of the polyhedra takes place in such a way that the M and X atoms often end up with an arrangement identical to that known from isolated metal clusters. The examples chosen for the present work (*cf.* Table 3) may provide convincing evidence for this idea; many more examples could be added. It should nevertheless be stressed that the "image-seeking" procedure illustrated with the aid of the examples shown here, is not yet always successful. Even in those cases where certain atomic arrangements can be interpreted in terms of condensed clusters, conclusions drawn from the crystal structure alone can be misleading. An example of this is the high pressure form of $Ag_2O$, which like $Ag_2F$ crystallizes in the anti-$CdI_2$ structure type[222] and therefore could be discussed as $Ag_{6/3}O_{2/2}$ within the concept of condensed clusters. In contrast to $Ag_2F$, the VEC is zero in the case of $Ag_2O$, and only van der Waals bonds exist between the $Ag^+$ ions. This example shows that further knowledge, above all about the VEC, is essential for the interpretation of structures of metal-rich compounds. It is well known that isostructural behaviour is no evidence for identical chemical bonding. Many of the metal-rich compounds under discussion possess structural antitypes (*e.g.* $Co_2P/PbCl_2$), for which the interatomic interactions postulated here are irrelevant. This is directly related to the question which arose for $U_3Si$ and $Ni_3Sn$ and which is particularly important for intermetallic phases. How far can the tendency to optimize space-filling (close-packing) be distinguished from the consequence of directional bonding? In particular, it may be very helpful that chemical bonding is

Table 3. Crystal data for the structures of compounds shown as projection, *cf.* footnotes on p. 4.

| Compound | Figure | Crystal system | Lattice constants [pm, °] | Ref. |
|---|---|---|---|---|
| $Ti_5Ti_4$ | 5a | tetragonal | $a=1016.4$, $c=377.2$ | [64] |
| $V_3As_2$ | 5b | tetragonal | $a=941.28$, $c=333.61$ | [74] |
| $Nb_7P_4$ | 5c, 15d | monoclinic | $a=1495.0$, $b=344.0$, $c=1384.8$, $\beta=104.74$ | [75] |
| $Nb_5Si_4Cu_4$ | 5d | tetragonal | $a=1019.08$, $c=360$ | [76] |
| $Nb_4As_3$ | 5e | o-rhombic | $a=351.6$, $b=1466.0$, $c=1883.0$ | [81] |
| $Ti_2Bi$ | 6a | tetragonal | $a=404$, $c=1450$ | [181] |
| $U_3Si$ | 6b | tetragonal | $a=601.7$, $c=867.9$ | [84] |
| $U_3Si_2$ | 6c | tetragonal | $a=731.51$, $c=389.25$ | [84] |
| $Mn_3As$ | 6d | tetragonal | $a=378.8$, $c=1629.0$ | [96] |
| TiO | 7 | monoclinic | $a=585.5$, $b=934.0$, $c=414.2$, $\gamma=107.53$ | [88] |
| $Ti_2S$ | 8a | o-rhombic | $a=1135$, $b=1406$, $c=332.0$ | [92] |
| $Nb_2Se$ | 8b | monoclinic | $a=1399.2$, $b=342.2$, $c=928.3$, $\beta=91.76$ | [95] |
| $Nb_{14}S_5$ | 8c | o-rhombic | $a=1848.0$, $b=337.4$, $c=1979.7$ | [97] |
| $Nb_{21}S_8$ | 8d | tetragonal | $a=1679.4$, $c=335.9$ | [98] |
| $Ti_8S_3$ | 8e | monoclinic | $a=3269.0$, $b=332.7$, $c=1936$, $\beta=139.9$ | [100] |
| $NaMo_4O_6$ | 9a | tetragonal | $a=955.9$, $c=286.0$ | [113, 136] |
| $Gd_2Cl_3$ | 9b | monoclinic | $a=1523.7$, $b=389.6$, $c=1017.9$, $\beta=117.66$ | [112] |
| $Tb_5Br_8$ | 9c | monoclinic | $a=2070.5$, $b=385.9$, $c=1336.7$, $\beta=133.07$ | [123] |
| $Er_4I_5$ | 9d | monoclinic | $a=1852.1$, $b=401.5$, $c=847.8$, $\beta=103.07$ | [124] |
| $Er_6I_7$ | 9e | monoclinic | $a=2138.7$, $b=387.4$, $c=1232.3$, $\beta=123.46$ | [125] |
| $Er_7I_{10}$ | 9f | monoclinic | $a=2096.6$, $b=418.7$, $c=1458.5$, $\beta=96.56$ | [124] |
| $Sc_7Cl_{10}$ | 9g | monoclinic | $a=1862.0$, $b=353.66$, $c=1225.0$, $\beta=91.98$ | [115] |
| *h,t*-TbCl | 9h, 9i | rhombohedral | $a_h=378.6$, $c_h=2746.1$ | [127] |
| $TlFe_3Te_3$ | 12a | hexagonal | $a=935$, $c=422.3$ | [154] |
| $Mn_5Si_3$ | 12b | hexagonal | $a=691.0$, $c=481.4$ | [156] |
| $Ru_7B_3$ | 12c | hexagonal | $a=695.9$, $c=454.6$ | [164] |
| $Ni_3Sn$ | 12d | hexagonal | $a=531.0$, $c=425.6$ | [181] |
| *o*-$Ni_4B_3$ | 14a | o-rhombic | $a=1195.4$, $b=298.15$, $c=656.8$ | [169] |
| $Rh_5Ge_3$ | 14b | o-rhombic | $a=542$, $b=1032$, $c=396$ | [170] |
| $Fe_2P$ | 14c | hexagonal | $a=586.5$, $c=345.6$ | [172] |
| $Co_2P$ | 14d | o-rhombic | $a=564.6$, $b=351.3$, $c=660.8$ | [174] |
| $Cu_2Sb$ | 14e | tetragonal | $a=399.2$, $c=609.1$ | [181] |
| $Hf_3P_2$ | 15a | o-rhombic | $a=1013.8$, $b=357.8$, $c=988.1$ | [182] |
| $Cr_3C_2$ | 15b | o-rhombic | $a=553.29$, $b=282.9$, $c=1147.19$ | [184] |
| $Ni_2Si$ | 15c | hexagonal | $a=384$, $c=500$ | [179] |
| $Nb_5P_3$ | 15e | o-rhombic | $a=2538.4$, $b=343.3$, $c=1148.3$ | [196] |
| $Nb_8P_5$ | 15f | o-rhombic | $a=2620$, $b=946.5$, $c=346.4$ | [198] |
| $Mo_8P_5$ | 15g | monoclinic | $a=939.9$, $b=320.9$, $c=653.7$, $\beta=109.59$ | [199] |
| $Mo_4P_3$ | 15h | o-rhombic | $a=1242.8$, $b=315.8$, $c=2044.0$ | [200] |

quantitatively related to the volumes of intermetallic phases within an isostructural family[223-225].

The objectives of further investigations have to be sought both in experimental work and in the more detailed analysis of structural data in the light of results obtained by other techniques. Our present knowledge of the existing metal-rich compounds and their structures appears in many respects fragmentary. The structural principles which have been recognized (for example, in the cases of the Ti sulphides and ternary metal-rich Mo compounds) allow us to be optimistic of finding many more compounds of this sort. One important area for further work is the correlation of information about composition, structure and VEC, which up to now has only been attempted for single cases in a preliminary way. Last but not least, the localized description of the often very complicated structures in terms of condensed clusters hopefully provides a guide for an appropriate quantitative description of electronic structure, and hence a detailed understanding of the chemical bonding in these compounds.

*Special thanks are due to my former co-worker Ch. Bauspieß, who assisted in the early stages of the development of the present concept, as well as K. Berroth, R. Eger, N. Holzer, Hj. Mattausch and E. Warkentin, who all helped to open up the chemistry of metal-rich lanthanoid halides. I had valuable discussions with my colleagues J. D. Corbett, R. E. McCarley and H. G. v. Schnering. I wish to thank Mrs. M. Raatz, K. Berroth and E. Warkentin for their help in producing the manuscript and the figures, also A. Griffiths for translating the text into English. Finally, I am indebted to the Verband der Chemischen Industrie—Fonds der Chemie—for their generous support of this work in the form of book donations.*

Received: November 3, 1980 [A 346 IE]
German version: Angew. Chem. *93*, 23 (1981)

---

[1] *H. Schäfer, H. G. von Schnering,* Angew. Chem. *76*, 833 (1964).
[2] *J. Lewis, R. S. Nyholm,* Sci. Prog. London *52*, 557 (1964).
[3] *J. Lewis,* Pure Appl. Chem. *10*, 11 (1965).
[4] *F. A. Cotton,* Q. Rev. Chem. Soc. *20*, 389 (1966).
[5] *M. C. Baird,* Prog. Inorg. Chem. 9, 1 (1968).
[6] *P. Chini,* Inorg. Chim. Acta Rev. *2*, 31 (1968).
[7] *F. A. Cotton,* Acc. Chem. Res. *1*, 257 (1968).
[8] *E. W. Abel, F. G. A. Stone,* Q. Rev. Chem. Soc. *23*, 325 (1969).
[9] *R. D. Johnston,* Adv. Inorg. Chem. Radiochem. *13*, 471 (1970).
[10] *R. B. King,* Prog. Inorg. Chem. *15*, 287 (1972).
[11] *J. E. Fergusson,* Prep. Inorg. React. *7*, 93 (1971).
[12] *R. A. Walton,* Prog. Inorg. Chem. *16*, 1 (1972).
[13] *T. J. Meyer,* Prog. Inorg. Chem. *19*, 1 (1975).
[14] *H. Vahrenkamp,* Struct. Bonding (Berlin) *32*, 1 (1977).
[15] *E. L. Muetterties, T. N. Rhodin, E. Band, C. F. Brucker, W. R. Pretzer,* Chem. Rev. *79*, 91 (1979).
[16] *F. Hulliger,* Struct. Bonding (Berlin) *4*, 83 (1968).
[17] *C. N. R. Rao, K. P. R. Pisharody,* Prog. Solid State Chem. *10*, 207 (1976).
[18] *H. F. Franzen,* Prog. Solid State Chem. *12*, 1 (1978).
[19] *H.-Y. Chen, H. F. Franzen,* Natl. Bur. Stand. U. S. Spec. Publ. *364*, 651 (1972).
[20] *A. Simon,* Chem. Unserer Zeit *10*, 1 (1976).
[21] *A. Simon, Hj. Mattausch, N. Holzer,* Angew. Chem. *88*, 685 (1976); Angew. Chem. Int. Ed. Engl. *15*, 624 (1976).
[22] *Ch. Bauspieß,* Thesis, Universität Münster 1977.
[23] *A. Simon,* Inst. Phys. Conf. Ser. *39*, 353 (1978).
[24] *A. Simon, Ch. Bauspieß,* VI. Intern. Conf. Solid Comp. Trans. Elements, Coll. Abstr., Stuttgart 1979, S. 98.
[25] *K. Wade,* Adv. Inorg. Chem. Radiochem. *18*, 1 (1976).
[26] *R. B. King, D. H. Rouvray,* J. Am. Chem. Soc. 99, 7834 (1977).
[27] *J. W. Lauher,* J. Am. Chem. Soc. *100*, 5305 (1978).
[28] *B. T. Matthias,* Prog. in Low Temp. Phys. *2* (1957).
[29] *A. Zalkin, D. E. Sands,* Acta Crystallogr. *11*, 615 (1958).
[30] *L. F. Dahl, D. L. Wampler,* Acta Crystallogr. *15*, 903 (1962).
[31] *A. Simon, H. G. von Schnering,* J. Less-Common Met. *11*, 31 (1966).
[32] *H. Schäfer, H. G. von Schnering, K.-J. Niehues, H. G. Niedervahrenholz,* J. Less-Common Met. 9, 95 (1965).
[33] *D. Bauer, H. G. von Schnering,* Z. Anorg. Allg. Chem. *361*, 259 (1968).
[34] *A. Simon, H. G. von Schnering, H. Wöhrle, H. Schäfer,* Z. Anorg. Allg. Chem. *339*, 155 (1965).
[35] *A. Simon, H. G. von Schnering, H. Schäfer,* Z. Anorg. Allg. Chem. *355*, 295 (1967).
[36] *H. Imoto, J. D. Corbett,* Inorg. Chem. *19*, 1241 (1980).
[37] *M. Spangenberg, W. Bronger,* Angew. Chem. *90*, 382 (1978); Angew. Chem. Int. Ed. Engl. *17*, 368 (1978).
[38] *J. D. Corbett, R. L. Daake, K. R. Poeppelmeier, D. H. Guthrie,* J. Am. Chem. Soc. *100*, 652 (1978).
[39] *K. Brodersen, G. Thiele, H. G. von Schnering,* Z. Anorg. Allg. Chem. *337*, 120 (1965).
[40] *F. A. Cotton, T. E. Haas,* Inorg. Chem. *3*, 10 (1964).
[41] *H. Müller,* Z. Phys. Chem. *249*, 1 (1972).
[42] *A. Broll, A. Simon, H. G. von Schnering, H. Schäfer,* Z. Anorg. Allg. Chem. *367*, 1 (1969).
[43] *J. V. Brencic, F. A. Cotton,* Inorg. Chem. *8*, 7 (1969).
[44] *F. A. Cotton,* Inorg. Chem. *4*, 334 (1965).
[45] *R. Siepmann, H. G. von Schnering, H. Schäfer,* Angew. Chem. *79*, 650 (1967); Angew. Chem. Int. Ed. Engl. *6*, 637 (1967).
[46] *D. L. Kepert, R. E. Marshall, D. Taylor,* J. Chem. Soc. Dalton Trans. *1974*, 506.
[47] *K. Jödden, H. G. von Schnering, H. Schäfer,* Angew. Chem. *87*, 594 (1975); Angew. Chem. Int. Ed. Engl. *14*, 570 (1975).
[48] *S. Stensrad, B. J. Helland, M. W. Babich, R. A. Jacobson, R. E. McCarley,* J. Am. Chem. Soc. *100*, 6257 (1978).
[49] *Z. Amilius, B. von Laar, H. M. Rietveld,* Acta Crystallogr. *B 25*, 400 (1969).
[50] *K. Selte, A. Kjekshus,* Acta Crystallogr. *17*, 1568 (1964).
[51] *O. Bars, J. Guillevic, D. Grandjean,* J. Solid State Chem. *6*, 48 (1973).
[52] *H. G. von Schnering, H. Wöhrle, H. Schäfer,* Naturwissenschaften *48*, 159 (1961).
[53] *A. F. J. Ruysink, F. Kadijk, A. J. Wagner, F. Jellinek,* Acta Crystallogr. *B 24*, 1614 (1968).
[54] *K. Selte, A. Kjekshus,* Acta Chem. Scand. *17*, 2560 (1963).
[55] *H. Krebs:* Grundzüge der Anorganischen Kristallchemie. Enke, Stuttgart 1968, p. 327.
[56] *F. C. Frank, J. S. Kasper,* Acta Crystallogr. *11*, 184 (1958); *ibid. 12*, 483 (1959).
[57] *E. E. Hellner,* Struct. and Bonding (Berlin) *37*, 61 (1979).
[58] *B. G. Hyde, S. Anderson, M. Bakker, C. M. Plug, M. O'Keeffe,* Prog. Solid State Chem. *12*, 273 (1979).
[59] *L. Pauling:* Die Natur der chemischen Bindung. Verlag Chemie, Weinheim 1973, p. 231.
[60] *A. Simon,* Struct. and Bonding (Berlin) *36*, 81 (1979).
[61] *E. T. Keve, A. C. Skapski,* Inorg. Chem. *7*, 1757 (1968).
[62] *J. Gaudé, P. l'Haridon, Y. Laurent, J. Lang,* Bull. Soc. Fr. Minér. Cristallogr. *95*, 56 (1972).
[63] *H. T. Künzel, A. Simon,* unpublished results.
[64] *F. Grønvold, A. Kjekshus, F. Raaum,* Acta Crystallogr. *14*, 930 (1961).
[65] *W. Klemm, W. Bronger, H. G. von Schnering,* Jahrbuch der Arbeitsgemeinschaft für Forschung des Landes Nordrhein-Westfalen. Westdeutscher Verlag, Köln 1966, p. 451.
[66] *H. Schäfer,* Jahrbuch der Arbeitsgemeinschaft für Forschung des Landes Nordrhein-Westfalen. Westdeutscher Verlag, Köln 1968, p. 7.
[67] *D. Eberle, K. Schubert,* Z. Metallkd. *59*, 306 (1968).
[68] *F. Grønvold, H. Haraldsen, P. Pedersen, T. Tufte,* Rev. Chim. Minér. *6*, 215 (1969).
[69] *E. Röst, L. Gjertsen,* Z. Anorg. Allg. Chem. *328*, 300 (1964).
[70] *S. Furuseth, A. Kjekshus,* Acta Chem. Scand. *18*, 1180 (1964).
[71] *S. Furuseth, A. Kjekshus,* Acta Chem. Scand. *19*, 95 (1965).
[72] *P. Jensen, A. Kjekshus,* Acta Chem. Scand. *20*, 1309 (1966).
[73] *H. Nohl, O. K. Andersen,* unpublished results.
[74] *R. Berger,* Acta Chem. Scand. *A 31*, 287 (1977).
[75] *S. Rundqvist,* Acta Chem. Scand. *20*, 2427 (1966).
[76] *E. Ganglberger,* Monatsh. Chem. 99, 549 (1968).
[77] *K. Yvon, A. Paoli, R. Flükiger, R. Chevrel,* Acta Crystallogr. *B33*, 3066 (1977).
[78] *K. Yvon, A. Paoli,* Solid State Commun. *24*, 41 (1977).
[79] *K. Yvon,* Curr. Top. Mater. Sci. *3*, 55 (1979).
[80] *R. Berger, P. Phavanantha, Mongkolsük,* Acta Chem. Scand. *A 34*, 77 (1980).
[81] *B. Carlsson, S. Rundqvist,* Acta Chem. Scand. *25*, 1742 (1971).
[82] *R. Berger,* Acta Chem. Scand. *A 28*, 771 (1974).
[83] *H. Auer-Welsbach, H. Nowotny, A. Kohl,* Monatsh. Chem. *89*, 154 (1958).
[84] *W. H. Zachariasen,* Acta Crystallogr. *2*, 94 (1949).
[85] *G. Kimmel, S. Nadiv,* Acta Crystallogr. *B31*, 1351 (1975).
[86] *G. Kimmel,* J. Less-Common Met. *59*, 83 (1978).
[87] *A. Taylor, N. J. Doyle,* J. Appl. Crystallogr. *4*, 109 (1971).
[88] *D. Watanabe, J. R. Castles, A. Jostsons, A. S. Malin,* Acta Crystallogr. *23*, 307 (1967).

[89] *H. Schäfer, R. Gruehn, F. Schulte*, Angew. Chem. *78*, 28 (1966); Angew. Chem. Int. Ed. Engl. *5*, 40 (1966).
[90] *A. Nyland*, Acta Chem. Scand. *20*, 2393 (1966).
[91] *S. Rundqvist, B. Carlsson, C. Pontchour*, Acta Chem. Scand. *23*, 2188 (1969).
[92] *J. P. Owens, B. R. Conard, H. F. Franzen*, Acta Crystallogr. *23*, 77 (1967).
[93] *H. F. Franzen, J. Smeggil, B. R. Conard*, Mater. Res. Bull. *2*, 1087 (1967).
[94] *S. Rundqvist, B. Carlsson*, Acta Chem. Scand. *22*, 2395 (1968).
[95] *B. R. Conard, L. J. Norrby, H. F. Franzen*, Acta Crystallogr. *B25*, 1729 (1979).
[96] *H. Nowotny, R. Funk, J. Pesl*, Monatsh. Chem. *82*, 513 (1951).
[97] *H.-Y. Chen, R. T. Tuenge, H. F. Franzen*, Inorg. Chem. *12*, 552 (1973).
[98] *H. F. Franzen, T. A. Beineke, B. R. Conard*, Acta Crystallogr. *B 24*, 412 (1968).
[99] *B. R. Conard, H. F. Franzen*, High Temp. Sci. *3*, 49 (1971).
[100] *J. P. Owens, H. F. Franzen*, Acta Crystallogr. *B 30*, 427 (1974).
[101] *N. C. Baenziger, R. E. Rundle, A. I. Snow, A. S. Wilson*, Acta Crystallogr. *3*, 34 (1950).
[102] *H. F. Franzen, J. G. Smeggil*, Acta Crystallogr. *B26*, 125 (1970).
[103] *H. F. Franzen, J. G. Smeggil*, Acta Crystallogr. *B 25*, 1736 (1969).
[104] *H.-Y. Cheng, H. F. Franzen*, Acta Crystallogr. *B28*, 1399 (1972).
[105] *W. Klemm, H. Bommer*, Z. Anorg. Allg. Chem. *231*, 138 (1937).
[106] *J. D. Corbett*, Rev. Chim. Minér. *10*, 239 (1973).
[107] *E. Warkentin, H. Bärnighausen*, Z. Anorg. Allg. Chem. *459*, 187 (1979).
[108] *C. Perrin, R. Chevrel, M. Sergent*, C. R. Acad. Sci. Ser. *C281*, 23 (1975).
[109] *J. E. Mee, J. D. Corbett*, Inorg. Chem. *4*, 88 (1965).
[110] *D. A. Lokken, J. D. Corbett*, J. Am. Chem. Soc. *92*, 1799 (1970).
[111] *D. A. Lokken, J. D. Corbett*, Inorg. Chem. *12*, 556 (1973).
[112] *A. Simon, N. Holzer, Hj. Mattausch*, Z. Anorg. Allg. Chem. *456*, 207 (1979).
[113] *C. C. Forardi, R. E. McCarley*, J. Am. Chem. Soc. *101*, 3963 (1979).
[114] *K.-J. Range, K. Bauer, F. Rau, W. Abriel*, private communication.
[115] *K. R. Poeppelmeier, J. D. Corbett*, Inorg. Chem. *16*, 1107 (1977).
[116] *K. R. Poeppelmeier, J. D. Corbett*, J. Am. Chem. Soc. *100*, 5039 (1978).
[117] *J. D. Corbett*, Adv. Inorg. Chem. Ser. *186*, in press.
[118] *N. Holzer*, Thesis, Universität Stuttgart 1978.
[119] *E. Warkentin, K. Berroth, A. Simon*, unpublished results.
[120] *K. Berroth*, Thesis, Universität Stuttgart 1980.
[121] *Hj. Mattausch, R. Eger, A. Simon*, unpublished results.
[122] *Hj. Mattausch, J. B. Hendricks, R. Eger, J. D. Corbett, A. Simon*, Inorg. Chem. *19*, 2128 (1980).
[123] *Hj. Mattausch, A. Simon, R. Eger*, Rev. Chim. Minér., in press.
[124] *K. Berroth, A. Simon*, J. Less-Common Met., in press.
[125] *K. Berroth, Hj. Mattausch, A. Simon*, Z. Naturforsch. *B35*, 626 (1980).
[126] *K. R. Poeppelmeier, J. D. Corbett*, Inorg. Chem. *16*, 294 (1977).
[127] *Hj. Mattausch, A. Simon, N. Holzer, R. Eger*, Z. Anorg. Allg. Chem. *466*, 7 (1980).
[128] *S. I. Troyanov*, Vestn. Mosk. Univ. Khim. *28*, 369 (1973).
[129] *D. G. Adolphson, J. D. Corbett*, Inorg. Chem. *15*, 1820 (1976).
[130] *R. L. Daake, J. D. Corbett*, Inorg. Chem. *16*, 2029 (1977).
[131] *W. Bauhofer, A. Simon*, Z. Naturforsch., in press.
[132] *D. W. Bullett*, Inorg. Chem. *19*, 1780 (1980).
[133] *G. Ebbinghaus, A. Simon*, Z. Naturforsch., in press.
[134] *J. D. Greiner, J. E. Smith, J. D. Corbett, F. J. Jelinek*, J. Inorg. Nucl. Chem. *28*, 971 (1966).
[135] *G. Czjzek, N. Holzer, A. Simon*, unpublished results.
[136] *R. E. McCarley*, private communication.
[137] *S. Andersson, S. Asbrink, B. Hochberg, A. Magneli*, Bull. Natl. Inst. Sci. India *14*, 136 (1958).
[138] *G. Argay, F. Náray-Szabo*, Acta Chim. Acad. Sci. Hung. *49*, 329 (1966).
[139] *A. L. Bowmann, T. C. Wallace, J. L. Yarnell, R. G. Wenzel, E. K. Storms*, Acta Crystallogr. *19*, 6 (1965).
[140] *G. L. Bacchella, P. Mériel, M. Pinot, R. Lallement*, Bull. Soc. Fr. Minéral. Crystallogr. *89*, 226 (1966).
[141] *M. Atoji, M. Kikuchi*, J. Chem. Phys. *51*, 3863 (1969).
[142] *H. G. von Schnering, K.-G. Häusler*, Rev. Chim. Miner. *13*, 71 (1976).
[143] *H. F. Franzen, J. Graham*, Z. Kristallogr. *123*, 133 (1966).
[144] *A. S. Izmailovich, S. I. Troyanov, V. I. Tsirel'nikow*, Russ. J. Inorg. Chem. *19*, 1597 (1974).
[145] *A. Grüttner, K. Yvon, R. Chevrel, M. Potel, M. Sergent, B. Seeber*, Acta Crystallogr. *B35*, 285 (1979).
[146] *B. Seeber, M. Decroux, Ø. Fischer, R. Chevrel, M. Sergent, A. Grüttner*, Solid State Commun. *29*, 419 (1979).
[147] *R. Chevrel, M. Sergent, B. Seeber, Ø. Fischer, A. Grüttner, K. Yvon*, Mater. Res. Bull. *14*, 567 (1979).
[148] *A. Lipka, K. Yvon*, Acta Crystallogr. *B 36*, 2123 (1980).
[149] *M. Potel, R. Chevrel, M. Sergent, M. Decroux, Ø. Fischer*, C. R. Acad. Sci. Ser. *C 288*, 429 (1979).
[150] *R. Chevrel, M. Potel, M. Sergent, M. Decroux, Ø. Fischer*, Mater. Res. Bull. *15*, 867 (1980).
[151] *M. Potel, R. Chevrel, M. Sergent*, Acta Crystallogr. *B 36*, 1319 (1980).
[152] *R. Chevrel, M. Potel, M. Sergent, M. Decroux, Ø. Fischer*, J. Solid State Chem. *34*, 247 (1980).
[153] *K. Klepp, H. Boller*, Acta Crystallogr. *A 34*, S 160 (1978).
[154] *K. Klepp, H. Boller*, Monatsh. Chem. *110*, 677 (1979).
[155] *W. Hönle, H. G. von Schnering, A. Lipka, K. Yvon*, J. Less-Common Met. *71*, 135 (1980).
[156] *B. Aronsson*, Acta Chem. Scand. *14*, 1414 (1960).
[157] *W. B. Pearson:* Handbook of Lattice Spacings and Structures of Metals. Int. Ser. Monogr. Metal Phys. Phys. Metallurgy, Vol. 2, Pergamon Press, Oxford 1967, p. 44.
[158] *G. Brauer, K. Gingerich, M. Knausenberger*, Angew. Chem. *76*, 187 (1964); Angew. Chem. Int. Ed. Engl. *3*, 231 (1964).
[159] *M. C. M. Farguhar, H. Lipson, A. R. Weill*, J. Iron Steel Inst. *152*, 457 (1945).
[160] *J.-P. Bouchaud, R. Fruchart*, Bull. Soc. Chim. Fr. *1965*, 130.
[161] *R. Fruchart, J.-P. Senateur, J.-P. Bouchaud, A. Michel*, C. R. Acad. Sci. *260*, 913 (1965).
[162] *R. Fruchart, A. Rouault*, Ann. Chim. (Paris) *4*, 143 (1969).
[163] *A. Rouault, P. Herpin, R. Fruchart*, Ann. Chim. (Paris) *5*, 461 (1970).
[164] *B. Aronsson*, Acta Chem. Scand. *13*, 109 (1959).
[165] *P. Rahlfs*, Metallwirtsch. *16*, 343 (1937).
[166] *K. Schubert, W. Burkhardt, P. Esslinger, E. Günzel, H. G. Meissner, W. Schütt, J. Wegst, M. Wilkens*, Naturwissenschaften *43*, 248 (1956).
[167] *U. Henning, F. Pawlek*, Z. Erzbergbau Metallhüttenwes. *18*, 293 (1965).
[168] *E. Adelson, A. E. Austin*, J. Phys. Chem. Solids *26*, 1795 (1965).
[169] *S. Rundqvist, S. Pramatus*, Acta Chem. Scand. *21*, 191 (1967).
[170] *S. Geller*, Acta Crystallogr. *8*, 15 (1955).
[171] *R. Berger*, Acta Chem. Scand. *A 30*, 363 (1976).
[172] *S. Rundqvist, F. Jellinek*, Acta Chem. Scand. *13*, 425 (1959).
[173] *R. Guérin, M. Sergent*, Acta Crystallogr. *B 33*, 2820 (1977).
[174] *S. Rundqvist*, Acta Chem. Scand. *14*, 1961 (1960).
[175] *H. Nowotny*, Z. Anorg. Chem. *254*, 31 (1947).
[176] *R. Berger, L.-E. Tergenius*, Acta Chem. Scand. *A 30*, 387 (1976).
[177] *S. Geller, V. M. Wolontis*, Acta Crystallogr. *8*, 83 (1955).
[178] *S. Rundqvist*, Acta Chem. Scand. *15*, 342 (1961).
[179] *S. Rundqvist*, Ark. Kemi *20*, 67 (1962).
[180] *M. Elander, G. Hägg, A. Westgren*, Ark. Kemi Mineral. Geol. *B12*, 38 (1936).
[181] *K. Schubert:* Kristallstrukturen zweikomponentiger Phasen. Springer, Berlin 1964.
[182] *T. Lundström*, Acta Chem. Scand. *22*, 2191 (1968).
[183] *B. Carlsson, M. Gölin, S. Rundqvist*, Acta Chem. Scand. *A 30*, 386 (1976).
[184] *S. Rundqvist, G. Runnsjö*, Acta Chem. Scand. *23*, 1191 (1969).
[185] *R. Berger*, Acta Chem. Scand. *A 34*, 231 (1980).
[186] *P. E. Ettmayer, G. Vinek, H. Rassaerts*, Monatsh. Chem. *97*, 1258 (1966).
[187] *Yu. D. Kondrashev*, Sov. Phys. Crystallogr. *11*, 492 (1967).
[188] *K. Toman*, Acta Crystallogr. *5*, 329 (1952).
[189] *W. B. Pearson:* The Crystal Chemistry and Physics of Metals and Alloys. Wiley, New York 1972.
[190] *D. C. Johnston*, Solid State Commun. *24*, 699 (1977).
[191] *Yu. B. Kuzma, N. S. Bilonizkko*, Dopov. Dokl. Akad. Nauk USSR *A 3*, 275 (1978).
[192] *A. Grüttner, K. Yvon*, Acta Crystallogr. *B35*, 451 (1979).
[193] *B. T. Matthias, E. Corenzwit, J. M. Vandenberg, H. E. Barz*, Proc. Natl. Acad. Sci. USA *74*, 1334 (1977).
[194] *W. A. Fertig, D. C. Johnston, L. E. DeLong, R. W. McCallum, M. B. Maple, B. Matthias*, Phys. Rev. Lett. *38*, 987 (1977).
[195] *J. M. Vandenberg, B. T. Matthias*, Science *198*, 194 (1977).
[196] *E. Hassler*, Acta Chem. Scand. *25*, 129 (1971).
[197] *S. Rundqvist, B. Carlsson*, Acta Chem. Scand. *22*, 2395 (1968).
[198] *S. Anugul, C. Pontchour, S. Rundqvist*, Acta Chem. Scand. *27*, 26 (1973).
[199] *T. Johnsson*, Acta Chem. Scand. *26*, 365 (1972).
[200] *S. Rundqvist*, Acta Chem. Scand. *19*, 393 (1965).
[201] *A. Simon*, Z. Anorg. Allg. Chem. *355*, 311 (1967).
[202] *B. E. G. Johnson, R. D. Johnston, J. Lewis*, Chem. Commun. *1967*, 1057.
[203] *P. Chini, G. Longoni, V. G. Albano*, Adv. Organomet. Chem. *14*, 285 (1976).
[204] *P. Chini, G. Longoni, S. Martinengo, A. Ceriotti*, Adv. Chem. Ser. *167*, 1 (1978).
[205] *P. Chini*, Gazz. Chim. Ital. *109*, 225 (1979).
[206] *V. G. Albano, S. Martinengo*, Nachr. Chem. Tech. Lab. *28*, 654 (1980).
[207] *R. G. Teller, R. Bau*, Struct. and Bonding (Berlin), in press.
[208] *A. W. Struss, J. D. Corbett*, Inorg. Chem. *16*, 360 (1977).
[209] *H. Nowotny, H. Boller, O. Beckmann*, J. Solid State Chem. *2*, 462 (1970).
[210] *H. H. Stadelmeier*, Z. Metallkd. *52*, 758 (1961).
[211] *H. Nowotny*, Berg. Hüttenmänn. Monatsh. *110*, 171 (1966).
[212] *F. Günther, H. G. Schneider*, Sov. Phys. Crystallogr. *11*, 585 (1967).
[213] *G. Bergerhoff*, Z. Kristallogr. *124*, 6 (1967).
[214] *E. Parthé, W. Rieger*, J. Dentl. Res. *47*, 829 (1968).
[215] *W. Rieger, H. Nowotny, F. Benesovsky*, Monatsh. Chem. *96*, 98 (1965).
[216] *J. P. Sénateur, J.-P. Bouchaud, R. Fruchart*, Bull. Soc. Fr. Minér. Cristallogr. *40*, 537 (1967).
[217] *H. Bärninghausen, M. Knausenberger, G. Brauer*, Acta Crystallogr. *19*, 1 (1965).

[218] *T. Lundström, P. O. Snell,* Acta Chem. Scand. *21*, 1343 (1967).
[219] *W. Rossteutscher, K. Schubert,* Z. Metallkd. *56*, 813 (1965).
[220] *M. Pötzschke, K. Schubert,* Z. Metallkd. *53*, 474 (1962).
[221] *R. Horyn, R. Kubiak,* Bull. Acad. Pol. Sci. Ser. Sci. Chim. *19*, 185 (1971).
[222] *S. S. Kabalkina, S. V. Popova, N. R. Serebrjanaja, L. F. Vereščagin,* Sov. Phys. Dokl. *8*, 972 (1964).
[223] *A. Simon, W. Brämer, B. Hillenkötter, H.-J. Kullmann,* Z. Anorg. Allg. Chem. *419*, 253 (1976).
[224] *A. Simon,* Coll. Abstr. 3rd Europ. Crystallogr. Meeting, Zürich 1976, p. 335.
[225] *A. Simon, H. G. von Schnering,* unpublished results.

# Production of High Temperatures in the Chemical Laboratory: Examples of Application in Lanthanoid Oxo-Chemistry

## By Hanskarl Müller-Buschbaum[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

High-temperature reactions have always been a fascinating although difficult field of experimentation for the chemist. In the case of solid-state reactions the problems with apparatus increase exponentially with rising temperature, so that especially in this area of inorganic chemistry the modern techniques of producing high temperatures—from the solar furnace to the high-power $CO_2$ laser—have yielded new and interesting possibilities, particularly in the field of metastable high-temperature compounds.

## 1. Introduction

On account of limited preparational possibilities, research into lanthanoid oxo-compounds during the first half of this century was rather limited, as demonstrated clearly by the repeated investigations[1-3] of the phase diagram of the trivalent lanthanoid oxides in accordance with *Goldschmidt*[4] (Fig. 1); up to some 30 years ago, *i. e.* the dawn of modern high-temperature chemistry, the stability ranges of the three crystalline forms at high temperatures were unknown. In addition to the physical and thermodynamic data at high temperatures (for the definition of the term "high-temperature chemistry", see [5]), the formation of compounds, the phase diagrams, the reversibility or irreversibility of phase transformations, and above all accurate structural data are of interest.

As a result of the advent of new methods for the generation and application of high temperatures, the study of lanthanoid oxo-chemistry has undergone a burgeoning development in the last 30 years. Some of the most important fundamental studies in the field of high-temperature chemistry were carried out at the Institute of Inorganic Chemistry of the University of Münster under the direction of Professor *Klemm*. In the following review article the methods used for the production of high temperatures are considered, with selected examples of applications from the sphere of lanthanoid oxo-chemistry.

High temperatures can be produced by either chemical or physical methods. A number of such processes is presented in Table 1. Some processes affording very high final temperatures are nevertheless of little use in preparational solid-state chemistry, and these are consequently dealt with only briefly.

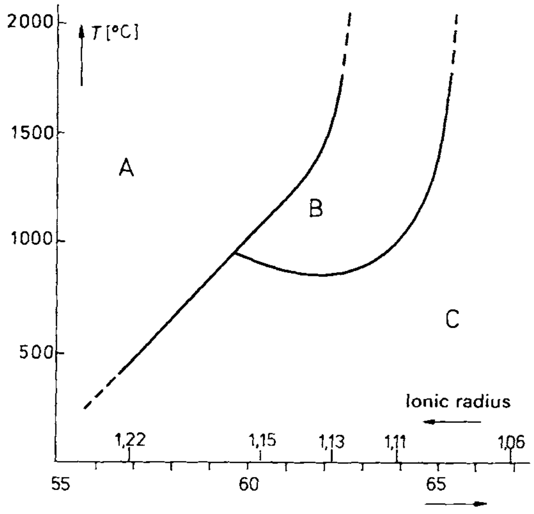


Fig. 1. Phase diagram for trivalent lanthanoid oxides, after *Goldschmidt*. For the A-, B-, and C-types, see text.

## 2. Methods of Limited Applicability for the Production of High Temperatures

### 2.1. Mechanical Techniques

The synthesis of new compounds by shock waves or a single adiabatic compression is the province of a few specialized teams. An explosive charge (*e. g.* hexogen) is set off and the

---

[*] Prof. Dr. Hk. Müller-Buschbaum
Institut für Anorganische Chemie der Universität
Olshausenstrasse 40/60, D-2300 Kiel (Germany)

0570-0833/81/0101-0022 $ 02.50/0

Table 1. Summary of the heat sources and heat production processes usable in chemical laboratories, and temperatures achievable in this way.

| *Mechanical processes* | | | *Thermochemical processes* | | *Natural heat sources* |
|---|---|---|---|---|---|
| Adiabatic compression ($>10^3$ °C) | | | Flames | Metallothermy | Solar furnaces |
| Adiabatic shock waves ($>10^4$ °C) | | | $2H_2+O_2$ (2660 °C) | Metal oxides, | ($\approx 3500$ °C) |
| | | | $C_2H_2+O_2$ (3100 °C) | sulphides, and halides | |
| | | | $C_2H_2+N_2O$ ($>3100$ °C) | +Al, Mg, Ca, Zr, *etc.* | |
| | | | Metal powder/$O_2$ flames | ($\approx 2000$—2500 °C) | |
| | | | "skating sun" | | |
| | | | ($\approx 2500$—4500 °C) | | |
| | | | *Electrical processes* | | |
| Resistance heating | | Electron-beam heating | Induction heating | Electric arc | Laser |
| Cr/Ni | (1100 °C) | Focal spot fusion | Inductive heating of electrically | Arc fusion | High-power $CO_2$ |
| SiC | (1500 °C) | Drip fusion ($>3000$ °C) | conducting substances | ($>3000$ °C) | laser ($>4000$ °C) |
| Pt/Rh | (1700 °C) | | Crucible-free fusion | Electric-arc plasma torch | |
| $MOSi_2$ | (1800 °C) | | Open plasma torch ($>10^4$ °C) | ($>10^4$ °C) | |
| $MO(H_2)$ | (2000 °C) | | Closed plasma torch | Arc-transport process | |
| C | (2500 °C) | | (thermal disequilibrium) | ($\approx 2000$—4000 °C) | |
| $ZrO_2$ | (2500 °C) | | ($\approx 10^3$—$10^4$ °C) | Artificial suns | |
| $MO_2+M_2O_3$ | (2000 °C) | | | ($\approx 2300$ °C) | |

shock front is passed through crystalline material; in addition to the pressure wave an equally steep temperature front is then formed, and the two together break the crystallites down to about 100 Å[7] to 10 Å[6], or about the order of magnitude of the elementary cells. This decomposition gives rise to a variety of structural disorders and lattice defects, raising the chemical reactivity to an extremely high level. The method has been used to synthesize ferrites[8,9], chromium[10] and tin[11] chalcogenides, and mixed tin dihalides ($SnCl_{0.5}Br_{1.5}$, SnClI, and SnBrI[12]). *Batsanow et al.*[13] found that the first few members of the lanthanoid oxide series $Ln_2O_3$ (Ln = La—Sm) react with water under the influence of shock waves to form $Ln(OH)_3$, whereas with $Eu_2O_3$ the product is the unexpected EuOH.

## 2.2. Thermochemical Techniques

The thermochemical methods are based on the principle of using the heat released in a chemical reaction for the production of the high temperatures. As far as manipulation is concerned, the most elegant examples of this type are hot flames, whose upper temperature is limited only by the chemical equilibrium of the combustion reaction, and in earlier years hot flames were in fact the only acceptable way for obtaining single crystals from the high-melting lanthanoid oxides. A disagreement between *Zachariasen*[14] and *Pauling*[15] on the structure of the hexagonal A-form of $La_2O_3$, a question that could not be decided definitively either way on microcrystalline powder preparations, was ultimately resolved by *Zachariasen*[16] on single crystals prepared by *Goldschmidt* with an oxyhydrogen flame. In 1956 *Tannenbaum* produced the first single crystals of the monoclinic B-form of $Sm_2O_3$ with an oxyacetylene flame. It was on this material that *Douglass* and *Staritzky*[17] were first able to determine the space group, the cell dimensions, and the optical properties, and *Cromer*[18] in 1957 was able to determine the crystal structure of the B-form of the lanthanoid oxides. This example illustrates the importance of high temperatures for the production of X-ray-perfect single crystals.

An obvious disadvantage of hot flames is that it is only possible to work with substances that can resist the oxidizing and reducing action of the flames at the high temperatures in question (Verneuil's process for the synthesis of rubies and sapphires). A particular difficulty is also presented by the extreme thermal expansion of the fuel gases as they heat up from room temperature to 2000—3000 °C: the strongly turbulent gases simply blast the molten samples out of the hot zone.

In metallothermic reactions (Al, Mg, Ca, Zr, *etc.* reacting with halides and oxides) the reacting metal intervenes to a far greater extent in the chemical process than the hot flames. For this reason the preparative applications are restricted to a few special examples, which will not be discussed in greater detail in the present review. The original method proposed by *Grosse* and *Conway*[19], of a metallic powder/$O_2$ flame, has also not been developed further. In one interesting variant, carrier materials coated with metals are combusted ("skating sun" phenomenon).

## 2.3. Electrical Techniques

### 2.3.1. Electron Beam Heating

The heating of metals by bombarding them with a beam of electrons, originated by *von Pirani*[20], was used by *Tiede*[21], *Tiede* and *Birnbräuer*[22], and *O'Bryan*[23] to melt metals, oxides, and carbides. In metallurgy, this technique, meanwhile perfected by the development of high-power electron guns (Fig. 2), has become a preferred method[24], since the melted material can be situated in a field-free space. Figure 2 shows *Stephan*'s 100 kVA apparatus[25]; the electron beam produced is focussed by magnetic lenses and emerges *via* a vacuum system into a field-free space likewise evacuated to about $10^{-3}$ mbar. The decisive advantages of this technique are protection of the cathode from evaporating material, suppression of perturbing glow discharge, and the simultaneous degassing and purification of the fused material. However, the use of the method is at the moment confined almost exclusively to metallic materials.

In this connection it is interesting to note that the heating of the extremely small samples in an electron microscope is identical with the older technique of preparation in the field. Thus, *Boulesteix et al.*[26] heated single crystals of the A-form of lanthanoid oxides to high temperatures (>2000 °C) by bombarding them with the electron beam of an electron microscope, to study the transition of the A-form into the Hand X-forms (high temperature modifications of $La_2O_3$) on the electron diffraction pattern (see Section 3.3).

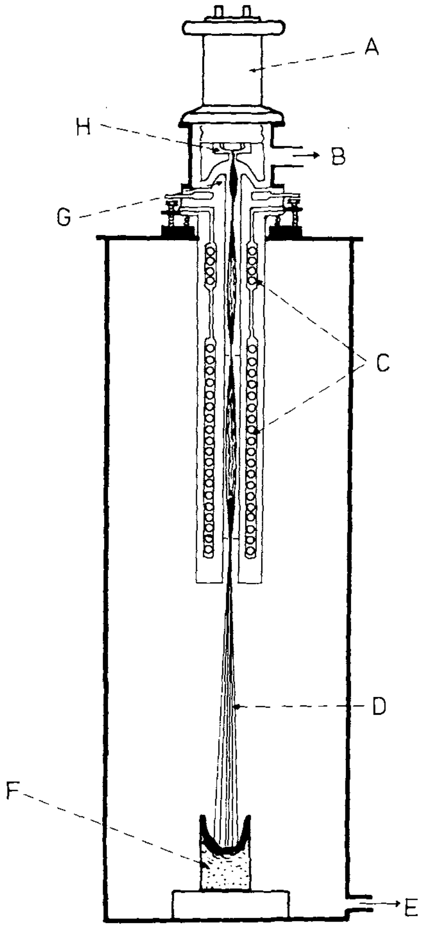


Fig. 2. Principle of an electron gun [25] for metal fusion in a field-free space. A: Insulator; B: pump for the electron gun; C: magnetic lenses; D: electron beam; E: pump for the preparation space; F: preparation; G: anode; H: cathode.

### 2.3.2. Electric Arc

Whereas the electric arc is used in a large number of ways for the production of high temperatures, in this section we shall consider only the direct application of arc fusion (heating in a d-c arc) and the original arc-transport process. The electric plasma-arc torches and electric arcs mentioned in Table 1 as artificial suns, are dealt with in Sections 3.4 and 3.3.

Direct heating in an electric arc resembles electron beam fusion, the principal differences being that

- in the electric arc the cathode drop is very small due to the low potential requirement ($\approx 10$ V),
- in the electric arc the power is produced by high currents,
- the substances to be heated are exposed to the material vaporizing in the arc (high-current arc).

In the high-intensity arc or the Beck arc temperatures of about 7000 °C are reached in long anode flames, *i. e.* temperatures much higher than are normally necessary for reactions in the solid state. Using a d-c arc, *Weir* and *Valkenburg*[27] reacted BeO with $Ga_2O_3$, $Y_2O_3$, and $La_2O_3$ and obtained, for example, the compound $BeY_2O_4$, whose structure—an $AB_2O_4$-type structure—was clarified later by *Harris* and *Yakel*[28]. *Miller* and *Daane*[29] prepared a number of lower-valence lanthanoid oxides ($LnO_{1.5-x}$) by the arc fusion of $Ln_2O_3$ with Ln (Ln = lanthanoid). As shown by density measurements, the deep-colored oxides $GdO_{1.495}$, $YO_{1.489}$, and $LuO_{1.485}$ obtained in this way contain a defect oxide lattice, which is also manifested in their formulas.

The arc-transport process described by *Drabble*[30], in which the material is transported by an electric arc, and which is particularly suitable for growing larger single crystals has so far received astonishingly little attention. A vertically burning arc between an electrode filled with a melt and a second electrode carrying the crystal is kept at a constant length by progressively raising the upper electrode (Fig. 3).

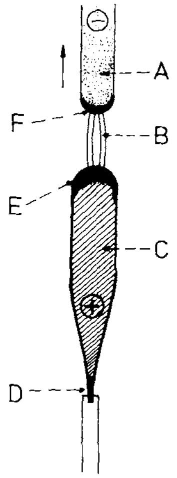


Fig. 3. Schematic representation of the arc transport process [30] for growing single crystals with transportation of the material in an arc. A: Feed electrode; B: arc; C: growing crystal; D: seed crystal; E: anode melt; F: cathode melt.

The fused oxides are transported by the arc from sintered $CeO_2$ or $La_2O_3$ electrodes to the opposite electrode, where they deposit and grow on the single crystal seed (the two electrodes can be tempered by additional heating). *Drabble*[30] investigated the dependence of the direction of transport on the chemical material, and found that both the material transport and its loss are a function of the length of the arc. However, careful maintenance of the constancy of the arc conditions is an extremely complicated experimental operation.

## 3. Universally Applicable Methods for the Production of High Temperatures

The conventional technique of resistance heating, long used in solid-state chemistry, the use of the sun as a natural source of heat, induction heating of electric conductors, and the various plasma torches are of differing practical significance, though all of them are more important than the methods outlined in the preceding section. The high-power $CO_2$ laser has been added in more recent times as an elegant and very promising energy source for solid-state chemistry. These techniques will now be discussed in chronological sequence.

### 3.1. Resistance Heating

Although few furnaces with resistance heating reach temperatures as high as 2000 °C, for many decades simple electric furnaces were the only usable heat sources and preparative chemists were forced to put up with their drawbacks. Many lanthanoid oxides were in fact prepared in such furnaces:

- Simple mixed crystals: $Ln_2O_3 \cdot Ln'_2O_3$ (Ln, Ln' = lanthanoid)
- Perovskites: $LnLn'O_3$
- Pyrochlore-type compounds: $M_2Ln_2O_7$ (M = tetravalent metals Zr, Th, *etc.*)
- Heterotype fluorite phases: $MO_2 + Ln_2O_3$ (M = Ce, Zr, Th, Hf, U, *etc.*)
- Compounds of the calcium ferrite-type: $MLn_2O_4$ (M = Ca, Sr, Ba, Eu, *etc.*)
- Compounds of the formula $Ln_2TiO_5$.

In addition to this there have been studies on binary systems, on the reversibility or irreversibility of the changes between allotropic modifications, and on higher and lower degrees of oxidation or phases and phase widths in lanthanoid-oxygen systems. Reviews of this work will be found in [31-35].

Lanthanoid oxo-compounds, for example the heterotype fluorite phases $MO_2 + Ln_2O_3$ (M = Zr, Th, Hf, Ce; Ln = lanthanoids and yttrium) showing oxygen-ionic conductivity can also themselves be used as resistance heating elements in high-temperature technology. Trivalent lanthanoid ions are incorporated at the lattice points of the tetravalent element in oxides such as $ThO_2$, $ZrO_2$, $HfO_2$, *etc.*, crystallizing in the fluorite lattice. The resulting oxygen-ionic conductors work particularly well in an oxidizing atmosphere. This is an advantage over heating elements that have to be protected against corrosive action of oxygen at high temperatures. Thus, a $ZrO_2$ resistance-heating furnace described by *Faucher, Dembinski* and *Anthony*[36] reached about 2500 °C both in inert and oxygen atmospheres. However, *Gorski* and *Dietzel*[37] showed that at such high temperatures contamination of the preparations by zirconia vapor is unavoidable. When an oxide furnace of this kind is started up the semiconducting material is preheated to 1000—1800 °C until, as a result of the fall in resistance, the size of the current increases constantly with rising temperature. An essential drawback of this fundamentally conventional technique is that because of the negative temperature coefficient of the resistance local hot zones appear in the heating conductors, leading eventually to destruction of the material through an accumulation of this effect[38,39].

Furnaces wound with molybdenum and tungsten resistance wires are not affected by these problems but are endangered by oxidation. This also applies to graphite (Tammann) heating conductors at temperatures above 1900 °C. Since even under a protective atmosphere or under vacuum significant quantities of carbon vapor are produced in the Tammann furnaces at temperatures above 2500 °C[40], it is preferable to reserve the use of these furnaces to reactions in which C and CO do not interfere; good examples of this are the experiments on the reduction of $Sm_2O_3$ with C or CO by *Smagina* and *Kutsev et al.*[41-43].

The main disadvantage of all heat conductor sources, however, is that the energy is invariably introduced into the sample from outside, through a boat or some other container. Since the sample is therefore somewhat colder than the vessel wall, there is always the risk of reaction with the crucible material.

### 3.2. Induction Heating

A high-frequency electric field induces eddy currents in conductors, and these can be utilized for the production of high temperatures. The temperatures achievable in this way are therefore limited only by the material, *i. e.* by the melting point of the inductively heated crucible material. The $LnO_{1.5-x}$ compounds mentioned in Section 2.3.2 were prepared by *Miller* and *Daane*[29] by this method. *Bedford* and *Catalano*[44] used induction furnaces with tungsten crucibles to investigate the systems Eu—$Eu_2O_3$, Sm—$Sm_2O_3$, and Yb—$Yb_2O_3$ between 1500 and 2300 °C. In 1977 *Greedan, Gibb,* and *Turner*[45] prepared $Eu_3TaO_6$ with divalent and trivalent europium using crucibles heated to 2200 °C by induction.

The use of high-frequency energy in induction furnaces is a relatively old technique, supplemented in the mid-sixties by inductively powered plasma torches (see Section 3.4.2).

### 3.3. Solar Furnaces and Artificial Suns

Solar furnaces, which have been used successfully both on the small scale as well as the large scale since 1960[51], represented a great step forward in high-temperature solid-state chemistry. A large-scale solar furnace plant has long been in operation on the technical scale at the Laboratoire des Ultra Réfractaires du Centre National de la Recherche Scientifique in Odeille/Fornt-Romeu.

Strictly speaking a solar furnace is not a furnace but an optical system by means of which sunlight is focussed onto a chemical preparation using parabolic mirrors and lenses (Fig. 4).

The mode of action of solar furnaces, *e.g.* the dependence of the flux density on the diameter of the focal spot, or that of the temperatures attained on the mirror aperture, has been described by *Noguchi*[46]. The precision with which a solar furnace can be operated for 1 h at about 2700 °C reaches the amazing value of ± 10 °C[47]. Solar furnaces can be designed in such a way that they allow heating of the samples under a protective atmosphere or under vacuum (*Laszlo*'s[48] and *Glaser*'s[49] construction, Fig. 5).

Special reference is made to the stripper inside the chamber, which mechanically removes evaporated material that would otherwise impair the transmission through the protective cap. *Noguchi et al.*[50] also describe solar furnaces for work under controlled gas atmospheres.

To eliminate the dependence of solar furnaces on the weather, and to preserve the elegant working technique of energy transfer by radiation, the next step was the development of "artificial suns", which make use of electric arcs, xenon high-pressure lamps, or high-frequency plasma torches as the energy sources in place of the sun. The principle of energy transfer by focussing with elliptical and parabolic mirrors is shown in Figure 6. To give an impression of the tech-

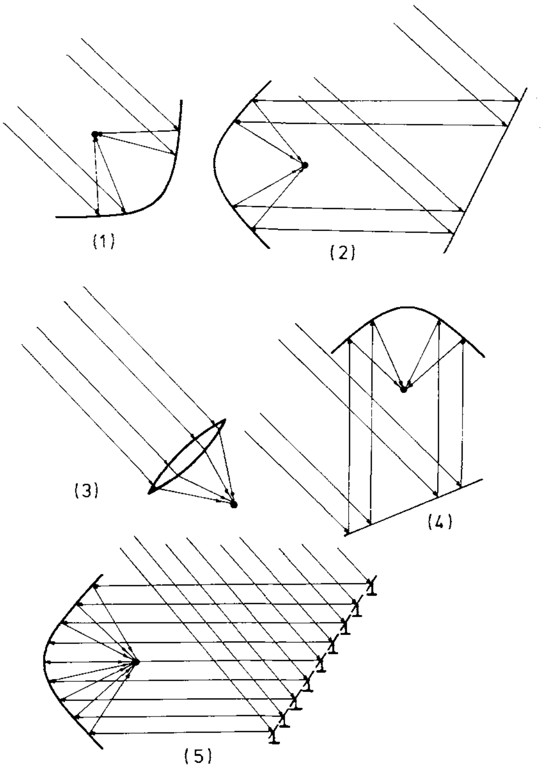


Fig. 4. Types of solar furnaces: (1) direct solar furnace; (2) horizontal heliostat; (3) type with a single lens; (4) vertical heliostat; (5) large-scale horizontal heliostat with illumination of the parabolic mirror by several plane mirrors.

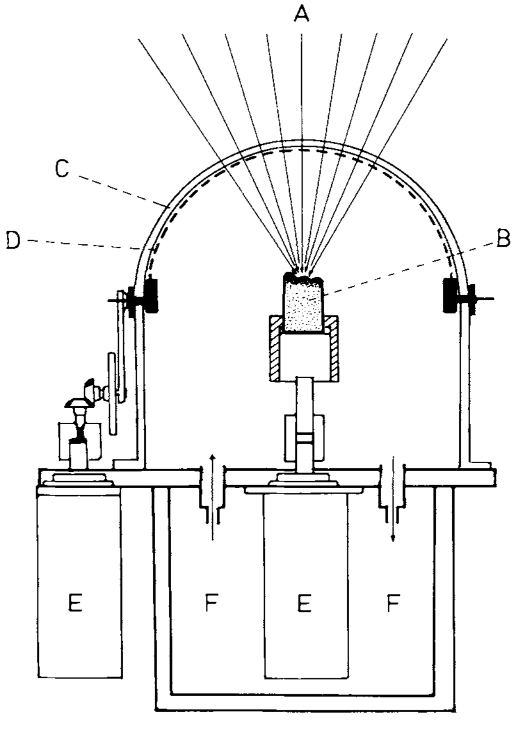


Fig. 5. Solid-state reaction, using a solar furnace and a specific gas atmosphere [48, 49] or vacuum. A: Sunlight; B: sample; C: quartz glass; D: stripper; E: motor; F: protective gas or vacuum.

nical embodiment of a radiation furnace of this kind, Figure 7 shows *Traverse*'s experimental construction[52], in which the preparation is again separated from the combustion space of the electric arc to prevent contamination by evaporating electrode material and to allow the performance of reactions under a special gas atmosphere.

Solar furnaces and artificial light optical systems have been responsible for a whirlwind advance of research into the high-temperature chemistry of the lanthanoid oxides.

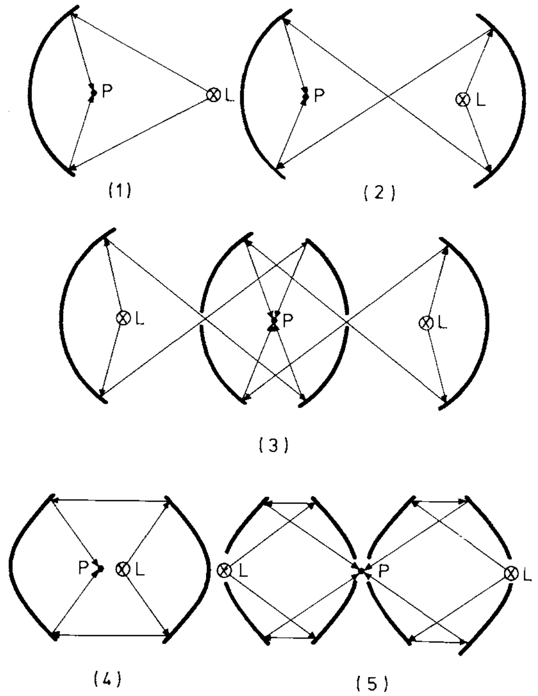


Fig. 6. Fundamental construction of optical heat sources (artificial suns). (1) Simple elliptical furnace; (2) double elliptical furnace; (3) multimirror system for two light sources with elliptical mirrors; (4) double mirror furnace with parabolic mirrors; (5) multimirror system for two light sources with parabolic mirrors (P = preparation; L = light source).

For example, *Foex*[53] and *Noguchi*[54] have determined the melting points of the trivalent oxides with a high degree of precision. *Trombe et al.*[55] used solar furnaces for zone melting, and *Kooy* and *Couruenberg*[56] and also *Collongues et al.*[57,58] for growing single crystals and for the purification of oxides. Using a solar furnace, *Segui* and *Trombe*[59] studied vaporization phenomena in the systems $La_2O_3$—$Nb_2O_3$/$TiO_2$/$Ta_2O_3$.

Numerous studies have been carried out on binary systems, *e.g.* $La_2O_3$—$Ln_2O_3$ (Ln = Sm, Ho, Yb, Y)[60], $ZrO_2$—$La_2O_3$[61], $ZrO_2$—$Nd_2O_3$[62], $ZrO_2$—$Sm_2O_3$/$Gd_2O_3$[63], and $ThO_2$—$La_2O_3$/$Sm_2O_3$[64-66]; the cooling curves[67] of the binary oxides $Ln_2O_3$ have been determined in the temperature range in which the Goldschmidt diagram (cf. Fig. 1) was still uncertain. In now already classical procedures, the phase diagram of the trivalent lanthanoid oxides (Fig. 8) has been conclusively elucidated, two new high-temperature forms (the H- and X-forms) having been found[68,69]. The allotropic conversions between the A-, B-, C-, H-, and X-forms[68,70] and the influence of alkaline earth metal oxides on the phase change between the C- and B-forms[71] have also been studied with solar furnaces. Since a low-valence oxide of europium EuO also exists, but cannot be readily obtained from $Eu_2O_3$, its isolation by *Achard*[96] by reduction of $Eu_2O_3$ under high vacuum with solar energy is noteworthy. In the early seventies, *Lopato* and *Kushewskii*[72] synthesized compounds of the composition $SrLn_2O_4$ (Ln = La—Lu) using solar furnaces at 2090 to 2240 °C.

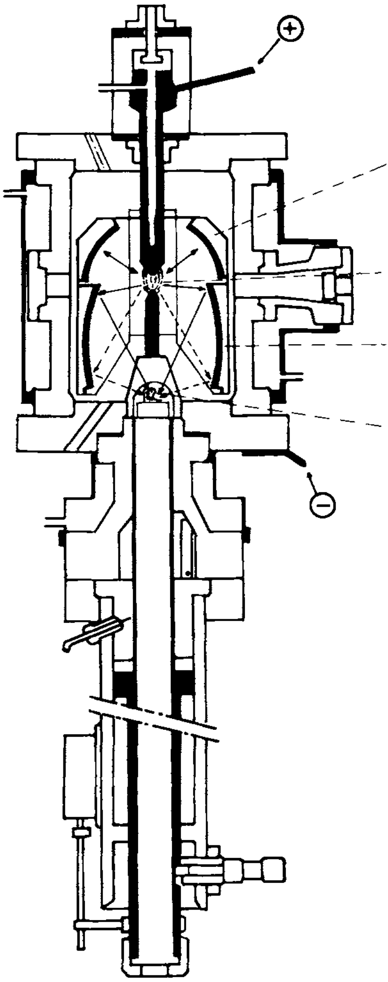


Fig. 7. Section through an electric arc furnace [52] for preparations under a specific gas atmosphere. A: Spherical mirror; B: electric arc; C: elliptical mirror; D: sample under a protective cap.

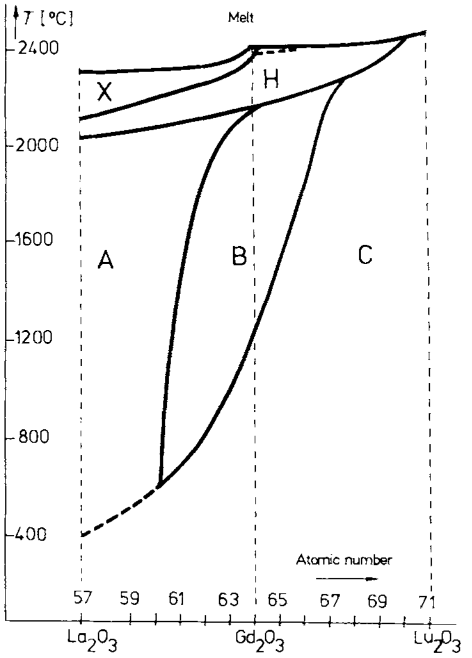


Fig. 8. Phase diagram for trivalent lanthanoid oxides [68, 69] with the new H- and X-high-temperature forms. For the A-, B- and C-types, see Section 1.

The essential problem in high-temperature chemistry is the prevention of wall reactions between the sample and its container. This is achieved by surface reactions on compressed finely divided material—the surface-acting solar furnaces are just as suitable for this as the $CO_2$ laser—or by a technique developed by *Trombe*[73], in which the molten material is processed in a centrifuge made of the same substance (Fig. 9). The advantage of this method, quite apart from the avoidance of wall reactions, is the utilization of the principle of a black body radiator for more accurate temperature measurement of the reaction mixture ("black body centrifuge"). For the problem of temperature measurement, see Section 3.5.

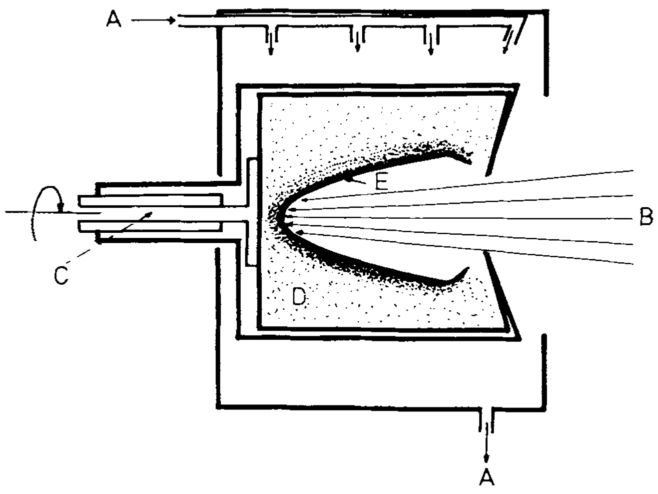


Fig. 9. Principle of the high-temperature centrifuge technique [73] for the prevention of wall reactions ("self-crucible method") in the heating of solids with radiant energy. A: Cooling; B: sunlight; C: centrifuge axis; D: solid phase; E: liquid phase.

### 3.4. Plasma Torches

The modern plasma torches can be classified according to the manner of the plasma production:

1. Electric arc plasma torch
2. High-frequency plasma torch
   a) capacitative plasma torch
   b) inductive plasma torch
      α) open (normal-pressure) plasma torch
      β) closed (low-pressure) plasma torch

#### 3.4.1. The Electric Arc Plasma Torch

In the electric arc plasma torch the jet is produced by an electric arc (for a definition of plasma see [77]). The principle of *Wendler*'s[78] plasma torch for handling metal powders is presented in Figure 10. A high-density arc, traversed by a fuel gas (*e.g.* argon or nitrogen) which in this process is converted into the plasma state, is struck between a tungsten cathode and a copper anode. The fast gas flow prevents the arc from touching the cooled anode, *i.e.* the total electrical energy is essentially transferred into the plasma jet. The physical basis of all electric plasma-arc torches is thus the Gerdien arc[79], since the water-cooled anode causes a constriction of the plasma jet (thermal pinch effect), the current intensity and the temperature rising so dramatically that the high field intensities also produce a magnetic pinch effect.

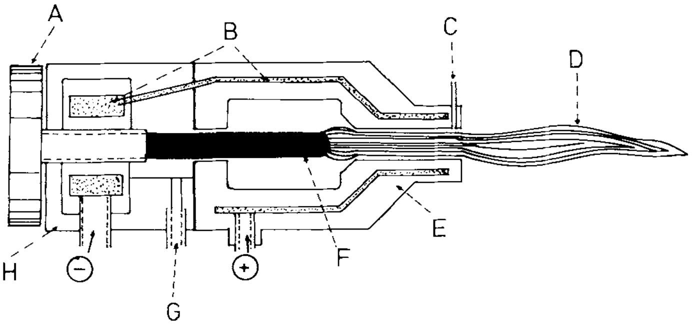


Fig. 10. Principle of an electric-arc plasma torch [78] for processing powdered materials. A: Adjustable electrode support; B: cooling; C: powder feed; D: plasma; E: anode; F: cathode; G: fuel gas supply; H: insulator.

The plasma jet can reach temperatures of 8000—50000 °C. Many descriptions of plasma torches and working techniques have been published[78,80-85], referring almost exclusively to material processing and treatment and to the synthesis of molecular compounds. Applications in the field of solid-state chemistry are hindered by the problems already mentioned in connection with hot flames (Section 2.2) and the extremely short residence time of the powdered samples within the plasma jet.

### 3.4.2. High-Frequency Plasma Torches

Of the two possibilities available for the transfer of high-frequency energy into plasma the method of inductive coupling is mainly preferred (for the use of capacitatively driven low-pressure plasma torches reference is made to *Veprek*'s work[86 91]). In inductive high-frequency plasma torches it is expedient to distinguish between the open and the closed variants.

*Open-high-frequency plasma torches:* open, inductively-coupled high-frequency plasma torches have been described by *Scholz*[92], *Reed*[93,94], and *Fricke*[95] (Fig. 11). Figure 11 shows two parallel quartz tubes surrounded by the induction coil of a conventional HF generator. At a working frequency of about 1—5 MHz a plasma torch, burning in the open air similarly to the electric plasma-arc torches against atmospheric pressure, is ignited by an electrode situated within the coil. However, the large thermal expansion of the fuel gas (ignition gas = argon, fuel gas = $N_2$, $O_2$, $H_2$, noble gases) causes an uncontrolled exhaustion of the plasma torch. To prevent this, *Reed*[93] designed a torch with a tangential feed of the fuel gas, producing a slight underpressure at the core of the jet. Because of this, charge carriers constantly flow back into the field of the induction coil. In this way it is even possible to carry finely divided material by the gas stream concentrically into the plasma jet, where it can react with the fuel gas[96] or can be fused and used for growing single crystals by the Verneuil process (cf. Fig. 11). *Reed*[97] grew centimeter-size single crystals of sapphires, $ZrO_2$ and metallic niobium in this way, since, given a suitable experimental setup, a fuel gas such as argon protects even extremely reactive substances such as niobium from the attack of $O_2$, $N_2$, $H_2O$, *etc.*

*Theta* and *Lejus*[98] obtained single crystals of $Nd_2O_3$ 2—3 cm in size by the Verneuil plasma torch process, which does not suffer from the disadvantages of an uncontrolled gaseous atmosphere of burning flames. The same authors also succeeded in making single crystals from oxide mixtures: CaO and $La_2O_3$ and also $Nd_2O_3$ and $La_2O_3$.

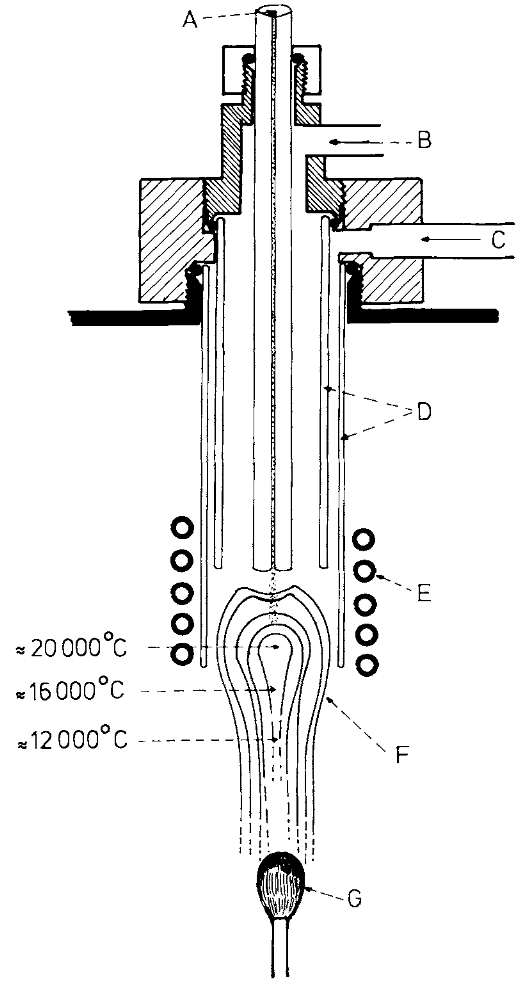


Fig. 11. Principle of an open (high-pressure) plasma torch [93, 94] with inductive coupling of the HF energy. A: Substance + carrier gas; B: plasma gas; C: cooling gas; D: quartz tube; E: induction coil; F: plasma torch; G: crystal.

Microwave plasma torches, whose operation has been described by *Scholz*[92], and which, depending on the frequency, lead to open point discharges, represent variants of the inductive high-frequency plasma torch shown in Figure 11. Figure 12 shows two designs, constructed as coaxial cavity resonators because of the high frequencies involved. The resonant cavity in Figure 12a is at the same time an anode oscillating circuit; by means of the capacitance $C_1$ a wavelength shortening is achieved, while $C_2$ allows adjustment to the transmitting tubes. Figure 12b shows a high frequency (2400 MHz) dipole coupling. The energy is taken by the electrode E from the cavity resonator, which serves as a transformer circuit, and conducted to the nozzle D. In both designs the plasma torch is stabilized by fuel gas escaping in the shape of a tubular envelope. For practical applications of microwave plasma torches reference may be made to a paper by *Seifert* and *Kappelt*[99], which deals with the growth of ferrite single crystals in a modification of the Verneuil process.

As against the above advantages of the open plasma torch, disadvantages arise in preparative solid-state chemistry, so that the applications in this field are restricted. Thus, the expansively burning flame—like chemical flames—makes it difficult to treat small quantities of the sample; powdered preparations can only be introduced into the jet in a stream, so that their residence time in the hot part of the plasma discharge is both short and uncontrolled. As a result of the steep temperature gradients of about 5000 °C inside the jet, it is almost impossible to carry out a homogeneous reaction combined with the establishment of a chemical equilibrium. For all these reasons the closed low-pressure plasma torch, developed in parallel with the open normal-pressure plasma torch, has proved more suitable for solid-state reactions.

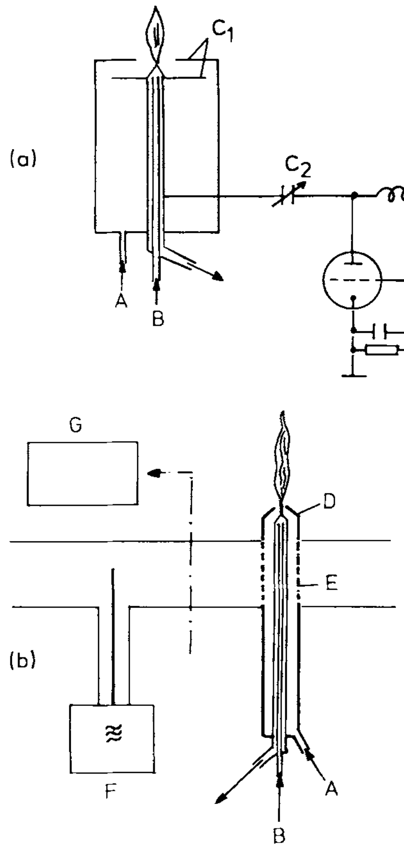


Fig. 12. Mode of operation of high frequency open plasma torches [92] (a) for several hundred MHz, (b) for 2400 MHz. A: Fuel gas; B: cooling; $C_1$, $C_2$: capacitators; D: nozzle; E: electrode; F: HF generator; G: cross section.

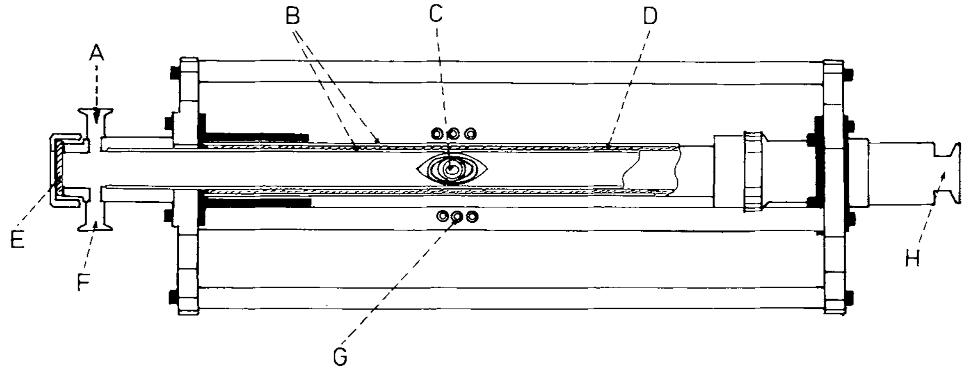


Fig. 13. Principle of a closed (low-pressure) plasma torch [100, 101] with inductive coupling of the HF energy. The torch can be displaced in a horizontal direction. The induction coil is fixed. A: Gas inlet (plasma gas); B: quartz tube; C: plasma; D: water cooling; E: window; F: pressure control; G: introduction coil; H: vacuum.

*Closed high-frequency plasma torches:* In contrast to the open, normal-pressure plasma torch, in the low-pressure variant there is a combustion chamber that can be evacuated (Fig. 13); the quartz tubes are cooled with water (tangential water cooling with a high pressure gradient).

If the inner tube is evacuated to 0.1—1 mbar, on inductive coupling of a high-frequency field (1—5 MHz) a steadily burning plasma jet is ignited at that point[100,101]. Samples pressed into pellets are situated in the cooled inner tube on a layer of MgO; rod-shaped pellets can be introduced coaxially into the plasma jet by moving the latter with a fixed induction coil. The sample temperature can be regulated sufficiently accurately *via* the HF power and the residual gas pressure. The energy is transferred from the plasma to the sample by collisions and radiation, by ionization and dissociation of primary species, by recombination of atoms to molecules, and in the case of a good intrinsic semiconductor by direct coupling of the heated sample to the high-frequency field. The advantages of the low-pressure plasma torch are the steadily burning and very hot plasma jet, the risk-free operation with hydrogen above temperatures of 3000 °C, and the introduction of energy as it were from within the tube onto the sample, so that, in contrast to conventional furnaces, the sample and not the furnace wall constitutes the hottest point in the entire system. The disadvantages of the closed plasma torch are the relatively low working pressure, which favors thermal decomposition of the reaction product, and the limitation of the available high-frequency power. Certain constructional prerequisites for water cooling of the quartz tube are already required at 12 kVA to prevent considerable delay in boiling. The fact that the low-pressure plasma torch works in a state of thermal disequilibrium, *i. e.* the electron and gas temperatures of the plasma torch can differ by $10^4$ °C, must be regarded as a drawback, but so far no perturbing influences have been observed in applications to solid-state reactions.

Originally only X-ray-perfect single crystals of lanthanoid oxides and their compounds were prepared with the closed plasma torch. Mention may be made at this point of the growing of $La_2O_3$ and $Nd_2O_3$ single crystals[102,103], whose structure proved to be more complicated than could be perceived in earlier works[14,16,104]. Stimulated by this result, which *Foex* and *Traverse* interpreted by the presence of a frozen metastable high-temperature modification, *Greis*[105] reinvestigated $La_2O_3$, heated to a relatively low temperature, by electron diffraction, while *Aldebert* and *Traverse*[106] studied the transitions between the A-, H-, and X-forms at high temperatures by neutron diffraction. Owing to the relatively low working pressure in the low-pressure plasma torch (0.1—10 mbar), $Tb_4O_7$ decomposes into $Tb_2O_3$[107] at high temperatures and dark-green to black single crystals are even obtained from the thermally stable $La_2O_3$[108], its color being due to a slight oxygen deficiency ($LaO_{1.5-x}$). Tempering of the black $La_2O_3$ single crystals in air regenerates the colorless form of $La_2O_3$.

The phase transformation between the monoclinic B-form and the hexagonal A-form in the $Sm_2O_3$—$La_2O_3$ system[109] has been studied by X-ray methods on single crystals from plasma torch reactions. Under appropriate experimental conditions, single crystals of $SrTb_2O_4$[110], $SrY_2O_4$[111], $LaYbO_3$[112], $LaErO_3$, $LaLuO_3$[113], $LaZr_2O_7$[114], and $Nd_2TiO_5$[115] have been obtained from oxide mixtures in low-pressure plasma torches to name but a few examples.

### 3.5. The $CO_2$ Laser

After it had become possible to raise the power of *Patel*'s[116] $CO_2$ laser by the admixture of nitrogen and helium[117–119] from the milliwatt range to 60—80 Watt per meter of discharge length, there was nothing left to hinder the development of high-power lasers into the kilowatt range. (For details of the energy transfer from the state of oscillation of the $N_2$ molecule to the laser level of the $CO_2$ molecule, the laser transfer into the $CO_2$ molecule, and the efficiency and power, see [120].) For preparative solid-state chemistry it is an important fact that the 10.6 μm radiation emitted by $CO_2$ lasers is absorbed and converted into heat by almost all substances. Thus, this working technique resembles those involving visible light, as already described in Section 3.3. For preparative purposes the laser radiation is generally focussed (KCl, $BaF_2$, or Ge lenses), the size of the focal spot influencing the power density; however, this can also be varied by continuous or pulsed energy output. Thus, according to our own experience[121], the size of the focal spot is limited only by the maximum laser power and the experimental conditions. Various working techniques for medium-power ($\approx 150$ W) and high-power ($\geq 450$ W) lasers have already been reported[121], so that here only the principle of a solid-state reaction with the $CO_2$ laser technique will be outlined. Figure 14 shows the way the focussed laser beam may be directed onto a sample, heating it to a high temperature in any desired atmosphere. The lenses and protective windows are made of KCl; a suitable gas flushing system should be used to ensure[121] that the windows do not become coated with vaporizing material, since even the thinnest film leads to absorption and hence destruction of the window. The sample can also be subjected to additional heating, by means of which the temperature gradient within it can be reduced from $\Delta_T \approx 2000\,°C$ to $\Delta_T \approx 500\,°C$.

The particular value of the laser technique lies in its possible applicability at high temperatures and pressures, *i. e.* conditions that frequently suppress the thermal decomposition of the reacting substances. High-temperature synthesis of lanthanoid oxometallates requires a high pressure of oxygen, which under these conditions is extremely reactive; so far only the laser autoclave technique[122] can prevent reaction of $O_2$ with the pressure vessel, in spite of the high sample temperatures. Figure 15 shows an autoclave with a window transparent to the laser radiation; the sample can be observed through a quartz side-port, using a television camera (for further details see [122]).

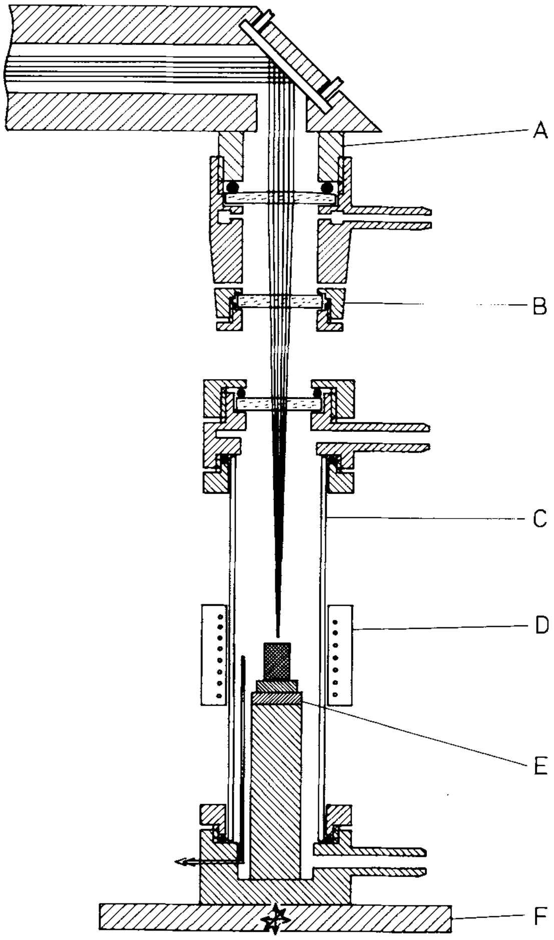


Fig. 14. Schematic representation of the performance of a high-temperature reaction with $CO_2$ laser energy under a specific atmosphere [121]. A: Collimator and focussing unit; B: protective window; C: sample space with the protective gas atmosphere; D: resistance heating; E: sample carrier; F: rotary, cross-slide and lifting stage.

The advantages and disadvantages of the laser technique have a decisive bearing on the course of a solid-state reaction. The advantageous features are, for example, high working temperatures kept constant over prolonged experimental periods, any desired gas atmosphere, and the very efficient transfer of energy to the sample. According to *Reed*[123-125], hot flames and laminar argon plasmas transfer 0.2 kW/cm$^2$ and a d-c arc transfers 16 kW/cm$^2$. The corresponding value for electron beams and lasers is $10^3$ kW/cm$^2$. A problem is that the energy absorbed in a thin surface layer is transported only poorly to the center of the sample, resulting in the build-up of an extremely steep temperature gradient. This gives rise to chemical disequilibria and in particular to the formation of metastable substances. This same disadvantage is of course the strength of the process when the aim is to prepare metastable high-temperature compounds. The metastable compounds $SrCa_2Sc_6O_{12}$[126], $SrCa_2Yb_{10}O_{18}$, and $SrCa_2Lu_{10}O_{18}$[127] have been synthesized by heating with plasma torches and quenching. *Foex*[70,71] as well as *Foex* and *Traverse*[67,69] describe impurity-stabilized modifications of lanthanoid oxides. Thus CaO, SrO *etc.* can, within wide limits (a few mol-% to molar concentrations) convert the cubic-C into the monoclinic B-form. The high-temperature reactions carried out with plasma torches and $CO_2$ lasers show that indeed small amounts of CaO "dissolve" in the lanthanoid oxides with stabilization of the monoclinic B-form; if the fraction of CaO *e.g.* in $Ho_2O_3$ exceeds 7%, a new, metastable compound $Ca_2Ho_2O_5$ is formed[128] with independent coordination polyhedra. Coincidentally, the positions of the metal atoms are identical with those in the monoclinic B-form; hence, the reason for the assumption in the cited papers of the presence of the monoclinic crystal form of the lanthanoid oxides on the basis of the X-ray powder diffraction patterns.

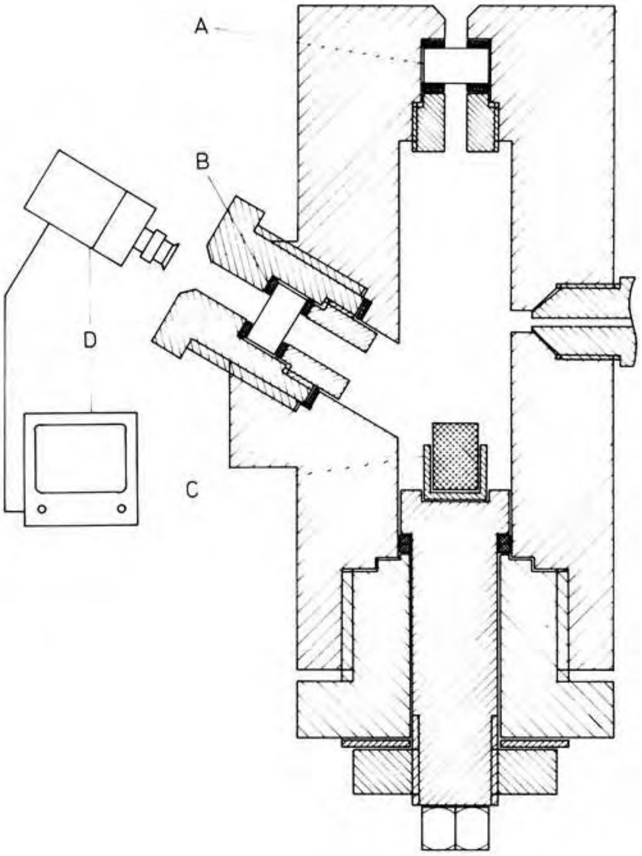


Fig. 15. Principle of a high-pressure autoclave for reactions with oxygen at high temperatures and pressures [122]. A: pressure-tight window permeable to the laser radiation; B: observation port; C: preparation support with solid preparation; D: TV camera with monitor.

A further interesting fact is that at high temperatures the calcium ferrite type ($MLn_2O_4$; M = Ca, Sr, Ba), normally stable in lanthanoid oxo-compounds, becomes unstable in the range of the light lanthanoids. The laser technique can be used to synthesize the metastable substances $Sr_3Nd_4O_9$[129] and $Sr_3La_4O_9$[130], in which $Sr^{2+}$ and $Nd^{3+}$ are distributed almost statistically, and $Sr^{2+}$ and $La^{3+}$ completely statistically, over the metal positions. Here a characteristic crystallochemical aspect of metastable lanthanoid compounds is recognizable.

The $CO_2$ laser technique allows risk-free operation with hydrogen atmospheres at temperatures in excess of 3000 °C, oxo-compounds of low oxidation state such as $La_2CoO_4$ and $Sm_2CoO_4$[131] being accessible with $Co^{2+}$ and $SrV_{10}O_{15}$ and $BaV_{10}O_{15}$[132,133] with a fraction of $V^{2+}$. By using high $O_2$ partial pressures above the reaction product single crystals of thermally unstable compounds can be synthesized at high temperatures[134], or higher oxidation states, such as $Ni^{3+}$ in $SrLaNiO_4$[135], can be stabilized.

Finally, let us consider briefly the problem of temperature measurement. With the exception of the laser and electron beam techniques, all other sources of heat emitting in the visible range (flames, furnaces, plasma torches, electric arcs, solar furnaces, *etc.*) give rise to considerable problems with accurate measurement of the surface temperature. The elegant pyrometric method requires a black-body radiator, *i.e.* the ratio of radiation emitted to that absorbed is equal to the intensity of the black-body radiator. This does not apply to the majority of substances having an absorption coefficient of less than one, so that elaborate calibration becomes necessary (cf. [52]). The $CO_2$ laser, however, emits in the infrared; as partially reflected radiation this is not recorded in the visible range in the pyrometric measurement, and the surface temperature of the sample can be obtained from its intrinsic emission.

## 4. Outlook

New methods for the generation and experimental application of high temperatures in the chemical laboratory have opened up new synthetic routes and facilitated the preparation of single crystals so important for structure determinations. Many compounds that cannot be synthesized at "lower" temperatures have now become accessible, the metastable substances being of special interest. Thus the metastable substances investigated so far are distinguished by daltonide compositions; however, considerable deviations are found in the micro region. Partial and total statistical occupation of point positions with metal ions of very different charge and electronic states are observed. In addition, under-population of certain regions of the metal lattice and stabilization effects of selected crystal structures by the incorporation of impurities are observed. These peculiarities of metastable oxometalates, observable in carefully performed structural investigations, lead to speculations about their possible physical properties. Thus, a mixture of metal ions with and without spin-orbit coupling having definite equivalent positions, *i.e.* in definite microsymmetry, could be interesting for magnetic studies. With metastable oxo-compounds a particularly small electronic work function can be expected within their range of stability and might provide stimulation to new investigations in the area of fluorescence phenomena of solids, extending beyond the investigation of doped pure substances. By skilful utilization of the thermal lability of various substances at sufficiently high temperatures it should be possible to obtain new nonstoichiometric compounds or phases. In particular, the possibility of working with atomic gases in plasma jets and the use of hydrogen at extremely hot sample surfaces (on bombardment with $CO_2$-laser jets) offer new ways to obtain low-valence compounds. Reaction of oxometalates with metals of low oxidation states beyond the first main- and sub-groups of the Periodic system can produce "anion-deficient" compounds which are distinguished by the extremely low coordination numbers of the metal ions. Compounds of this type constitute the scientifically fascinating transition to the metal-rich sub- and cluster compounds.

Finally, also of great interest to the high-temperature chemist is how methods which are already realizable shall one day find application in preparative chemistry. It is conceivable that nuclear energy and energy-rich particles could be employed, not as previously for radiative decomposition, but in combination with known methods for high-temperature radiative syntheses. For this reason many chemists are now eagerly awaiting future developments in the field of high-temperature chemistry, particularly with regard to the possible synthesis of new solid state compounds.

Received: September 1, 1980 [A 345 IE]
German version: Angew. Chem. 93, 1 (1981)
Translated by AD-EX Translations Ltd. (London)

---

[1] *M. W. Shafer, R. Roy,* J. Am. Ceram. Soc. *42,* 152 (1959).

[2] *R. S. Roth, S. J. Schneider,* J. Res. Nat. Bur. Stand. Sect. *A 64,* 309 (1960).

[3] *J. Warshaw, R. Roy,* J. Phys. Chem. *65,* 2048 (1961).

[4] *V. M. Goldschmidt, F. Ulrich, T. Barth,* Skrifter Norske Videnskaps-Akad. Oslo I. Mat.-Naturv. Kl. No. 2 (1926).

[5] For the definition of the term "high-temperature chemistry", see a) *E. Ryshkewitsch* in Ullmanns Encyklopädie der technischen Chemie. 3 rd Edit Vol. 2/1. Urban and Schwarzenberg, München 1961, p. 985; b) *R. J. Thorn,* Annu. Rev. Phys. Chem. *17,* 83 (1966); c) *P. Goldfinger,* Adv. High Temp. Chem. *1,* 1 (1967).

[6] *M. Klein, P. Rudman,* Phil. Mag. *14,* 1199 (1966).

[7] *P. de Carli, J. Jamieson,* J. Chem. Phys. *31,* 1675 (1959).

[8] *Y. Kimura,* J. Appl. Phys. (Tokyo) *2,* 312 (1963).

[9] *G. A. Adurov, G. V. Novikov, N. S. Ovanesyan, V. A. Truhtanov, V. M. Shetman,* Fiz. Tverd. Tela *11,* 1988 (1969).

[10] *S. S. Batsanov, E. S. Zolotova,* Dokl. Akad. Nauk SSSR *180,* 93 (1968).

[11] *S. S. Batsanov, N. A. Shestakova, V. P. Stupnikov, G. S. Litvak, V. M. Nigmatullina,* Dokl. Akad. Nauk SSSR *185,* 330 (1969).

[12] *S. S. Batsanov, V. F. Lyachowa, E. M. Moroz,* Zh. Neorg. Khim. *16,* 231 (1971).

[13] *S. S. Batsanov, A. A. Deribas, G. N. Kustova,* Zh. Neorg. Khim. *12,* 2283 (1967).

[14] *W. H. Zachariasen,* Z. Phys. Chem. *123,* 134 (1926).

[15] *L. Pauling,* Z. Kristallogr. Mineral. Petrogr. *A 69,* 415 (1928).

[16] *W. H. Zachariasen,* Z. Kristallogr. Mineral. Petrogr. *A 70,* 187 (1929).

[17] *R. M. Douglas, E. Staritzky,* Justus Liebigs Ann. Chem. *552,* 28 (1956).

[18] *D. T. Cromer,* J. Phys. Chem. *61,* 753 (1957).

[19] *A. V. Grosse, J. B. Conway,* Ind. Eng. Chem. *50,* 663 (1958).

[20] *M. von Pirani,* DRP 188466 (1905).

[21] *E. Tiede,* Ber. Dtsch. Chem. Ges. *46,* 2229 (1913).

[22] *E. Tiede, E. Birnbräuer,* Z. Anorg. Allg. Chem. *87,* 129 (1914).

[23] *H. M. O'Bryan,* Rev. Sci. Instrum. *5,* 125 (1914).

[24] *H. Gruber,* Z. Metallk. *52,* 291 (1961).

[25] *H. Stephan,* Umsch. Wiss. Tech. *60,* 211 (1960).

[26] *C. Boulesteix, P. Caro, M. Gasgner, Ch. H. la Blanchetais, G. Schiffmacher,* Proc. Colloq. Int. C. N. R. S. *205,* 361 (1971).

[27] *C. E. Weir, A. V. Valkenburg,* J. Res. Natl. Bur. Stand. *A 64,* 103 (1960).

[28] *L. A. Harris, H. L. Yakel,* Acta Crystallogr. *9,* 1025 (1956).

[29] *A. E. Miller, A. H. Daane,* J. Inorg. Nucl. Chem. *27,* 1955 (1965).

[30] *J. Drabble,* J. Cryst. Growth *3,* 804 (1968).

[31] *G. Brauer,* Prog. Sci. Technol. Rare Earths *1,* 152 (1964).

[32] *G. Brauer,* Prog. Sci. Technol. Rare Earths *2,* 312 (1966).

[33] *C. Keller,* MTP Int. Rev. Sci. Ser. 1, *7,* 47 (1972).

[33a] *A. K. Gschneidner, L. Eyring:* Handbook on the Physics and Chemistry of Rare Earths. Vol. 3. North-Holland, Amsterdam 1979.

[34] *L. Eyring* in [33a], S. 337.

[35] *D. J. M. Bevan, E. Summerville* in [33a], S. 401.

[36] *M. Faucher, K. Dembinski, A.-M. Anthony,* Rev. Int. Hautes Temp. Refract. *6,* 17 (1969).

[37] *W. Gorski, A. Dietzel,* Rev. Int. Hautes Temp. Refract. *6,* 105 (1969).

[38] *W. H. Davenport, S. S. Kistler, W. M. Wheildon, O. J. Whittemore, Jr.,* J. Am. Ceram. Soc. *33,* 333 (1950).

[39] *R. F. Geller,* J. Am. Ceram. Soc. *33,* 339 (1950).

[40] *E. A. Ballik, D. A. Ramsay,* Astrophys. J. *137,* 61 (1963).

[41] *E. I. Smagina, V. S. Kutsev, B. F. Ormont,* Zavod. Lab. *10,* 1249 (1956).

[42] *E. I. Smagina, V. S. Kutsev,* Zavod. Lab. *14,* 511 (1962).

[43] *V. S. Kutsev, E. I. Smagina, R. N. Morzheedova,* Russ. J. Inorg. Chem. *8,* 543 (1963).

[44] *R. G. Bedford, E. Catalano,* J. Solid State Chem. *3,* 112 (1971).

[45] *J. E. Greedan, H. F. Gibbs, C. W. Turner,* Inorg. Chem. *16,* 332 (1977).

[46] *T. Noguchi,* Adv. High Temp. Chem. *2,* 236 (1969).

[47] *T. Noguchi, M. Mizuno, T. Kozuka, M. Yoshida, T. Yamamoto,* Nagoya Kogyo Gijutsu Shikensho Hokoku *14,* 28 (1965).

[47a] U. N. Conf. New Sources of Energy, Rom 1961. III-F. United Nations, New York 1964. E/3577/rev. 1. Doc, ST/ECA/72.

[48] *T. S. Laszlo* in [47a], p. 5.

[49] *P. E. Glaser* in [47a], p. 16.

[50] *T. Noguchi, M. Mizuno, N. Nakayama, H. Hayashi* in [47a], p. 57.

[51] *T. S. Laszlo:* Imaging Furnace Techniques. Wiley, New York 1965.

[52] *J. P. Traverse:* Thèse, Université de Grenoble 1971.

[53] *M. Foex,* Rev. Int. Hautes Temp. Refract. *3,* 309 (1966).

[54] *T. Noguchi, M. Mizuno,* Sol. Energy *11,* 90 (1967).

[55] *F. Trombe, M. Foex, Ch. L. Blanchetais* in [47a], p. 35.

[56] *G. Kooy, H. J. Courvenberg,* Philips Tech. Rundsch. *23,* 161 (1962).

[57] *A. Revcolevski, R. Collongues,* C. R. Acad. Sci. *266,* 1767 (1968).

[58] *M. Saurat, A. Revcolevski, R. Collongues,* C. R. Acad. Sci. *271,* 58 (1970).

[59] *M. Segui, F. Trombe,* C. R. Acad. Sci. *267,* 1039 (1968).

[60] *J. A. Coutures, A. Rouanet, R. Verges, M. Foex,* J. Solid State Chem. *17,* 171 (1976).

[61] *A. Rouanet,* C. R. Acad. Sci. *267,* 395 (1968).

[62] *A. Rouanet,* Rev. Int. Hautes Temp. Refract. *8,* 161 (1971).

[63] *A. Rouanet, M. Foex,* C. R. Acad. Sci. *267,* 873 (1968).

[64] *C. Keller, U. Berndt, H. Engerer, L. Leitner,* J. Solid State Chem. *4,* 453 (1972).

[65] *A. M. Diness, R. Roy,* J. Mater. Sci. *4,* 613 (1969).

[66] *S. Sibieude, M. Foex,* J. Nucl. Mater. *56,* 229 (1975).

[67] *M. Foex, J. P. Traverse,* Rev. Int. Hautes Temp. Refract. *3,* 429 (1966).

[68] *M. Foex, J. P. Traverse,* C. R. Acad. Sci. *262,* 636 (1966).

[69] *M. Foex, J. P. Traverse,* Bull. Soc. Fr. Mineral. Cristallogr. *89,* 184 (1966).

[70] *M. Foex,* Z. Anorg. Allg. Chem. *337,* 313 (1965).

[71] *M. Foex,* Bull. Soc. Fr. Mineral. Cristallogr. *88,* 521 (1965).

[72] *L. M. Lopato, A. E. Kushewskii,* Ukr. Khim. Zh. *39,* 7 (1973).

[73] *F. Trombe,* Rev. Hautes Temp. Refract. *1,* 5 (1964).

[74] *B. Selton, J. A. Sheward,* J. Mater. Sci. *4,* 302 (1969).

[75] *A. V. Grosse, P. J. McGonigal, W. J. Murphy, C. S. Stokes,* Mater. Res. Stand. *5,* 173 (1965).

[76] *J. Achard* in [47a], p. 108.

[77] *H. Maecker,* Chem.-Ing.-Tech. *42,* 629 (1968).

[78] *F. Wendler,* Elektrotech. Z. *15,* 6 (1963).

[79] *H. Gerdien, A. Lotz,* Z. Tech. Phys. *4,* 157 (1923).

[80] *G. Hessler,* Z. Maschinenmarkt Nr. 93 (1960).

[81] *H. Meyer,* Umschau *23,* 713 (1961).

[82] *M. Thorpe,* Res. Dev. Mag. *12,* 79 (1961).

[83] *F. Wendler, G. Nette,* Elektrotech. Z. *A 85,* 737 (1964).

[84] *F. Wendler,* Jahrb. Oberflächentech. *20,* 233 (1964).

[85] *U. Landt,* Chem.-Ing.-Tech. *42,* 617 (1970).

[86] *S. Vepřek, C. Brendel, H. Schäfer,* Z. Naturforsch. *A 24,* 2025 (1969).

[87] *S. Vepřek,* Proc. Xth Int. Conf. Phenomenes in Ionized Gases, Oxford 1971.

[88] *S. Vepřek, C. Brendel, H. Schäfer,* J. Cryst. Growth *9,* 266 (1971).

[89] *S. Vepřek,* Habilitationsschrift, Universität Zürich 1977.

[90] *C. Braganza, H. Stüssi, S. Vepřek,* J. Nucl. Mater. *87,* 331 (1979).

[91] *C. Braganza, S. Vepřek, E. Wirz, H. Stüssi, M. Textor,* Proc. 4th Int. Sympos. Plasma Chemistry, Zürich 1979.

[92] *O. Scholz,* Elektrotechnik *42,* 288 (1960).

[93] *T. B. Reed,* J. Appl. Phys. *32,* 821 (1961).

[94] *T. B. Reed,* Adv. High Temp. Chem. *1,* 259 (1967).

[95] *H. W. Fricke,* Glas Instrum.-Tech. *9,* 49 (1965).

[96] *K. Hartl,* Chem.-Ing.-Tech. *39,* 1253 (1967).

[97] *T. B. Reed,* J. Appl. Phys. *32,* 2534 (1961).

[98] *R. Theta, A. M. Lejus,* Rev. Chim. Miner. *11,* 27 (1974).

[99] *G. Seifert, R. Kappelt,* Exp. Tech. Phys. *13,* 124 (1965).

[100] *Hk. Müller-Buschbaum,* Habilitationsschrift, Universität Gießen 1966.

[101] *Hk. Müller-Buschbaum,* Z. Anorg. Allg. Chem. *355,* 30 (1967).

[102] *Hk. Müller-Buschbaum, H. G. von Schnering,* Z. Anorg. Allg. Chem. *340,* 232 (1965).

[103] *Hk. Müller-Buschbaum,* Z. Anorg. Allg. Chem. *343,* 6 (1966).

[104] *L. Pauling,* Z. Kristallogr. Mineral. Petrogr. *A 69,* 415 (1928).

[105] *O. Greis,* Interner Bericht: The Flinders University of South Australia 1978.

[106] *P. Aldebert, J. P. Traverse,* Mat. Res. Bull. *14,* 303 (1979).

[107] *E. Hubbert-Paletta, Hk. Müller-Buschbaum,* Z. Anorg. Allg. Chem. *363,* 145 (1968).

[108] *Hk. Müller-Buschbaum,* J. Inorg. Nucl. Chem. *30,* 895 (1968).

[109] *Hk. Müller-Buschbaum,* Z. Anorg. Allg. Chem. *355,* 41 (1967).

[110] *E. Paletta, Hk. Müller-Buschbaum,* J. Inorg. Nucl. Chem. *30,* 1425 (1968).

[111] *Hk. Müller-Buschbaum,* Z. Anorg. Allg. Chem. *358,* 138 (1968).

[112] *Hk. Müller-Buschbaum, Ch. Teske*, Z. Anorg. Allg. Chem. *369*, 255 (1969).
[113] *Hk. Müller-Buschbaum, P.-H. Graebner*, Z. Anorg. Allg. Chem. *386*, 158 (1971).
[114] *H.-J. Deiseroth, Hk. Müller-Buschbaum*, Z. Anorg. Allg. Chem. *375*, 152 (1970).
[115] *Hk. Müller-Buschbaum, K. Scheunemann*, J. Inorg. Nucl. Chem. *35*, 1091 (1973).
[116] *C. K. N. Patel*, Phys. Rev. *136*, 1187 (1964).
[117] *C. K. N. Patel, P. K. Tien, J. H. McFee*, Appl. Phys. Lett. *7*, 290 (1965).
[118] *T. G. Roberts, G. J. Hutcheson, J. J. Ehrlich, W. L. Hales, T. A. Barr*, J. Quant. Electronics *QE-3*, 605 (1967).
[119] *K. Gürs*, Z. Angew. Phys. *25*, 379 (1968).
[120] *H. Pausch*, Dissertation, Universität Kiel 1976.
[121] *Hk. Müller-Buschbaum, H. Pausch*, Z. Naturforsch. *B 34*, 371 (1979).
[122] *Hk. Müller-Buschbaum, H. Pausch*, Z. Naturforsch. *B 34*, 375 (1979).
[123] *T. B. Reed:* Directed Heating with Atoms, Electrons and Photons. ASM Tech. Dep. New York 9.1.61 (1962).
[124] *T. B. Reed*, Proc. Natl. Electron Conf. XIX, Chicago 1963, p. 654.
[125] *T. B. Reed*, Sci. Ind. (Eindhoven) *12*, 1 (1965).
[126] *Hk. Müller-Buschbaum, W. Muschick*, Z. Anorg. Allg. Chem. *412*, 209 (1975).
[127] *W. Muschick, Hk. Müller-Buschbaum*, Z. Naturforsch. *B 31*, 1064 (1976).
[128] *W. Muschick, Hk. Müller-Buschbaum*, Z. Naturforsch. *B 32*, 495 (1977).
[129] *A.-R. Schulze, Hk. Müller-Buschbaum*, Z. Anorg. Allg. Chem. *461*, 48 (1980).
[130] *A.-R. Schulze, Hk. Müller-Buschbaum*, Z. Anorg. Allg. Chem., im Druck.
[131] *U. Lehmann, Hk. Müller-Buschbaum*, Z. Anorg. Allg. Chem. *460*, im Druck.
[132] *D. Chales de Beaulieu, Hk. Müller-Buschbaum*, Z. Anorg. Allg. Chem., im Druck.
[133] *D. Chales de Beaulieu, Hk. Müller-Buschbaum*, Z. Naturforsch. *B 35*, im Druck.
[134] *H. Pausch, Hk. Müller-Buschbaum*, Z. Anorg. Allg. Chem. *426*, 184 (1976).
[135] *H. Pausch, Hk. Müller-Buschbaum*, Z. Naturforsch. *B 34*, 378 (1979).

# Homoatomic Bonding of Main Group Elements

## By Hans Georg von Schnering[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

Clusters of main group elements are not rare. On the contrary, it is becoming difficult to avoid the discovery of new substances of this type. Clusters are the natural intermediate stages between an element and its isolated atoms or ions. In the form of polycations and polyanions they offer models for the stepwise oxidation and reduction of an element and represent a bridge between the elements. The great majority of homonuclear bonded structures are already present in the solid phases of simple systems. Mobilization of these clusters as molecules represents a great challenge.

*"Then says little Max: that's easy!"*
[*Wilhelm Klemm*, lecture on inorganic chemistry, university of Münster 1951]

This, the birthday celebrants own, pithy introduction to the discussion of difficult factual material gives both courage and a warning that the greatest caution is needed. Even he who is advanced requires courage in order to apply himself, armed with insufficient knowledge and means, to that which is not yet really understood; but he will do it! The right and the duty to be sceptical lie with the reader; he should keep them alive.

## 1. Clusters: Aggregates of Things of the Same Kind

The term "cluster" was introduced as an attractive designation for the formation of $M_n$ groups of directly-bonded metal atoms M in metal compounds which are otherwise "normal"[1]. Such behavior is unexpected according to classical valence rules. There is no reason why this term should not be applied quite generally to emphasize regions of homonuclear bonding. Overlap with customary molecular descriptions, above all for compounds of the main group elements, are more useful than otherwise, since nothing disturbs the insight into the indivisibility of chemistry more than the staking of claims. Reference to the molecules $Na_2(g)$ and $F_2(g)$, which are in principle analogous, may be sufficient to illustrate this. Also, whether a cluster $E_n$ already counts as a cluster with $n=2$ or only when $n\geq 3$, whether polymers $E_\infty$ belong to the "claim" or not, whether electron deficiency is essential or not, these problems do not really exist. Let everyone use his own judgement and keep the boundaries open.

Today, cluster compounds are known of practically all elements. They occur as polycations, as polyanions and as neutral molecules. The selection given in Figure 1 shows that the size and stereochemistry of the cluster $E_n$ are variable within wide limits. In the solid state the clusters are often found linked *via* ligand bridges or directly condensed[2,3]. The consideration of the homonuclear bonded regions as quasi-isolated, "bare" units is, nevertheless extraordinarily helpful to a complete understanding.

Certain groups of elements form cluster compounds preferentially. These are: the heavy 5A, 6A and 7A elements, elements of the Fe group, the elements of the main groups 4B and 5B as well as, finally, boron. Since the atomic binding energies are highest for the above elements (Fig. 1), the con-

---

[*] Prof. Dr. H. G. von Schnering
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 90 (Germany)

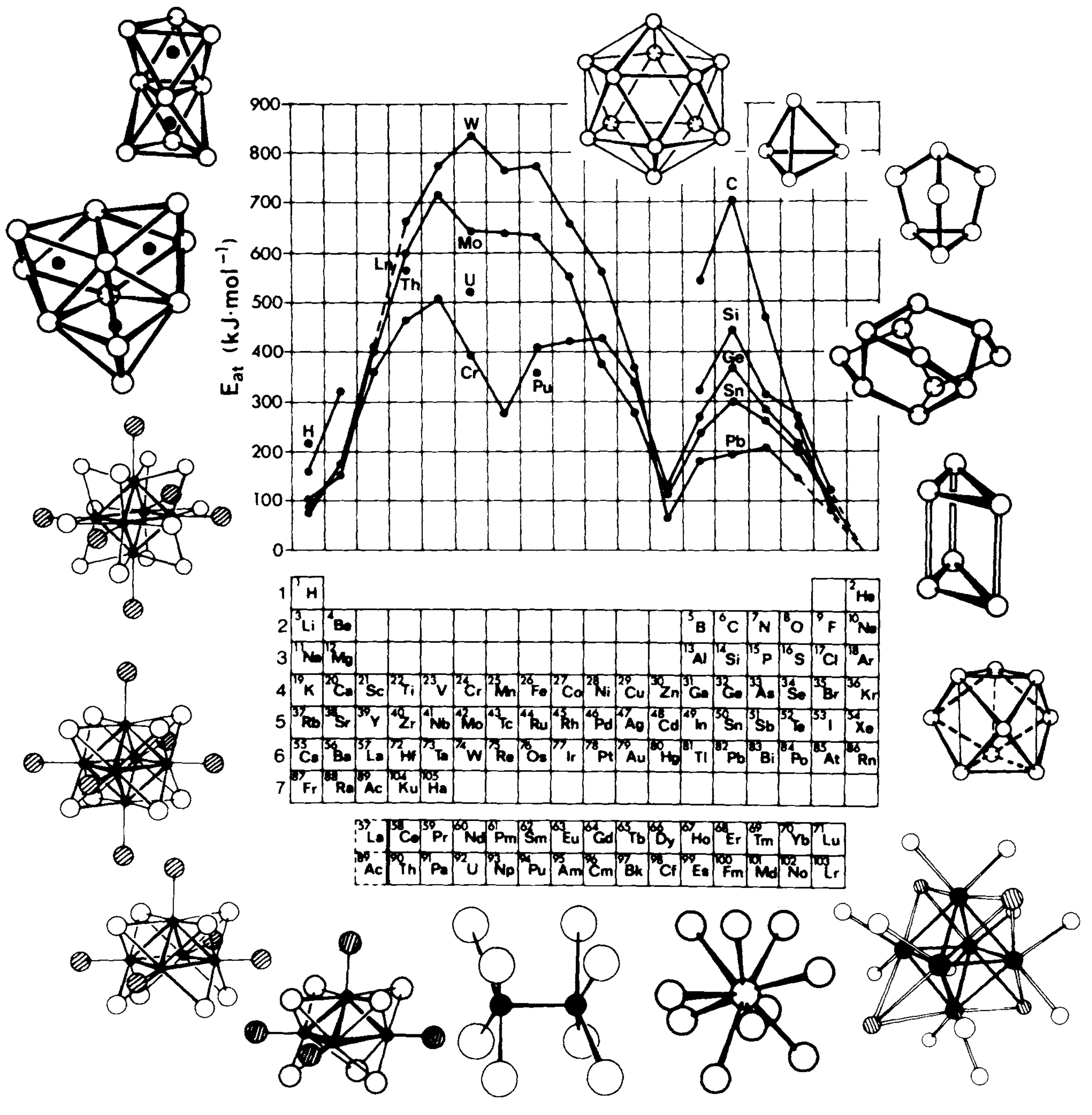


Fig. 1. Atomization energy $E_{at}$ of the elements [163]. Examples of clusters (clockwise) $B_{12}H_{12}^{2-}$, $P_4$, $P_7^{3-}$, $P_{11}^{3-}$, $Te_6^{4+}$, $Bi_9^{5+}$, $Rh_6(CO)_{16}$, $Au_{11}^{3+}$, $Re_2Cl_8^{2-}$, $Mo_4I_{11}^{2-}$ $Mo_5Cl_{13}^{2-}$, $Mo_6Cl_{14}^{2-}$, $Nb_6Cl_{18}^{4-}$, $Cs_{11}O_3^{5+}$, $Rb_9O_2^{5+}$.

nection between the occurrence of cluster compounds and the size of the homonuclear bond energy is obvious[2]. This energy, however, cannot be the only factor, as shown by the example of the $Hg^I$ compounds. After all, the homonuclear bond only has to be able to compete energetically with the heteronuclear bond.

The compounds with homonuclear linkages are often conspicuous because of their abnormal composition (as, for example, $Cs_{11}O_3$[4] or $Na_3P_{11}$[5]), which turns out to be normal in the sense of classical valence rules when one knows the structure and properties. A "normal" composition, however, does not rule out homonuclear bonds. ZnS, for example, is fully capable of building a tetrahedral structure as a Zn(I) disulfide with $Zn_2$ and $S_2$ pairs. The argument that this is a case of an oxidizing agent bound to a reducing agent without anything happening, is not serious, since there are many such examples, right up to charge transfer complexes. The clusters $E_n$ are in any case frozen-in redox steps between the element E and its electron-saturated formal cation or anion. The structural change which takes place parallel to these redox processes can be followed particularly well for the non-metals and meta-metals with predominantly localized bonds. The particular fascination of these compounds consists, therefore, not only in the occurrence of element-element bonds E—E, but also in the quasi-stepwise "break-up of element structures". Structural fragments are also formed in this process, of course, which are not formed as stable arrangements at all by the element; these correspond to excited states. The change in the electron balance often leads to structures which are typical for the neighboring elements. In this way, one crosses the periodic table step by step using "pseudo-elements" as a crutch. The cluster compounds lead finally to model structures, showing the first stages of reduction or oxidation of an element. The group $Cs_{11}O_3^{5+}$, the essential unit of the suboxide $Cs_7O$[4], shows that the oxidation of cesium leads to a localized elimination of oxygen while the rest of the metal remains intact. Oxygen is, therefore "precipitated" and not "dispersed". The structure of the cage compound $K_8Ge_{46}$[6]—corresponding to the gas hydrates $Xe_8(H_2O)_{46}$—with exclusively tetravalent Ge, shows that nothing happens to the germanium in the first stage of the reduction with potassium. The K atoms do not transfer their electrons to the Ge atoms, but form $K^+$ and give up the electrons to a conduction band without any appreciable Ge participation. A striking analogy to the solvation of electrons: germanium as "solvent" for $(K^+ + e^-)$!

The world of cluster compounds has found its place in the textbooks and the progress of recent years[7] has been described in detail in many articles[1–5,8]. The present article will concentrate on small regions of homonuclear linkage among main group elements.

## 2. On the Bonding

The bonding in clusters has been treated in various ways. The schemes for counting electrons developed by *Cotton et al.*[9], *Wade*[10] and *Lauher*[11] may be mentioned in this context. Each theory works well for particular types of cluster and leads in other cases to rather desperate efforts. A universal description of saturated and unsaturated systems does not seem to be easy to find. Apart from the boranes[12], the clusters of the main group elements can be treated extremely effectively using the comparatively simple valence rules of *Grimm* and *Sommerfeld*[13], of *Zintl*[14], of *Klemm* and *Busmann*[15,16] or of *Mooser, Pearson, Kjekshus* and *Hulliger*[17]. One should bear in mind, however, that the compounds are defenceless against our descriptions[18]. A description must be judged according to its effectiveness in relating stoichiometry, structure and properties.

The old (8-$N$) rule, generalized by *Mooser* and *Pearson*[17] uses a covalent model with collective counting of electrons. *Zintl*[4] and *Klemm*[15] examine local configurations in a setting of formal ions. Both descriptions are based on the assumption that the more electronegative partner B of a binary compound $A_mB_n$ obtains an octet configuration preferentially. With the first method, the sum of the valence electrons yields a universal statement on the number of homonuclear A—A and B—B bonds or on the number of nonbonding electrons. With the second method, one generates formal ions $A^{p+}$, $B^{q-}$, and ascribes to these, as pseudoelements E*, the homonuclear bonding of isoelectronic elements[5]. This yields for example, the well-known equivalence: $Si^{2-} \hat{=} P^{1-} \hat{=} S^0 \hat{=} Cl^{1+}$ for homonuclear bivalent units (2b)X. Finally, the Gillespie-Nyholm rules[19] are helpful in assembling the elements and pseudoelements together to form structures, or in analyzing structural principles. These electronic counting rhymes seem to be equivalent in many respects and can be summarized thus: (a) electron clouds repel each other.—(b) Isoelectronic units behave practically the same.—(c) The 8e rule and the 18e rule hold.—(d) Formal ions can be used with the bonding of isoelectronic elements or groups.—(e) for the same number of bonds various structural configurations are possible.—(f) Homonuclear bonds are supplemented by heteronuclear bonds in the sense of formal donor-acceptor interactions.

As mentioned above, the most important thing is to understand the relationship between stoichiometry ($\hat{=}$ number of valence electrons), structure ($\hat{=}$ electron distribution) and properties (color, conductivity, magnetism, reactivity *etc.*). Here are two examples of this: (1) The compound $K_8Ge_{46}$ (cf. Section 1) is a metallic conductor, since the K atoms have not given their electrons up to the Ge atoms (otherwise $(3b)Ge^-$ would be present and not $(4b)Ge^0$). If 8 Ge are substituted by 8 Ga, however, these fit into the structural framework as $(4b)Ga^-$. The conducting electrons are captured in the valence states and $K_8Ga_8Ge_{38}$ is a semi-conductor[20].–(2) $Sr_2As$ is described as a red compound, and must therefore be a semiconductor or insulator[21]. This is contradicted by the proposed structure, in which, besides "isolated" $As^{3-}$, only Sr atoms are supposed to exist with no indication of homonuclear interactions $(Sr^{2+} + e^-?)$. The electron balance, and therefore the formula, must be wrong. A new investigation shows that the compound is really $Sr_4As_2O$[22].

## 3. Structural Principles

Alone, the binary compounds which are formed between the electropositive metals and the non-metals and meta-metals are enough to constitute an overwhelming variety of substances, structures and properties. Figure 2 shows schematically which compounds have been identified up to the present time in one small region of the periodic table. The following compounds are formed, for example, between the alkali metals and phosphorus: $M_3P$, $MP_x$ $(x<1)$, MP, $M_4P_6$, $M_3P_7$, $M_3P_{11}$, $MP_5$, $MP_7$, $MP_{10.3}$, $MP_{11}$, $MP_{15}$. The substances are black up to the composition $M_4P_6$, and react immediatly with protic solvents. $M_3P_7$ and $M_3P_{11}$ are yellow or orange, but just as reactive. The remaining compounds are red or brown and, with increasing P content, more and more inert to mineral acids[5]. The remarkable variability in stoichiometry and properties is reflected in the structures, which indicate in multifarious ways the stepwise transition from the isolated $P^{3-}$ to elementary phosphorus. The structural variety can nevertheless be reduced to a few quasi-molecular building blocks, which are sections out of the various P modifications, or which could be structural parts of hypothetical forms of this element. Finally, all the structures can be built up from the atoms and pseudo-atoms $(3b)P^0$, $(2b)P^{1-}$, $(1b)P^{2-}$ and $(0b)P^{3-}$. A wide variety of structures is therefore based on relatively simple principles.

This holds in principle for all elements of groups 3B to 7B, even when the variety is not always so wide according to present knowledge. Silicon and phosphorus are developing visibly into "worthy" neighbors of boron and carbon, whose outstanding properties arise from a marked gregariousness. The structures which form are determined primarily by the number of valence electrons and are almost independent of the type of elements involved (Fig. 3). The decisive factor is the homonuclear bonding of the following: $(4b)Tl^{1-}$, $Si^0$, $P^{1+}$ or $(3b)Tl^{2-}$, $Si^{1-}$, $P^0$, $S^{1+}$ or $(2b)Si^{2-}$, $P^{1-}$, $S^0$ or

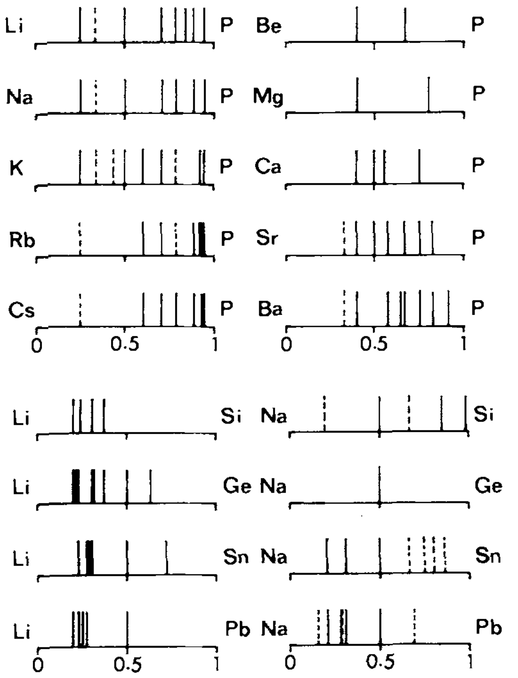


Fig. 2. Schematic representation of some binary systems. Compounds whose structures are certain are shown as continuous lines.

(1b)$Si^{3-}$, $P^{2-}$, $S^{1-}$, $Cl^0$, which lead to the formation of structures which are stereochemically identical or analogues. The great majority of homonuclear bonded groups are present in the solid state. They are, therefore, not "isolated", but bound to each other *via* heteronuclear interactions. In these intracollective interactions, the interatomic and intermolecular bonds between the pseudo-atoms E* and the pseudo-molecules M* (clusters), these units also behave just like the isoelectronic atoms and molecules. The heterobond can, as mentioned in Section 2, be treated independently of the intracluster bonding as an additional ionogenic bond or as a covalent donor-acceptor bond.

Some questions remain open despite the apparently closed picture (cf. Sections 2 and 6): in the treatment of degenerate bonds, in multicenter bonding, in the "assignment" of electrons used for external bonds. For example, the system $Si_4^0$[23], which has been proven to exist in an argon matrix, can be compared with $B_4Cl_4$. The tetrahedral cluster is—in contrast to $P_4$—formed by four three-center bonds, which in this manner provide each cluster atom with three shared electron pairs. The Si atoms in $Si_4^0$ complete their tetrahedral electron configuration (octet) by using free electron pairs, the B atoms in $B_4Cl_4$, on the other hand, by σ bonds to the Cl atoms. The equivalence can be described either by removing the "ligands" $[(B^+)_4 \triangleq (Si^{2+})_4]$ or by counting the electron pairs as part of the cluster $[(B^-)_4 \triangleq (Si^0)_4]$. This arbitrary method of cutting the outer bonds in different ways is capable of opening up interesting new aspects, *e.g.* a tetrahedral cation $(P^+)_4$.

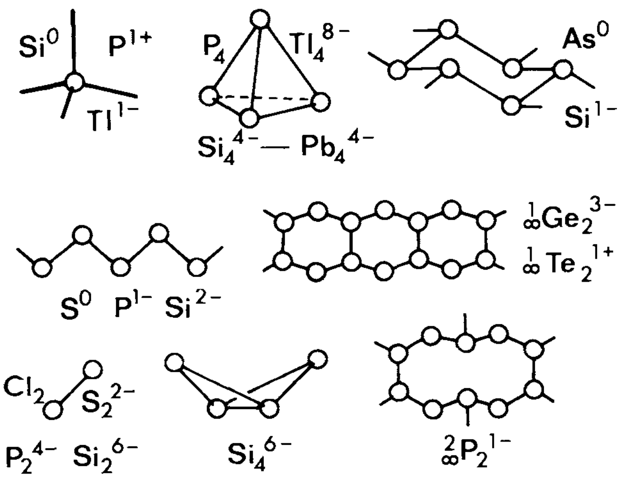


Fig. 3. Homonuclear bonds for isoelectronic elements E and pseudoelements E*.

## 4. Chain Structures

A series of compounds of the elements Zn, Cd, Hg and In are known which contain *polycations* of increasing chain length (Fig. 4). Examples are $In_2^{4+}$ and $In_3^{5+}$ in $In_6Se_7$ and $In_4Se_3$ respectively[24], $Zn_2^{2+}$ in the black $ZnP_2$, and $Cd_2^{2+}$ in the isostructural $CdP_2$[25]. In the case of mercury, the $Hg_2^{2+}$ groups are typical for $Hg^{I}$, and $Hg_3^{2+}$ and $Hg_4^{2+}$ have also been found in yellow and red salts respectively[26]. The final member of this condensation is also known: the metallic compound $Hg_{2.86}[AsF_6]$ contains the infinite, linear polycation $Hg_{2.86}^{1+}$ with the formal oxidation state $Hg^{0.35+}$[27]. In this way, an isolated metallic thread of mercury forms step by step from a molecular cation. A special feature of this compound is that the translational identity of the Hg atoms belonging to the "string" is incommensurate with that of the anions $[AsF_6]^-$; a strong indication of the autonomy of this string of pearls in its box.

The polyanions of phosphorus, arsenic and antimony in their compounds with the electropositive metals provide impressive examples of the configuration and conformation of homonuclear, two-bonded elements (2b)E or (2b)E*. The stepwise dismantling of 1-dimensional infinite chains can be studied using these structures. The *polyanion* $^1_\infty(X^{1-})$ is characteristic, not only for the alkali metal compounds MX, but also for the $MX_2$ compounds of the bivalent cations. There is a series of structure types, all of which possess the same helical construction, but which differ in the conformation of the helices and in their packing[28]. The diphosphides and the diarsenides of the lanthanoids form two structure types: the $LaP_2$ type[29] and the $CeP_2$ type[5,30], which are stable at high and low temperatures respectively. In the first structure type an $X_3^{5-}$ group occurs together with an $X_5^{7-}$ group, while the second structure type only contains $X_4^{6-}$ anions. In structures of the $Ca_2As_3$ type the groups $X_4^{6-}$ and $X_8^{10-}$ exist side by side[31], while the structures of $Eu_2Sb_3$[32] and $Sr_2Sb_3$[33] contain only $X_6^{8-}$ anions. The $Sr_3As_4$ structure, which is formed by almost all phosphides and arsenides of the divalent cations, is also characterized by $X_4^{6-}$ chains, although with a different conformation (torsional angle 90°)[34–36]. The adaptability of these polyhedra to external conditions, such as size and coordination of the cations, is shown in Figure 4 for the conformation of several $^1_\infty(2b)X^-$ chains. Each chain is labeled here by the sequence of the torsional angles γ and by the (analogous) conformational type: s ≙ staggered and e ≙ ecliptic.

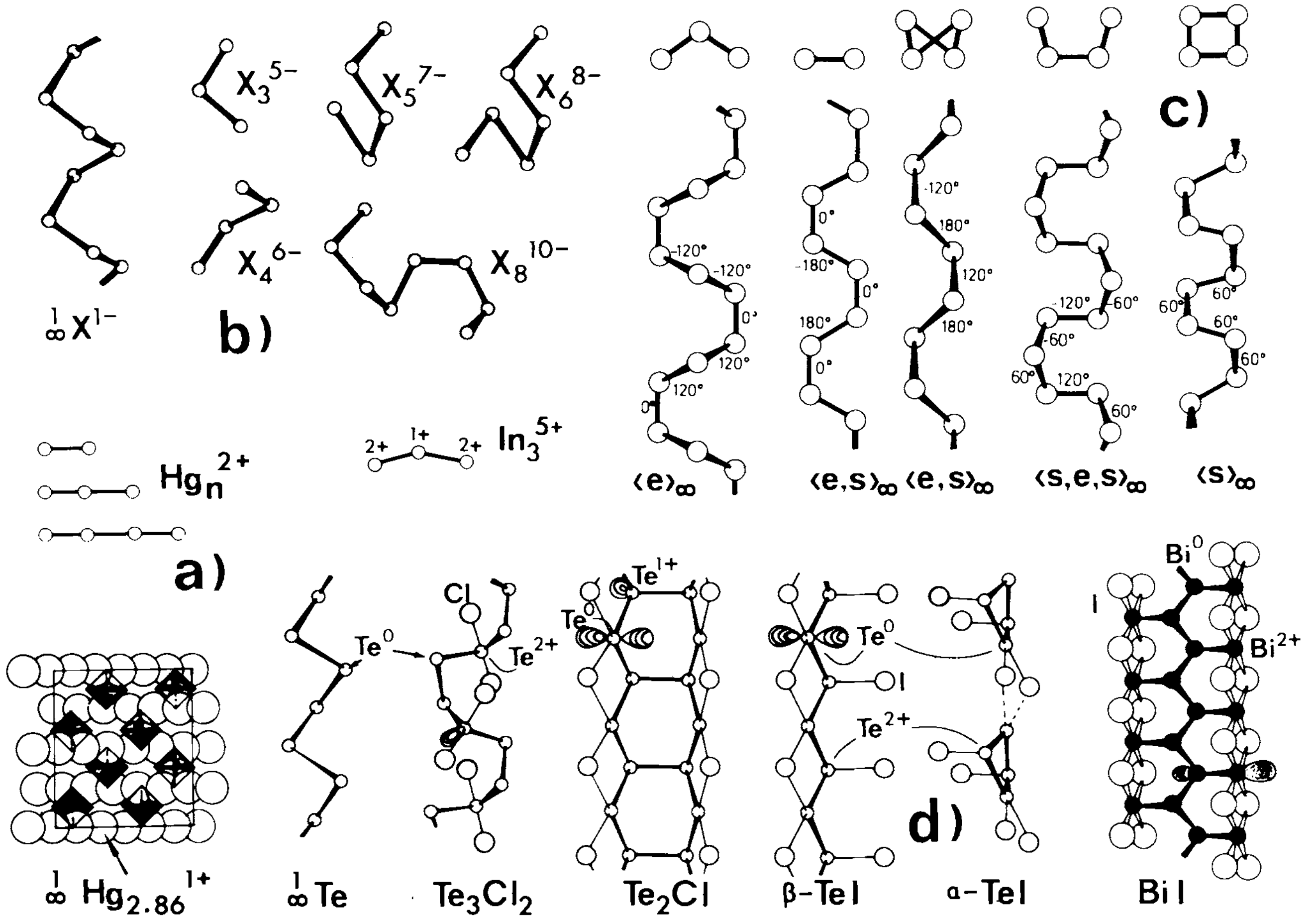


Fig. 4. Homonuclear chains. a) Polycations of Hg and In. b) Polyanions of P, As and Sb. c) Conformation of one-dimensional infinite polyanions in (from the left): BaAs$_2$ [94], GdPS [164], EuAs$_2$ [94], BaAs$_2$ and LiAs [105]: the projection in the chain direction (top), the dihedral angles and the conformation (s, e) are given. d) Linkage of Te and Bi in subhalides; the formal electron configuration is drawn for some atoms.

Several examples of polyanions with branched chains can be found among the subhalides of bismuth and tellurium: BiBr[37], BiI[38], Te$_3$Cl$_2$, TeCl and TeI[39]. The monohalides BiX possess several modifications, all, however, with the same structural principle (Fig. 4d). The branched one-dimensional infinite Bi chain can be regarded as a strip, which has been cut from the two-dimensional structure of condensed six-membered rings found in elementary bismuth. The Bi atoms are bonded in different ways. One half of them control three homonuclear bonds as (3b)Bi$^0$, the other half, in contrast, only one. Only these (1b)Bi$^{2+}$ possess Bi—X bonds so that these monohalides are mixed-valence Bi$^0$/Bi$^{2+}$ compounds of the type $\{$Bi$^0$[BiX$_2$]$\}$. In the subhalides of tellurium, modifications of the $^1_\infty$(2b)Te$^0$ chain can be found. Te$_3$Cl$_2$ still contains this chain, but every third Te atom is additionally bound to two Cl atoms (Cl$^-$ as donor). This Te atom has, therefore, a ψ-trigonal bipyramidal configuration, when the remaining free e$_2$ pair is included; a conceivable arrangement for Te$^{2+}$: $\{$Te$_2$[TeCl$_2$]$\}$. In the TeCl$_2$ structure, two Te chains are united to form a band of condensed six-membered rings. This Te$^{2+}$ band has the same structure as the Ge$_2^{3-}$ unit in the compound Sr$_3$Ge$_4$[8a] (Fig. 3). The three-bonded atoms behave like Sb atoms: (3b)Te$^+$. The others possess two additional Cl bonds (Cl$^-$ donor) as in Te$_3$Cl$_2$, but in a configuration which, according to *Gillespie*[19], corresponds to a ψ octahedral coordination: (2b)Te$^0$. At first glance, it appears strange that Te$^0$ is bound to Cl and not Te$^+$, but polar structures like $\{$Te$^+$[TeCl$_2$]$^-\}$ are not unusual. α-TeI and β-TeI are also mixed-valence compounds with, formally, ψ-tetrahedral (2b)Te$^{2+}$ and ψ-octahedral (2b)Te$^0$ (Fig. 4d). The Te$_4$ ring in α-TeI (as Te$_4^{4+}$) corresponds to the As$_4^{4-}$ anion in CoAs$_3$[40].

The polysulfides and polyiodides, which have been known for a long time, also belong to the group of compounds with homonuclear chains. They have been discussed in detail, for example, by *Steudel*[41] and *Tebbe*[42]. Sulfur linkages give examples of conformational variations which allow both cyclic and helical structures. For the iodides, on the other hand, gliding transitions between weak interactions I—I···I$^-$ and degenerate bonding states (I--I--I)$^-$ are typical, in which a local simulation of the non-metal→metal transition can be seen. One finds I$_\infty$ chains formed from regular or irregular series of I$^-$, I$_2$, I$_3^-$ and I$_4^{2-}$ units in compounds which possess rigid frameworks with suitable cavities. This is realized in various ways, *e.g.* with complex cations[43], with dextrins[44], in Tl$_3$I$_4$[42] or the variable iodides of the type M$_x$Tl$_6$I$_6$(I$_4$)[45]. I$_\infty^{z-}$ anions of this type are found to have incommensurable transitions, as for the (Hg$^{0.35+}$)$_\infty$ cations mentioned above. With regard to the non-metal→metal transition, the I chains represent the state below the critical temperature $T_c$ (partially localized bonds) and the Hg chains the state above $T_c$ (degenerate bonds).

## 5. Rings

Small homonuclear rings have been studied and described many times in detail, as for example, those in the silanes by *Hengge*[46] and those in the phosphanes by *Baudler*[47]. In particular, the latter investigation has recently led to the statement that the $P_3$ ring is apparently the most stable three-membered ring system[48]. Therefore, only a few structures will be treated here which can be discussed as π-systems, as well as some larger ring systems in polymeric structures.

The butterfly anion, $Si_4^{6-}$ in $Ba_3Si_4$[49] is, as a 22-electron system, the opened $Si_4^{4-}$ tetrahedrane[16,50,51]. It is also the monomeric structure of the polymeric ${}^1_\infty Ge_2^{3-}$ or ${}^1_\infty Te_2^{1+}$ (Fig. 3). At the same time, the $Si_4^{6-}$ butterfly, as a localized bonded system, can be equated to the isoelectronic groups $Bi_4^{2-}$[52] and $Te_4^{2+}$[53] with delocalized π bonds (Fig. 5).

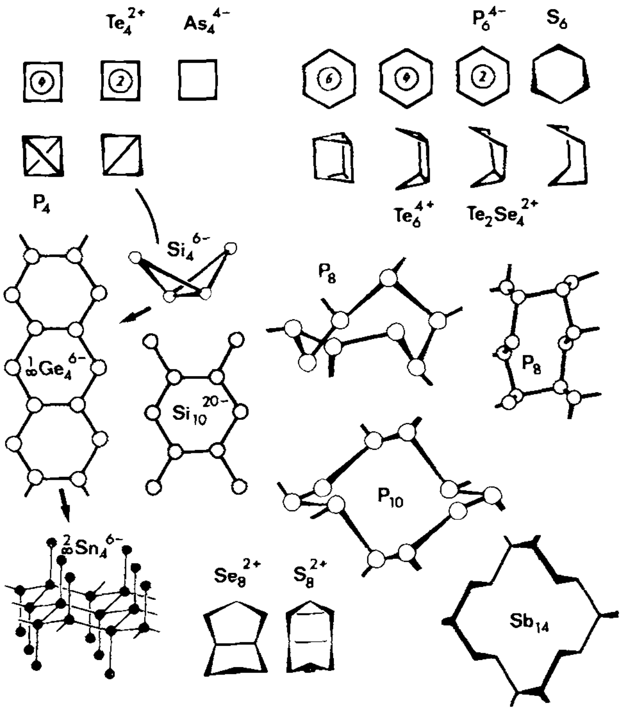


Fig. 5. Homonuclear ring systems (cf. text). On the lower right hand side are the condensed $P_8$ rings from $EuP_7$ [64] and $Th_2P_{11}$ [65], the $P_{10}$ ring from $EuP_7$ and the $X_{14}$ ring from the $MX_3$ compounds (M = Ca, Sr, Ba, Eu; X = P, As, Sb).

These systems behave, then, just like the cations $S_8^{2+}$ and $Se_8^{2+}$[54]. The heavy alkali metals form the compounds $M_4X_6$ with phosphorus and arsenic, in which strictly planar $X_6$ rings occur[55,56]. The bond distances P—P = 215 pm and As—As = 237 pm are noticeably shorter than the single bond lengths (221 and 245 pm, respectively). The formula $X_6^{4-}$ yields a "cyclohexene system" (here with a delocalized double bond). The existence of the isoelectronic $Te_6^{2+}$ is not yet certain, but for the cation $Te_6^{4+}$ a variant of the prismane series analogous to cyclohexadiene has actually been proven to exist[57] (Fig. 5).

The planar $Si_5$ rings and $Ge_5$ rings in the compounds $Li_{12}Si_7$[58] and $Li_{11}Ge_6$[59] must be mentioned as well. Higher bond-orders in the sense of cyclopentenes with delocalized double bonds can be argued for these compounds as well[58]. On the other hand, crystal fields can also stabilize excited molecular states. The first of the two SrSi modifications[60,61] contains normal ${}^1_\infty Si^{2-}$ chains with $(2b)Si^{2-}$. The other form possesses, however, the unusual planar ion $Si_{10}^{20-}$ (Fig. 5) with four $(3b)Si^-$, two $(2b)Si^{2-}$ and four $(1b)Si^{3-}$, that is, with three different states of charge. In this connection it is interesting to look at the polyanion ${}^2_\infty Sn_2^{3-}$ in $Li_5NaSn_4$[62]. It has the same structure as the isoelectronic carbon monofluoride $(CF)_n \mathrel{\hat{=}} (SnSn^{3-})_n$ (Fig. 5). With this ion, we have not only monomeric and polymeric variations of the homonuclear combinations $E_2E_2^*$ with $Bi_4^{2-}$, $Si_4^{6-}$, $Ge_4^{6-}$ or $Sn_4^{6-}$, but also all the limiting cases of formal charge distribution:

$$\{(2\tfrac{1}{2}b)Bi^{1.5-} + (2\tfrac{1}{2}b)Bi^{1.5-}\} \rightarrow \{(2b)Si^{2-} + (3b)Si^{1-}\} \rightarrow \{(1b)Sn^{3-} + (4b)Sn^{0}\}$$

Polymeric anions often contain large, linked ring systems, which are worthy of some interest because of their conformations. Examples are (Fig. 5): the $Ge_8$ ring of LiGe[63] with the $S_8$-crown conformation, the $P_8$ rings of $EuP_7$[64] and $Th_2P_{11}$[65], the $X_{14}$ rings of $CaP_3$[66], $SrAs_3$[67] and $BaSb_3$[68], and the $P_{12}$ rings of $LaP_5$[5,69] (cf. Section 11). Unfortunately, chemical methods are not yet available which can systematically separate and isolate such systems from the polymeric structures in solids.

## 6. Polycyclic Systems

The polycyclic polyhedra are particularly interesting for chemists, because they provide an immediate link between the structures of solid materials and known isolated molecules. In principle, the polyhedra span the surface of a sphere; their vertices are the atoms of a cluster. Two-center bonds correspond to the polyhedral edges, multicenter bonds the polyhedral faces. If one expects for the main group elements in the simplest case an electron octet with tetrahedral configuration, then those polyhedra are most interesting whose vertices are shared by three edges or three faces: *e.g.* tetrahedron $A_4$, trigonal prism $A_6$, cube $A_8$, pentagonal prism $A_{10}$, pentagonal dodecahedron $A_{20}$ and others. The faces correspond in chemical language to the rings of polycyclic systems, *e.g.* three-membered rings in the tetrahedron. The edges of the polyhedra can be bridged by additional atoms, which then represent "improper" two-bonded vertices (2b)A, without violating the Euler relationship between vertices, edges and faces of convex polyhedra[5,70]. The adamantane structure remains analogous to the tetrahedron despite the six two-bonded bridges. In such polyhedra, the missing bond functions will be directed outwards and be characterized by free electron pairs $e_2$ (donor), empty orbitals (acceptor) or ligands. Each atom which occupies a "proper" vertex of a cluster of this type with two-center bonds must contribute at least 5 electrons or 3 electrons and one ligand, while a bridging atom requires a configuration analogous to $>CH_2$. In this way, the elements of main group 5 (or isoelectronic pseudoelements E*) are the natural building bricks for polyhedra of this kind, as for all other "peripheral" structures. If the number of electrons per atom is less than five, only polycyclic groups with multicenter bonds remain, if one neglects for a moment the possibility of three-dimensional linkages. In clusters of this sort, more than three edges meet at a vertex (octahedron, icosahedron, among others) and polyhedra with triagonal faces seem to be preferred. The large family of the boranes was first described by *Lipscomb*[12] using a sophisticated system of two 2-center and three-center bonds, which span the surface of the polyhedra while including the H atoms. *Wade*[10], *Lauher*[11], *Williams*[71] and *Mingos*[72] have chosen MO treatments, which were also applied to clusters in general.

The real problem is actually the question: when is an arrangement with only one *exo*-bond per atom electronically saturated, and therefore particularly stable and, do the atoms involved strive for an 8e shell or an 18e shell? Playing with these electron counting rules[73] can be very stimulating (cf. the examples in Fig. 6).

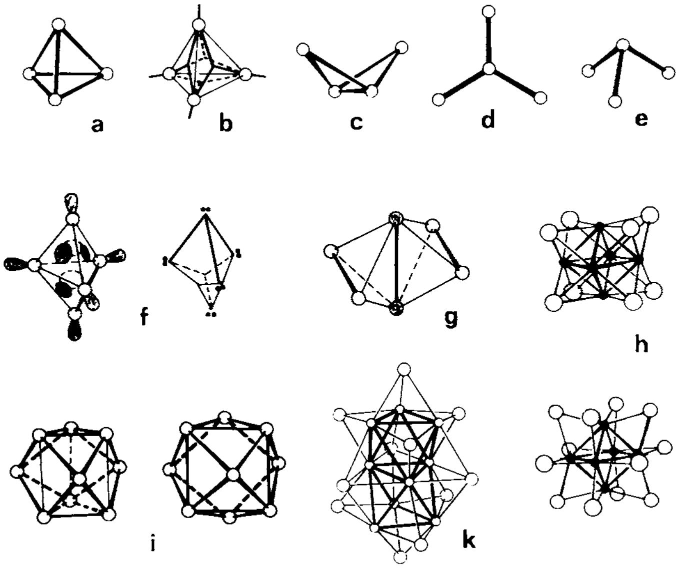


Fig. 6. Polycyclic systems I (cf. text): a) $P_4$, $Si_4^{4-}$ *etc.*; b) $B_4Cl_4$ or $Si_4$ with 3c-2e bonds; c) $Si_4^{6-}$; d) $Si_4$ star; e) $P_4^{6-}$; f) two views of $Bi_5^{3+}$; g) $Nb_2S_4^{4+}$ as double tetrahedron; h) $M_6X_8$ and $M_6X_{12}$; i) $Bi_9^{5+}$ or $Sn_9^{4-}$ as {3,3,3}-polyhedron and as {1,4,4}-polyhedron; k) $Mo_9S_{11}^{4-}$.

The stable configuration of a *closo*-$E_4$ tetrahedrane should be a 10e system according to *Wade*, if the *exo*-bonds are neglected. It could be described with one 4c-2e bond[*] and four 3c-2e bonds, which, however, together with the *exo*-bonding implies that the octets of the atoms are exceeded. Examples are not known. Instead, $B_4Cl_4$ and $Si_4$[23] exist with, in each case, 8 electrons in the skeleton, for which four 3c-2e bonds yield a tetrahedral configuration of the vertices. Since an additional electron pair cannot improve this configuration for any of the atoms involved, this is presumably the reason why a tetrahedral cluster is not stabilized with exactly 4+1 bonds. The same may be true for the other polyhedra whose vertices are shared by three faces. The saturated $P_4$ tetrahedrane is, as a 20e system, that is, with 12 electrons for skeletal bonds, without doubt the most stable configuration. Its isoelectronic relatives should be mentioned again (see Section 3): $As_4$, $Sb_4$, $Bi_4$, $Si_4^{4-}$, $Ge_4^{4-}$, $Sn_4^{4-}$, $Pb_4^{4-}$, $Tl_4^{8-}$ and, last but not least, the carbon compounds $C_4R_4$[74]. This is another case where a further electron pair is superfluous after the six 2c-2e bonds along the polyhedral edges have been built up into a formal tetrahedral electron configuration. The treatment of this cluster as a *nido*-$E_5$-polyhedron according to *Wade* conceals, however, a fascinating component. The $E_4$ tetrahedron would, in this sense, be a trigonal bipyramid with one missing vertex, which implies that we have a "tetrahedron" opened on one side—that is, a trigonal pyramid. Since this opening can take place in four different ways, the tetrahedral topology of $P_4$ would perhaps only result from a dynamic process. On the other hand, the tetrahedral cluster with exactly 20 electrons fits into the bonding scheme of *Lauher*[11], which requires 60 electrons in the stable configuration for 18e components. For the higher homologues one only has to add the electrons from the complete $d^{10}$ shell. For $P_4$ and $Si_4^{4-}$, we can imagine the empty 3d states as "reserving places" for 4 × 10 electrons, and in this strange way we come back to the participation of d orbitals in the bond scheme of these elements. But: "God is just!"[75], the carbon tetrahedrane is not satisfied with this description.

The uptake of two electrons certainly causes the tetrahedron to open up and form the butterfly cluster or its analogous forms with 22 electrons such as $Si_4^{6-}$ (see Section 5). With six electrons one of the three-membered rings is fully opened. This 26e system is isoelectronic with $SO_3^{2-}$ and is realized as a homonuclear unit in *e. g.* the trigonal pyramidal $P_4^{6-}$ anion of the polyphosphide $La_6Ni_6P_{17}$[76]. Meanwhile, the $Si_4$ cluster of the compound $Li_{12}Si_7$[58] sets us a real problem. The cluster forms a trigonal planar $Si_4$ star (Fig. 6d), a topology which is very appropriate for Stuttgart! $Li_{12}Si_7$ is a diamagnetic semiconductor, which removes all excuse for not treating it because it is an intermetallic phase. The compound $[Li_{24}Si_4(Si_5)_2]$ contains, besides the $Si_4$ star, two planar $Si_5$ rings. If these rings are described as saturated cyclopentanes $Si_5^{10-}$, then the 20e-system $Si_4^{4-}$ remains. This really should be a tetrahedron! Is this an excited state of the $P_4$ molecule, stabilized by the crystal field? This trigonal structure, on the other hand, reminds us directly of the $CO_3^{2-}$ anion, a 24e system. Using this description, with the units $Si_4^{8-}$ and $Si_5^{8-}$, the $Si_5$ rings would be left with the 28 electrons of a cyclopentene with a delocalized double bond. The bond lengths in both groups point at first glance against higher bond orders. They lie clearly in the range of single bonds with $d(Si—Si) = 236$ to 239 pm. This question will be discussed again in Section 13.

The trigonal bipyramidal 22e systems $Pb_5^{2-}$[77] and $Bi_5^{3-}$[78] are representatives of the $E_5$ cluster. Both *Lauher*'s rule (72e after adding 5 × 10 d electrons) and *Wade*'s rule (6 $e_2$ pairs for the skeleton) hold here. According to *Gillespie*[79], six 3c-2e bonds are present in these clusters (Fig. 6f). Here, the two apex atoms would have "tetrahedral", the three equatorial atoms "square pyramidal" electron configurations. If one chooses to describe the system as a mesomeric state between two limiting cases, with in each case three 3c-2e bonds and three 2c-2e bonds (Fig. 6f), all atoms would have, formally "tetrahedral" electron configurations. On homolytic separation one obtains the distribution of positive charge in $Bi_5^{3+}$ according to (a): $2 \times Bi^{+} + 3 \times Bi^{1/3+}$ or (b): $2 \times Bi^{1/2+} + 3 \times Bi^{2/3+}$. Model (b) yields, with 3c and 2c bonds, a more even distribution of charge on all atoms and, in fact, for both $Bi_5^{3+}$ and $Pb_5^{2-}$. Of course, only an exact analysis of the *exo*-contacts and, above all, a quantitative calculation, can show whether this is correct.

Octahedral $E_6$ clusters are typical for the transition metals. Among the main group elements only $B_6H_6^{2-}$ and the

---

[*] 4c-2e bond stands for a four-center two electron bond *etc.*

linked $B_6$ octahedra in the hexaborides of the type $CaB_6$ are known. In this case, the skeleton is formed from 14 electrons ($\hat{=}6+1e_2$). This agrees with the Wade rules. An 86e system (7 $e_2$ for the framework, 6 *exo*-$e_2$, 6 × 10 d electrons) is analogous for 18e components[11]. Unfortunately this method of counting is wrong, both for the well-known $Rh_6(CO)_{16}$ and for the apparently equally stable $M_6X_8$ and $M_6X_{12}$, clusters, which enrich the chemistry of the heavy transition metals in such an unusual way and are in addition the essential units for the concept of condensed clusters[80]. In any case, the MO treatment of *Cotton* and *Haas* of 1964[9] seems to me to be still topical. It describes the $M_6X_{12}$ cluster as a stable unsaturated unit with eight 3c-2e bonds (16 electrons in the skeleton) and the $M_6X_8$ cluster as a saturated unit with twelve 2c-2e bonds (24 electrons in the skeleton). The six M atoms obtain a complete 18e shell on including the 24 M—X bonds and the six potential bonds to outer ligands $:X^a$. The unsaturated state yields a 76e system, the saturated state of the $M_6$ cluster an 84e system (instead of 86e). *Lauher*'s description leads, however, to a quite unexpected aspect, which one should follow up in regard to cluster systems with formal similarities to spherical close-packing: the unit $M_6X_8$ possesses the structure of a face-centred cube. *Lauher* expects a stable system with 180e for this. In fact, if *all* M and X atoms are treated the same, then $Mo_6Cl_8^{4+}$, with the Mo atoms (6 × 6 electrons) and the Cl atoms ($8\times7+8\times10$ electrons), the six potential *exo*-electron pairs and the cationic charge, possesses exactly 180 electrons!

The 40e systems $Bi_9^{5+}$[81], $Sn_9^{4-}$[82] and $Ge_9^{4-}$[82,83] form one of the most beautiful clusters known. The existence of such large groups was derived by *Zintl et al.*[84] from the unusual behavior of the intermetallic phases $Na_4Sn_9$ and $Na_4Pb_9$. The structure however (Fig. 6i) was only determined a few years ago, and can be described in two ways, according to one's point of view; as a tricapped trigonal prism {3,3,3} or as a monocapped archimedean antiprism {1,4,4}. The two forms can easily be derived from each another, as is well known. The different points of view have theoretical foundations, and for this reason the original {3,3,3} polyhedron is gradually giving way to the {1,4,4}-polyhedron as the theory is consolidated. The latter polyhedron is, in fact, expected according to both *Wade* (*nido*-$E_{10}$ cluster) and *Lauher* (130e system including the d electrons). The assignment of bonding electrons to the edges and faces of the polyhedron is not possible, at least not in any simple way. According to *Gillespie*[79] all nine atoms possess a free electron pair and the remaining 11 electron pairs form eight 3c-2e bonds and three 4c-2e bonds, according to the faces of the {3,3,3} polyhedron. This would give $3\times Bi^{1/3-}$ and $6\times Bi^+$ (or $Sn^{4/3-}$ and $Sn^0$) with a sandwich-like charge distribution. The same result is obtained with two 3c-2e bonds and twelve 2c-2e bonds, but with only six *exo*-electron pairs on the prism atoms. The two clusters $Bi_9(e_2)_{11}^{5+}$ and $Mo_9Se_{11}^{4-}$[85] show a remarkable topological analogy to the "twins" $M_6X_{12}$ and $M_6X_8$, which can be derived from each other formally by exchanging the positions of electron pairs and X atoms. This may be useful for a better understanding. The $Ge_9^{2-}$ cluster, described by *Corbett et al.*[83] satisfies *Wade* ($E_9$ polyhedron) as well as *Lauher* (threefold capped trigonal prism, 128 e) and is also a hint for the remarkable valence behavior of this unit.

It will have become clear that the bonding in clusters can be viewed in quite different ways. At any rate, there is plenty of room for phantasy, and anomalous results mean, after all, that the next generation can still hope to find out something new. Above all, the unusual way in which main group elements fit into the 18e scheme as well, provides us with a striking insight. It has already been mentioned that the clusters $M_6X_8$ and $M_6X_{12}$ (Fig. 6h), of all things, do not fulfil *Lauher*'s rules (84e instead of 86e). But, to be fair, the rules do work for the group $[Nb_2(S_2)_2]^{4+}$, which one certainly would not look for, here (Fig. 6g). The remarkable orthogonal orientation of the two $S_2^{2-}$ anions to the $Nb_2$ pair in the structure of $NbS_2Cl_2$ has been referred to already[86]. If one counts 16 electrons for sulfur and takes the eight Nb—Cl bonds into account as *exo*-electron pairs, the group receives exactly 86 electrons. An 86e—$E_6$ cluster is, according to *Lauher*, not only stable as an octahedron, but also as an edge-sharing double tetrahedron—exactly the structure of $[Nb_2(S_2)_2]^{4+}$.

A series of fascinating polycyclic anions has been identified in recent years among the structures of the metal phosphides (Fig. 7), which at last allows well-founded statements to be made about the systematic structures of the lower Stock polyphosphanes[5]. A large number of phosphanes have been clearly identified from the homologous series $P_nH_{n-m}$ and $P_{m+n}H_n$ through the fundamental investigations made by *Baudler et al.*[87]. These should be derivatives of $P_2$ ($m=2$), of tetrahedrane $P_4$ ($m=4$), of prismane $P_6$ ($m=6$) and of cubane $P_8$ ($m=8$) with a considerable number of possible isomers[5]. The corresponding polyanions already show similarities to the structure of the molecular element in its real form ($P_2$ and $P_4$) as well as hypothetical forms ($P_6$ and $P_8$).

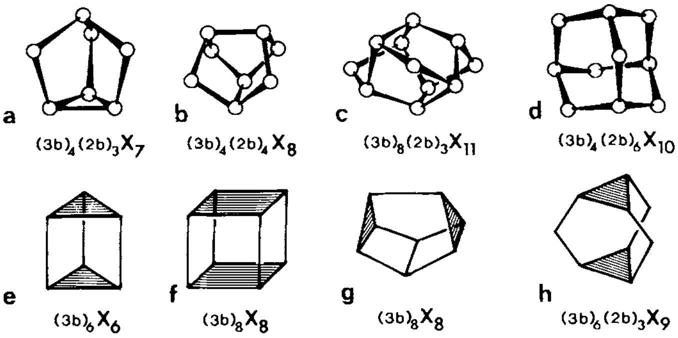


Fig. 7. Polycyclic systems II (cf. text): a) $P_7^{3-}$, $As_7^{3-}$, $Sb_7^{3-}$; b) $As_4S_4$, structural element in $P_{15}^-$; c) $P_{11}^{3-}$, $As_{11}^{3-}$; d) $P_{10}^{6-}$; e) prismane; f) cubane; g) cuneane; h) trigonal asterane as a possible structure for $P_9^{3-}$ or $P_9R_3$ [103].

The anion $P_7^{3-}$ is typical for the $M_3P_7$ compounds of the monovalent cations $M^+$, and for the $M_3P_{14}$ compounds of the divalent cations $M^{2+}$[5]. In accordance with the formula, it contains four $(3b)P^0$ and three $(2b)P^-$ and is isoelectronic with the well-known molecule $P_4S_3$. This nortricyclene system is a derivative of the $P_4$ tetrahedron; the bridging atoms over the three edges are improper vertices in the sense of the Euler polyhedra (Fig. 7a). The analogous nortricyclenes $As_7^{3-}$[88] and $Sb_7^{3-}$[89] are also known, and have been studied in detail. A comparison between the configurations of the $X_7^{3-}$ polyanions and those of $P_4S_3$ and the molecules $P_7(SiMe_3)_3$ and $P_4(SiMe_2)_3$[90] shows that the height of the anions is relatively small and that the distance between the two-bonded bridging atoms is relatively large. This is good evidence for the localization of finite formal charges on these two-bonded atoms[91]. It was recently possible to confirm this interpretation by the quantitative evaluation of the NMR spectra of $Li_3P_7$ in solution[92]. *Zintl* and *Klemm*'s concept of formal ions, which these days seems very crude, is, therefore, still capable of providing statements which are both sensible and far-reaching. The $P_7^{3-}$ anion is not only stable in suitable solvents[88,92]; it can also be found in melts at 720 K[5,93]. This explains the unusual thermal behavior of $K_3P_7$, for example. While the higher phosphides decompose by loss of P[94] and the lower phosphides by loss of K[95], the yellow $K_3P_7$ "sublimes"[94]. The equilibrium vapor contains, however, only K(g) and $P_4$(g); in other words, the sublimation corresponds somewhat to that of $NH_4Cl$. The considerable solubility of phosphorus in salt melts, above all in the presence of metals[5], can also be understood with the aid of these polyanions. The dynamic behavior of this system provides the final twist: according to *Baudler et al.*[92] this is the first inorganic "bullvalene" with valence tautomerism above 350 K, as suspected by *Bues et al.*[93]. The same structure was proposed for the corresponding heptaphosphane(3), $P_7H_3$[5]. This has also been proven recently by *Baudler et al.*[95].

The realgar molecule $As_4S_4$ has been known for a long time. Its structure is shared by the molecule $P_4S_4$[96], and very probably by the octaphosphane(4), $P_8H_4$, as well (Fig. 7b). This configuration is frequently found in polymeric form as a fourfold linked unit (4b)$P_8^0$, as, for example, in Hittorf's phosphorus[97] and in many polyphosphides[5] (cf. Section 8). Decaphospha-adamantane (Fig. 7d) is the last stage in the $P_4$ tetrahedrane derivatives with bridged edges. This system turns up as the anion $P_{10}^{6-}$ in the compound $Cu_4SnP_{10}$[98], which is otherwise characterized by a 4c-2e cluster $Cu_3Sn$. Unfortunately, it has not yet proven possible to obtain a neutral molecule from this polyanion (cf. Section 7).

The polyanion $P_{11}^{3-}$ is present, for example, in $Na_3P_{11}$[99] and $Cs_3P_{11}$[94,100]. It may be understood as a derivative of the much sought, but never found, octaphosphacubane $P_8$. This beautiful, chiral molecule with the symmetry $D_3$ is made up of eight (3b)$P^0$ and three (2b)$P^-$ atoms. By bridging three edges of cubane, six five-membered rings are obtained from the original six four-membered rings (Fig. 7c). Anyone who has rotated a model of this group about its threefold axis understands the name "UFOsane"[99] immediately. The undecaphosphane(3) $P_{11}H_3$ should also possess this structure, which has the highest symmetry of all conceivable isomers. Compounds with the $P_{11}^{3-}$ anion form under very similar conditions to those with the $P_7^{3-}$ group. It can be shown that the brilliant yellow $Na_3P_7$ and the orange $Na_3P_{11}$ can be readily (and reversibly) converted into each other, when in equilibrium with $P_4$(g)[101]. This transition can be well understood with the aid of the model[5]. In this connection, the occurrence of mixed crystals among the alkali metal phosphides is also important. These lead to phases containing both polyanions $P_7^{3-}$ and $P_{11}^{3-}$ (cf. Section 9). Important too, is the observation by *Bues* and *Somer*[102] that the $P_{11}^{3-}$ group remains intact in melts at 720 K, and can be identified spectroscopically. The analogous arsenic unit $As_{11}^{3-}$, recently described by *Belin*[156], shows impressively that surprising results could be expected in this region of chemistry.

The $P_{11}^{3-}$ cluster, as a derivative of cubane, certainly opens up new possibilities in the search for $P_8$ cubane, especially since the anions can be converted into neutral molecules (Section 7). The polymeric unit (4b)$P_8^0$ (see above) also shows that the great structural flexibility of phosphorus should enable the formation of cubane. The (4b)$P_8^0$ group can be understood as the polymerization product of an octaphosphacuneane (Fig. 7g), which is itself an isomer of cubane. Analogous statements can be made for a $P_6$ prismane. The structural units of the heptaphosphides $LiP_7$ or $RbP_7$[5] are not only derivatives of the $P_7^{3-}$ cluster, but can at the same time be considered to be derivatives of the polymeric $P_6$-prismane (Section 8).

## 7. Reactions at Polycyclic Anions

Obtaining molecules from metal salts is a familiar procedure—the preparation of acetylene from $CaC_2$ is one example. As far as the protolytic decomposition of the, in general very sensitive, phosphides, arsenides, silicides, germanides *etc.* is concerned, one has not got much further than the small hydrides, although (a) the existence of flexible polyanions such as $Sn_9^{4-}$ and $Sb_7^{3-}$ has already been proven by *Zintl*[84], (b) a whole series of higher hydrides were identified by *Baudler* among the insoluble *Stock*'s phosphanes, and finally (c) despite the fact that many research groups have worked on this problem. Refined chemical and physical methods have in recent years enabled the decisive first step to be made towards a systematic study of this class of substances. When one looks at the very simple methods, it seems puzzling today that this step was made so late and, partly, by chance. *Corbett* obtained crystalline salts of $Pb_5^{2-}$, $Sn_9^{5-}$, $Ge_9^{4-}$, $Ge_9^{2-}$ and $Sb_7^{3-}$ by using crown ethers[77,82,83,89]. *Kummer* obtained $Sn_9^{5-}$ and $Ge_9^{5-}$ from ethylenediamine in the form of solvated salts[82]. The last important step to substituted molecular clusters has not yet been made. If one thinks of the tetrahedral cluster $Si_4^{4-}$ or the $Si_4$ star (cf. Section 6), it should be worth every effort.

After the discovery of the polycyclic phosphides it was shown that they could yield $P_7H_3$, $P_{11}H_3$ and other phosphanes[5]. It also became clear that the yellow insoluble *Stock*'s phosphanes possess quite different characteristics according to the phosphide used [$(PH)_x$ from NaP with the $^1_\infty P^-$ chain; $P_7H_3$ from $Na_3P_7$ with the $P_7^{3-}$ group]. In 1979, *Baudler et al.* succeeded for the first time in obtaining the colorless $P_7H_3$ on a preparative scale by careful hydrolysis of $Li_3P_7$[95].

For the future, however, the synthesis of substituted clusters such as $P_7(SiMe_3)_3$ is of decisive importance. In 1975, *Fritz* and *Hölderich* succeeded in this synthesis, together with the preparation of Si-substituted groups such as $P_4(SiMe_2)_3$ in a one-pot process[90]. Soon afterwards, $P_{11}R_3$ and $As_7R_3$ were obtained and characterized[103] (Fig. 8). Their structures clearly prove that a description of this cluster system according to *Wade* (cf. *Belin*[156]) does not fit, because without doubt 14 electron pairs are reserved for the *exo*-cyclic bonds.

The synthesis is now fairly well optimized and gives high yields[104]. In this case, an old piece of chemical wisdom turned out once more to be true; that only microcrystalline ("amorphous") starting materials can be used for this heterogeneous reaction. Well-crystallized samples of $Na_3P_7$ and $Cs_3P_{11}$, for example, hardly react at all with $SiMe_3Cl$[104].

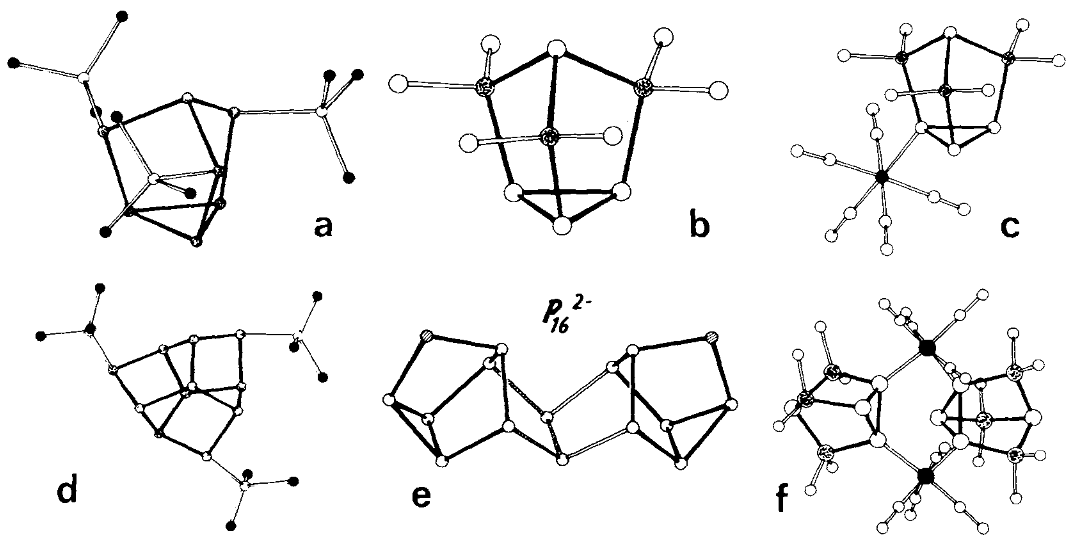


Fig. 8. Cluster molecules $P_7R_3$ and $As_7R_3$ (a), $P_4Si_3R_6$ (b) and $P_{11}R_3$ (d). Metal(0) complexes with $P_4Si_3R_6$ ligands (c, f) and the novel polyanion $P_{16}^{2-}$ (e) (cf. text).

The remarkable flexibility of the P—P bonds is not only reflected in the valence tautomerism of $P_7^{3-}$ and the abundance of different structures, but shows itself as well in the thermal decomposition and build-up of the phosphides, phosphanes, and substituted phosphanes. Molecules such as $P_9R_3$, $P_{14}R_4$ and $P_{16}R_2$ have already been discovered in mass spectra[90,103]. The anion $P_{16}^{2-}$ belonging to $P_{16}R_2$ (Fig. 8e)—the largest phosphide known—was only very recently trapped as a $Ph_4P^+$ salt[106]. The cluster $P_{16}^{2-}$ can be considered as a condensation product of $P_7^{3-}$ and $P_9^{3-}$. The salt is, by the way, the first polyphosphide without a metal cation and, because of its solvent properties, indicates a way of synthesizing polyanions at fairly low temperatures.

Some of the cluster molecules mentioned are excellent complexing agents for metal carbonyls[107-109] (cf. Fig. 8c, f). A lot more reactions are expected here. The chirality of $P_7R_3$ and $P_{11}R_3$ is also worthy of note; it could become useful for selective syntheses.

## 8. Condensed Polyanions

The condensation of chains to rings and finally to nets, as well as the condensation of polycyclic anions, lead with progressive oxidation successively to the structures of the elements. The richness in forms observed for phosphorus is reflected in the various structures of the condensed anions, which lead directly to *Hittorf*'s phosphorus, to black phosphorus, to gray arsenic and also to possible new forms of a three-bonded element[5].

It has already been shown for the one-dimensional infinite chains of two-bonded atoms and their fragments that, for the same number of homonuclear bonds and with constant bond angles, different types of structure can occur through changes in conformation, such as a torsional rotation. For higher condensed systems, the number of structural possibilities is still larger. Six-membered rings can occur in the chair or boat form and the additional linkages to tetrahedral or ψ-tetrahedral atoms can take place equatorially and axially (Fig. 9). The poly-phosphides, -arsenides and -antimonides, as well as silicides, germanides and stannides[7a,110] offer plenty of impressive examples.

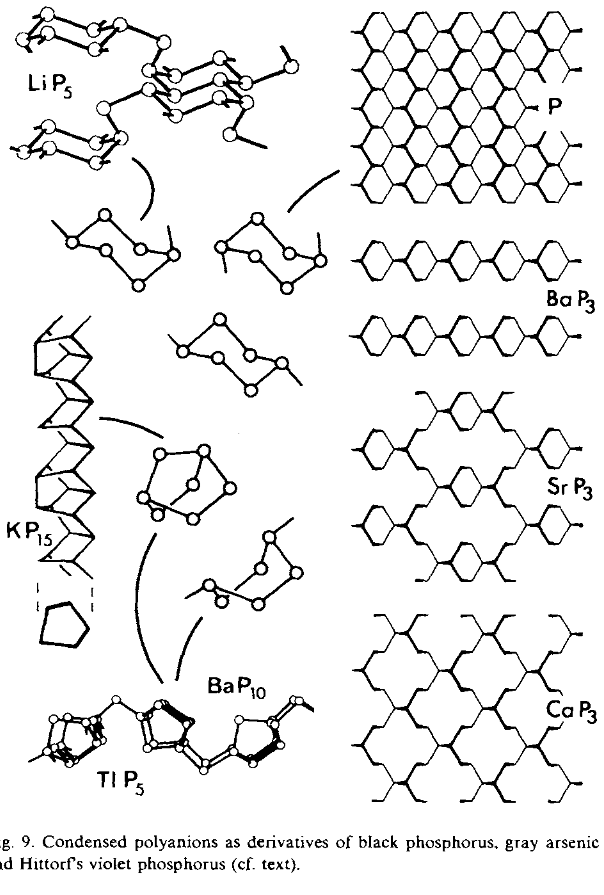


Fig. 9. Condensed polyanions as derivatives of black phosphorus, gray arsenic and Hittorf's violet phosphorus (cf. text).

The structures of orthorhombic black phosphorus and gray rhombohedral arsenic are known to differ solely in the

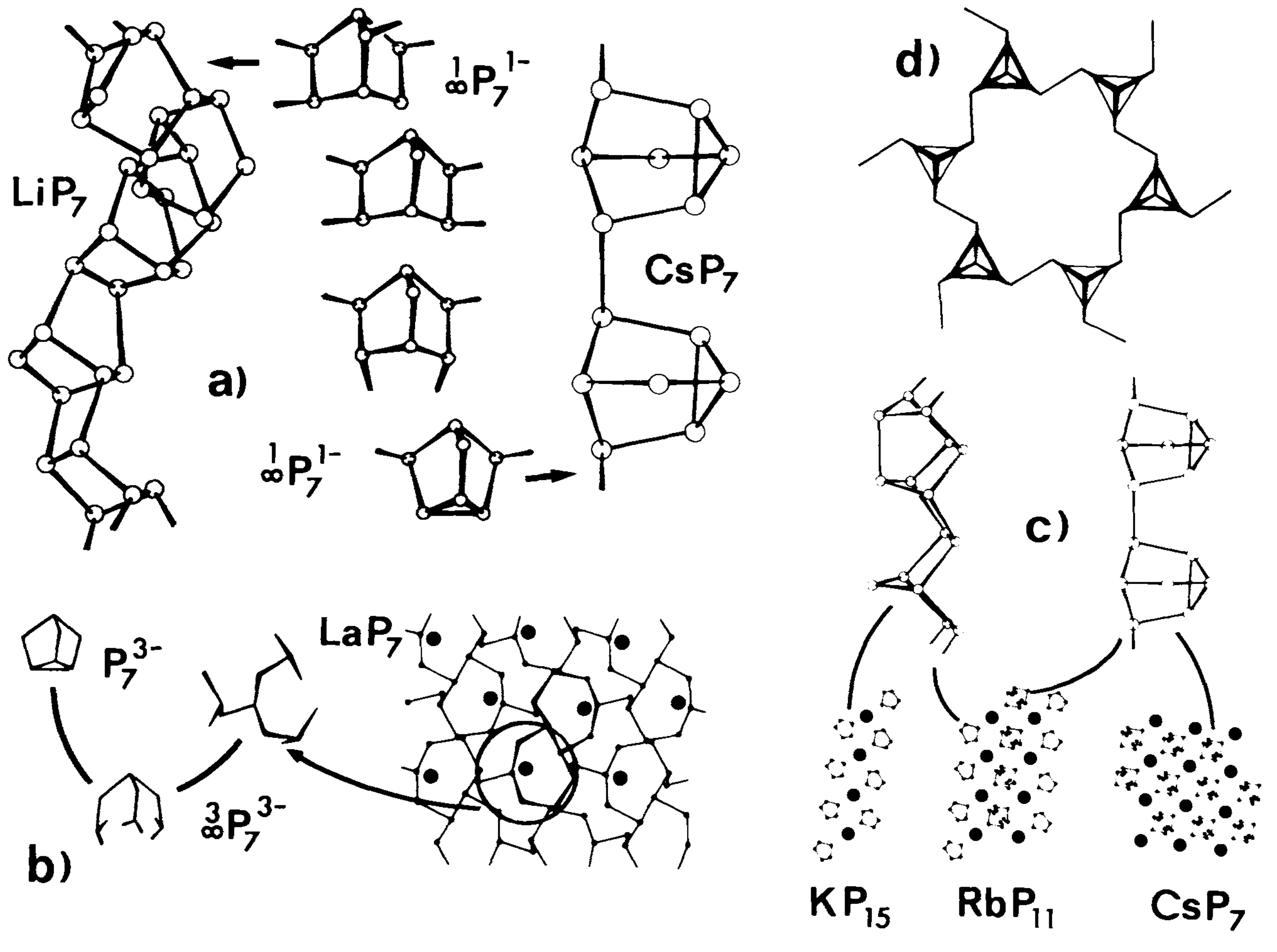


Fig. 10. Condensed polyanions from $P_7$ and $P_8$ clusters. a) Four sterical variants of $(3b)_6(2b)_1P_7^{1-}$; they lead to the helical LiP$_7$ structure and the linear CsP$_7$ structure, from which the monomeric $P_7^{1-}$ prismane derivative could be obtained by a further ring-closure. The two norbornane analogues (center) form the two-dimensional structure of $K_4IP_{21}$, for example. b) The nortricyclene $P_7^{3-}$ forms, after ring-opening, the three-dimensional polymeric LaP$_7$ structure. c) The combinations of the translationally commensurate units $P^1_{15}$ and $(P_7^{1-})_2$ leads to the RbP$_{11}$ structure. A peculiar feature of the $P^{1-}_{15}$ structure is the $P_8$ unit, which can be regarded as the polymeric form of an octaphosphacuneane. d) Six-membered ring of $P_7^-$ cluster, which with its chair conformation and its exocyclic bonds could built up a hypothetical "superphosphorus" of the gray arsenic type.

linkage of their condensed six-membered rings in the chair conformation, which in the case of arsenic is fully equatorial, for black phosphorus, however, partly axial. This leads in one case to a relatively slightly puckered structure, in the other case to a strong buckling of the layers. The phosphides, arsenides and antimonides $MX_3$ of the divalent metals modify the structure of black phosphorus in the sense that one quarter of the three-bonded atoms are removed from the two-dimensional framework. In this way, structures come into being which only contain one $(3b)X^0$ and two $(2b)X^-$, in accordance with the formulation. The overall picture remains of a structure with strongly buckled two-dimensional infinite polyanions[5]. The positions of the atoms which form the polyanion also remain almost unchanged from those in black phosphorus. The structures of CaP$_3$[66], SrP$_3$[111] and BaP$_3$[112] differ, however, in the arrangement of the vacancies, in that, in the first case, all the six-membered rings are broken up, in the second case only some of the six-membered rings exist, and in the third case one-dimensional infinite chains of linear condensed six-membered rings remain (Fig. 9).

The linkage of the six-membered rings is different in the structure of LiP$_5$[120]. Here, bands of condensed six-membered rings in the chair form are connected *via* two-bonded P atoms, which take up equatorial and axial positions in equal numbers. This structure is, in a sense, an intermediate stage between the structures of black phosphorus and gray arsenic.

If the six-membered rings are present in the boat form, there is a notable limitation: the possibility of an axial-equatorial linkage in the 1,4 position, as realized in LiP$_5$, is missing, since the boat is closed up to a norbornane structure as soon as one axial position is occupied (Fig. 9). The linkage of these $E_7$ units can take place in different ways. Important examples are KP$_{15}$, HgPbP$_{14}$, TlP$_5$ and BaP$_{10}$[114-117], in whose structures units of this type occur as sections of characteristic one-dimensional infinite tubes with a five-cornered cross-section. Also found in the structures are known elements such as the $As_4S_4$ molecule, which is present in KP$_{15}$ as a $P_8$ unit with four equatorial linkages in the *trans* position (Fig. 10c). The analogy between this unit and an (in this case polymeric) octaphosphacuneane has already been discussed in Section 6. The structures of TlP$_5$ and BaP$_{10}$ are completed by six-membered rings in the boat conformation with 1,4-equatorial linkages. This configuration leads in this case to linkage of the five-cornered tubes to two-dimensional infinite layers.

The linkage of the mentioned norbornane $E_7$ offers a series of possibilities which have been realized in its structural chemistry. If we assume that one of the 7 atoms is 2-bonding and the rest 3-bonding, then the 2-bonding atom is either, as the bridging atom across the six-membered ring, a member of both five-membered rings, or is just a member of the six-membered ring. Four atoms are in a position to form further bonds in both axial and equatorial directions (Fig. 10a). If the 2-bonded atom is in the bridge position, the linking bonds are in the equatorial direction and a linear structure results. If the linkages are both equatorial and axial, a two-dimensional aggregate results. These two elements govern the structure of $K_4IP_{21}$ and $Rb_4IP_{21}$[5,56,118].

If axial bonds in the 1,3 position saturate each other, a three-membered ring can form and give the above-mentioned nortricyclene system which is typical for $P_4S_3$ and the $X_7^{3-}$ anions. Here, however, the system is bonded at two extra positions, so that in the case of the polyphosphides the polyanion ${}^{1}_{\infty}P_7^{1-}$ forms. This structure is typical of the heptaphosphides of the large alkali metals $RbP_7$ and $CsP_7$[5,118]. The monomeric form of the anion ${}^{1}_{\infty}P_7^{1-}$, which is still hypothetical, can be obtained by a further ring-closure. The anion is particularly interesting as a prismane derivative. The linkage of the polymeric ${}^{1}_{\infty}P_7^{1-}$ chain can be broken by two electrons, giving the isolated anion $P_7^{3-}$. This unit does not have to be molecular, of course, it can polymerize as well by breaking the three-membered ring. In this form it builds the spatial network of the polyanion ${}^{3}_{\infty}P_7^{3-}$ in $LaP_7$ and $CeP_7$[5,119] (Fig. 10b).

If the two-bonded atom of the $X_7^{1-}$ unit is a member of the six-membered ring, then further linkage must lead to a helical structure. This is typical of the heptaphosphides of the small alkali metals $LiP_7$ and $NaP_7$[5,120]. It can be shown using the structures of the alkali metal heptaphosphides that K is too large for the $LiP_7$ structure and too small for the $RbP_7$ structure. In agreement with this, no "$KP_7$" has been prepared; instead, in the presence of iodine, only the "ersatz-$KP_7$", $KI \cdot 3KP_7 = K_4IP_{21}$ is formed[56].

The dimensions of the one-dimensional infinite linked $P_7^{1-}$ units in the $RbP_7$ structure agree exactly with the dimensions of the one-dimensional infinite five-cornered tubes of the $P_{15}^{1-}$ type, which are contained in the alkali metal compounds $MP_{15}$ (Fig. 10c). In fact, both units occur together in the compounds $RbP_{11}$ and $CsP_{11}$ and the geometrical commensurability allows us to expect the existence of further phases[5,118].

Not many chemical elements can, like phosphorus, claim to be produced and used in large quantities and simultaneously keep the secret of their structure so stubbornly. The latest investigations have done nothing to change this[121]. For red phosphorus one can say: Where nothing is known, one can speculate! *(K. Lorenz)*. The structural variety of the polyphosphides offers sufficient encouragement. A particularly colorful aspect is supplied by the $P_7^{3-}$ and $P_{11}^{3-}$ clusters, which, with the three 2-bonded P atoms polymerize exactly three times and form a "superphosphorus". A model consisting of condensed six-membered rings of pseudo-atoms (3b)[$P_7$] can at any rate be easily built and represents one of many possibilities (Fig. 10d). Also the condensation of these six-membered rings to a two-dimensional infinite structure can be easily realized by a model.

## 9. Mixed Phases and Phase Widths

Both terms are often used as an alibi for non-treatment. In textbooks and articles on cluster compounds, the "intermetallic compounds" which include much of what is discussed here, are often disposed of with the remark: they often possess large phase widths. In fact, this is only true for very few phases, since, more often than not, a series of closely-spaced stoichiometric compounds turns up. Genuine statistical distributions of various atoms over equivalent positions are, at most, preferred at high temperatures to the separation into suitably organized structures. The formation of clusters, whether strongly or weakly bound, is one of the possibilities for such suitably organized structures. Clusters, or analogous structural regions, take the place of the single atoms. The breakdown of a region of homogeneity into closely-spaced phases can be regarded as the formation of a series of compounds of "higher order". This kind of phenomena has not been studied enough up to now. The value of such studies will be briefly indicated with the following examples.

$Rb_3P_7$, $Rb_3P_{11}$, $Cs_3P_7$ and $Cs_3P_{11}$ possess practically the same structure; namely, a cubic $Li_3Bi$ arrangement in which the Bi atoms are replaced by the centers of $P_7^{3-}$ or $P_{11}^{3-}$ groups[122] (cf. Fig. 11a), as observed for $Na_3PO_4$, for example[123]. The orientation of the anions is random, as in plastic phases. There is good evidence for a continuous series of mixed crystals $M_3(P_7, P_{11})$ which is strange, since apart from the charge the anions have little in common. An interesting question is whether the reaction described above, $Na_3P_7 + P_4 \rightleftarrows Na_3P_{11}$, takes place here in the solid state, *e.g.*

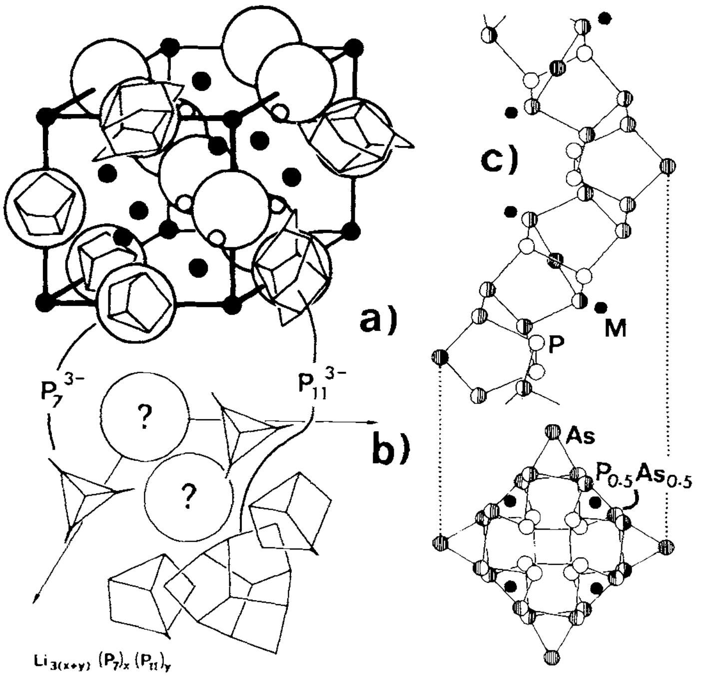


Fig. 11. Mixed crystals: a) $Li_3Bi$ as parent structure for $Cs_3P_7$, $Cs_3P_{11}$ and the mixed crystals $Cs_3$ ($P_7$, $P_{11}$) with statistical distribution and orientation of the cluster anions. b) Section of the hexagonal structure of the "red lithium phosphide" $LiP_x$ with partially ordered $P_7^{3-}$ and $P_{11}^{3-}$ as well as disordered (?) polyanions. c) Structure of the helical polyanions ${}^{1}_{\infty}X_7^{1-}$ in $LiX_7$ and $NaX_7$ with $X = P_{0.5}As_{0.5}$ (projections perpendicular to and along the fourfold helix). The As atoms occupy preferentially the peripheral positions, the P atoms the central part of the polyanion.

by $P_4$ diffusion. Mixed-order phases have not yet been observed here, but in the system Li/P, besides yellow $Li_3P_7$, a red phosphide $LiP_x$ exists with ordered $P_7^{3-}$ and $P_{11}^{3-}$ groups in the ratio 2:1, as well as a further orientation-disordered group[124]. The compounds $RbP_{11}$ and $CsP_{11}$ can also be treated as ordered phases in a mixed-crystal series between $MP_7$ and $MP_{15}$ (cf. Section 8). The marked tendency to twinning also indicates great mobility and perhaps also a variation in the stoichiometry at high temperatures (Fig. 11a, b).

Mixed crystals with different cluster-forming atoms can supply information on the function of the individual atomic positions. The peripheral positions of the ${}^1_\infty P_7^{1-}$ helix of $LiP_7$ and $NaP_7$ show a distinct preference for arsenic in $LiP_{3.5}As_{3.5}$[125] (Fig. 11c), while in $EuP_{3-3x}As_{3x}$ the preference of As for the $(2b)X^-$ position is weaker[126]. EuP forms the NaCl structure with $Eu^{III}$, but EuAs the $Na_2O_2$ structure with $Eu^{II}$. Mixed crystals with the EuAs structure go as far as 5 atom-% As; the rest possess the EuP structure[126]. Two important questions remain: (a) does the distribution of $P_2^{4-}$, $(PAs)^{4-}$ and $As_2^{4-}$ obey a mass-effect law? (b) How does the system behave at the boundary of the mixed series with respect to the redox reactions $2(Eu^{3+}+X^{3-}) \leftrightarrows 2Eu^{2+}+X_2^{4-}$?

## 10. Defect Structures

Several of the $MX_n$ compounds with homonuclear chains and rings (Sections 4 and 5) can be described as trigonal-prismatic defect structures. In these structures the metal atoms M form trigonal prisms in whose centers the X atoms lie. Two structure types with trigonal prisms which occur very frequently are $AlB_2$ and $\alpha$-$ThSi_2$ (Fig. 12). They differ in the relative orientation of the $M_6$ prisms, which, because of the three square faces of these polyhedra, can be varied in many different ways[127]. In the hexagonal $AlB_2$ type, all M prisms are oriented in the same way. The occupation of all centers by X atoms generates the well-known two-dimensional honeycomb structure of graphite. $Rb_4P_6$[55] and $Cs_4As_6$[56] are direct derivatives of this $Al_4B_8$ type, since, according to $M_4X_6\square_2$, a quarter of the X sites remain vacant in an ordered way and leave isolated planar $X_6$ rings. The defects and their order apparently depend on the valency.

If the prisms are rotated through 90° from one layer to the next, one obtains the $\alpha$-$ThSi_2$ type structure, which, on complete occupation of the prism centers, shows a characteristic three-dimensional network of three-bonded X atoms (Fig. 12). If the rotation takes place every second layer, an unknown tetragonal $MX_2$ type would result, containing a three-dimensional network of bands of $X_6$ rings rotated with respect to each other. The compounds $Eu_3P_4$[36], $Eu_3As_4$[35], $Sr_3As_4$[34], $Eu_2Sb_3$[32], $Ca_2As_3$[31] and $Sr_2Sb_3$[33] are defect structures of these two types with $M_3X_4\square_2$ or $M_4X_6\square_2$[128]. The ordering of the defects caused by the valency conditions can lead to chains of various lengths and conformations (Fig. 12). The pair of compounds $Ca_2As_3$ and $Sr_2Sb_3$ are noteworthy, since a chemical reaction, $X_4^{6-}+X_8^{10-} \leftrightarrows 2X_6^{8-}$, can take place simply by a reordering of the defects in the $M_6$ prisms. The search for such phase transitions would certainly be worthwhile.

While describing these structures as defect variants of $AlB_2$ and $\alpha$-$ThSi_2$ we were reminded that, in the case of the "disilicides" of the lanthanoids, compositions such as $MSi_{1.7}$ or $MSi_{1.4}$ are given, with very few exceptions[127]. Detailed studies have shown: (a) Only $EuSi_{2.0}$ possesses a completely occupied tetragonal $\alpha$-$ThSi_2$ structure, which fits into the picture of $Eu^{2+}$ and $(3b)Si^-$.—(b) The other silicides form the orthorhombic defect variant of $\alpha$-$ThSi_2$ ($\alpha$-$GdSi_2$) with $LnSi_{1.7}$ (Ln = lanthanoid) or the defect $AlB_2$ with $LnSi_{1.4}$ without noticeable phase widths.—(c) The vacancies in the defect $\alpha$-$GdSi_2$ structure can be filled with Ni, Cu, Ag, Au, Al, Ga. The structures are then, and only then, tetragonal. The occurrence of defects agrees with the model of finite $Si_x^{n-}$ chains, since the additional electrons from $Ln^{3+}$ should break Si—Si bonds. The length of the $Si_x^{n-}$ chains is, however, variable and their orientations are disordered[128].

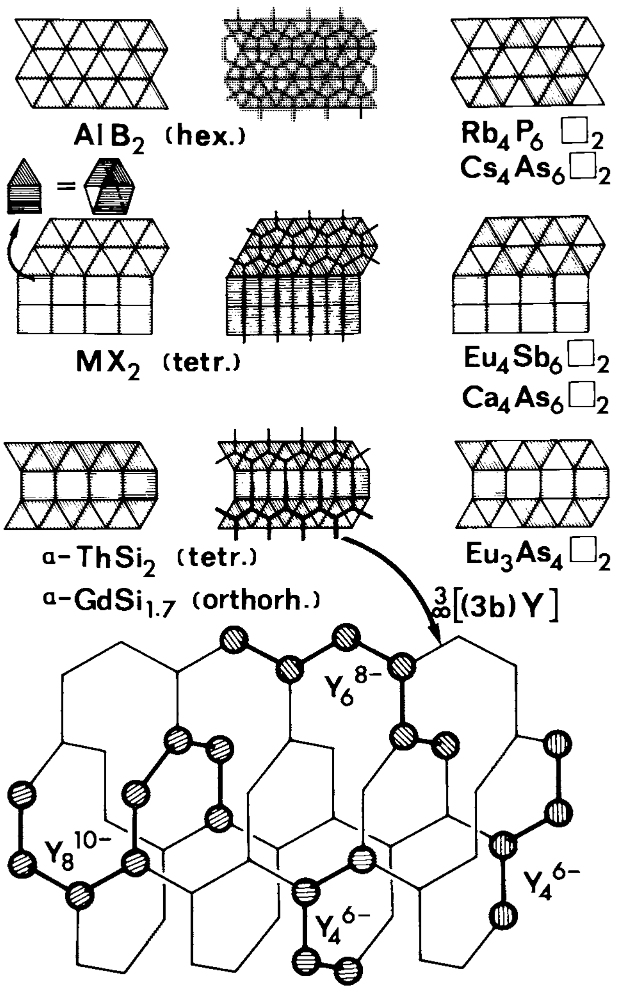


Fig. 12. Structures with metal prisms of the type $AlB_2$, $\alpha$-$ThSi_2$ and a hypothetical $MX_2$ compound with some defect variants. (above left: arrangement of the $M_6$ prisms; above center: prisms with the anion network; above right: order of defects; empty prisms are not shaded.) The ordering of the defects leads for $Rb_4P_6$ to isolated $P_6$ rings, but for the other structures to various anionic chains. In the lower part such chains are shown as sections of the Si sublattice of $\alpha$-$ThSi_2$.

A series of compounds apparently exists too, in whose structures the Si network of the $\alpha$-$ThSi_2$ type is broken up step by step. The final member of the series is the NbAs structure type with isolated $X^{n-}$ anions[127].

## 11. Real and Hypothetical Reactions in the Solid State

*Dunitz* and *Bürgi* have shown how one can obtain far-reaching information on chemical reaction paths from the details of static crystals structures[129]. Compounds with cluster anions can also be used for such studies. Firstly, the comparison between configurations and conformations of the polyanions on changing the cation allows statements to be made on the dynamics of the homonuclear structure. The various compounds can be regarded as frozen-in reaction steps and assigned to a reaction coordinate. Secondly, phase transitions are excellent subjects of study, above all when they go to higher order. Only a few investigations have been made in this area, and it would be of interest to mention some potential examples:

1. The phosphides $MP_{15}$ and $MP_{11}$ form, without exception, twinned crystals, the orientation of which stems from the ordering of the cations in channels of the structure. At high temperature, a mobility of the cations can be assumed which is accompanied by changes in the covalent bonds in the polyanion.

2. The possible reordering of the $X_n$ chains in derivatives of the $ThSi_2$ and $AlB_2$ structures has been referred to in Section 10. The diphosphides and diarsenides of the lanthanoids $LnX_2$ offer a similar example of a molecular reaction in the course of a phase transition. At low temperature, the $CeP_2$ type forms[5,30,130] with $X_4^{6-}$ and at high temperature the $LaP_2$ type[29] with $(X_3^{5-} + X_5^{7-})$ (cf. Fig. 13a).

3. $Th_2P_{11}$, the compound with the highest non-metal content known for a four-valent metal, is a particularly attractive example of a frozen-in ring-opening reaction with an $S_N2$ mechanism[65]. The polyanion sublattice forms bands of condensed $P_6$ rings (boat) and $P_8$ rings ($C_{2h}$ symmetry). Inserted between these are $P_6$ rings in the chair conformation and $P_3$ fragments of such rings. The $P_3$ fragments are all joined to the polyanion bands. A periodic modulation is present in the crystal resulting from a sequence of closed and opened $P_6$ rings. This modulation is, therefore, caused by a valency effect and is generated by the turning of a single P—P bond which opens the ring and joins the fragments to the polymeric anion with a simultaneous 1,4-charge transfer (Fig. 13b). At room temperature both of the boundary states are frozen in, giving the environment of the "mobile" P atom the configuration of the boundary states of an $S_N2$ reaction. The evidence suggests that at higher temperatures this process takes place in the crystal (perhaps with varying modulation wavelength).

4. The pentaphosphides of the trivalent lanthanoid cations, $LnP_5$, form a polyanion $^1_\infty(P_5^{3-})$ out of condensed $P_{12}$ rings. The structure can be derived from a hypothetical P modification with condensed six-membered rings in the boat form[5,69,131]. The polyanion adapts itself to the size of the

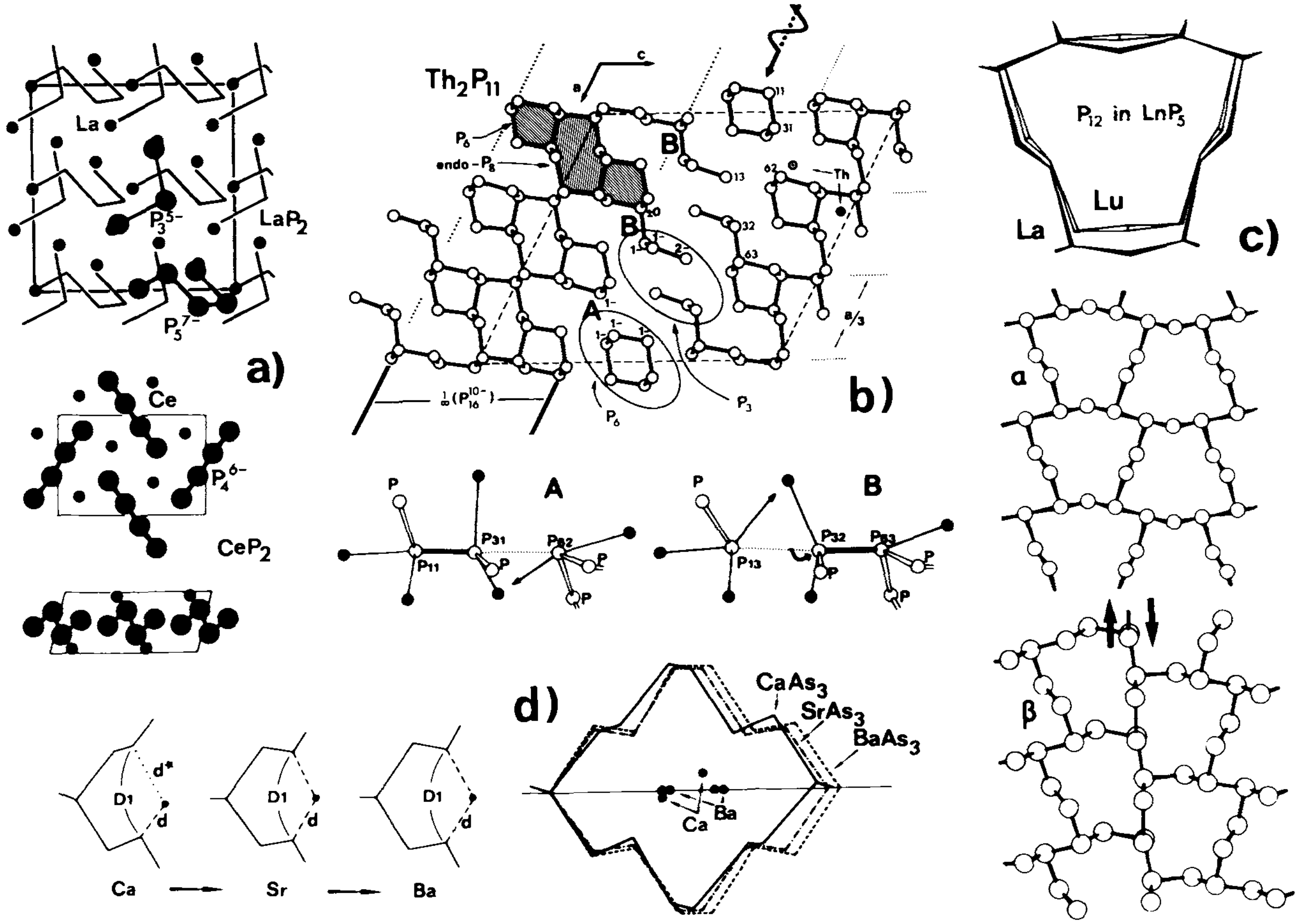


Fig. 13. Solid structures as models for reactions and reactions paths. a) High temperature and low temperature forms of $LnP_2$ and $LnAs_2$ with $X_4^{6-}$, and $X_3^{5-} + X_5^{7-}$, respectively. b) Part of the $Th_2P_{11}$ structure with the polyanionic band, built up from $P_6$ and $P_8$ together with the inserted $P_6$ rings and $P_3$ fragments. The modulation (arrow) along the *a*-axis results from a sequence of closed (A) and fragmented (B) $P_6$ rings. The configurations A and B exhibit the details of a frozen-in $S_N2$ reaction (center of the figure). Notice the formal charge transfer. c) Adaption of the $P_{12}$ ring to the sizes of the $Ln^{3+}$ ions in $LnP_5$ as a model for a reaction induced by pressure. The transition from α-$YbP_5$ to β-$YbP_5$ exhibits besides the volume contraction a shearing of the polyanion. d) Change in the conformation of the $As_{14}$ rings on substituting Ca by Sr and Ba as steps in a phase transition. The abnormal change in the conductivity goes hand-in-hand with the changes in non-bonding As—As distances D1.

cation in the series La–Lu by altering the P—P bond lengths and by conformational changes (Fig. 13c). β-$YbP_5$ forms a more closely-packed variant of the structure, which results formally from the first by a relative shift of the points where the condensation occurs at the twelve-membered rings. The structures of the $LnP_5$ series can be interpreted as stages of a reaction path brought about by application of pressure.

5. Triclinic $CaP_3$ passes at 990 K through a phase transition to give the monoclinic $SrAs_3$ structure. The induction period for this transition is very long[132]. The bonding in the polyanion remains unchanged; the only changes take place in the conformation. The details have not yet been investigated, but $T_c$ can, for example, be changed progressively in the isostructural mixed-crystal series $Ca_xEu_{1-x}As_3$[133]. The stages of the supposed reaction path are given by the series $CaAs_3$ (triclinic), $SrAs_3$ (monoclinic) and $BaAs_3$ (monoclinic). It is remarkable in this context that this series represents a transition from a semiconductor to a meta-metal and back to a semiconductor, which is connected with the change in a non-bonding distance in the polyanion $^2_\infty(As_3^{2-})$[134].

## 12. The Electrostatic Treatment of Cluster Compounds

Terms like ions or ionic bond elicit no more than a cynical smile from the colleagues of the ruling covalent clique. As always in times of an all-powerful doctrine, the dissenter has to knuckle under and recite his creed in secret, but anyone who wants to harvest in his lifetime cannot afford to wait for the *ab initio* theory of weather! Chemists are like farmers: they believe in rules, but are cunning enough to be able to interpret them as the occasion demands.

The compounds with homonuclear linkages which are discussed here actually have nothing to do with electrostatically balanced systems, since, in the formal ion model, equally-charged particles are close neighbors. *Kapustinskii*, however, has pointed out a remarkable phenomenon[135]: he showed that the enthalpy of formation of a solid can be calculated with sufficient accuracy from the Born-Haber cycle if one treats the transition $a\cdot M^{m+}(g) + b\cdot X^{n-}(g) \rightarrow M_aX_b(s)$—whatever its structure may be—with the expression $U_K = k\cdot A\cdot \nu\cdot z_1\cdot z_2\cdot R^{-1}$ ($k$ = constant; $A$ = Born repulsion; $\nu$ = sum of the ions $a+b$; $z_i$ = charge on ion "i", *e.g.* $m+$ and $n-$; $R$ = distance M—X, *e.g.* sum of the ionic radii). If $\nu z_1 z_2$ is replaced by $\sum z_i^2$, the relationship to the lattice potentials of the individual ions is obtained directly[136]. The decisive thing is that the constant $k$, apart from some conversion factors, contains *solely* the Madelung constant of the NaCl structure ($k \sim \frac{1}{2}\text{MF(NaCl)} = 0.8738$), *i.e.* with respect to the total energy: "Everything is rock salt!" in other words, nature does not do any more than it has to. Whatever the details of a real crystalline structure $\{M^{\delta+}X^{\delta-}\}_{\text{real}}$, however large the effective charges δ+ and δ− and the covalent part of the bond might be, it is energetically no more than if rigid particles with the picture-book charges $m+$ and $n-$ were joined together with the typical distance $R$ for condensed phases to a NaCl structure. The lattice energy $U_{BH}$ of a compound MX, which is inserted in the Born-Haber cycle, can therefore be written:

$$U_{BH}(\text{MX-real structure}, \delta+, \delta-) = U_K(\text{NaCl-structure}, 1+, 1-)$$

I would like to comment at this point that *Klemm* gave "effective Madelung constants" as early as 1931 for tetrahedral structures, for example, which made such structures energetically similar to NaCl[138]. The covalent age, which was then just beginning, prevented these ideas from being followed up.

The surprising example of niobium monoxide NbO has already been referred to [2]. This structure is, independent of the covalent Nb—O bonds, strongly characterized by the Nb—Nb bonds. Nevertheless, the experimental enthalpy of formation $\Delta H_f$ yields an "experimental" lattice energy $U_{ex}$ for the real structure, which is just as large as NbO would have with $Nb^{2+}$ and $O^{2-}$ in the NaCl structure.

On the other hand, if one calculates the electrostatic lattice energy of the real structure with the ideal charges 2+ and 2− (MAPLE after *Hoppe*[137]), the difference between $U_K$ and MAPLE is $\Delta E = 560\ \text{kJ}\cdot\text{mol}^{-1}$, which could certainly be the energy of the entire metal-metal bonding of an $Nb_6$ cluster

$$U_{BH} = U_K = \text{MAPLE} + \Delta E$$

with $\text{MAPLE} \mathrel{\hat{=}} U(\text{MX-real structure}, 2+, 2-)$ and $\Delta E \mathrel{\hat{=}}$ non-electrostatic part of the lattice energy.

The first problem is how to count up the energy of the individual bonds in an $M_6$ cluster of this type. This is different for the clusters of the main group elements. As shown above, these compounds largely follow the simple rules of bonding. For the following calculation, the binary MX compounds were used. These include, for example, NaS ($Na_2S_2$), NaP with $^1_\infty P^{1-}$, NaSi with $Si_4^{4-}$ and all the appropriate homologs. The formal ion $X^{1-}$ is common to all these compounds,

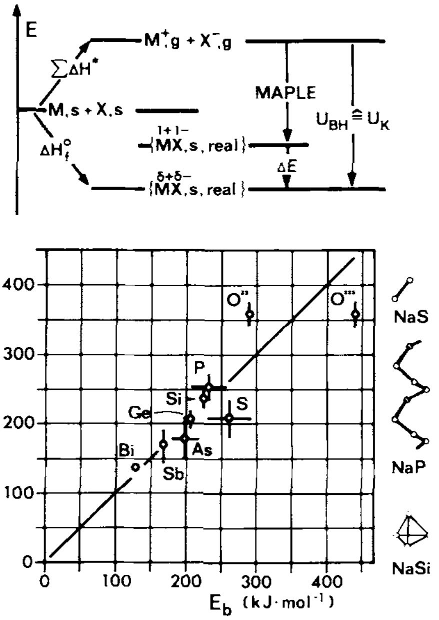


Fig. 14. Simplified Born-Haber cycle (top) with the enthalpy of formation $\Delta H_f$, the various terms of the excitation energy $\sum\Delta H^*$ and the lattice energy $U_{BH}$. According to *Kapustinskii* $U_K$ can be used as a good approximation for $U_{BH}$. $U_K$ should be composed of the Madelung part of the lattice energy MAPLE (calculated for the real structure with $z = \pm 1$) and the homonuclear bond energy $\Delta E$. Below: correlation of $\Delta E$ with the homonuclear bond energy $E_b$ [139] for representatives of the NaS, NaP and NaSi families. The deviations of $\Delta E$ result from various structures (cf. Table 1). The deviations in $E_b$ for some elements result from taking the repulsive electronic effects into account, *e.g.* O'' and O''' [139].

but it possesses different homonuclear X—X contacts (Fig. 14). The MAPLE lattice energy was calculated for the real structure $\{M^{1+}X^{1-}\}_{real}$, and subtracted from the $U_K$ calculated for a hypothetical NaCl structure according to *Kapustinskii*. For the calculation of $U_K$, $R$ was determined from the real molar volumes $V_m$, as the distance M—X in an NaCl structure with the volume 4 $V_m$. The differences $\Delta E$ agree surprisingly well with the usual homonuclear binding energies[139] (Fig. 14). The number of bonds was counted in the classical manner for the atoms in the polyanions; *e.g.* $Si_4^{4-}$ tetrahedrane contains six Si—Si bonds. The individual values for the various compounds do not show much scatter (Table 1), but have a certain trend $\Delta E \sim R$. This is related to the fact that, for constant homonuclear bond lengths, the cluster atoms get, *relatively,* closer together, as the elementary cell or the M—X distance becomes larger. Whether this really points to increasing $\Delta E$ values, or is compensated for by sinking effective charges, or is simply the result of incorrect methods, still has to be investigated. Whatever the answer, this electrostatic treatment of cluster compounds promises to provide, for the metal cluster too, a useful estimation of the binding energy for the homonuclear regions.

Table 1. Homonuclear bond energy $\Delta E$(X—X) from electrostatic calculations. See text and Figure 14 for the definitions of MAPLE and $U_K$. The Born repulsion was not taken into account. $R$ is the distance MX of an NaCl structure and a $CaF_2$ structure, respectively, with the same molar volume. The factor $m$ accounts for the number of X—X bonds per formula unit.

| MX | Ref. | MAPLE [a] | $U_K$ [a] | $R$ [pm] | $\Delta E$ [a] | $m$ | $\Delta E$(X—X) [a] |
|---|---|---|---|---|---|---|---|
| NaSi | [50] | 492 | 838 | 290 | 346 | 0.67 | 231 |
| KSi | [16] | 430 | 769 | 316 | 339 | 0.67 | 227 |
| RbSi | [16] | 393 | 744 | 326 | 351 | 0.67 | 235 |
| CsSi | [16] | 354 | 720 | 338 | 366 | 0.67 | 245 |
| NaGe | [50] | 514 | 824 | 295 | 310 | 0.67 | 208 |
| KGe | [16] | 457 | 760 | 320 | 303 | 0.67 | 203 |
| RbGe | [16] | 424 | 736 | 330 | 312 | 0.67 | 209 |
| CsGe | [16] | 390 | 710 | 342 | 320 | 0.67 | 214 |
| NaP | [28] | 635 | 871 | 279 | 236 | 1 | 236 |
| KP | [28] | 531 | 803 | 302 | 272 | 1 | 272 |
| LiAs | [105] | 776 | 926 | 262 | 150 | 1 | 150 |
| NaAs | [94] | 657 | 839 | 289 | 182 | 1 | 182 |
| KAs | [94] | 558 | 772 | 314 | 214 | 1 | 214 |
| NaSb | [105] | 640 | 783 | 310 | 143 | 1 | 143 |
| KSb | [113] | 551 | 722 | 336 | 171 | 1 | 171 |
| RbSb | [140] | 526 | 697 | 348 | 171 | 1 | 171 |
| CsSb | [140] | 489 | 678 | 358 | 189 | 1 | 189 |
| $PtAs_2$ [b] | [141] | 2628 | 2824 | 258 | 196 | 1 | 196 |
| $PtBi_2$ [b] | [141] | 2379 | 2517 | 289 | 138 | 1 | 138 |
| $Na_2O_2$ | [142] | 876 | 1048 | 231 | 172 | 2 | 344 |
| $K_2O_2$ | [142] | 735 | 908 | 267 | 173 | 2 | 346 |
| $Rb_2O_2$ | [142] | 675 | 864 | 281 | 189 | 2 | 378 |
| $Cs_2O_2$ | [142] | 631 | 818 | 297 | 187 | 2 | 374 |
| α-$Na_2S_2$ | [143] | 770 | 860 | 282 | 90 | 2 | 180 |
| β-$Na_2S_2$ | [143] | 772 | 861 | 282 | 89 | 2 | 178 |
| $K_2S_2$ | [143] | 659 | 778 | 312 | 119 | 2 | 238 |
| $BaS_2$ [b] | [144] | 2042 | 2284 | 306 | 242 | 1 | 242 |
| $FeS_2$ [b] | [145] | 2916 | 3110 | 234 | 194 | 1 | 194 |
| $CaC_2$ [b] | [145] | 2209 | 2807 | 249 | 598 | 1 | 598 |

[a] $kJ \cdot mol^{-1}$. [b] $d_0(CaF_2)$; M(2+), X(1−).

The calculations yield an average value of $\Delta E = 361$ $kJ \cdot mol^{-1}$ for the O—O bond. This fits, in a qualitative way, the model that in the structures under study, the repulsive effect of free electron pairs is considerably reduced by the influence of the cations[139].

## 13. Again: The Bonding

*Schäfer, Eisenmann* and *Müller* discussed the Zintl phases some years ago in detail[8a], and contributed much more to this subject later[146]. They also dealt in depth with the question of those compounds for which the Zintl concept apparently fails, those which can be counted as belonging to metallic systems. Among these are above all the compounds of Li with the meta-metals[110], whose structures are variants of the body-centred cubic structure of metals. Clusters of metametal atoms $X_n$ are certainly found, but the valency sum often does not agree with the concept of formal ions. This effect has been explained by the agreement between the metallic radii of Li and X[147,148], that is, using the terminology of metallic phases. On the other hand, a significant relationship has been observed between the X—X distances and the electronegativity $\chi(M)$[8a], which, for example, leads to smaller distances $d_{XX}$ for lithium. This reduction in $d_{XX}$ can be traced back, not only to a reduction in the effective charge, but also to an increase in the classical Pauling bond order[149]. The two effects are interdependent. Lithium, the most electronegative of the alkali metals, also possesses the smallest cation and therefore the one with the largest polarizing influence. The reduction in the anion charge affects above all those states which are antibonding with regard to the X—X bonds, resulting in an increase in the bond order $n_{XX}$. Before these substances are pigeon-holed as intermetallic phases and removed in this way from simple valency considerations, one should remember that most of these phases are described as shiny metallic *and brittle.* Only a few are metallic and ductile. The decisive electrical properties have hardly been examined[150]. We recently established semiconductor behavior for some of these brittle Li phases. The violet $Li_{2.33}Si$ (formerly $Li_2Si$) belongs to these[151]. The diamagnetic phase contains $Si_2$ dumb-bells and, as $Li_{4.67}Si_2$, possesses a defect $M_5X_2$ structure *without* any sign of a significant phase width ($\rightarrow Li_{14}Si_6$).

With the help of several examples, it will now be shown that the bond-order concept leads to interesting results for the Zintl phases too. One obtains the bond order $n$ by comparing the bond lengths $d_n$ and $d_1$ according to *Pauling*[149] ($d_n = d_1 - k \log n$; $k = 60$—$71$ pm) or *Donnay-Allmann*[152] ($n = \{d_1/d_n\}^5$). The two expressions are equivalent, which can be shown by suitable transformation. We now turn to the Li-stannides[110] (Table 2). Using the simplified Mooser-Pearson relationship[17], the expected average bond orders for the anions X, $\bar{n}_{XX}$, can be calculated using the total number of electrons in the compound, $\sum e$, the number of "anions", $m_X$, and the average number of homonuclear bond lines observed in the structure, $\bar{b}_0$:

$$\bar{n}_{XX} = \bar{b}_c/\bar{b}_0, \quad \bar{b}_c = 8 - \sum e/m_X.$$

As shown in Table 2, $\bar{n}$ and the average distance $\bar{d}_{XX}$ agree with the Pauling formula $d_1(Sn^-) = 301$ pm. The values $\bar{n}_{XX}$ are apparently consistent with the variation in the distance $d_{XX}$. $d_1$ is, however, about 20 pm longer than the familiar single bond length $d_1(Sn) = 281$ pm. The same observation can be made for the polyanions of other elements. For example, $d_1(Sb^-) = 286$ pm, which is 12 pm longer than $d_1(Sb) = 274$ pm[140] and the same is true for other elements (*e.g.* $Li_2Sn_5$[8a], compared with β-Sn). An increase of 10—20 pm can be expected in the homonuclear bond lengths, if formal anions $X^-$ are directly bonded in place of neutral atoms $X^0$. If this is taken account of in the expected bond lengths $d_1(X^-)$ a clear indication of higher bond orders is obtained, which allows the Zintl phases to be treated as compounds with normal valency, even though this is forbidden according to the simple total number of topological linkages. The simple comparison between $d(X^-—X^-)$ and the distances in the element X is not very meaningful. Only if both near and far contacts are taken into account are the normal distances, $d_1(X) = 2r_{cov}$, obtained, as for example in the case of P, As, Sb, Bi with the condition $\sum n = 3$. For these elements, $n < 1$ holds for the shorter bonds too. This effect was used before by *Pauling* in deriving the metallic single bond radii.

Table 2. Effective bond order $\bar{n}_{XX}$, formal single bond lengths in polyanions $d_1(X\ \ )$ and the difference $\Delta d_1$ to the single bond lengths of neutral atoms $d_1(X)$ (cf. Text).

| | Ref. | $\bar{d}(X—X)$ [pm] | $\sum e$ | $\bar{b}_c$ | $\bar{b}_0$ | $\bar{n}_{XX}$ | $d_1(X\ \ )$ [a] [pm] | $\Delta d_1$ [pm] |
|---|---|---|---|---|---|---|---|---|
| $Li_7Sn_3$ | [110] | 294 | 19 | 1.67 | 1.33 | 1.25 | 301 | 20 |
| $Li_5Sn_2$ | [110] | 288 | 13 | 1.50 | 1.00 | 1.50 | 300 | 19 |
| $Li_{13}Sn_5$ | [110] | 286 | 33 | 1.40 | 0.80 | 1.75 | 303 | 22 |
| $Li_7Sn_2$ | [110] | 300 | 15 | 0.50 | 0.50 | 1.00 | 300 | 19 |
| $Li_{14}Si_6$ | [151] | 233 | 38 | 1.67 | 1.00 | 1.67 | 248 | 13 |
| $Li_{12}Si_7$ | [58] | 237 | 40 | 2.29 | 1.86 | 1.23 | 244 | 9 |

[a] $k = 70$ pm.

The above mentioned semiconductors, $Li_{14}Si_6$ ($Si_2$ pairs) and $Li_{12}Si_7$ ($Si_4$, $Si_5$) also turn out to be "normal" using this treatment. For the $Si_2$ pairs, the 233 pm distance, which is stretched by the charge, would correspond to the bond order $n = 1.67$. The $Si_4$ star with $\sum n = 3.7$ would be comparable to the carbonate anion and the $Si_5$ rings with $\sum n = 6.2$ would be comparable to cyclopentene[58].

Finally, a reference to $SiP_2$, a pyrite structure with short P—P distances (215 pm)[153,154]. The comparison with $PtP_2$ (P—P = 223 pm[155]) shows above all that the effective bonding state appears to lie between the limits ($Si^{4+} + P_2^{4-}$) with a P—P single bond and ($Si^{2+} + P_2^{2-}$) with a P=P double bond.

## 14. Plastic Phases

Crystals of plastic phases are soft and easily deformed. They form from the melt with a minimum thermal effect since the molecules or complex groups only lose their translatory degrees of freedom. The complex structural units often surround the positions of atoms in highly symmetrical simple structures and carry out free or only slightly hindered rotations. Sharp X-ray lines with rapidly falling intensity are typical for the plastic phases. Examples of these phases among the compounds discussed here are $Rb_3P_7$ and $Cs_3P_{11}$ (cf. Section 9) as well as white phosphorus and β-$P_4S_3$. While the two phosphides take up the structure of the intermetallic phase $Li_3Bi$ ($P_7$ and $P_{11}$ surround the Bi positions), it is interesting that $P_w$ and β-$P_4S_3$ do not follow simple metal structures. In crystalline white phosphorus, 58 $P_4$ tetrahedra surround the positions of the 58 Mn atoms in the unusually complex α-Mn structure[122,157], while the molecules in β-$P_4S_3$ envelope the positions of the 20 Mn atoms in the also complex β-Mn structure[122]. This behavior leads directly to the question of whether $P_4/P_4S_3$ mixed crystals can form, which has not yet been studied, but which could perhaps explain the strange behavior in the metastable part of the P/S system at around "$P_2S$". Four crystallographically different $P_4$ tetrahedra are present in crystalline white phosphorus. They are subjected to different crystal fields and differ from one other in their movement (Fig. 15). This difference is not observed in the NMR spectrum[158]. At 133 K only one of the $P_4$ tetrahedra is "frozen-in" (Fig. 15). A splitting in the NMR signals was attributed here to a lowering of the symmetry.

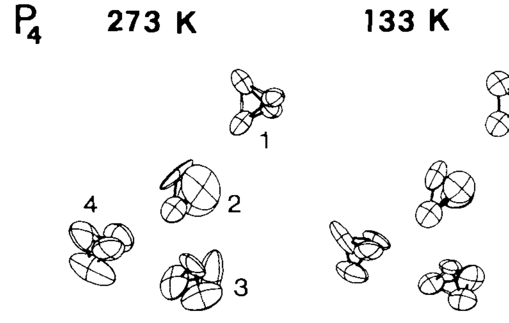


Fig. 15. The four independent $P_4$ tetrahedra in the structure of white phosphorus at 273 K and 133 K [122]. The hindered rotation is poorly described by the vibrational ellipsoids. The considerable changes on cooling to 133 K can, however, be recognized.

For β-$P_4S_3$, $Rb_3P_7$ and $Cs_3P_{11}$, the electron density in the region of the mobile clusters has not yet been analyzed in terms of preferred orientation. This has been done for white phosphorus, but the distances P—P = 195—200 pm are much too short. This effect is, however, typical, and results from the unsuitable algebraic treatment of the problem. The same is true for the P—P distances in the complex $[(np_3)Ni(P_4)]$[*] for example, which are also unreal[159].

## 15. Outlook

I had the impression a few years ago that there was not much more to learn about the cluster compounds of the main group elements. The astounding developments of recent years have taught me better. Apart from the work discussed here I would like to mention the studies made by my fellow-countrymen *Jeitschko*[160], *Schuster*[161] and *Schäfer*[146], who–representative of many colleagues in the world–by combining main group elements with transition elements, opened up new aspects of the problems of homonuclear linkages. The systematic investigation of simple classes of substances seems to promise a wealth of unforseeable experiences for the hunter and collector. Clear vision is, of course necessary, but, provided with the right pair of spectacles, one can even see cluster units in NaCl (Fig. 16).

Cluster compounds are sophisticated redox systems in the solid state, and simultaneously potential generators of interesting molecular compounds. The systematic investigation of physical properties and of chemical behavior are equally im-

---

[*] $np_3$ = tris[2-(diphenylphosphino)ethyl]amine.

portant. As always, we are just at the beginning. This was emphasized by *Klemm* as early as 1943, with a remark that is still topical today: in determining physical data one has to struggle less with the method than with the unyielding substance[162].

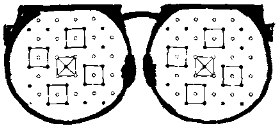


Fig. 16. The author's spectacles for discovering clusters in any structure.

One important aim is to bridge the unnatural gap between molecular chemists and solid state chemists, that is, between moleculists and collectivists. The clusters $P_7$, $As_7$, $Sb_7$, $P_{11}$, $As_{11}$, $Ge_9$, $Sn_9$, $Bi_9$, $Si_4$(I), $Si_4$(II) are impressive examples of the senselessness of all attempts by moleculists to ignore solid substances and by collectivists to let localized bonds in solids merge into bands. For a full understanding of the relationship stoichiometry-structure-properties one needs—after determining the facts—both, the fearless drawing of bond lines *and* the spreading of nets through packed structures. The elimination of language barriers between chemists of both faiths seems to me to be sometimes more difficult than between chemists and physicists. Stacked coordination polyhedra and condensed ring systems are often the same thing. Finally, young chemists have the right to learn at the beginning that, besides $SiCl_4$ and $SiRR'R''R'''$, NaSi exists as well and that "intermetallic phases" are not indecent. Otherwise they might think that elements can only be added from the right-hand side to the left-hand side.

*I wish to thank my wife Christa and my three daughters for putting up with me during the preparation of this work, also my co-workers for their active cooperation over many years. I am also indebted to Dr. W. Hönle, Dr. R. Nesper, Dr. M. Wittmann and Dr. W. Bensmann for their technical help, Mrs. C. Fowler for typing the manuscript, and Dr. A. Griffiths for translating the text into English. Our research was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for their support over many years.*

Received: November 17, 1980 [A 347 IE]
German version: Angew. Chem. *93*, 44 (1981)

---

[1] *F. A. Cotton,* Q. Rev. Chem. Soc. *20*, 389 (1966).

[2] *H. Schäfer, H. G. von Schnering,* Angew. Chem. *76*, 833 (1964).

[3] *A. Simon,* Chem. Unserer Zeit *10*, 1 (1976).

[4] *A. Simon,* Struct. Bonding (Berlin) *36*, 81 (1979).

[4a] *A. L. Rheingold:* Homoatomic Rings, Chains and Macromolecules of Main Group Elements. Elsevier, Amsterdam 1977.

[5] *H. G. von Schnering* in [4a], p. 317.

[6] *J. Gallmeier, H. Schäfer, A. Weiss,* Z. Naturforsch. *B 24*, 665 (1969).

[7] A certain hectic etate is unmistakable, which for example, due to "up-to-date" properties of compounds, has also led to the rediscovery of knowledge which was "lost" for 15 jears (no comment).

[8] a) *H. Schäfer, B. Eisenmann, W. Müller,* Angew. Chem. *85*, 742 (1973); Angew. Chem. Int. Ed. Engl. *12*, 694 (1973); b) *R. B. King,* Prog. Inorg. Chem. *15*, 387 (1972); c) *F. A. Cotton, ibid. 21*, 1 (1976); d) *J. D. Corbett, ibid. 21*, 129 (1976); e) *H. Vahrenkamp,* Struct. Bonding (Berlin) *32*, 1 (1977).

[9] *F. A. Cotton, T. E. Haas,* Inorg. Chem. *3*, 10 (1964).

[10] *K. Wade,* Adv. Inorg. Chem. Radiochem. *18*, 1 (1976).

[11] *J. W. Lauher,* J. Am. Chem. Soc. *100*, 5305 (1978).

[12] *W. N. Lipscomb:* Boron Hydrides. Benjamin, New York 1963.

[13] *H. O. Grimm, A. Sommerfeld,* Z. Phys. *36*, 36 (1926).

[14] *E. Zintl,* Angew. Chem. *52*, 1 (1939); cf. also [5] and [8a].

[15] *W. Klemm,* Proc. Chem. Soc. London *1958*, 329; see also in: Festkörperprobleme, Vol. III, Vieweg, Braunschweig 1963.

[16] *E. Busmann,* Z. Anorg. Allg. Chem. *313*, 90 (1961).

[17] *E. Mooser, W. B. Pearson,* Phys. Rev. *101*, 1608 (1956); cf. detailed discussion by *A. Kjekshus* and *T. Rakke,* Struct. Bonding (Berlin) 9, 45 (1974).

[18] *H. Schäfer,* Diskussionsbemerkung, Münster 1962.

[19] *R. J. Gillespie, R. S. Nyholm,* Q. Rev. Chem. Soc. *11*, 339 (1957).

[20] *H. G. von Schnering, H. Menke,* unpublished work (1975).

[21] *B. Better, A. Hütz, G. Nagorsen,* Z. Metallkd. *67*, 118 (1976).

[22] *W. Schmettow, H. G. von Schnering,* 1st Conf. of the GdCh-Fachgruppe Festkörperchemie, Giessen 1978; cf. also: *Y. Wang, L. D. Calvert, E. J. Gabe, J. B. Taylor,* Acta Crystallogr. *B33*, 3122 (1977); *F. Hulliger,* Z. Kristallogr. *150*, 125 (1979).

[23] *T. P. Martin, H. Schaber,* Z. Phys. *B35*, 61 (1979).

[24] *J. H. C. Hogg,* Acta Crystallogr. *B27*, 1630 (1971); *J. H. C. Hogg, H. H. Sutherland, D. J. Williams, ibid. B29*, 1590 (1973).

[25] *I. J. Hegyi, E. E. Loebner, E. W. Poor, Jr., J. G. White,* J. Phys. Chem. Solids *24*, 333 (1963); *J. Goodyear, G. A. Steigmann,* Acta Crystallogr. *B25*, 2371 (1969).

[26] *R. J. Gillespie, J. Passmore,* Adv. Inorg. Chem. Radiochem. *17*, 49 (1975).

[27] *I. D. Brown, B. D. Cutforth, C. G. Davies, R. J. Gillespie, P. R. Ireland, J. E. Vekris,* Can. J. Chem. *52*, 791 (1974).

[28] *H. G. von Schnering, W. Hönle,* Z. Anorg. Allg. Chem. *456*, 194 (1979).

[29] *H. G. von Schnering, W. Wichelhaus, M. Schulze-Nahrup,* Z. Anorg. Allg. Chem. *412*, 193 (1975).

[30] *H. G. von Schnering, W. Wichelhaus, M. Wittmann,* Abstr. V. Int. Conf. Solid Compounds of Transition Elements (ICSTE), Uppsala 1976.

[31] *K. Deller, B. Eisenmann,* Z. Naturforsch. *B31*, 1023 (1976).

[32] *G. Chapuis, F. Hulliger, G. Schmelczer,* J. Solid State Chem. *31*, 59 (1980); *M. Wittmann, W. Schmettow, D. Sommer, W. Bauhofer, H. G. von Schnering,* Abstr. VI. Int. Conf. Solid Compounds of Transition Elements (ICSTE), Stuttgart 1979.

[33] *B. Eisenmann,* Z. Naturforsch. *B34*, 1162 (1979).

[34] *K. Deller, B. Eisenmann,* Z. Naturforsch. *B 32*, 1368 (1977).

[35] *Y. Wang, L. D. Calvert, M. L. Smart, J. B. Taylor, E. J. Gabe,* Acta Crystallogr. *B35*, 2186 (1979).

[36] *M. Wittmann, H. G. von Schnering,* Z. Anorg. Allg. Chem., in press.

[37] *H. von Benda, A. Simon, W. Bauhofer,* Z. Anorg. Allg. Chem. *438*, 53 (1978).

[38] *H. G. von Schnering, H. von Benda, C. Kalveram,* Z. Anorg. Allg. Chem. *438*, 37 (1978).

[39] *A. Rabenau* in: *J. Wood, O. Lindquist, C. Helgesson, N.-G. Vannerberg:* Reactivity of Solids. Plenum Press, New York 1977, p. 731 and references cited therein.

[40] *A. Kjekshus, T. Rakke,* Acta Chem. Scand. *A 28*, 99 (1974).

[41] *R. Steudel,* Angew. Chem. *87*, 683 (1975); Angew. Chem. Int. Ed. Engl. *14*, 655 (1975).

[42] *K. F. Tebbe* in [4a], p. 551.

[43] *H. Endres, H. J. Keller, W. Moroni, J. Weiss,* Acta Crystallogr. *B31*, 2357 (1975).

[44] *W. Saenger,* Angew. Chem. 92, 343 (1980); Angew. Chem. Int. Ed. Engl. *19*, 344 (1980).

[45] *A. Rabenau, W. Stoeger,* Angew. Chem. *90*, 627 (1978); Angew. Chem. Int. Ed. Engl. *17*, 599 (1978).

[46] *E. Hengge* in [4a], p. 235.

[47] *M. Baudler,* Pure Appl. Chem. *52*, 755 (1980).

[48] *H. Quast,* Nachr. Chem. Tech. Lab. *27*, 120 (1979).

[49] *B. Eisenmann, K. H. Janzon, H. Schäfer, A. Weiss,* Z. Naturforsch. *B 24*, 457 (1969).

[50] *J. Witte, H. G. von Schnering,* Z. Anorg. Allg. Chem. *327*, 260 (1964).

[51] *H. Schäfer, K. H. Janzon, A. Weiss,* Angew. Chem. *75*, 451 (1963); Angew. Chem. Int. Ed. Engl. *2*, 393 (1963).

[52] *A. Cisar, J. D. Corbett,* Inorg. Chem. *16*, 2482 (1977).

[53] *T. W. Couch, D. A. Lokken, J. D. Corbett,* Inorg. Chem. *11*, 357 (1972).

[54] *C. Davies, R. J. Gillespie, J. J. Park, J. Passmore,* Inorg. Chem. *10*, 2781 (1971); *R. K. Mullen, D. J. Prince, J. D. Corbett, ibid. 10*, 1749 (1971).

[55] *W. Schmettow, A. Lipka, H. G. von Schnering,* Angew. Chem. *86*, 10 (1974); Angew. Chem. Int. Ed. Engl. *13*, 5 (1974).

[56] *W. Hönle,* Dissertation, Universität Münster 1975.

[57] *R. C. Burns, R. J. Gillespie, W.-Ch. Luk, D. R. Slim,* Inorg. Chem. *18*, 3086 (1979).

[58] *H. G. von Schnering, R. Nesper, J. Curda, K.-F. Tebbe,* Angew. Chem. *92*, 1070 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1033 (1980).

[59] *U. Frank, W. Müller,* Z. Naturforsch. *B 30*, 313 (1975).

[60] *G. Rocktäschel, A. Weiss,* Z. Anorg. Allg. Chem. *316*, 261 (1962).

[61] *B. Eisenmann, H. Schäfer, K. Turban,* Z. Naturforsch. *B 29*, 464 (1974).

[62] *K. Volk, W. Müller,* Z. Naturforsch. *B33*, 593 (1978).

[63] *E. Menges, V. Hopf, H. Schäfer, A. Weiss,* Z. Naturforsch. *B 24*, 1351 (1969).

[64] *H. G. von Schnering, M. Wittmann,* Z. Naturforsch. *B35*, 824 (1980).

[65] *H. G. von Schnering, M. Wittmann, R. Nesper,* J. Less Common Met. *76*, 213 (1980).

[66] *W. Dahlmann, H. G. von Schnering,* Naturwissenschaften *60*, 518 (1973).

[67] *K. Deller, B. Eisenmann,* Z. Naturforsch. *B 31,* 1550 (1976).

[68] *K. Deller, B. Eisenmann,* Z. Naturforsch. *B 33,* 676 (1978).

[69] *W. Wichelhaus, H. G. von Schnering,* Z. Anorg. Allg. Chem. *419,* 77 (1976).

[70] *L. Euler,* „Elementa doctrinae solidorum", in Novi Commentarii Academiae Scientiarum Imperialis Petrolitanae, 1758, p. 109-140.

[71] *R. E. Williams,* Adv. Chem. Radiochem. *18,* 67 (1976).

[72] *D. M. P. Mingos,* Nature (London) Phys. Sci. *236,* 99 (1972); J. Chem. Soc. Dalton Trans. *1974,* 133.

[73] *R. Grinter,* Chem. Unserer Zeit *11,* 176 (1977).

[74] a) *G. Maier, S. Pfriem, U. Schäfer, R. Matusch,* Angew. Chem. *90,* 552 (1978); Angew. Chem. Int. Ed. Engl. *17,* 520 (1978); b) *H. Bock, B. Roth, G. Maier, ibid. 92,* 213 (1980) bzw. *19,* 209 (1980); c) *G. Rauscher, T. Clark, D. Poppinger, P. von R. Schleyer, ibid. 90,* 306 (1978) bzw. *17,* 276 (1978).

[75] *R. Hoppe,* private communication.

[76] *D. J. Braun, W. Jeitschko,* Acta Crystallogr. *B 34,* 2069 (1978).

[77] *P. A. Edwards, J. D. Corbett,* Inorg. Chem. *16,* 903 (1977).

[78] *J. D. Corbett,* Inorg. Chem. *7,* 198 (1968).

[79] *R. J. Gillespie:* Molecular Geometrie. Van Nostrand-Reinhold, London 1972.

[80] *A. Simon,* Angew. Chem. *93,* 23 (1981); Angew. Chem. Int. Ed. Engl. *20,* 1 (1981).

[81] *A. Hershaft, J. D. Corbett,* Inorg. Chem. *2,* 979 (1963); *R. M. Friedman, J. D. Corbett,* Inorg. Chim. Acta *7,* 525 (1973); Chem. Commun. *1971,* 422.

[82] *L. Diehl, K. Khodadadeh, D. Kummer, J. Strähle,* Chem. Ber. *109,* 3404 (1976).

[83] *C. H. E. Belin, J. D. Corbett, A. Cisar,* J. Am. Chem. Soc. *99,* 7163 (1977).

[84] *E. Zintl, J. Goubeau, W. Dullenkopf,* Z. Phys. Chem. *A 154,* 1 (1931); *E. Zintl, A. Harder, ibid. A 154,* 47 (1931); *E. Zintl, W. Dullenkopf,* Z. Phys. Chem. *B 16,* 183 (1932); *E. Zintl, H. Kaiser,* Z. Anorg. Allg. Chem. *211,* 113 (1933).

[85] *A. Lipka, K. Yvon,* Acta Crystallogr. *B 36,* 2123 (1980).

[86] *H. G. von Schnering, W. Beckmann,* Z. Anorg. Allg. Chem. *347,* 231 (1966).

[87] *M. Baudler, H. Ständeke, M. Borgardt, H. Strabel, J. Dobbers,* Naturwissenschaften *53,* 106 (1966).

[88] *W. Schmettow, H. G. von Schnering,* Angew. Chem. *89,* 895 (1977); Angew. Chem. Int. Ed. Engl. *16,* 857 (1977).

[89] *D. G. Adolphson, J. D. Corbett, D. J. Merryman,* J. Am. Chem. Soc. *98,* 7234 (1976).

[90] *G. Fritz, W. Hölderich,* Naturwissenschaften *62,* 573 (1975); *G. Fritz, R. Uhlmann,* Z. Anorg. Allg. Chem. *440,* 168 (1978).

[91] *W. Hönle, H. G. von Schnering,* Z. Anorg. Allg. Chem. *440,* 171 (1978).

[92] *M. Baudler, T. Pontzen, J. Hahn, H. Ternberger, W. Faber,* Z. Naturforsch. *B 35,* 517 (1980).

[93] *W. Bues, M. Somer, W. Brockner, D. Grünewald,* Naturwissenschaften *64,* 583 (1977).

[94] *H. G. von Schnering, W. Wichelhaus, W. Hönle, W. Schmettow, M. Wittmann, D. Sommer, J. Curda, C. Mensing,* unpublished results.

[95] *M. Baudler, H. Ternberger, W. Faber, J. Hahn,* Z. Naturforsch. *B 34,* 1690 (1979).

[96] *P. C. Minshall, G. M. Sheldrick,* Acta Crystallogr. *B 34,* 1326 (1978).

[97] *H. Thurn, H. Krebs,* Acta Crystallogr. *B 25,* 125 (1969).

[98] *W. Hönle, H. G. von Schnering,* Z. Kristallogr. *153,* 339 (1980).

[99] *W. Wichelhaus, H. G. von Schnering,* Naturwissenschaften *60,* 104 (1973).

[100] *W. Bues,* private communication (1978).

[101] *W. Wichelhaus,* Dissertation, Universität Münster 1973.

[102] *M. S. Somer,* Dissertation, Technische Universität Clausthal 1979.

[103] *H. G. von Schnering, D. Fenske, W. Hönle, M. Binnewies, K. Peters,* Angew. Chem. *91,* 755 (1979); Angew. Chem. Int. Ed. Engl. *18,* 679 (1979).

[104] *H. G. von Schnering, W. Bensmann, C. Mujica, V. Manriquez, W. Hönle,* unpublished results (1980).

[105] *D. T. Cromer,* Acta Crystallogr. *12,* 36, 41 (1959).

[106] *H. G. von Schnering, V. Manriquez, W. Hönle,* Angew. Chem. and Angew. Chem. Int. Ed. Engl., in press.

[107] *G. Fritz, R. Uhlmann,* Z. Anorg. Allg. Chem. *456,* 59 (1980).

[108] *W. Hönle, H. G. von Schnering,* Z. Anorg. Allg. Chem. *456,* 72 (1980).

[109] *C. A. Ghilardi, S. Midollini, A. Orlandini, L. Sacconi,* Inorg. Chem. *19,* 301 (1980).

[110] *U. Frank, W. Müller,* Z. Naturforsch. *B 30,* 316 (1975).

[111] *W. Dahlmann, H. G. von Schnering,* Naturwissenschaften *60,* 429 (1973).

[112] *H. G. von Schnering, W. Dahlmann,* Naturwissenschaften *58,* 623 (1971).

[113] *E. Busmann, S. Lohmeyer,* Z. Anorg. Allg. Chem. *312,* 53 (1961); *W. Hönle, H. G. von Schnering,* Z. Kristallogr., in press.

[114] *H. G. von Schnering, H. Schmidt,* Angew. Chem. *79,* 323 (1967); Angew. Chem. Int. Ed. Engl. *6,* 356 (1967).

[115] *H. Krebs, T. Ludwig,* Z. Anorg. Allg. Chem. *294,* 257 (1958).

[116] *O. Olofsson, J. Gullman,* Acta Chem. Scand. *25,* 1327 (1971).

[117] *H. G. von Schnering, G. Menge,* Z. Anorg. Allg. Chem., in press; *G. Menge,* Dissertation, Universität Münster 1977.

[118] *W. Schmettow,* Dissertation, Universität Münster 1975.

[119] *W. Wichelhaus, H. G. von Schnering,* Naturwissenschaften *62,* 180 (1975).

[120] *H. G. von Schnering, W. Wichelhaus,* Naturwissenschaften *59,* 78 (1972).

[121] *J. Brunner, M. Thüler, S. Vepřek, R. Wild,* J. Phys. Chem. Solids *40,* 967 (1979); *H. U. Beyeler, S. Vepřek,* Phil. Mag. *B 41,* 327 (1980).

[122] *H. G. von Schnering,* Int. Conf. Phosphorus Chem. Halle, Coll. Abstr. III., 356 (1979).

[123] *D. M. Wiench, M. Jansen,* Z. Anorg. Allg. Chem. *461,* 101 (1980).

[124] *W. Hönle, H. G. von Schnering,* Int. Conf. Phosphorus Chem. Halle, Coll. Abstr. III., 418 (1979).

[125] *W. Hönle, H. G. von Schnering,* IV. Eur. Crystallogr. Meet. Oxford, Coll. Abstr. B, 552 (1977).

[126] *W. Schmettow, D. Sommer, C. Mensing, H. G. von Schnering,* 2nd Conf. of the GdCh-Fachgruppe Festkörperchemie, Stuttgart 1980.

[127] *W. B. Pearson:* The Crystal Chemistry and Physics of Metals and Alloys. Wiley-Interscience, New York 1972.

[128] *H. G. von Schnering, M. Wittmann, R. Nesper, J. Curda,* Z. Kristallogr., in press.

[129] *J. D. Dunitz,* Perspect. Struct. Chem. *2,* 1 (1968); *H.-B. Bürgi,* Angew. Chem. *87,* 461 (1975); Angew. Chem. Int. Ed. Engl. *14,* 460 (1975).

[130] *Y. Wang, R. D. Heyding, E. J. Gabe, L. D. Calvert, J. B. Taylor,* Acta Crystallogr. *B 34,* 1959 (1978).

[131] *G. Menge, H. G. von Schnering,* Z. Anorg. Allg. Chem. *422,* 226 (1976).

[132] *M. Wittmann, H. G. von Schnering,* J. Solid State Chem., in press.

[133] *H. G. von Schnering, M. Wittmann, W. Bauhofer,* unpublished (1980).

[134] *W. Bauhofer, M. Wittmann, H. G. von Schnering,* J. Phys. Chem. Solids, in press.

[135] *K. F. Kapustinskii,* Z. Phys. Chem. *B 22,* 257 (1933); Q. Rev. Chem. Soc. *10,* 283 (1956).

[136] *H. G. von Schnering,* unpublished; cf. also [137].

[137] *R. Hoppe,* Angew. Chem. *78,* 52 (1966); Angew. Chem. Int. Ed. Engl. *5,* 95 (1966).

[138] *W. Klemm,* Z. Phys. Chem. *B 12,* 1 (1931).

[139] *R. T. Sanderson:* Chemical Bonds and Bond Energy. 2nd Edit., Academic Press, New York 1976.

[140] *H. G. von Schnering, W. Hönle, G. Krogull,* Z. Naturforsch. *B 34,* 1678 (1979).

[141] *A. Kjekshus,* Acta Chem. Scand. *14,* 1450 (1960).

[142] *H. Föppl,* Z. Anorg. Allg. Chem. *291,* 12 (1957).

[143] *H. Föppl, E. Busmann, F.-K. Frorath,* Z. Anorg. Allg. Chem. *314,* 12 (1962).

[144] *H. G. von Schnering, Ngoh-Khang Goh,* Naturwissenschaften *61,* 272 (1974).

[145] *R. W. G. Wyckhoff:* Crystal Structures. 2nd Edit., Wiley-Interscience, New York 1963.

[146] Cf. *H. Schäfer* et al. and *B. Eisenmann* et al. as well as *W. Müller* et al. in Z. Naturforsch. *B* (1975-1980).

[147] *A. Zalkin, W. J. Ramsay,* J. Phys. Chem. *62,* 689 (1958); *60,* 234 (1956).

[148] *A. Zalkin, W. J. Ramsay, D. H. Templeton,* J. Phys. Chem. *60,* 1275 (1956).

[149] *L. Pauling:* Die Natur der chemischen Bindung. Verlag Chemie, Weinheim 1964; *L. Pauling:* The Nature of the Chemical Bond, 3 ed., Cornell Univ. Press Ithaca (1960).

[150] *F. Hulliger* in *K. A. Gschneider, Jr., L. Eyring:* Handbook on the Physics and Chemistry of Rare Earth. North-Holland, Amsterdam 1979, Chap. 33.

[151] *H. G. von Schnering, R. Nesper, K.-F. Tebbe, J. Curda,* Z. Metallkd. *71,* 357 (1980).

[152] *R. Allmann,* Monatsh. Chem. *106,* 779 (1975); and references cited therein.

[153] *P. C. Donohue, W. J. Siemons, J. L. Gillson,* J. Phys. Chem. Solids *29,* 807 (1968).

[154] *H. G. von Schnering, T. Chattopadhyay, W. Hönle,* unpublished refinement (1979).

[155] *A. Baghdadi, A. Finley, P. Russo, R. J. Arnott, A. Wold,* J. Less-Common Met. *34,* 31 (1974).

[156] *C. H. E. Belin,* J. Am. Chem. Soc. *102,* 6036 (1980).

[157] *D. E. C. Corbridge:* The Structural Chemistry of Phosphorus. Elsevier, Amsterdam 1974.

[158] *H. W. Spiess, R. Grosescu, U. Haeberlin,* Chem. Phys. *6,* 226 (1974).

[159] *P. Dapporto, S. Midollini, L. Sacconi,* Angew. Chem. *91,* 510 (1979); Angew. Chem. Int. Ed. Engl. *18,* 469 (1979).

[160] Cf. *D. J. Braun, W. Jeitschko,* Z. Anorg. Allg. Chem. *445,* 157 (1978); *W.* Jeitvschko, R. Rühl, Acta Crystallogr. *B 35,* 1953 (1979).

[161] Vgl. *U. Schuster* et al. in Z. Naturforsch. *B* (1975-1980).

[162] *W. Klemm,* Angew. Chem. *56,* 1 (1943).

[163] *R. C. Weast:* Handbook of Chemistry and Physics. 54th Edit., CRC Press, Cleveland 1973, Table F-212.

[164] *F. Hulliger, R. Schmelczer, D. Schwarzenbach,* J. Solid State Chem. *21,* 371 (1977).

# Ternary Sulfides: Model Compounds for the Correlation of Crystal Structure and Magnetic Properties

By Welf Bronger[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

Relationships between crystal structure and magnetic properties enable an insight into the nature of the binding of atoms or ions in the solid state. Suitable as model substances are transition metal compounds in which the collective bonds that are generally present are directively degraded by incorporation of diamagnetic cations. This requirement of progressive degradation is met with in sulfides of the general composition $A_xM_yS_z$, where $A \triangleq$ alkali metal and $M \triangleq$ transition metal.

## 1. Introduction

Examination of the metal chalcogenides from the standpoint of the arrangement of the metals in the periodic system reveals a striking change in properties at the site of insertion of the transition metals. For example, the sulfides of the main group elements have considerable salt-like character, whereas those of the transition elements often have covalent-metallic character. Moreover, it is noteworthy that structures with distinct anisotropic atomic arrangements occur in the transition regions: thus, in the compounds MX of metals of the fourth period ($M \triangleq$ metal, $X \triangleq$ chalcogen) the CuS-type structure represents a transition to a layer structure, while the CuTe-type, which in the case of the iron chalcogenides also appears at the boundary to the salt-like manganese compounds, represents a real layer structure. These structural types form a transition to the NiAs-type, which is commonly met with in the transition-metal chalcogenides. In this type of structure the metal atoms occupy the octahedral sites of hexagonally packed layers of sulfur, selenium or tellurium, with relatively short metal-metal distances in the direction of the c-axis—a structure results which is obviously predestined for metallic bonding.

An analogous situation is found in the $MX_2$ compounds: The anisotropic structure type which here enables transitions from predominantly salt-like to predominantly covalent-metallic bonding, is realized only by the $CdI_2$ layer structure type. The dichalcogenides $TiS_2$, $TiSe_2$ and $TiTe_2$ crystallizing with this type of structure serve as typical examples.

These relationships between crystal structure and chemical bonding described for MX and $MX_2$ compounds of metals of the fourth period are also found in compounds of other stoichiometry as well as in the case of metals of higher periods. The anisotropic arrangements of the atoms occurring in the transition from extremely ionic to extremely covalent-metallic bonding, are always associated with characteristic electric and magnetic properties.

The variety of chalcogenides of the non-transition metals on the one hand and of chalcogenides of the transition metals on the other prompts the following question: what properties can be expected in the case of chalcogenides containing both a non-transition metal as well as a transition metal? In this context the most informative combination would be that of an alkali metal with a transition metal. This concept urged us to investigate compounds of the general composition $A_xM_yX_z$, where $A \triangleq$ alkali metal, $M \triangleq$ transition metal, and $X \triangleq$ chalcogen.

Regarding structural properties the prerequisites here are similar to those in the case of Zintl phases, in which the anisotropic crystal structures of the elements in the transition range between non-metals and metals can be copied and varied by combination of an electropositive metal with a semimetal. In the case of ternary chalcogenides appropriately containing an electropositive metal A and a transition metal M, one can similarly expect that the anisotropic arrangements of the atoms in the border region between ionic and metallic metal chalcogenides are copied and, moreover, so diversely modified that $[M_yS_z]$-framework structures are formed which resemble those of binary metal sulfides. In addition, as a result of incorporation of transition metals, the magnetic properties, in particular, might yield important information about the nature of the bonding and thus make a valuable contribution to the elucidation of chemical bonding in the solid state.

In the following paper, therefore, an account is given of the relationships between structure and magnetic properties in the case of the alkali metal-transition metal chalcogenides, with particular emphasis on the sulfides.

## 2. Synthesis of Ternary Alkali Metal—Transition Metal Sulfides

The first investigations on the existence of ternary sulfides of alkali metals and transition metals date back to about 1840 to 1875. Particularly worth noting are the works of *Völker*[1] and *Schneider*[2,3], from which it emerges that ternary sulfides such as $KFeS_2$, $NaCrS_2$ and $KCrS_2$ are formed on fusing together salts of the transition metals with sulfur and soda or potash. Some of these earlier findings were later confirmed around the turn of the century by *Milbauer*[4,5], who was able to synthesize ternary sulfides by reaction of KSCN with metal oxides at elevated temperatures. These older works then fell for a long time into oblivion, and it was not until the middle of the forties before new results were published by *Rüdorff et al.*[6-8], mainly on chromium and copper compounds. Analogies and interrelationship have now been recognized and are represented by a great number of new al-

---

[*] Prof. Dr. W. Bronger
Institut für Anorganische Chemie der Technischen Hochschule
Prof.-Pirlet-Strasse 1, 5100 Aachen (Germany)

© Verlag Chemie, GmbH, D-6940 Weinheim, 1981 0570-0833/81/0101-0052 \$ 02.50/0 Angew. Chem. Int. Ed. Engl. 20, 52-62 (1981)

kali metal-transition metal sulfides and selenides which have been characterized in recent times.

Based on earlier findings on the preparation of ternary sulfides, methods have been developed for the isolation of pure, above all oxygen-free, substances. For this purpose hydrides or the metals themselves are used as alkali metal components besides the carbonates, sulfides or polysulfides. The reaction partners are then transition metals in elemental form and sulfur or hydrogen sulfide. The reactions generally occur between 800 and 1300 °C in the melt, and on cooling under suitable conditions the ternary sulfides can be obtained as well formed, often beautifully colored crystals.

Parallel and as an extension to the fusion reactions ternary sulfides can be prepared by intercalation of alkali metals in the layer structures of metal chalcogenides. The disulfides and diselenides of transition metals of the 4th, 5th and 6th groups as well as those of rhenium and platinum usually serve as host structures. The reactions are generally carried out in liquid ammonia.

Table 1 contains a list of the ternary sulfides of alkali metals and transition metals which have so far been investigated in detail. The aforementioned intercalation compounds, which usually have wide ranges of homogeneity, are not listed. $AVS_2$ and $ACrS_2$ can still be regarded as borderline compositions for the incorporation of alkali metal A in the metastable disulfides $VS_2$ and $CrS_2$. Ternary sulfides for which accurate data on crystal structure and magnetic properties are not available are likewise not considered, or are regarded as a group with A $\triangleq$ alkali metal. In recent years some of the corresponding ternary selenides have also been synthesized. As far as known, their structural and magnetic properties are in all cases similar to those of the sulfides.

Table 1. Data on the crystal structure and magnetic properties of ternary alkali metal-transition metal sulfides.

| Compound | Structural characteristics | Shortest bond lengths M—M [pm] | Shortest bond lengths M—S [pm] | Magnetic properties | Ref. |
|---|---|---|---|---|---|
| $LiVS_2$ | Fully occupied $CdI_2$ type (cf. Fig. 1b) | 338.03(2) | 243(1) | Antiferromagnetic; still no three-dimensional arrangement of the moments at 4.2 K | [9]<br>[10] |
| $NaVS_2$ | Fully occupied $CdCl_2$ type (cf. Fig. 2b) | 357 | 246 [a] | Paramagnetic with delocalized moments corresponding to $V^{3+}$; antiferromagnetic arrangement below 50 K | [11]<br>[12] |
| $LiCrS_2$ | Corresponding to $LiVS_2$ | 346.37(3) | 240(1) | Antiferromagnetic arrangement of the moments at 4.2 K | [9]<br>[13] |
| $NaCrS_2$ | Corresponding to $NaVS_2$ | 355.44(2) | 243.4 | Paramagnetic with localized moments corresponding to $Cr^{3+}$; antiferromagnetic below 19 K ($NaCrS_2$) and 38 K ($KCrS_2$), resp. θ: 30 K ($NaCrS_2$); 112 K ($KCrS_2$) | [16]<br>[14]<br>[15] |
| $KCrS_2$ | Corresponding to $NaVS_2$ | 360.2(6) | 242.8 | | |
| $KCr_5S_8$ | Sulfur octahedra with central chromium atoms, linked *via* common edges and, in part, *via* common surfaces. The framework structure thus formed contains channels in which the alkali metal ions are arranged linearly | from 298(2)<br>to 366(1) | from 235(3)<br>to 251(2) | | [16] |
| $RbCr_5S_8$ | | from 296(1)<br>to 366(1) | from 235(1)<br>to 250(1) | | [16] |
| $CsCr_5S_8$ | | from 297(2)<br>to 363(1) | from 234(2)<br>to 252(2) | | [16] |
| $Rb_2Mn_3S_4$ | Sulfur tetrahedra linked *via* edges in which the manganese atoms are incorporated corresponding to $^2_\infty[Mn_{0.75}\square_{0.25}S]$. Separation by alkali metal atom layers (cf. Fig. 3b) | 296.7(1)<br>304.4(2) | 240.7(2)<br>242.4(3)<br>244.6(3) | Antiferromagnetic | [17]<br>[18]<br>[19] |
| $Cs_2Mn_3S_4$ | | 300.6(1)<br>310.3(1) | 241.9(2)<br>244.2(2)<br>246.0(2) | Antiferromagnetic | [17]<br>[18]<br>[19] |
| $Na_3FeS_3$ | Isolated $[Fe_2S_6]$-units (cf. Fig. 6) | 287.7(2) | 224.9(2)<br>225.2(2)<br>226.0(3)<br>229.8(2) | Antiferromagnetic coupling of the iron atoms in the binuclear complex | [20] |
| $Na_3Fe_2S_4$ | $^1_\infty[FeS_{4/2}]$-chains | 274.5(1)<br>274.9(1) | 228.4(1)<br>228.9(1)<br>229.8(2)<br>233.5(1) | | [21] |
| $KFeS_2$ | $^1_\infty[FeS_{4/2}]$-chains (cf. Fig. 4) | 270 | 218<br>229 | Linear antiferromagnetism; threedimensional arrangement of the moments below 250 K ($KFeS_2$), 188 K ($RbFeS_2$), and 66 K ($CsFeS_2$), resp. | [22]<br>[27]<br>[23] |
| $RbFeS_2$ | | 271 | 220<br>222 | | [24] |
| $CsFeS_2$ | $^1_\infty[FeS_{4/2}]$-chains (cf. Fig. 5) | 269.6(7)<br>272.5(7) | 222.7(6)<br>223.4(5) | | |
| $Cs_2Co_3S_4$ | Isotypic with $Cs_2Mn_3S_4$ | 288.3(1)<br>301.1(1) | 230.6(3)<br>233.8(4)<br>234.2(3) | Antiferromagnetic | [17]<br>[18] |

Table 1 (continued).

| Compound | Structural characteristics | Shortest bond lengths M—M [pm] | M—S [pm] | Magnetic properties | Ref. |
|---|---|---|---|---|---|
| $A_2Ni_3S_4$<br>($A \triangleq K$, Rb, Cs) | Probably isotypic with the corresponding palladium compounds | | | Diamagnetic | [25] |
| $KCu_4S_3$ | Double layers of edge-linked sulfur tetrahedra, all of which are occupied by copper atoms. The alkali metal atoms are incorporated between the double layers (cf. Fig. 9) | 275.7<br>297.0(2) | 231.2(2)<br>245.1(1) | Pauli paramagnetism | [8]<br>[28] |
| $RbCu_4S_3$ | | 278<br>298 | 233<br>246 | | [8] |
| $CsCu_4S_3$ | | 281.0(0)<br>292.2(3) | 231.5(2)<br>246.6(1) | | [29] |
| $K_3Cu_8S_6$ | Copper-Sulfur layers separated by alkali metal atoms, with almost trigonal planar or distorted tetrahedral environment of copper atoms | from 254<br>to 292 | from 223<br>to 284 | | [30] |
| $Rb_3Cu_8S_6$ | | from 254<br>to 293 | from 223<br>to 290 | | [30] |
| $Na_3Cu_4S_4$ | ${}^{1}_{\infty}[CuS_{3/3}]$ chains which are separated by the sodium atoms | 261.9(1)<br>295.5(1)<br>304.6(1)<br>306.0(1) | 225.1(1)<br>229.5(1)<br>231.2(1) | | [31] |
| $Li_4Re_6S_{11}$ | Fully occupied $Nb_6I_{11}$-type; $[Re_6S_8]S_{6/2}^{4-}$ framework (cf. Fig. 10) | from 259.1(1)<br>to 262.3(1) | from 237.9(3)<br>to 248.7(3) | | [32] |
| $Na_2Re_3S_6$ | ${}_{\infty}\{[Re_6S_8]S_{4/2}(S_2)_{2/2}\}^{4-}$ framework | from 259.3(1)<br>to 261.9(1) | from 236.9(2)<br>to 248.2(2) | | [33] |
| $K_2Re_3S_6$ | Isotypic with $Na_2Re_3S_6$ | from 261.0(1)<br>to 263.5(1) | from 239.1(2)<br>to 247.5(2) | | [33] |
| $Cs_4Re_6S_{13}$ | ${}_{\infty}\{[Re_6S_8]SS_{2/2}(S_2)_{3/2}\}^{4-}$ framework | from 261.9(1)<br>to 265.3(1) | from 237.2(3)<br>to 247.8(3) | | [34] |
| $Na_2PdS_2$ | The planar sulfur environments of the palladium atoms are one-dimensionally linked side to side | 354 | 235<br>239 | | [35] |
| $K_2Pd_3S_4$ | The planar sulfur environments of the palladium atoms are two-dimensionally linked side to side | 305<br>307 | 234 | Diamagnetic | [36] |
| $Rb_2Pd_3S_4$ | Stacking variant of the $K_2Pd_3S_4$-type (cf. Fig. 7) | 306<br>311 | 235<br>236 | Diamagnetic | [36] |
| $Cs_2Pd_3S_4$ | Isotypic with $Rb_2Pd_3S_4$ (cf. Fig. 7) | 308<br>314 | 232<br>234<br>235 | | [36] |
| $Na_2PtS_2$ | Isotypic with $Na_2PdS_2$ | 355 | 234<br>238 | | [35] |
| $K_2PtS_2$ | The planar sulfur environments of the platinum atoms are one-dimensionally linked side to side | 359 | 236 | | [38] |
| $Rb_2PtS_2$ | | 364 | 236 | | [38] |
| $Rb_2Pt_3S_4$ | The palladium-sulfur framework corresponds to that of $Cs_2Pd_3S_4$ | 314<br>319 | 248<br>251 | | [39] |
| $Cs_2Pt_3S_4$ | Isotypic with $Rb_2Pt_3S_4$ | 315<br>319 | 238<br>242 | | [39] |
| $K_2Pt_4S_6$ | Layer structure with $Pt^{2+}$ in planar, and $Pt^{4+}$ in octahedral sulfur environment | 350 | 235 | | [40] |

[a] Calculated using the z-parameter of $NaCrS_2$.

## 3. Crystal Structures with Characteristic $[M_yS_z]$-Frameworks

The ternary sulfides presented in Table 1 do not show any, or only slight, phase widths. The combination of alkali metal and transition metal, moreover, leads to oxidation states of the transition metals which are typical for salt-like compounds. Phase widths and associated alloy-like properties are observed only on transition to intercalation compounds. The structures in this region also show a continuous transition. Thus the atomic arrangement in $LiVS_2$ or $LiCrS_2$ corresponds, on the one hand, to the nickel arsenide type with a layer distribution of the cations; on the other hand, it can also be described as a filled-up $VS_2$- or $CrS_2$-structure ($CdI_2$-type, cf. Fig. 1) and thus forms a direct transition to the lithium-deficient intercalation compounds, which crystallize with the same structure type with only partially occupied lithium positions. In the stoichiometrically analogous alkali metal compounds $NaVS_2$, $NaCrS_2$ and $KCrS_2$ the structure of the $MS_2$-framework does not correspond to the $CdI_2$-type, but to the $CdCl_2$-type. Here the sulfur layers are arranged in the sequence —ABCA— (Fig. 2a), so that the occupation of all octahedral sites with A and M atoms can be described in terms of the rock-salt structure with layerwise ordered cation distribution (cf. Fig. 2b). In the alkali-metal deficient $ACr_5S_8$ compounds which follow (in Table 1), the three-dimensional $[Cr_5S_8]$-framework is preserved. The linking of the sulfur octahedra is obviously directionally dependent, so that channels are formed in which alkali metal atoms with short A—A distances are incorporated.

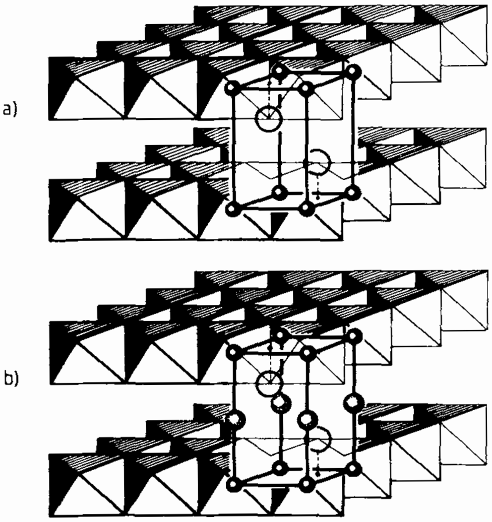


Fig. 1. a) $CdI_2$-type layer structure of many dichalcogenides $MX_2$. Open circles: X-, closed circles M-positions. b) Fully occupied $CdI_2$-structure ($LiCrS_2$-type). Dotted circles: alkali-metal positions. These symbols are also used in the following Figures.

In the alkali metal thiomanganates the structure of the $[Mn_3S_4]$-framework largely corresponds to the tetragonal CuTe layer structure-type (cf. Fig. 3a). The metal atoms occupy alternately every second layer of tetrahedral sites of a sequence of chalcogen atom layers. The only differences are that in the $[Mn_3S_4]$-framework, according to the stoichiometry, only three of four tetrahedral sites are occupied and that the layers, unlike in CuTe, are not arranged in the sequence —ABAB— but in the sequence —ABBA—. This enables the alkali metal atoms incorporated between layers of the same sequence to be coordinated by sulfur atoms in a cubic arrangement (cf. Fig. 3b).

The alkali metal thioferrates $AFeS_2$ crystallize in chain structure types. The $[FeS_2]$-framework corresponds to the $SiS_2$ structure: The iron atoms are coordinated tetrahedrally by sulfur atoms, while the sulfur tetrahedra are linked one-dimensionally *via* edges. The alkali metal atoms are incorporated between the chains, with differing coordination number according to size (cf. Fig. 4 and 5). The compound $Na_3Fe_2S_4$ also has an analogous framework structure. In the

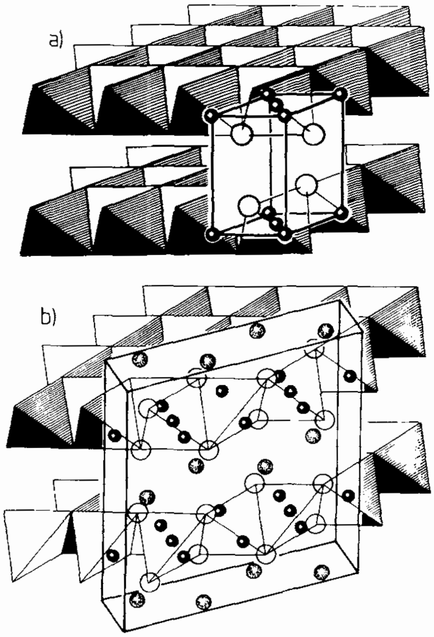


Fig. 3. a) CuTe structure. b) Fully occupied CuTe structure ($Cs_2Mn_3S_4$-type) with modified layer sequence.

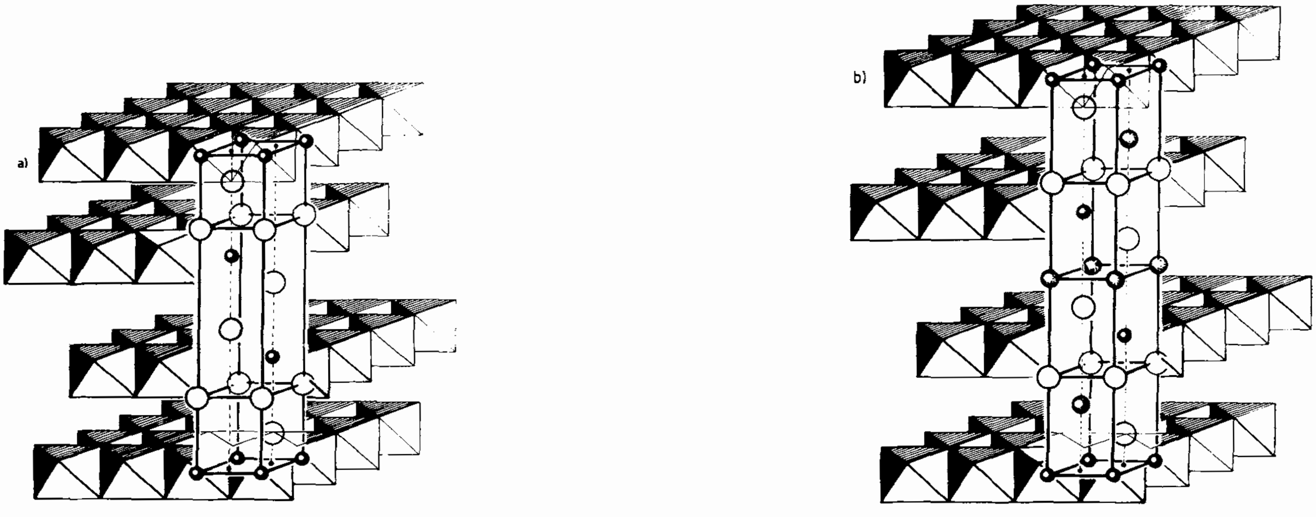


Fig. 2. a) $CdCl_2$-type, as layer structure previously not observed in metal dichalcogenides. b) Fully occupied $CdCl_2$ structure ($\alpha$-$NaFeO_2$ type). Characteristic atomic arrangement for many ternary sulfides of the composition $AMS_2$.

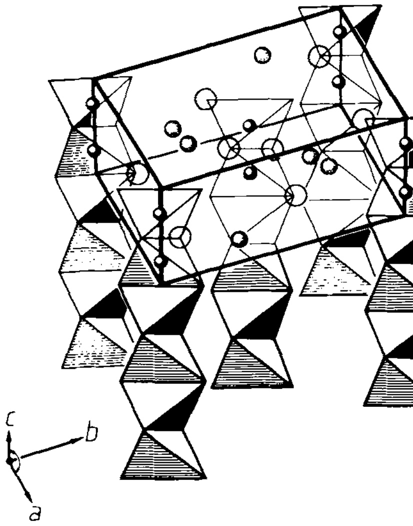


Fig. 4. $KFeS_2$-type structure.

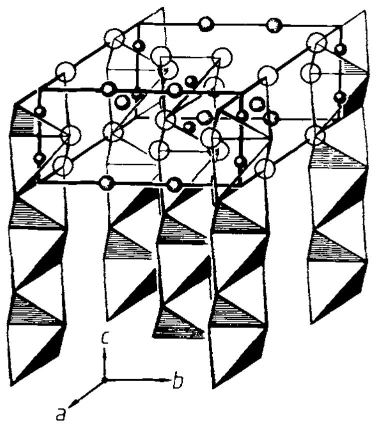


Fig. 5. $CsFeS_2$-type structure.

more sodium-rich compound $Na_3FeS_3$, however, even the one-dimensional framework is broken: only isolated $[Fe_2S_6]$ double tetrahedra are found which are arranged with the sodium atoms in a three-dimensional array (cf. Fig. 6).

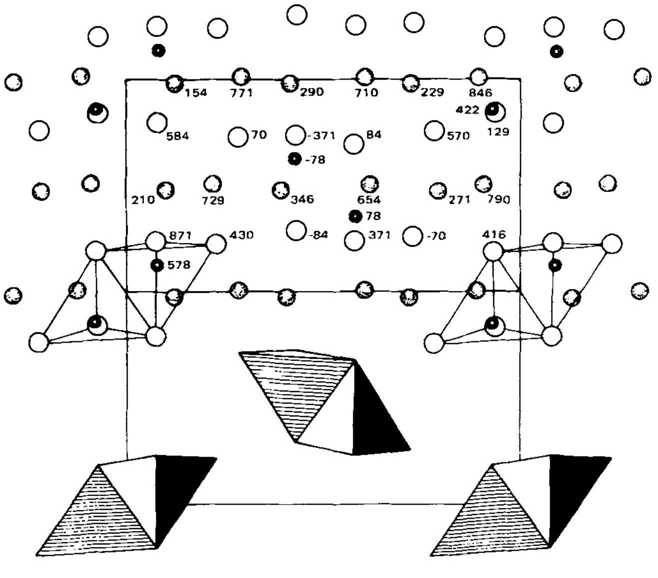


Fig. 6. $Na_3FeS_3$, atomic arrangement.

The ternary cobalt compound $Cs_2Co_3S_4$ is isotypic with the corresponding manganese compound (cf. Fig. 3). The nickel sulfides $A_2Ni_3S_4$, for which a detailed structure determination on single crystals is still lacking, have, on the other hand, a completely different structure. According to previous investigations they are isotypic with the analogous palladium and platinum compounds. The underlying constructional principle of these structures is illustrated in Figure 7 for the $Cs_2Pd_3S_4$-type as example: The palladium atoms are surrounded by a planar arrangement of sulfur atoms and the resulting rectangular arrays are linked with one another two-dimensionally *via* sides in a honeycomb-fashion. The sulfur-palladium-sulfur layer assemblies are finally separated from one another by double layers of alkali metal atoms. The observed planar coordination of transition metal atoms with $d^8$-configuration is in keeping with expectation; the layer structure of the $[Pd_3S_4]$-framework had hitherto not been observed in binary compounds. Moreover, ternary alkali metal thiopalladates and thioplatinates of the composition $A_2PdS_2$ and $A_2PtS_2$, respectively, could be synthesized. Their framework structure corresponds to that of $PdCl_2$: Here the arrangements with planar sulfur coordination are linked with one another one-dimensionally *via* sides. Figure 8 illustrates this with the $K_2PtS_2$-type as example. Finally, ternary platinum sulfides have been reported in which platinum atoms of oxidation states +4 and +2 are incorporated between sulfur layers with octahedral and planar coordination, respectively. The sulfur-platinum-sulfur layer assemblies are once again separated by alkali metal atoms. An accurate crystal structure investigation of $K_2Pt_4S_6$ is available.

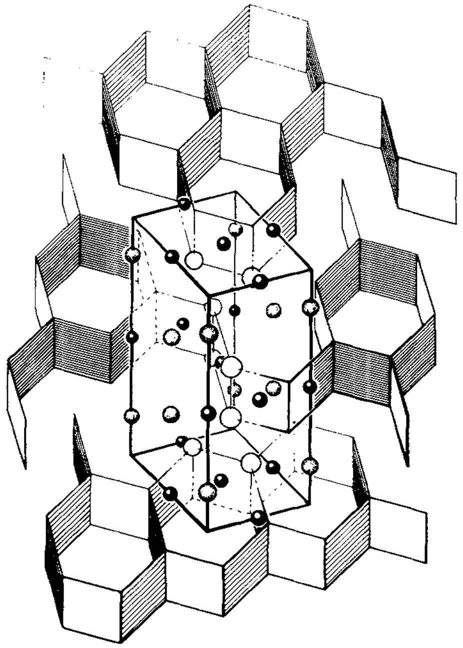


Fig. 7. $Cs_2Pd_3S_4$-type structure.

A number of ternary sulfides of alkali metals and copper have already been known for some time. The compositions (Table 1) indicate mixed valence compounds. Detailed structural investigations reveal, however, that a crystallographic differentiation between $Cu^{1+}$ and $Cu^{2+}$ is not possible. Thus, the copper atoms in the $KCu_4S_3$-type structure occupy equivalent positions. The atomic arrangement is once again

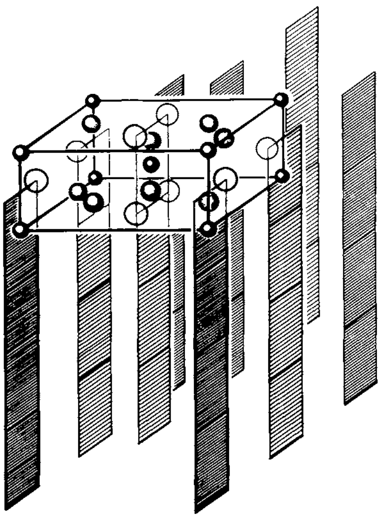


Fig. 8. $K_2PtS_2$-type structure.

describable as a layer structure, in which the copper atoms occupy double layers of tetrahedral sites built up by sulfur atoms and these arrays are separated by the alkali metal atom layers (cf. Fig. 9). A layer structure is also recognizable in the $K_3Cu_8S_6$-type structure. The copper atoms—here also a differentiation of oxidation numbers on the basis of coordination numbers and Cu—S distances is not possible—have approximately trigonal planar or distorted tetrahedral environments. Of the thiocuprates listed in Table 1, $Na_3Cu_4S_4$ is the most rich in alkali metal; it is typical, therefore, that the degree of cross-linking of the framework structure is further reduced. The copper-sulfur arrays form one-dimensional strands, in which the copper atoms have coordination number three. Besides the compounds listed here, there also exist some in which all copper atoms have completely filled d-levels, *i.e.* in which copper no longer functions as a transition metal. Corresponding diamagnetic compounds of silver are also known. Detailed information on alkali metal thioaurates is so far lacking.

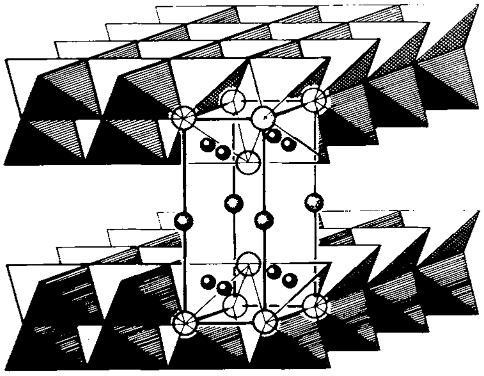


Fig. 9. $KCu_4S_3$-type structure.

In the case of 4d- and 5d-transition metals ternary chalcogenides of the general composition $A_xM_yX_z$ were unknown, apart from the aforementioned palladium and platinum compounds and intercalation phases in which alkali metals are intercalated in $MX_2$ layer structures. Only very recently molybdenum and rhenium compounds were discovered which contain isolated $[M_6S_8]$ clusters or, in the case of the alkali metal molybdenum sulfides, also condensed units of these clusters[41]. The structural data determined on single crystals of the rhenium compounds are given in Table 1; corresponding values for the molybdenum compounds are so far lacking. In the case of $Li_4Re_6S_{11}$ a framework structure was discovered which is already known for a binary system: linkage of the $[Re_6S_8]S^{4-}_{6/2}$ type is analogous to that in $Nb_6I_{11}$ ($\triangleq [Nb_6I_8]I_{6/2}$) (cf. Fig. 10).

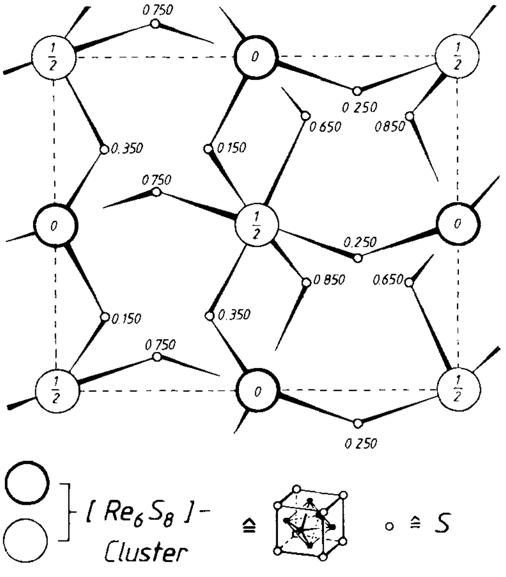


Fig. 10. $Li_4Re_6S_{11}$, structure of the $[Re_6S_8]S^{4-}_{6/2}$-framework.

Not to be overlooked are ternary sulfides which contain an f-element besides an alkali metal. For example, in the lanthanoid series (general symbol Ln) compounds of the composition $ALnS_2$ exist. At a radius ratio $r_{Ln^{3+}}/r_{A^+}$ above $\approx 0.9$ a random distribution of the cations can be found in the octahedral sites of cubic close packed layer sequences of the anions. At a smaller radius ratio an ordered distribution which deviates from the $CdCl_2$ framework structure becomes stable (cf. Fig. 2b).

At this juncture we might summarize as follows: The crystal structures of the ternary alkali metal-transition metal sulfides $A_xM_yS_z$ contain $[M_yS_z]$ frameworks which form three-, two- or one-dimensional arrays. Some of the atomic arrangements in these arrays were observed in binary compounds in which directed bonding entities lead to an anisotropic structure. Apparently, the Zintl-Klemm-Busmann principle[42] can be further extended beyond the explanation of the structure and bonding of Zintl phases, and as a matter of fact, quite generally, if ionic partners in a compound determine the makeup of covalent framework structures. Metallic properties can conceal the picture, but do not have to!

## 4. Magnetic Properties and their Correlation with Structure

In the ternary sulfides described here, magnetic properties can—in addition to the crystal structures—enable further insights into the bonding. Unfortunately, accurate data are still not available for all compounds (cf. Table 1). From the picture gained so far, however, it can be recognized that the covalent bonding moieties in the $[M_yS_z]$-framework structures can link *via* the direct interaction of neighboring M- and S-atoms to give ferro- or antiferromagnetic arrangements. Thereby direct exchange interactions of the paramagnetic centers might recede into the background compared to the indirect linkages *via* the sulfur ligands. These collective covalent bondings can now be correlated with each of the respective crystal structures *via* an analysis of the magnetic properties. Thus, *e.g.*, in the accurately investigated layer structures of the alkali metal thiovanadates and chromates (cf. Table 1) below the Néel temperatures one finds spin orders at which the coupling constants in the sulfur-transition metal-sulfur layer assemblies are markedly greater than between the layer assemblies. As a result of this anisotropy of the collective bonds furnished by the framework structure there can occur, *e.g.*, metamagnetic behavior, a phenomenon which makes itself manifest by the fact that at a critical field strength an external magnetic field perpendicular to the layers turns the antiferromagnetic arrangement of the spin moments between the layers into an energetically more favorable ferromagnetic arrangement. Since the strong ferromagnetic couplings in the layers thereby remain unaltered this spin flop mechanism makes itself significantly perceptible in the susceptibility values or in the neutron diffraction diagram. In a more accurate analysis a similar behavior might possibly be found in the layered tetrahedral framework structures of the alkali metal thiomanganates and thiocobaltates.

The chain structures of the sulfides $KFeS_2$, $RbFeS_2$, and $CsFeS_2$ behave like linear antiferromagnets at elevated temperatures. Here the couplings of the magnetic moments in the tetrahedral chains survive up to the decomposition temperatures. The antiferromagnetic interactions are correlated with remarkably short Fe—Fe and Fe—S distances of *ca.* 271 and 223 pm, respectively, within the chains (cf. Table 1). Corresponding distances in the thiomanganates(II), which are isoelectronic with regard to the M atoms, are longer; the resulting weaker collective bonds are also clearly recognized by the higher susceptibility values. In the ferrates it can also be observed that the anisotropy of the coupling phenomena increases on going from the potassium to the cesium compound, since the Néel points for the three-dimensional arrangements of the moments decrease on going from $KFeS_2$ to $CsFeS_2$—a clear demonstration that the atomic distances in the chains in the same sequence hardly change, in contrast to the distances between the chains. For the dinuclear complex $[Fe_2S_6]^{6-}$ in the atomic arrangement of the alkali-metal-rich compound $Na_3FeS_3$ the spin configurations of the individual atoms can be recognized directly *via* the temperature dependence of the magnetic susceptibilities (cf. Section 5.2).

Thioniccolates, thiopalladates and thioplatinates with planar ligand configurations of the transition metal atoms were found to be diamagnetic, thus indicating spin pairing of the $d^8$ system. The degree of diamagnetism corresponds, within the accuracy of measurement, to the values calculated from the increments. Of the copper compounds, only $KCu_4S_3$ has been investigated in detail. It is so far the only ternary alkali metal-transition metal sulfide which exhibits metallic conducting properties. The weak, almost temperature-independent paramagnetism of this compound might therefore be due to the conducting electrons.

In previous investigations the rhenium cluster compounds proved to be diamagnetic. This can also be expected from quantum mechanical calculations, for, with 24 valence electrons per $[Re_6]$-unit, all bonding orbitals are fully occupied. At the same time this implies that single bonds exist between the rhenium atoms in the almost regular $[Re_6]$-octahedra[43-45].

In the lanthanoid compounds $ALnS_2$ the expected magnetism of the trivalent ions was found at elevated temperatures. At very low temperatures Néel points can be observed. Accurate measurements of the magnetic susceptibilities have shown, moreover, that deviations from the linear $1/\chi - T$ law, *i.e.* from the Curie or Curie-Weiss behavior, occur far above the Néel temperatures. On the basis of quantum mechanical calculations there is the possibility of interpreting the measured behavior in terms of crystal field effects and exchange interactions and thus of gaining a deeper insight into the bonding[46,47]. This will be discussed in detail in Section 5.1 for the example of $NaCeS_2$.

It generally holds for the relationships between crystal structure and magnetic properties of the ternary sulfides presented here that the anisotropic $[M_yS_z]$-framework induced by incorporation of alkali metal ions is distinguished by strong covalent bonds. These bonds give collective couplings in non-spin-paired configurations of the M atoms and can be detected by anisotropic antiferromagnetic behavior. In spin-paired configurations of the M atoms, as enforced *e.g.* in ternary nickel(II), palladium(II) and platinum(II) sulfides by the M—S bonds of the planar oriented S ligands, diamagnetic behavior results. In this connection it should be mentioned that it is of importance for assessment of the magnetic behavior whether or not a compound has metallic properties. Conductivity measurements carried out so far[48] show that metallic properties occur exclusively in the mixed-valence compound $KCu_4S_3$.

## 5. Characterization of the Chemical Bond: Chemical Bonding and the Relationship between Structure and Magnetism

A further insight into the relationships between structure and magnetism is achieved if, as an extension to the analysis of the collective interactions, it is possible to measure the direct influence of the ligands on an individual central atom and to find a good fit of the measured values with model calculations. This will be discussed in the following Sections for two very different examples:

a) In $NaCeS_2$ the influence of the ligands on the cerium atom is relatively weak. An antiferromagnetic arrangement is first indicated at 4.8 K, so that above this temperature the influence of the crystal structure on the magnetic properties of the cerium atom can be observed directly[46,47].

b) In $CsFeS_2$ the influence of the ligand field is strong and, at the same time, collective couplings are present up to high temperatures. To gain information about the bonding from the magnetic properties, the antiferromagnetic interactions in the chains must be disturbed by the incorporation of diamagnetic ions. This has been successful in the series of mixed crystals $CsGa_{1-x}Fe_xS_2$[24].

### 5.1. First Example: $NaCeS_2$

$NaCeS_2$ crystallizes in the rock-salt structure. $Na^+$ and $Ce^{3+}$ ions are statistically distributed at the cation sites, their ionic radii, 116 and 115 pm, respectively, are practically equal. The sulfide, which has no phase width, can be obtained from the melt in very pure form as red crystals[49,50]. Figure 11 shows the $1/\chi_{mol}-T$ diagram[*]; the susceptibility

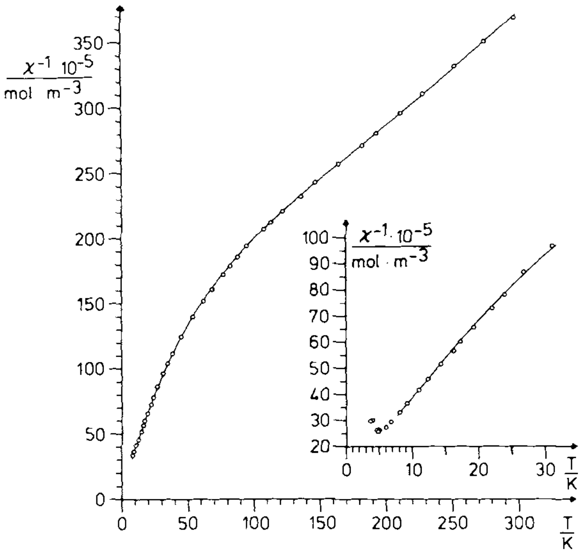


Fig. 11. $1/\chi_{mol}-T$ diagram of $NaCeS_2$: ○○○○ experimental values; —— calculated curves, using the susceptibility formula (4).

values were determined between 3.7 and 297 K by the Faraday method[46]. In the upper temperature range linear dependence is observed, below 4.8 K there exists an antiferromagnetic arrangement of the magnetic moments. The moment calculated from the linear region is in good agreement with the moment calculated for a free $Ce^{3+}$ ion. Below 150 K there are strong deviations from the Curie-Weiss law. This behavior has been successfully explained with the assumption of crystal field effects which could be taken into account by means of a point charge model, and by exchange interactions which were taken care of by a molecular field approximation. The parameters then obtained after a least squares fit to the experimentally determined susceptibility values provided information about the bonding of this sulfide.

The quantum mechanical calculations were performed using the perturbation method. The energy equation of the free $Ce^{3+}$ ion was assigned to the unperturbed system. In the case of compounds of the lanthanoids it is generally essential that the 4f electrons effecting the paramagnetism of the ions lie deep in the electronic sheath and hence are shielded by the outer 5s and 5p electrons. Thus, on incorporation into a crystal lattice not only are the spin moments essentially preserved but also the orbital moments. Moreover, the spin-orbital coupling is relatively strong, so that at room temperature generally only the lowest J-multiplet is occupied. The relevant ground state is given by Hund's rule. For the $Ce^{3+}$ ion it is more essential that expansion of the 4f orbitals in comparison to the ionic radius is greater than in the other lanthanoids and thus the influence of the ligands, promoted by the crystal structure, is distinctly more noticeable, and that quantum mechanical calculations for the $4f^1$-system with only one electron, necessary for calculation of these effects, are simpler than with other configurations.

The sixfold energy-degenerate $\psi$-functions, which correspond to the ground state of $Ce^{3+}$ with $J=5/2$ are suitable as basis functions for the calculations. The distance of the multiplet to the next term ($J=7/2$) is 2250 $cm^{-1}$. This was not taken into account in the calculations. The influence of the cubic crystal field leads to a splitting of the sixfold degenerated ground state into a doublet ($\Gamma_7$) and a quartet ($\Gamma_8$), whose energy difference $\Delta$ depends on the charge and the position of the atoms in the environs of the cerium atom under consideration[51]. A reduction in symmetry of the cubic crystal field caused by a non-homogeneous distribution of the cations in the outer coordination spheres of the cerium ions is of minor importance. The effect on the calculation of the susceptibility values is only slight, leading to a deviation of about 0.3%. Starting from the Van Vleck relation[52] for the calculation of the susceptibilities $\chi$

$$\chi = -\frac{N}{H}\,\frac{\sum\limits_i (\partial E_i/\partial H)\exp(-E_i/kT)}{\sum\limits_i \exp(-E_i/kT)} \tag{1}$$

in which $N$ is the Avogadro number and $-(\partial E_i/\partial H)=\mu_i$ the magnetic moment assigned to the energy state in the direction of the externally established field, a perturbation calculation with exclusive consideration of the influence of the crystal field gives

$$\chi_{KF} = \frac{5Ng^2\mu_B^2}{18kTZ}\,\{(5/2+16kT/\Delta)\exp(\Delta/kT)+13-16kT/\Delta\} \tag{2}$$

where $Z=2+\exp(\Delta/kT)$.

Exchange interactions can be taken into consideration by means of an additional perturbation calculation. In keeping with a Weiss formulation assuming a molecular field then gives for the magnetic susceptibility in the paramagnetic region

$$1/\chi = 1/\chi_{KF}-\lambda \tag{3}$$

with $\lambda$ as molecular field parameter. This effect requires a parallel shift in the $1/\chi-T$ curve, as is known for the linear case of the extension of the Curie law to the Curie-Weiss law. If anisotropic components besides the isotropic components are taken into account in the exchange interactions between the cerium atoms, which essentially occur *via* the sulfur atoms (superexchange), then the simple model must be extended so as to take into consideration the different influence of the exchange interactions on the crystal field states[53-55]. For calculation of the susceptibilities we finally arrive at the following relation:

$$\chi = \frac{(5/2+16kT/\Delta)\exp(\Delta/kT)+13-16kT/\Delta}{\dfrac{18kTZ}{5Ng^2\mu_B^2}-\left(\dfrac{5}{2}\lambda_1+\dfrac{16kT}{\Delta}\lambda_3\right)\exp\left(\dfrac{\Delta}{kT}\right)-13\lambda_2+\dfrac{16kT}{\Delta}\lambda_3} \tag{4}$$

---

[*] In order to facilitate a better comparison with values in the literature $\chi_{mol}$ is given in cgs units, the corresponding values in the SI system are obtained therefrom by multiplication with $4\pi\times10^{-6}$.

Here the molecular field parameters $\lambda_1$ and $\lambda_2$ give the exchange effects referred to the $\Gamma_7$ and $\Gamma_8$ functions, respectively; $\lambda_3$ describes to what extent the wave functions of the ground state are mixed with functions of the excited state by the molecular field (terms of the molecular field, which correspond to the 2nd order Zeemann effect).

Table 2. Parameters obtained from best fits using the susceptibility formulas (2), (3) and (4).

| Formula | $\Delta$ [cm$^{-1}$] | $\lambda_n \times 10^{-5}$ [m$^{-3}$ mol] $n=1$ | $n=2$ | $n=3$ | $R$-value [a] |
|---|---|---|---|---|---|
| (2) | 420 | 0 | 0 | 0 | 0.023 |
| (3) | 416 | −0.5 | − 0.5 | − 0.5 | 0.021 |
| (4) | 470 | −4 | −166 | 35 | 0.0075 |

[a] $R = \left[\sum_{i=1}^{n} |\chi_i(\text{obs.}) - \chi_i(\text{calc.})|\right] \Big/ \left[\sum_{i=1}^{n} \chi_i(\text{obs.})\right]$.

Table 2 lists the parameters determined from best fits using the susceptibility formulas (2), (3) and (4). The fit to the measured values was carried out by the method of least squares. The $R$ value can be regarded as a reliability factor. It is noteworthy that the $R$ value shows a decisively better fit on going from formula (3) to formula (4). If one considers the individual parameters obtained with the formula (4) in detail, it immediately follows from the positive sign of $\Delta$ that $\Gamma_7$ is the ground state. For $Ce^{3+}$, which is octahedrally surrounded by atoms with negative charges, this is to be expected. Figure 12 illustrates this result. Thus, the $\Gamma_8$ states have their maximum electron densities on the x, y and z axes if the $Ce^{3+}$ lies at the origin, *i. e.* in the direction of the negatively charged sulfur ligands, while the electron density maxima for the $\Gamma_7$ state lie along the cube diagonals. But it is also understandable that the $\Gamma_8$ state is decisive in the exchange interactions *via* the sulfur ligands, for only here is essential overlap of the orbitals of central atom and ligand to be expected. Thus the molecular field constant $\lambda_2$, which is assigned to the $\Gamma_8$ state, is also greater by a factor of 41.5 than the value of $\lambda_1$ assigned to the $\Gamma_7$ state. The negative signs of $\lambda_1$ and $\lambda_2$ correspond to antiferromagnetic interactions. These collective covalent bonds are also essentially consistent with the energy difference between the states $\Gamma_7$ and $\Gamma_8$ obtained from the fit with $\Delta = 470$ cm$^{-1}$, being about 57% greater than the value which can be calculated assuming purely ionic bonding (point charge model)[46].

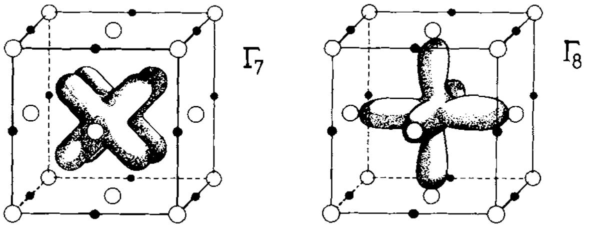


Fig. 12. Electron density distributions of the crystal field states $\Gamma_7$ and $\Gamma_8$. ○ ≙ $S^{2-}$, ● ≙ $Ce^{3+}/Na^+$.

Accordingly, from the change in magnetic susceptibilities of $NaCeS_2$ above the antiferromagnetic Néel temperature an insight can be gained into the chemical bonding: The purely electrostatic components enable an accurate reproduction of the experimental values *via* crystal field effects by point charge models and the covalent components *via* exchange interactions by a molecular field approximation.

### 5.2. Second Example: $CsFeS_2$

$CsFeS_2$ crystallizes in the structure already illustrated in Figure 5. The iron atoms are tetrahedrally surrounded by sulfur atoms, and the tetrahedra are linked one-dimensionally *via* edges to give chains. In the chains the Fe—Fe and, above all, Fe—S distances are markedly short (cf. Table 1); the chains themselves are relatively well separated from one another by the alkali metal atoms.

The magnetic properties of $CsFeS_2$ are closely related to the structural anomalies. Susceptibility measurements gave values which reveal antiferromagnetic interactions of the paramagnetic transition metal species; however, results of neutron diffraction experiments and Mössbauer spectra show that a three-dimensional arrangement of the magnetic moments occurs only below 55 K[24,27,56-58]. Above this Néel temperature $CsFeS_2$ exists as a linear antiferromagnet.

In order to measure the magnetic moment of an iron atom in the tetrahedral field of its sulfur ligands the collective bonds, recognizable by the antiferromagnetic behavior, must be broken. This possibility became feasible after the crystal structure determination of $CsGaS_2$ had shown a structure isotypic with $RbFeS_2$ (Fig. 4)[59], and thus the synthesis of a series of mixed crystals $CsGa_{1-x}Fe_xS_2$ with the two atomic arrangements shown in Figures 4 and 5 as terminal members appeared to be possible[24].

X-ray crystallographic investigations on the system $CsGa_{1-x}Fe_xS_2$ showed with reference to the phase sequences, that in the monoclinic $CsGaS_2$ structure gallium atoms can be replaced by iron atoms up to the approximate composition $CsGa_{0.75}Fe_{0.25}S_2$, that also a monoclinic phase with a small homogeneous region exists in which $x \approx 0.45$, and that the rhombic $CsFeS_2$ structure can take up only little gallium ($x \gtrsim 0.95$). The sequence of the lattice constants led to the following picture: On incorporation of iron atoms in the monoclinic $CsGaS_2$ structure the cell volume decreases with increasing $x$. The lattice constants $a$, $b$ and $\beta$ remain virtually constant with only slight variations, while $c$ decreases significantly. The $c$ axis represents the direction of the chains. Conversely, on incorporation of gallium atoms in the rhombic $CsFeS_2$ structure $c$ increases, while $a$ and $b$ once again scarcely alter. Structural investigations on single crystals confirm these results: The atomic distance of the cations in the chains significantly decreases with increasing $x$, *i.e.* with increasing iron content. Moreover, the distances to the four sulfur ligands in $CsFeS_2$ are also markedly smaller than in $CsGaS_2$ (Fe—Fe: 271.1 pm; Ga—Ga: 295.3 pm; Fe—S 231.1 pm; Ga—S: 227.4 pm). This finding is surprising, for the ionic radius of $Ga^{3+}$ (61 pm) is smaller than that of $Fe^{3+}$ (63 pm).

Here again it is clear that strong covalent bonding occurs in the iron-sulfur chains, *i. e.* the iron atoms are exposed to a strong ligand field of the tetrahedrally coordinating sulfur atoms.

The magnetic susceptibilities of some of the crystallographically investigated mixed crystals have been measured be-

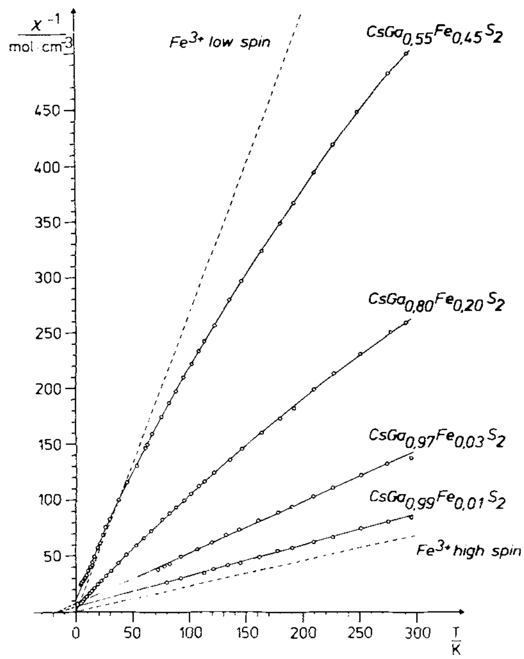


Fig. 13. $1/\chi_{mol}-T$ diagrams of a few mixed crystals $CsGa_{1-x}Fe_xS_2$: ○○○○ experimental values; —— curves calculated with the parameters from Table 3; ---- calculated curves for $Fe^{3+}$ low spin and $Fe^{3+}$ high spin.

Table 3. Calculation of $C$ ($\mu = 2.828\,C^{1/2}\,\mu_B$), $\theta$ and $\chi_0$ from the relation (5) for some mixed crystals of the series $CsGa_{1-x}Fe_xS_2$ (cf. Fig. 13)

| Composition | $\mu\,[\mu_B]$ | $\theta$ [K] | $\chi_0$ [$cm^3\,mol^{-1}$] |
|---|---|---|---|
| $CsGa_{0.99}Fe_{0.01}S_2$ | 5.39 | −15.5 | 0 |
| $CsGa_{0.97}Fe_{0.03}S_2$ | 4.21 | −17.4 | 0 |
| $CsGa_{0.80}Fe_{0.20}S_2$ | 2.66 | − 2.9 | $906\times10^{-6}$ |
| $CsGa_{0.55}Fe_{0.45}S_2$ | 1.81 | − 5.3 | $646\times10^{-6}$ |

tween 3.7 and 295 K using the Faraday method[24]. Figure 13 shows the $1/\chi_{mol}-T$ diagrams of some mixed crystals[*]. The curves obtained can be described by the relation (5)

$$\chi = C/(T-\theta)+\chi_0 \qquad (5)$$

where $\chi_0$ indicates a weak temperature-independent paramagnetism, which was set equal to zero for $x=0.03$ and $x=0.01$. The values of the parameters of eq. (5) determined by the method of least squares are collected in Table 3. For small values of $x$ the magnetic moments are close to that of $Fe^{3+}$ ions with $5.92\,\mu_B$, a value which corresponds to the high-spin state with five unpaired electrons in the 3d level ($S=5/2$). The magnetic moments become smaller with increasing ligand field strength and at $x=0.45$ reach a value which corresponds to a spin state with $S=1/2$.

Apparently a low-spin state is present with a tetrahedral ligand arrangement; this combination has so far never been observed. Figure 14 shows the corresponding electron configuration in a one-electron term system, which can be used here as an approximation assuming that the influence of the ligand field is strong compared to the electronic interactions.

An interpretation of the susceptibility curves (Fig. 13) assuming iron ions in the high-spin state and increasing antiferromagnetic coupling with increasing $x$ is not possible, since the susceptibility part from the coupling would then increase by a measurable amount with falling temperature—which cannot be expected for antiferromagnetic coupling. The concept of low-spin configuration in the tetrahedral field is also supported following investigations on the magnetic behavior of the recently discovered compound $Na_3FeS_3$ (cf. Fig. 6). The Fe—Fe and Fe—S atomic distances lie between those in $CsFeS_2$ and the corresponding ones in $CsGaS_2$. The susceptibility curves, however, still reveal a relatively strong ligand field, for apart from the high-spin state with $S=5/2$ one finds, with three shorter and one longer Fe—S distance (cf. Table 1), a spin state with $S=3/2$ for the two iron atoms of the dinuclear complex[60].

Measurements of the magnetic properties of $CsGa_{1-x}Fe_xS_2$ mixed crystals with $x\geq0.95$, which crystallize in the rhombic $CsFeS_2$-type structure, indicated strong perturbations of the antiferromagnetic interactions even at very low gallium contents. This observation prompted an attempt to mechanically perturbate the magnetic coupling in pure $CsFeS_2$. For this purpose crystals were carefully ground in a purified argon atmosphere. $1/\chi_{mol}-T$ diagrams of such samples are given in Figure 15. Curve I shows a plot of the susceptibility of pure coursely crystalline $CsFeS_2$. The X-ray

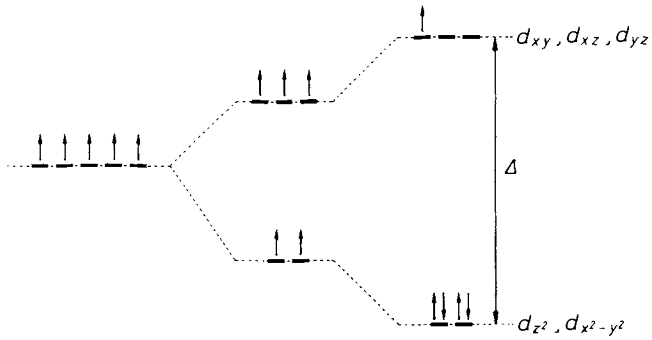


Fig. 14. Crystal field splitting in the case of tetrahedral symmetry, represented in a one-electron scheme.

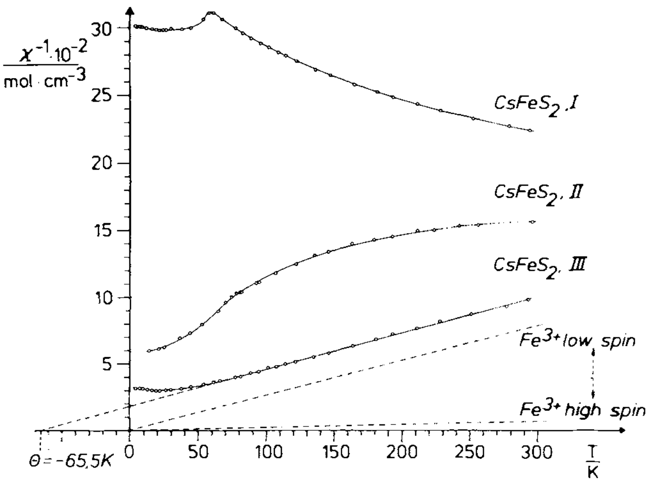


Fig. 15. $1/\chi_{mol}-T$ diagram of coarsely crystalline (I), ground (II), and powdered (III) $CsFeS_2$ samples; ○○○○ experimental values; —— mean curve of the measurements; ---- calculated curves for $Fe^{3+}$ low spin and $Fe^{3+}$ high spin.

---

[*] See footnote on p. 59.

powder diagram of sample II already shows strong broadening of reflections. Associated with the perturbation of long-range order observed here, the susceptibility values change significantly. In the case of sample III the powder diagram shows only weak diffuse reflections. The extensive loss of long-range order yields a Curie-Weiss curve for the temperature-dependence of the susceptibility. With a $\theta$-value of $-66$ K the magnetic moment per iron ion is calculated as $1.7\,\mu_B$. This result is further confirmation of the assumption that in the substances investigated here the previously unobserved low-spin configuration of a transition metal atom is present in the tetrahedral field of its ligands. It should also be mentioned that the Mössbauer spectra of $CsFeS_2$ and $CsGa_{1-x}Fe_xS_2$ mixed crystals[61] are likewise consistent with an extensive spin-pairing in the iron atoms. From the results of neutron diffraction experiments, previously carried out on $RbFeS_2$ and $KFeS_2$, magnetic moments can be derived for the temperature range of the three-dimensional spin order which correspond to those expected for low-spin states[60].

Finally, it can be said that in the anisotropic structure of $CsFeS_2$ the iron atoms are strongly influenced by the sulfur atoms tetrahedrally coordinated to them—an influence, which is subsidized by the collective coupling of the sulfur tetrahedra to chains which then even changes the spin states of the iron atoms contrary to Hund's rule and which thus leads to the observed low-spin configuration.

## 6. Conclusion

The relationships outlined here between crystal structure and magnetism in ternary sulfides of alkali metals and transition metals should make a valuable contribution to our understanding of chemical bonding in the solid state and ought to stimulate further experiments in this sector. Our achievements so far in this area are certainly not only coupled with the compounds selected here; numerous transition metal compounds are already known whose magnetic and/or structural properties allow interesting conclusions to be drawn about the nature of chemical bonding. Having examined the ternary alkali metal-transition metal sulfides the next obvious candidates of interest are certainly the corresponding selenides and tellurides, followed by the phosphides or arsenides where one will find stronger transitions to metallic bonding. A similar and equally informative approach would be the replacement of the alkali metal components by less electropositive elements. In all cases, of course, it is important to synthesize pure substances and to determine both the crystal structure as well as the magnetic properties with high precision.

*I sincerely thank all my coworkers, present and past, who have valuably contributed to this work. We thank the Deutsche Forschungsgemeinschaft, the Landesamt für Forschung in Nordrhein-Westfalen and the Fonds der Chemischen Industrie for financial support.*

Received: September 18, 1980 [A 344 IE]
German version: Angew. Chem. 93, 12 (1981)

---

[1] *A. Völker,* Justus Liebigs Ann. Chem. *59,* 35 (1846).
[2] *R. Schneider,* Poggendorffs Ann. Phys. Chem. *151,* 437 (1874).
[3] *R. Schneider,* J. Prakt. Chem. Ser. 2, Vol. *209,* 10 (1874).
[4] *J. Milbauer,* Z. Anorg. Allg. Chem. *42,* 333 (1904).
[5] *J. Milbauer,* Z. Anorg. Allg. Chem. *42,* 450 (1904).
[6] *W. Rüdorff, K. Stegemann,* Z. Anorg. Allg. Chem. *251,* 376 (1943).
[7] *W. Rüdorff, W. R. Ruston, A. Scherhaufer,* Acta Crystallogr. *1,* 196 (1948).
[8] *W. Rüdorff, H. G. Schwarz, M. Walter,* Z. Anorg. Allg. Chem. *269,* 141 (1952).
[9] *B. van Laar, D. J. W. Ijdo,* J. Solid State Chem. *3,* 590 (1971).
[10] *D. W. Murphy, C. Cros, F. J. DiSalvo, J. V. Waszczak,* Inorg. Chem. *16,* 3027 (1977).
[11] *C. F. van Bruggen, J. R. Bloembergen, A. I. A. Bas-Alberdink, G. A. Wiegers,* J. Less-Common Met. *60,* 259 (1978).
[12] *W. Rüdorff,* Chimica *19,* 489 (1965).
[13] *J. G. White, H. L. Pinch,* Inorg. Chem. *9,* 2581 (1970).
[14] *F. M. R. Engelsman, G. A. Wiegers, F. Jellinek,* J. Solid State Chem. *6,* 574 (1973).
[15] *B. van Laar, F. M. R. Engelsman,* J. Solid State Chem. *6,* 384 (1973).
[16] *J. Huster,* Z. Anorg. Allg. Chem. *447,* 89 (1978).
[17] *W. Bronger, P. Böttcher,* Z. Anorg. Allg. Chem. *390,* 1 (1972).
[18] *W. Bronger, P. Böttcher, U. Hendriks,* unpublished.
[19] *W. Bronger, U. Hendriks,* Rev. Chim. Miner., in press.
[20] *P. Müller, W. Bronger,* Z. Naturforsch. *B34,* 1264 (1979).
[21] *K. Klepp, H. Boller,* Monatsh. Chem., in press.
[22] *J. W. Boon, C. H. MacGillary,* Recl. Trav. Chim. Pays-Bas *61,* 910 (1942).
[23] *W. Bronger,* Z. Anorg. Allg. Chem. *359,* 225 (1968).
[24] *W. Bronger, P. Müller,* J. Less-Common Met. *70,* 253 (1980).
[25] *W. Bronger, J. Eyck, W. Rüdorff, A. Stössel,* Z. Anorg. Allg. Chem. *375,* 1 (1970).
[26] *W. Bronger,* unpublished.
[27] *H. P. Nissen, K. Nagorny,* Z. Phys. Chem. (Frankfurt am Main) *99,* 14 (1976).
[28] *D. B. Brown, J. A. Zubiete, P. A. Vella, J. T. Wrobleski, T. Watt, W. E. Hatfield, P. Day,* Inorg. Chem. *19,* 1945 (1980).
[29] *Ch. Burschka,* Z. Anorg. Allg. Chem. *463,* 65 (1980).
[30] *Ch. Burschka,* Z. Naturforsch. *B 34,* 675 (1979).
[31] *Ch. Burschka,* Z. Naturforsch. *B 34,* 396 (1979).
[32] *W. Bronger, H. J. Miehsen, M. Spangenberg,* unpublished.
[33] *W. Bronger, M. Spangenberg,* J. Less-Common Met., in press.
[34] *M. Spangenberg, W. Bronger,* Angew. Chem. *90,* 382 (1978); Angew. Chem. Int. Ed. Engl. *17,* 368 (1978).
[35] *W. Bronger, O. Günther, J. Huster, M. Spangenberg,* J. Less-Common Met. *50,* 49 (1976).
[36] *J. Huster, W. Bronger,* J. Solid State Chem. *11,* 254 (1974).
[37] *W. Bronger, J. Huster,* J. Less-Common Met. *23,* 67 (1971).
[38] *W. Bronger, O. Günther,* J. Less-Common Met. *27,* 73 (1972).
[39] *O. Günther, W. Bronger,* J. Less-Common Met. *31,* 255 (1973).
[40] *W. Rüdorff, A. Stössel, V. Schmidt,* Z. Anorg. Allg. Chem. *357,* 264 (1968).
[41] *M. Potel, R. Chevrel, M. Sergent, M. Decroux, O. Fischer,* C. R. Acad. Sci. *288,* 429 (1979).
[42] *H. Schäfer, B. Eisenmann, W. Müller,* Angew. Chem. *85,* 742 (1973); Angew. Chem. Int. Ed. Engl. *12,* 694 (1973).
[43] *F. A. Cotton, T. E. Haas,* Inorg. Chem. *3,* 10 (1964).
[44] *L. H. Guggenberger, A. W. Sleight,* Inorg. Chem. *8,* 2041 (1969).
[45] *O. K. Andersen, W. Klose, H. Nohl,* Phys. Rev. *B 17,* 1209 (1978).
[46] *H. Lueken, W. Brüggemann, W. Bronger, J. Fleischhauer,* J. Less-Common Met. *65,* 79 (1979).
[47] *C. M. Plug,* Dissertation, Universität Leiden 1977.
[48] *P. Vits,* Dissertation, Technische Hochschule Aachen 1975.
[49] *R. Ballestracci, E. F. Bertaut,* Bull. Soc. Fr. Minéral. Cristallogr. *87,* 512 (1964).
[50] *R. Ballestracci, E. F. Bertaut,* Bull. Soc. Fr. Minéral. Cristallogr. *88,* 207 (1964).
[51] *K. R. Lea, M. J. M. Leask, W. P. Wolf,* J. Phys. Chem. Solids *23,* 1381 (1962).
[52] *J. H. Van Vleck:* The Theory of Electric and Magnetic Susceptibilities. Oxford University Press, London 1932.
[53] *J. H. Van Vleck,* Rev. Math. Fis. Teorica, Universidad National de Tucumán *14,* 189 (1962).
[54] *P. M. Levy,* Phys. Rev. *177,* 509 (1969).
[55] *P. M. Levy* in *D. J. Craik:* Magnetic Oxides. Part 1. Wiley-Interscience, New York 1975, p. 181 ff.
[56] *D. Raj, S. P. Puri,* J. Chem. Phys. *50,* 3184 (1969).
[57] *C. A. Taft, D. Raj, J. Danon,* J. Phys. (Paris) Colloq. *C6, 35,* 241 (1974).
[58] *H. P. Nissen, K. Nagorny,* Z. Phys. Chem. (Frankfurt am Main) *95,* 301 (1975).
[59] *D. Schmitz, W. Bronger,* Z. Naturforsch. *B 30,* 491 (1975).
[60] *W. Bronger, P. Müller,* unpublished, cf. *P. Müller,* Dissertation, Technische Hochschule Aachen 1980.
[61] *P. Gütlich, J. Ensling,* private communication.

# Recent Progress in Oxo- and Fluorometalate Chemistry

By Rudolf Hoppe[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

About a quarter of a century ago a review article having almost the same title appeared in this journal[1]. Since then many hundreds of new fluorides and oxides of metals have been synthesized, and repeatedly subjected to detailed investigation. Why, and to what end are such compounds still studied[2]? Has our knowledge been not only widened but also deepened? What advances have been made in synthetic chemistry in this sector? Have new ideas led to unforeseen results and have unexpected findings forced the revision of tested concepts? This area of research belongs to solid state chemistry, and in the meantime has become almost unsurveyable even for a committed researcher. In this paper, therefore, an attempt is made to outline any relevant advances that have been made and to present open questions and new aspects using selected examples, mainly from the chemistry of the *first row of the transition metal series.* Those not directly involved in this area may be surprised to find that even substances with a simple composition are also cited. They might ask whether such compounds mentioned in text books are not already understood. Although it is a widely-held view that such compounds are well known, this is incorrect: Probably no-one has ever prepared a sample of $CrF_2$ or $Na_2O$ whose composition "adequately" exactly corresponded to the quoted formula[3]. Typical examples which demonstrate the considerable effort necessary for finally proving what others long ago already assumed to know, can be taken from the area of inorganic chemistry (*e.g.*: $As_2O_5$[4]) as well as from organic chemistry (*e.g.* $C_4[C(CH_3)_3]_4$[5]).

## *Part A: Fluorometalates of the 3d-Metals*

In Kiel, November 1947, *W. Klemm* and *E. Huss* heated an intimate mixture of two chlorides ($2\,KCl + NiCl_2$, previously totally dried in a stream of HCl) in elemental fluorine. I watched, fascinated. It was not clear whether a *mixture* (*e.g.* $2\,KF + NiF_2$) or a *homogenous compound* (*e.g.* instead of $KNiF_3 + KF$: $K_2NiF_4$ or $K_2NiF_6$) would result. The intervening time was whiled away by discussion and prognostication of possible formulas and colors. My tip was: If $K_2NiF_6$, then red. When the sintered corundum boat was carefully drawn to the end of the reaction tube, the original *pale yellow* mixture of the chlorides was now *bright red*; $K_2NiF_6$ had been produced[6,7]. This, and another experiment carried out almost simultaneously, but independently, in Cambridge by *H. J. Emeléus* and *A. G. Sharp*[8], who by reaction of liquid $BrF_3$ on gold obtained $AuF_3$—already observed by *Moissan*[9]—pure for the first time as a *brown* powder, heralded the development of inorganic fluorine chemistry in the post-war era.

## 1. Characterization of Metal Fluorides

All fluorometalates are first obtained as powders in this "fluorination". On exposure to air many of them react, in some cases almost spontaneously, with the moisture of the atmosphere. Thereby hydrolysis often occurs, sometimes the formation of hydrates.

*"Fluorine-active"* substances in particular attack the surface (quartz, glass, metal) of the vessels in which they are contained, sometimes even in the cold and the dark. Most fluorometalates are insoluble in the usual solvents or react with decomposition.

After their preparation, only a few fluorides of the 3d-metals can be purified by sublimation (for example: lustrous *deep blue* crystals[10] of $TiF_3$). Recrystallization from the *melt* also usually meets with unprecedented difficulties. Added difficulties occur if on fluorination *volatile* metal fluorides (for example: $TiF_4$[11]) are formed.

For the above mentioned and other reasons, a compound obtained by fluorination generally cannot be *further purified*, as is otherwise usual.

The *analysis*, therefore, gives only the *over-all composition* of the compound. The accuracy of the *fluorine determination* is frequently unfavorably influenced by reactions which occur because of the reactivity of the samples during the necessary *solubilization*. This is also the case in the *iodometric* determination of *oxidation states*.

Problems are also met with in the *X-ray crystallographic characterization* of the powder samples. The lattice constants can be determined with certainty from the X-ray powder diagram only if an isotypic compound of known crystal structure exists, from which reliable indexing can be obtained. But even here care is required: Guinier-Simon patterns of $Pb_2RhF_7$[12] show an amazing similarity to those of $K_2[NbF_7]$[13] and can be correspondingly indexed. However, no $[RhF_7]$ groups are present having for $Rh^{3+}$, the "sensational" coordination number (C.N.) of *seven*. The structural elucidation performed on single crystals of $Pb_2RhF_7$ showed that indeed the same space group occurs and all particles occupy corresponding equivalent positions; however, the F-pa-

---

[*] Prof. Dr. R. Hoppe
Institut für Anorganische und Analgetische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)

Angew. Chem. Int. Ed. Engl. 20, 63-87 (1981) 0570-0833/81/0101-0063 $ 02.50/0

rameters are numerically so different that an *octahedral* $[RhF_6]^{2-}$ group and and *"isolated"* $F^-$ are present (see Fig. 1).

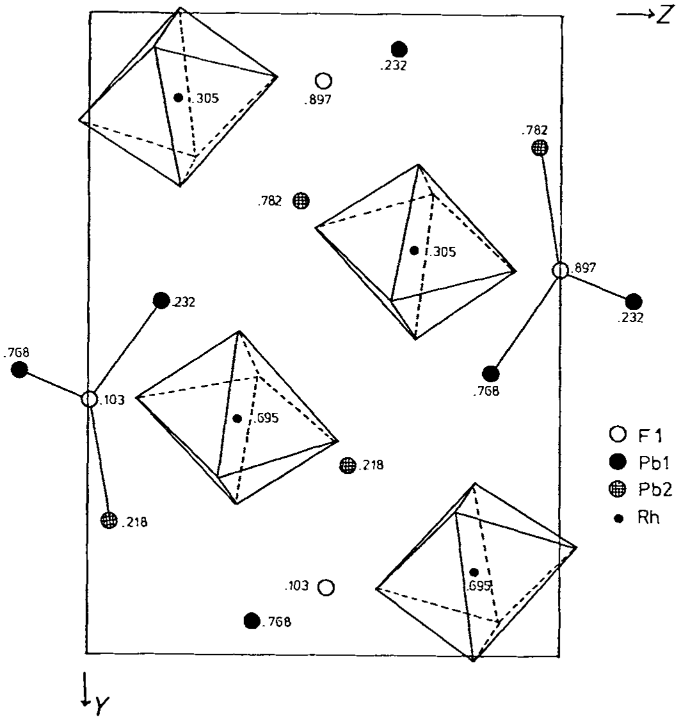


Fig. 1. Projection of the structure of $Pb_2RhF_7$ along [100].

It is especially difficult to prove the presence of impurities, and an exact determination of the *lattice constants* (even with substances crystallizing in the cubic system) is far less possible than one would suppose from the standard deviations.

The *growing* of sufficiently pure *single crystals* is tedious even for thermally stable fluorides, because of possible reactions with the surface of the container and above all with traces of moisture or $O_2$ (for example: $K_2NiF_4 \rightarrow K_2[Ni^{II}_{1-\delta}Ni^{III}_{\delta}F_{4-\delta}O_{\delta}]$[14]). It seemed hopeless ever to obtain single crystals of low-temperature forms (example: $\alpha$-$Ba_3Al_2F_{12}$, cf. Section 2.6) or of *thermally* less stable fluorides ($Li_2CrF_6$[15] disproportionates at room temperature, $Ba[MnF_6]$[16] decomposes on heating). *High-pressure fluorination* in Monel autoclaves [up to 4500 bar, $F_2$, $T = 600\,°C$] with the use of suitable *additives* (*e.g.* $O_2$, $BrF_5$, and also Ar), the choice of which requires much experience, opens up new possibilities for the first time[18] for growing single crystals, even in the case of especially *fluorine-active* compounds, apparently by making use of *chemical transport*[17].

An increasing number of physical measurements are being carried out on fluorides (even on those which are difficult to handle), *e.g.* magnetic measurements on $K_2Na[NiF_6]$[19] or $PdF_2$[20]. Considerable effort is often required to prove that special effects are not due to contaminants, but rather to the "pure" substance corresponding to the formula adopted.

## 2. New Results

A complete survey of new results would require space far in excess of that permitted here, while a summary (*e.g.* arranged according to oxidation states, formula types or crystal structures) might only be of interest to the specialist. Only *special features* have therefore been singled out. A glance at the corresponding fluorides of the 4d- and 5d-metals would seem most expedient.

### 2.1. New Oxidation States

*Tetravalent copper* was obtained for the first time in $Cs_2[CuF_6]$[21] and $Rb_2[CuF_6]$[22] by *high-pressure fluorination.* Both compounds are *orange,* as is $K_2CuF_6$[21], which, because of the even greater instability of the samples prepared so far, has not been characterized in detail.

The synthesis of these highly fluorine-active samples is critical. Only a slight deviation from optimum conditions (pressure of fluorine, time, temperature control) can lead to samples which are either incompletely fluorinated or have already undergone reaction with the crucible material with formation of black decomposition products.

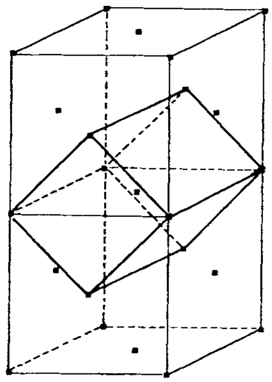


Fig. 2. Unit cell of $A_2[Cu^{IV}F_6]$ with A = Cs, Rb, derived from the $K_2[PtCl_6]$-type ($Cs_2CuF_6$: $a = 8.87_1$, $b/\sqrt{2} = 8.87_1$, $c/\sqrt{2} = 8.92_4$; $Rb_2CuF_6$: $a = 8.38_5$, $b/\sqrt{2} = 8.45_4$, $c/\sqrt{2} = 8.49_5$ Å; both are orange).

*Orthorhombic distortion of the $K_2PtCl_6$-type* (see Fig. 2) is slight. The *magnetic behavior* is here determined by the anomalously high value of the spin-orbital coupling constant ($\lambda_0 = -960\ cm^{-1}$)[23] and by the fact that the "mixing" of the first excited state ($^4T_{1g}$) with the ground state ($^2E_g$) does not necessarily lead to an increase in the magnetic moment in relation to the "spin-only" value ($\mu = 1.73\,\mu_B$).

We also obtained samples of *dark orange* "$Cs_2AgF_6$", about which we communicated only privately[24] because of incomplete characterization owing to its exceedingly easy decomposition. In the meantime, this fluoride has also been prepared by other workers[25] and has been formulated as $Cs_2Ag^{III}_{0.5}Ag^{V}_{0.5}F_6$[26]. Since ESR measurements on $Cs_2[CuF_6]$ clearly indicate the presence of $Cu^{4+}$ [21] (see Fig. 3) we are somewhat sceptical of this formulation.

The question of *tetravalent gold,* first raised some 30 years ago[27], is again of current interest: The *light-yellow* samples "$Cs_2AuF_6$" obtained at that time react with water (in contrast to $Cs[AuF_4]$[27], which likewise immediately decompose), but with vigorous *evolution of gas.* The state of development of X-ray crystallography at that time (only Debye-Scherrer patterns could be photographed on compounds sensitive to air) did not allow a detailed characterization. We now know that these compounds also contained *light-yellow*

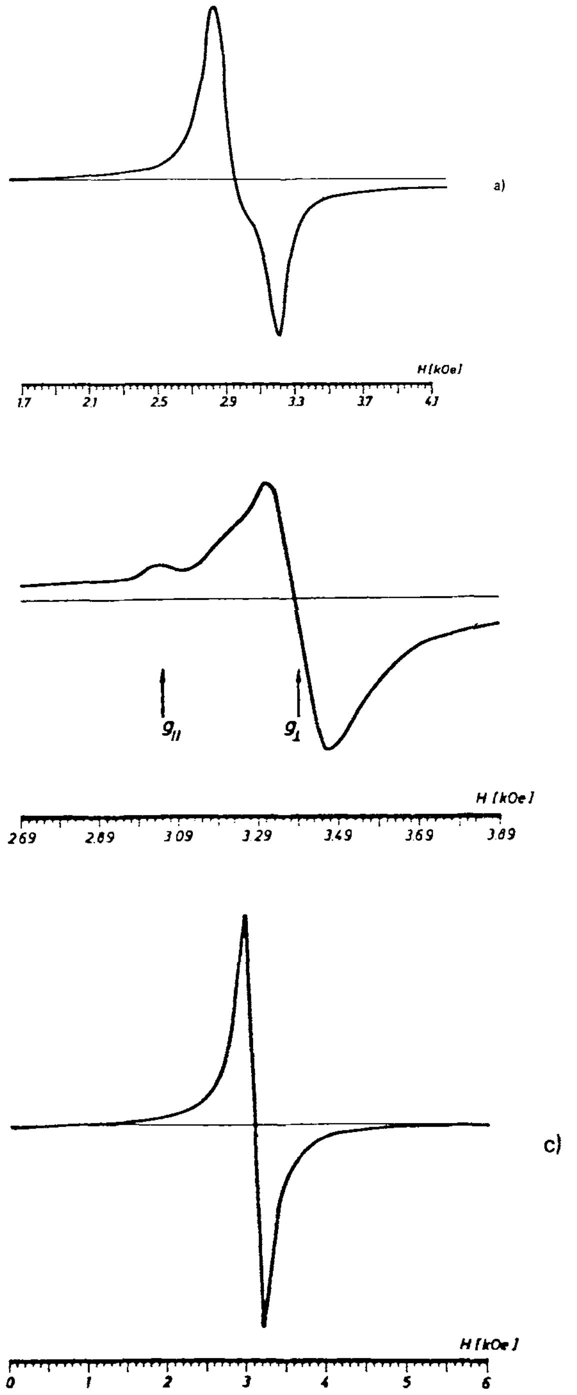


Fig. 3. ESR-spectra of a) Cs$_2$[Cu$^{IV}$F$_6$], b) Cu$^{II}$F$_2$, and c) Cs$_2$K[Cu$^{III}$F$_6$] at 297 K.

Cs[AuF$_6$][28], a fluoro complex of AuF$_5$[29]. New experiments using *high-pressure fluorination* of BaAuF$_5$ or SrAuF$_5$ have led to samples of the composition BaAuF$_7$ or SrAuF$_7$ respectively, while CaAuF$_5$ furnishes CaAuF$_6$; all the products are *light yellow*[30]. (NO)$_2^+$[Au$^{IV}$F$_6$]$^{2-}$ is also said to exist[31]. *Tetravalent cobalt* should also be mentioned here: Following the first report on "K$_3$CoF$_7$"[32], *P. Pfeiffer* doubted the existence of the coordination number 7, and in this he was right:

A detailed investigation showed that K$_3$[CoF$_6$] was responsible for the characteristic properties of the samples (*light blue*, paramagnetism with $\mu = 5.4\mu_B$ between 90 and 300 K). All the fluorides A$_3$[CoF$_6$] (A = Li to Cs) were then prepared as the pure compounds from the analogous, *colorless* (as macrocrystals *pale yellow*) cyanides A$_3$[Co(CN)$_6$][33,34]. These *sky-blue* fluorocobaltates(III) are the only known *high-spin complexes* of Co$^{3+}$. The confusion arose as a result of correct values in the F-analysis, but side-reactions of a mixture of 3KCl + CoCl$_2$ with HF residues in F$_2$ produced a mixture of 2K$_3$[CoF$_6$] + CoF$_3$ + 3KHF$_2$ instead of K$_3$CoF$_6$. However, the criticism stimulated further research: Cs$_2$[CoF$_6$][34] and its well-investigated analogues Rb$_2$[CoF$_6$] and K$_2$[CoF$_6$][35,36] are *brownish-yellow*. These cubic compounds (K$_2$[PtCl$_6$]-type) show a complicated magnetic behavior (on transitions between high-spin and low-spin behavior, *cf.* Section 2.12). Therefore, according to the Boltzmann-distribution, two states of different multiplicity ($^6A_{1g}$ and $^2F_{2g}$) are occupied (a "quasi-thermal" equilibrium between high-spin and low-spin states). Meanwhile, in the continued search for the *"genuine" K$_3$CoF$_7$*, numerous fluorides of the composition doubted by *Pfeiffer* have been obtained, *e.g. carmine red* Cs$_3$NiF$_7$ = Cs$_3$F[NiF$_6$] and the analogous, *bright yellow* Cs$_3$MnF$_7$[37] (*cf.* Section 2.7).

I am convinced that the continuing search for K$_3$F[CoF$_6$] will meet with success.

## 2.2. Fluorometalates with Unusual Coordination Numbers

Fluorocuprates(III) such as *green* K$_3$CuF$_6$[6,38] (see Table 1) closely follow the fluorides of the trivalent 3d-metals preceding copper in the periodic table; they are *paramagnetic*, the "central ion" Cu$^{3+}$ has C.N. 6. This is proved for the cubic elpasolite representatives such as K$_2$Na[CuF$_6$][38] by the structural type. A contrast to the known fluorides of trivalent silver and gold emerges here. These are all *yellow* and *diamagnetic* whether they are of the formula type Cs[AgF$_4$][39], BaAgF$_5$[40], K[AuF$_4$][27], BaAuF$_5$ or Ba[AuF$_4$]$_2$[40] (see Table 1). This striking difference is probably best explained in terms of the difference between 3d- and 4d- or 5d-orbitals.

In the meantime we have found an important connecting link—*intense red, paramagnetic* Cs$_2$K[AgF$_6$], a cubic elpasolite[41]. It follows, therefore that a much closer relationship should exist between the fluorides of the *coinage metals:* The long search (1951—1980) for a *tetrafluorocuprate(III)* finally

Table 1. Complex fluorides of the coinage metals (typical ecamples).

| | | | | | |
|---|---|---|---|---|---|
| K$_3$CuF$_6$<br>($a$ = 8.50 Å) | pale green<br>$\mu = 2.83\mu_B$<br>$\theta$ = 0 K | KAgF$_4$<br>$a$ = 5.90 Å<br>$c$ = 11.15 Å | yellow<br>diamagnetic | KAuF$_4$<br>$a$ = 5.99 Å<br>$c$ = 11.38 Å | yellow<br>diamagnetic |
| Rb$_3$CuF$_6$<br>($a$ = 8.91 Å) | brownish-green<br>$\mu = 2.82\mu_B$<br>$\theta$ = 0 K | RbAgF$_4$<br>($a$ = 6.0 Å)<br>($c$ = 11.8 Å) | yellow<br>diamagnetic | RbAuF$_4$<br>$a$ = 6.18 Å<br>$c$ = 11.85 Å | yellow<br>diamagnetic |
| Cs$_2$KCuF$_3$<br>$a$ = 8.92$_4$ Å | yellow-brown<br>$\mu = 2.83\mu_B$<br>$\theta$ = 0 K | Cs$_2$KAgF$_6$<br>$a$ = 9.17$_5$ Å | red<br>$\mu = 2.6\mu_B$ | — | |
| CsCuF$_4$<br>$a$ = 5.84$_7$ Å<br>$c$ = 12.03 Å | orange<br>diamagnetic | CsAgF$_4$<br>— | yellow<br>diamagnetic | CsAuF$_4$<br>— | yellow<br>diamagnetic |

led, on using high-pressure fluorination, to the preparation of *diamagnetic, orange* Cs[$CuF_4$], which, like Cs[$AgF_4$], crystallized as expected in the tetragonal K[$BrF_4$]-type structure; *i.e.* planar [$CuF_4$]-groups are present[42] (see Table 1). This stimulates continuation of the hitherto unsuccessful[43] search for *(probably) red, paramagnetic gold fluorides* such as $Cs_2K[AuF_6]$.

### 2.3. Fluorometalate or Double Fluoride?

According to *Werner*[44], a complex unit such as $[CuF_6]^{3-}$ or $[CuF_4]^-$ is a *fluorometalate* if it reacts in solution as an entity or is present in a crystal. In contrast, *double fluorides*[45] are those in which *structurally geometrically equivalent* positions (random or ordered) are occupied by *chemically different* entities (example: $MgMnF_6$[16], $ReO_3$-type = $Mg_{0.5}Mn_{0.5}F_3$; see Fig. 4). Compounds containing the same chemical entity in different oxidation states are also to be grouped under this heading. An example is *black* "$PdF_3$" = $Pd^{II}Pd^{IV}F_6$[46].

$LiYF_4$ would doubtlessly be formulated as "antischeelite" Y[$LiF_4$] because of its structural geometry; the $d$(Li—F) distances are substantially shorter than $d$(Y—F)[47]. This prompted the preparation of new scheelites with unusual oxidation states, *e.g.* $Pr^{IV}Cd^{II}[LiF_4]_2$[48], and therefore confirms that such different formulations for the same compound are more than "artificial" for systematic classification. But can bond lengths? Is the structure governed *only by the shortness of the bond lengths* as has been hitherto frequently supposed? With such a demarcation in the presuppositions, the fluorides cited in Table 2, which belong to the $ReO_3$-, $PdF_3$-, $VF_3$- or $LiSbF_6$-type, are double fluorides.

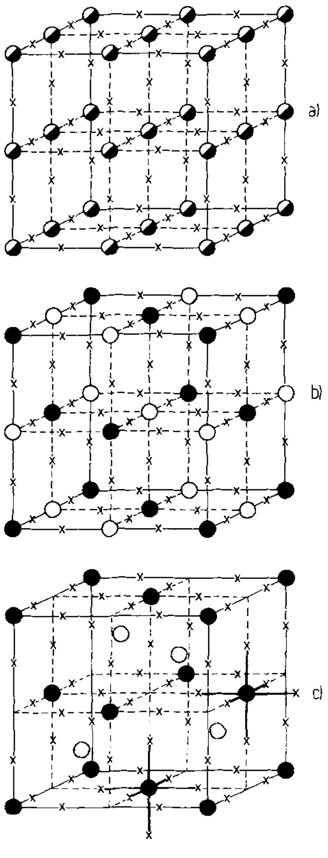


Fig. 4. a) $ReO_3$-type, example $A^{II}B^{IV}F_6$; ◑: $(1A^{II}+1B^{IV})/2$, ×: F.—b) Order variant with $A^{II}$ and $B^{IV}$ at structurally geometrically equivalent positions.—c) $A^{II}[M^{IV}F_6]$ with the anionic part of the crystal structure $M^{IV}\square F_6$ arranged corresponding to the $ReO_3$-type and $A^{II}$ at other positions.

Table 2. Compounds $A^{II}M^{IV}F_6$ and their colors.

| | | | |
|---|---|---|---|
| $VF_3$-Typ (Space group $R\bar{3}c$) | | | |
| $NiMnF_6$ | ocher-yellow | $NiTiF_6$ | pale yellow |
| $ZnMnF_6$ | orange-yellow | $ZnTiF_6$ | colorless |
| $MnTiF_6$ | colorless | $NiCrF_6$ | brown |
| $CoTiF_6$ | lilac | $ZnCrF_6$ | orange-yellow |
| $LiSbF_6$-Typ (Space group $R\bar{3}$) | | | |
| $HgMnF_6$ | orange | $CdCrF_6$ | pink |
| $CdMnF_6$ | yellow | $CaPtF_6$ | light-yellow |
| $CaMnF_6$ | yellow | $MgPtF_6$ | light-yellow |
| $MgMnF_6$ | yellow | $MnPtF_6$ | ocher |
| $CdTiF_6$ | colorless | $ZnPtF_6$ | light-yellow |
| $MgPdF_6$ | yellow | $CoPtF_6$ | light-brown |
| $ZnPdF_6$ | yellow | $NiPtF_6$ | egg-yellow |
| $CdPdF_6$ | yellow | $CaRhF_6$ | light-yellow |
| $CaPdF_6$ | yellow | $MgRhF_6$ | light-yellow |
| $CaCrF_6$ | pink | $ZnRhF_6$ | light-yellow |
| $MgCrF_6$ | pink | $CdRhF_6$ | light-yellow |
| $HgCrF_6$ | orange | $HgRhF_6$ | orange |
| | | $NiRhF_6$ | light-brown |
| $BaGeF_6$-Typ (Space group $R\bar{3}m$) | | | |
| $BaMnF_6$ | yellow | $PdPtF_6$ | green |
| $SrMnF_6$ | yellow | $PbPtF_6$ | light-yellow |
| $BaRhF_6$ | lemon-yellow | $BaCrF_6$ | yellow |
| $SrRhF_6$ | lemon-yellow | $SrCrF_6$ | yellow |
| $BaCrF_6$ | light-yellow | $BaTiF_6$ | colorless |
| $SrCrF_6$ | yellow | $SrTiF_6$ | colorless |
| $BaPtF_6$ | yellow | $SrNiF_6$ | carmine-red |
| $SrPtF_6$ | yellow | $BaNiF_6$ | carmine-red |

However, for those cited fluorides with *tetravalent chromium,* chemical arguments can be found for their classification as *double fluorides* or *fluorochromates*(IV): The cited *double fluorides disproportionate, e.g.,* during storage under inert gas at room temperature, into $CrF_5$ and fluorochromates(III). Compounds of the Ba[$SiF_6$]-type or the $K_2[PtCl_6]$-type and its "stacked variants" (*e.g.* of the $(NH_4)_2[GeF_6]$-type) are not *only fluorochromates(IV)* with respect to the geometrical aspects of the structure, but are also *stable for years* against disproportionation under the same conditions. Such classifications therefore should not be the subject of serious discussion as long as the "covalency" or "ionicity" of the chemical bond concerned has not been directly determined by experiment.

### 2.4. Thermochemistry of the Fluorometalates

There is little data available on the standard values of the *enthalpy of formation* of complex fluorides, and their accuracy is doubtful (see Table 3). More is known about ternary oxides[49]. Some characteristic values given in Table 3 show that in the series $K^+ > Na^+ > Ba^{2+} > Li^+ \simeq Sr^{2+} > Ca^{2+}$, the enthalpy of formation of comparable ternary oxides (from their binary components) markedly decreases under normal conditions, *i.e.* the energy of complex formation becomes smaller.

If one assumes that this general trend observed in the ternary metal oxides also applies in the case of fluorides, then it is understandable that in the mentioned series of *"counter cations"*, difficulties increase in trapping an "anomalously high" oxidation state of a 3d-metal. Table 4 lists as examples

Table 3. Standard values of the enthalpy of formation, $\Delta H^0_{298}$, of some metasilicates from the binary oxides, and of some fluoro complexes from the binary fluorides (all values in kcal/mol).

| | | |
|---|---|---|
| $K_2SiO$ | −65.5 | ±3.0 |
| $Na_2SiO_3$ | −55.5 | ±3.5 |
| $BaSiO_3$ | −38.0 | ±1.0 |
| $Li_2SiO_3$ | −33.4 | ±2.0 |
| $SrSiO_3$ | −31.2 | ±0.5 |
| $CaSiO_3$ | −21.3 | ±0.3 |
| $MgSiO_3$ | − 8.7 | ±0.7 |
| $CdSiO_3$ | − 4.8 | ±0.05 |
| $BaSiF_6$ | −31 | |
| $Na_2SiF_6$ | −16 | |
| $K_2SiF_6$ | −24 | |
| $Rb_2SiF_6$ | −20 | |
| $K_2GeF_6$ | −41 | |

Table 4. Known hexafluoroniccolates(IV); all are carmine red.

| Compound | $a$ [Å] | $b$ [Å] | $c$ [Å] | $\beta$ ($\gamma$) [°] |
|---|---|---|---|---|
| $Cs_2NiF_6$ | $8.90_6$ ($8.90_4$) | | | |
| $CsRbNiF_6$ | $8.69_1$ ($8.68_6$) | | | |
| $Rb_2NiF_6$ | $8.45_1$ ($8.46_3$) | | | |
| $RbKNiF_6$ | $8.30_2$ ($8.29_3$) | | | |
| $K_2NiF_6$ | $8.11_7$ ($8.11_8$) | | | |
| $Cs_2Mn_{0.5}Ni_{0.5}F_6$ | $8.94_3$ | | | |
| $Na_2NiF_6$ | $7.56_4$ | $5.68_6$ | $5.73_8$ | 92.28 |
| β-$BaNiF_6$ | $9.46_5$ | $4.95_0$ | $9.51_8$ | 103.34 |
| α-$BaNiF_6$ | $7.26_8$ (7.29) | | $6.98_1$ (7.00) | 120.0 |
| α-$SrNiF_6$ | $7.07_4$ | | $6.65_6$ | 120.0 |

The lattice constants in brackets were previously estimated.

Table 5. Fluorides containing $Pd^{II}$ or $Ag^{II}$.

| | | | $KBrF_4$-Typ; C.N. ($M^{II}$) = 4 | | | | |
|---|---|---|---|---|---|---|---|
| | | $a$ [Å] | $c$ [Å] | | | $a$ [Å] | $c$ [Å] |
| $BaPdF_4$ | orange | $6.12_0$ | 10.98 | $BaAgF_4$ | violet | $6.03_8$ | 11.46 |
| $SrPdF_4$ | red | $5.79_3$ | 10.75 | $SrAgF_4$ | violet | $5.73_9$ | 11.12 |
| $CaPdF_4$ | purple | $5.52_5$ | 10.56 | $CaAgF_4$ | violet | $5.49_3$ | 10.86 |
| $PbPdF_4$ | purple | $5.87_3$ | $10.83_3$ | $CdAgF_4$ | violet | $5.42_3$ | 10.80 |
| | | | | $HgAgF_4$ | violet | $5.52_4$ | 10.92 |
| $CdPdF_4$-Typ; C.N. ($N^{II}$) = 6(+2) | | | $GdFeO_3$-Typ; C.N. ($M^{II}$) = 6 | | | | |
| | | $a$ [Å] | | | $a$ [Å] | $b$ [Å] | $c$ [Å] |
| $CdPdF_4$ | blue | $5.40_3$ | $KPdF_3$ | brown-violet | $5.98_6$ | $6.00_1$ | $8.50_3$ |
| $HgPdF_4$ | black | 5.43 | $KAgF_3$ | brown | $6.48_9$ | $6.27_0$ | $8.30_0$ |
| *HP*-$PdF_2$ | black | $5.32_7$ | | | | | |
| $CaTiO_3$-Typ; C.N. ($M^{II}$) = 6 | | | | $KCuF_3$-Typ; C.N. ($M^{II}$) = 4(+2) | | | |
| | | $a$ [Å] | | | | $a$ [Å] | $c$ [Å] |
| $RbPdF_3$ | brown-violet | $4.29_8$ | | $RbAgF_3$ | brown | $6.33_5$ | 8.44 |
| $TlPdF_3$ | brown-violet | $4.30_1$ | | $CsAgF_3$ | brown | $6.48_9$ | 8.52 |
| $CsAgFeF_6$-Typ; C.N. ($M^{II}$) = 6(2+4) | | | | | $RbNiCrF_6$-Typ; C.N. ($M^{II}$) = 6 | | |
| | | $a$ [Å] | $b$ [Å] | $c$ [Å] | | | $a$ [Å] |
| $CsAgAlF_6$ | blue | $7.38_0$ | $7.24_1$ | 10.35 | $CsPdScF_6$ | brown-violet | 10.82 |
| $CsAgFeF_6$ | green | $7.31_8$ | $7.46_9$ | 10.45 | $CsPdInF_6$ | brown-violet | 10.89 |
| $CsAgGaF_6$ | turquoise | $7.33_8$ | $7.56_4$ | 10.55 | $CsPdFeF_6$ | red-brown | 10.64 |
| $RbAgAlF_6$ | blue | $7.15_2$ | $7.18_2$ | 10.13 | $CsPdRhF_6$ | red-brown | 10.65 |
| $RbAgFeF_6$ | blue-green | $7.15_3$ | $7.41_9$ | 10.25 | $CsAgScF_6$ | green | 10.79 |
| $RbAgGaF_6$ | blue | $7.17_5$ | $7.52_1$ | 10.36 | $CsAgInF_6$ | green | 10.84 |
| | | $T = 77$ K | $T = 290$ K | $T > 750$ K | $CsAgTlF_6$ | green | 10.88 |
| $CsAgFeF_6$ | | blue | green | black-green | | | |
| $Cs_2CuF_4$-Typ; C.N. ($M^{II}$) = 4(+2) | | | | | | | |
| | | $a$ [Å] | $c$ [Å] | | | | |
| $Cs_2AgF_4$ | violet | $4.58_1$ | 14.19 | | | | |

the hexafluoroniccolates(IV): The formation of $K_2[NiF_6]$ with fluorine can hardly be avoided even under unfavorable conditions ($N_2$:$F_2$ = 10:1; 450 °C); $Na_2NiF_6$[50] can be obtained free from impurities only under $F_2$-pressure (150 bar). The synthesis of $Ba[NiF_6]$ and $Sr[NiF_6]$[52] was very difficult; we finally succeeded, after a 25 year search, by *high-pressure fluorination*. The resulting $BaNiF_6$ did not show the expected modification, which is isotypic with $BaSiF_6$, but a new monoclinic form previously unknown for fluorides $A^{II}M^{IV}F_6$ (A = Ba, Sr; M = 3d-metal) and which only transforms under high static pressure (50 kbar, 350 °C, 6 h) into the rhombohedral modification. This finding prompted the repreparation of *e.g.* $Ba[MnF_6]$[16] and $Ba[CrF_6]$[53] under analogous conditions, in order to observe the possible occurrence of a corresponding monoclinic form.

Thus, it is also understandable that all previous attempts to synthesize $CaNiF_6$ or $CdNiF_6$ remained unsuccessful. The examples of *carmine-red* $SrNiF_6$ and the still unknown (probably *red*) $Li_2NiF_6$ show that the formula type, and hence the crystal structure, also has a substantial influence on the producibility of such fluorides.

It is now clear why it is relatively easy to prepare samples of $Li_3[NiF_6]$[54] which are free of $Ni^{IV}$, and why $Cs_3[NiF_6]$[48] has so far not been obtained in pure form.

### 2.5. Fluorometalates with Different Coordination Numbers of the Same Central Atom

All known fluorides of bivalent nickel are *light green-yellow* as a powder; $Ni^{2+}$ has the C.N. 6 (macrocrystals [*e.g.* $BaNiF_4$[55]: diameter up to 3 cm] have also been described as red). The *composition* (examples: $KNiF_3 = K[NiF_{6/2}]$[56];

$K_2NiF_4 = K_2[NiF_{4/2}F_{2/1}]$[57]; $Ba_2NiF_6 = Ba_2F_2[NiF_{4/2}F_{2/1}]$[58]) has here *no influence* on the C.N. and color. The situation is different in the case of fluorides of bivalent palladium[59] (and silver[60]) (see Table 5): If there are *planar* $[PdF_4]^{2-}$ groups with *C.N. 4* present, then the compounds are *yellow* to *red* and *diamagnetic* ($Ag^{II}$-fluorides are naturally paramagnetic and of other colors). However, if the composition necessitates $Pd^{II}$ having *C.N. 6* and octahedral coordination, then the compounds are *blue* to *violet* and *paramagnetic*. Is it possible to prepare fluorides which exhibit both possible types of coordination for $Pd^{2+}$ at the same time? The first success is observed in recent attempts to resynthesize the scarcely known "$CsPdF_3$"[59]: As the X-ray structure analysis demonstrates[61] the *orange-brown* single crystals of $CsPd^{II}Pd^{II}F_5$ contain square and octahedrally coordinated $Pd^{II}$ in a ratio of 1:1.

We now know that $Cu^{III}$ in $Cs[CuF_4]$ also has a C.N. 4 with a planar arrangement of the four ligands. Would this not signal that renewed and more concerted effort to prepare such fluorides with "mixed" coordination, in which $Cu^{3+}$ is replaced by the isoelectronic $Ni^{2+}$ is warranted? "$PdF_3$" $= Pd^{II}Pd^{IV}F_6$[46] is a kind of counter-example, and demonstrates that clearly different oxidation states in a fluoride may lead to the *same* coordination.

## 2.6. Are there Oligo-Fluorometalates?

Arsenic and antimony form *binuclear* as well as the well-known *mononuclear* fluorocomplexes (example: colorless $K[AsF_6]$[62]); "salts" of the type $(XeF_3)^+[Sb_2F_{11}]^-$[63] are of special interest (*cf.* Section 2.13). Are there analogous fluorometalates of the d-metals?

Until recently, all compounds of the almost limitless number of multicomponent metal fluorides belonged to *one of only* two groups: a) with mononuclear units (*e.g. lime-green* $K_2Na[VF_6]$[64]), b) with "high-polymer" linked coordination polyhedra. These may be linked *one-dimensionally* (*e.g. deep-red* single crystals of $Sr[RhF_5] = Sr[RhF_{4/1}F_{2/2}]$[65]), *two-dimensionally* (*e.g. sky-blue* $K[CoF_4] = K[CoF_{2/1}F_{4/2}]$[66]) or *three-dimensionally* (*e.g. light-pink* $K[MnF_3] = K[MnF_{6/2}]$[67]).

Two new findings show that surprises must be reckoned with: *Colorless* $Cs_3[Fe_2F_9] = Cs_3[F_3FeF_3FeF_3]$[68] verifies that d-metals can also form *binuclear* fluorometalates. Moreover, there is here a linkage of two octahedra *via* a *common face*, previously regarded as unfavorable for electrostatic reasons. This was already known as a chain building unit from light yellow $Cs[NiF_3] = Cs[F_{3/2}NiF_{3/2}]$[69] (here in the form of infinite chains of octahedra connected by faces on both sides).—We detected the first *tetrameric fluoro-complex* in the low-temperature form of $Ba_3Al_2F_{12}$[70]. The analogy of this "ring" $[Al_4F_{20}]^{8-} = [F_{4/1}AlF_{2/2}]_4^{8-}$ (see Fig. 5) to pentafluorides such as $Ru_4F_{20}$[71] is surprising, and it refutes the theory that the ring formation takes place *via* the 4d- or 5d-orbitals[72] or, that it even requires d-orbitals.

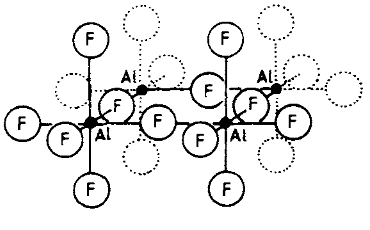


Fig. 5. The tetrameric $[Al_4F_{20}]^{8-}$ group in $Ba_3Al_2F_{12}$ (low temperature form).

The preparation of "mixed" fluorides such as $Ba_6Al_3FeF_{24}$ or $Ba_6AlFe_3F_{24}$ would therefore seem possible. $Na_5[F_6ZrFZrF_6]$[73] should also be mentioned. It contains two trigonal prisms (!) of $6F^-$, each "capped", the cap being bridging. Such fluorides are extremely important for the development of the theory of magnetic interactions between weakly paramagnetic ions (*cf.* Section 2.12).

## 2.7. Fluorometalates with "Single" and "Solitary" F-Atoms

The controversy surrounding $K_3CoF_7$ (*cf.* Section 2.1) stimulated the search for fluorides such as "$K_3NiF_7$" or "$K_3MnF_7$". For, in contrast to $K_2CoF_6$[36], which is difficult to obtain and very sensitive, compounds with $Ni^{4+}$ or $Mn^{4+}$ in place of Co such as *yellow* $K_2[MnF_6]$[74] are comparatively stable and are well-known. However, all experiments with these compounds as potential precursors remained unsuccessful. This was astonishing. The two *colorless* fluorosilicates $(NH_4)_3SiF_7 = (NH_4)_3[SiF_6]$ and $K_3F[SiF_6]$[75] have been known for some time, $(NH_4)_2TiF_7$ was found later[76]. Octahedral groups *e.g.* $[SiF_6]$ are present in their tetragonal crystal structure. Now, $Si^{4+}$ has, like $Ti^{4+}$, a "closed" electron configuration. Therefore, as suggested by *Klemm*[77], at least ions such as $Co^{4+}$ with "half-closed 3d-shells" should be able to form analogous fluorides. We decided to repeat some old experiments[78] and at once obtained a whole series of the desired fluorides $A_3MF_7$ (see Table 6). The use of a passivated Mg-metal boat instead of a sintered corundum one proved to be of vital importance in the success of our prepa-

Tabele 6. a) Tetragonal fluorides $A_3F[MF_6]$ of the $(NH_4)_3SiF_7$-type (above) and b) cubic fluorides $A_3[MF_7]$ of the $(NH_4)_3[ZrF_7]$-type below; $M^{IV}$ = Ce, Pr, Tb: colorless; $M^{IV}$ = Nd, Dy: orange).

| Compound | $a$ [Å] | $c$ [Å] | $c/a$ |
|---|---|---|---|
| $Cs_3SiF_7$ | 8.306 | 6.170 | 0.743 |
| $Rb_3SiF_7$ | 7.959 | 5.823 | 0.732 |
| $Cs_2RbSiF_7$ | 8.198 | 6.019 | 0.734 |
| $Cs_2KSiF_7$ | 8.115 | 5.972 | 0.732 |
| $Rb_2CsSiF_7$ | 8.099 | 5.899 | 0.728 |
| $Rb_2KSiF_7$ | 7.883 | 5.724 | 0.726 |
| $Cs_3TiF_7$ | 8.473 | 6.313 | 0.745 |
| $Rb_3TiF_7$ | 8.202 | 5.979 | 0.729 |
| $Cs_3CrF_7$ | 8.390 | 6.247 | 0.745 |
| $Rb_3CrF_7$ | 8.084 | 5.902 | 0.730 |
| $Cs_3MnF_7$ | 8.369 | 6.233 | 0.745 |
| $Rb_3MnF_7$ | 8.050 | 5.890 | 0.732 |
| $Cs_3NiF_7$ | 8.307 | 6.192 | 0.745 |
| $Rb_3NiF_7$ | 7.978 | 5.857 | 0.734 |
| $K_3MnF_7$ | $a = 11.146$<br>$b = 11.005$ | 5.631 | 0.719 |

| Compound | $a$ [Å] | Compound | $a$ [Å] | Compound | $a$ [Å] |
|---|---|---|---|---|---|
| $CsRbKCeF_7$ | $9.44_1$ | $K_2RbPrF_7$ | $9.27_9$ | $K_3TbF_7$ | $9.07_9$ |
| $Rb_3CeF_7$ | $9.53_7$ | $Rb_2KPrF_7$ | $9.38_3$ | $K_2RbTbF_7$ | $9.16_6$ |
| $Rb_2CsCeF_7$ | $9.66_6$ | $Rb_3PrF_7$ | $9.51_1$ | $Rb_2KTbF_7$ | $9.26_5$ |
| $Cs_2RbCeF_7$ | $9.79_0$ | $CsRbKPrF_7$ | $9.52_1$ | $Rb_3TbF_7$ | $9.39_6$ |
| $Cs_3CeF_7$ | $9.94_9$ | $Cs_2KPrF_7$ | $9.65_9$ | $CsRbKTbF_7$ | $9.39_6$ |
| | | | | $Cs_2KTbF_7$ | $5.52_3$ |
| $Rb_2CsPrF_7$ | $9.63_9$ | $Cs_2KNdF_7$ | $9.60_5$ | $Rb_2CsTbF_7$ | $5.52_9$ |
| $Cs_2RbPrF_7$ | $9.77_6$ | $Cs_2RbNdF_7$ | $9.74_8$ | $Cs_2RbTbF_7$ | $9.69_7$ |
| $Cs_3PrF_7$ | $9.91_8$ | $Cs_3NdF_7$ | $9.87_3$ | $Cs_3TbF_7$ | $9.80_1$ |
| | | | | $Cs_2KDyF_7$ | $9.47_4$ |
| | | | | $Cs_2RbDyF_7$ | $9.63_0$ |
| | | | | $Cs_3DyF_7$ | $9.79_5$ |

ration (cf. Section 3.6). The existence of these substances shows that the "single $F^-$" is no "remarkable exception". The structural difference from the cubic fluorides of the $(NH_4)_3[ZrF_7]$-type with C.N. 7 is noteworthy (see Table 6).

The energetic reasons for the formation of the fluorides $A_3F[MF_6]$ ($M = Ti^{IV}$, $Cr^{IV}$, $Mn^{IV}$, $Ni^{IV}$) are still unclear, but such compounds are apparently thermodynamically stable as regards decomposition, *e.g.*, $Cs_3F[MnF_6]_{(solid)} \rightarrow Cs_2[MnF_6]_{(solid)} + CsF_{(solid)}$. *Colorless* $Ca_2F[AlF_6]$[80] should be mentioned as a fluoride of another formula-type with a "single $F^-$" (see Fig. 6).

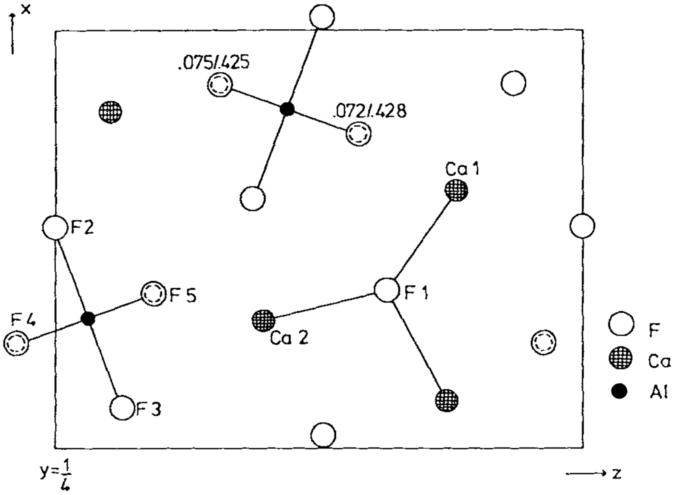


Fig. 6. Structure of $Ca_2AlF_7$ at $y = 1/4$. It can be seen that the $F1^-$ is surrounded by only $3Ca^{2+}$ as well as the $[AlF_6]^{3-}$ groups.

We speak here of a *"single $F^-$"*, because it is not directly coordinated in the classical sense within the "complex-building" moiety. The example of $Ca_2F[AlF_6]$ illustrates that such a $F^-$ coordinates to the "completing cations". Hence, the question immediately arises as to whether there is also a *"solitary $F^-$"* which does not coordinate either in one sense or another. Fluorides of thorium (and zirconium) would indicate that an examination of the d-metals is worthwhile. In the case of $KNaThF_6$[81], C.N. 6, as indicated by the composition, is not found, but C.N. 9, corresponding to $KNa[ThF_{3/1}F_{6/2}]$. Here, as with the analogous fluorides (*e.g.* also with $K_2[ZrF_6] = K_2[ZrF_{4/1}F_{4/2}]$[82]) the increase in C.N. by bridge formation was attributed to the *"size"* of the central ion. This is certainly incorrect. If it were so, C.N. 9 should be present all the more in fluorine-rich thorium compounds. This is not the case, however[83], because in $(NH_4)_4ThF_8$[84], even though the $Th^{4+}$ has C.N. 9 with respect to $F^-$, *one* of the $8F^-$ is a "single $F^-$" and, without any recognizable reason, is not coordinated to the $Th^{4+}$. In $K_5ThF_9$[85] there are sufficient $F^-$ for a C.N. 9, but $Th^{4+}$ again has C.N. 8, one of the $F^-$ remaining "single". Especially interesting, however, is the crystal structure of $K_7Th_6F_{31}$[85]; it is a compound comparable with $KNaThF_6$: Here *one of the 31 $F^-$* is not coordinatively attributed to either $Th^{4+}$ or $K^+$, rather one "solitary $F^-$" is present with only other $F^-$ in the *first sphere of coordination*[83].

## 2.8. Order/Disorder in Fluorometalates

Chemically very similar fluorides may differ markedly regarding the "arrangement" of the "cations": Thus *orange-yellow* $ZnCrF_6 = Zn_{0.5}Cr_{0.5}F_3$ and *brown* $NiCrF_6 = Ni_{0.5}Cr_{0.5}F_3$ have $VF_3$-type structure with random distribution of $M^{2+}$ and $Cr^{4+}$, and in *pink* $CdCrF_6$ and *orange-yellow* $HgCrF_6$ the cations are ordered[53] ($LiSbF_6$-type, see Table 2).

It is still unclear whether in such cases the "disorder" is simulated, *i. e.* there are micro-domains of *ordered* distribution which for their part are *disordered.*

Neither here nor in the case of the analogous fluorides, despite many attempts, has it been possible to prepare *both* types in the *same* substance, *e.g.* to prepare a modified form of $NiCrF_6$ with $LiSbF_6$-type structure. The $RbNiCrF_6$-type[68] (see Table 7) proved to be of special interest regarding the question of the disorder of cations. Here $M^{2+}$ and $M^{3+}$ are "statistically" distributed over the octahedral interstices, thereby decisively determining the magnetic behavior (*cf.* Section 2.12).

Table 7. Fluorides of the $RbNiCrF_6$-type.

| Compound | Color | *a* [Å] |
|---|---|---|
| $CsCuTiF_6$ | light-blue | 10.39 |
| $CsCuNiF_6$ | dark-brown | 10.14 |
| $CsMgFeF_6$ | colorless | 10.35 |
| $CsMgCoF_6$ | light-blue | 10.27 |
| $CsMgGaF_6$ | colorless | 10.23 |
| $CsMnGaF_6$ | pale pink | 10.42 |
| $CsMnFeF_6$ | pale green | 10.55 |
| $CsMnRhF_6$ | red-brown | 10.58 |
| $CsNiScF_6$ | light-yellow | 10.60 |
| $CsNiTlF_6$ | light-yellow | 10.60 |
| $CsNiRhF_6$ | light red-brown | 10.37 |
| $CsZnGaF_6$ | colorless | 10.29 |
| $CsZnInF_6$ | colorless | 10.58 |
| $CsNiInF_6$ | light-yellow | 10.64 |
| $CsZnTlF_6$ | colorless | 10.62 |
| $CsZnScF_6$ | colorless | 10.58 |
| $CsZnTiF_6$ | light-blue | 10.50 |
| $CsZnVF_6$ | light-green | 10.43 |
| $CsZnMnF_6$ | red-brown | 10.40 |
| $CsZnFeF_6$ | colorless | 10.42 |
| $CsZnCoF_6$ | light-blue | 10.34 |
| $CsZnNiF_6$ | dark-brown | 10.17 |
| $CsZnCuF_6$ | brown | 10.24 |
| $CsZnRhF_6$ | red-brown | 10.41 |

Calculations of the Madelung Part of the Lattice Energy (MAPLE)[87] show that an ordered distribution is usually so much more favorable, that under normal equilibrium conditions, disorder should not occur. In the case of the $RbNiCrF_6$-type structure, on the other hand, the situation is different, none of the possible ordered variants were, according to MAPLE, more favorable than the disordered $Rb(Ni_{0.5}Cr_{0.5})_2F_6$[88]. Such cases are rare.

However, new experimental investigations on single crystals established that ordered fluorides such as $CsAgFeF_6$[89] can be prepared (see Table 5); but, an *orthorhombic* unit cell is observed rather than the *cubic "aristo-type"*[90].

*Trirutiles* are derived from rutiles (see Fig. 7) with triplication of the *c*-axis (surprisingly, *"dirutiles"* have, as yet, not been described). Table 8 gives typical examples. It is remarkable that *ocker-colored* $Li_{1/3}Cd_{1/3}Co_{1/3}F_2$[91] is a genuine rutile, whereas according to magnetic measurements, *sky-blue* $LiZnCoF_6$ exists in a partially ordered form $(Li_{0.5}Zn_{0.5})_2CoF_6$ (cf. Fig. 7).

Table 8. Examples of mono- and trirutiles (fluorides).

| Compound | *c* [Å] | *c/a* (*c*/3*a*) | Color |
|---|---|---|---|
| $LiZnRhF_6$ | 9.235 | 0.660 | brown |
| $LiZnCrF_6$ | 9.10 | 0.655 | green |
| $LiNiVF_6$ | 9.142 | 0.656 | yellow-green |
| $LiMgGaF_6$ | 8.96 | 0.650 | light-gray |
| $LiZnCoF_6$ | $9.16_6$ | 0.661 | light-blue |
| $LiMgCoF_6$ | $9.05_4$ | 0.656 | light-blue |
| $LiNiCoF_6$ | $9.07_1$ | 0.656 | brown |
| $LiCuCoF_6$ | $3.10_5$ | 0.673 | ocher |
| $LiCuCrF_6$ | 3.035 | 0.662 | yellow-green |
| $MgF_2$ | 3.045 | 0.658 | white |
| $MgMgFeF_6$ | 3.130 | 0.673 | gray |
| $MgFeFeF_6$ | 3.120 | 0.665 | gray |
| $FeCoNiF_6$ | 3.175 | 0.678 | orange |

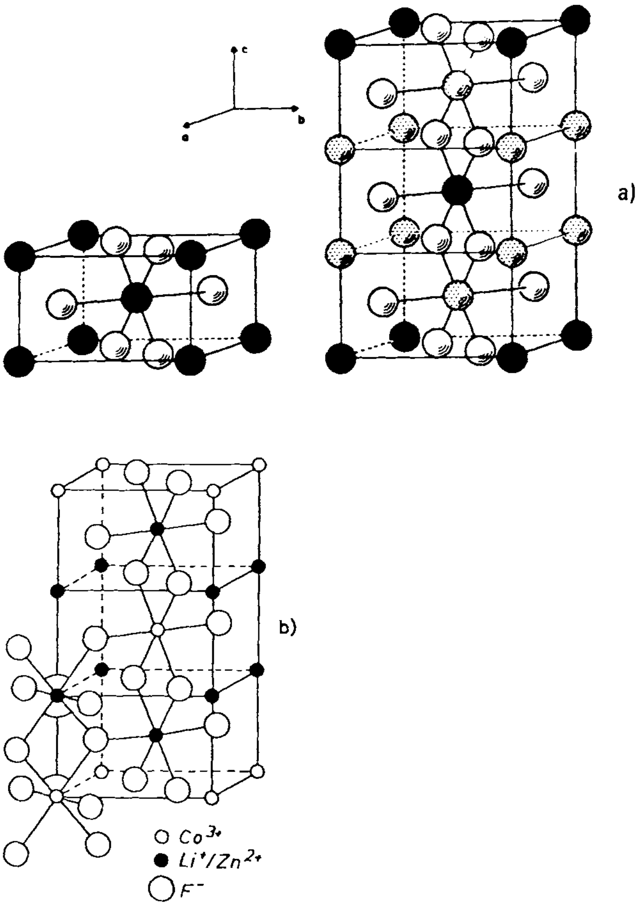


Fig. 7. a) The rutile-type structure and the unit cell of trirutiles which is derived from it. b) Trirutile $LiZnCoF_6$ with ordered distribution of $Co^{III}$ according to $(Li_{1/2}Zn_{1/2})_2Co^{III}F_6$.

*Ordered variants* for the same formula-type occur with larger differences in the ionic radii of the cations, namely the $LiCaAlF_6$-type[92] with *C.N. 6 for* $Li^+$ and $Ca^{2+}$ (*e.g.* $LiCaCoF_6$[91]) or the $LiBaCrF_6$-type[93] with *C.N. 4 for* $Li^+$ and *C.N. 12 for* $Ba^{2+}$ (*e.g.* $LiBaCoF_6$[91]). The *colorless* $LiSrFeF_6$[91] can be classified between them (Table 9), with *C.N. 6 for* $Li^+$ and *C.N. 8 for* $Sr^{2+}$.

Table 9. Motifs of mutual adjunction and coordination numbers in $LiCaAlF_6$, $LiSrFeF_6$ und $LiBaCrF_6$.

a) $LiCaAlF_6$

| | F | C.N. |
|---|---|---|
| Li | 6/1 | ⑥ |
| Al | 6/1 | 6 |
| Ca | 6/1 | 6 |
| C.N. | 3 | |

b) $LiSrFeF_6$

| | F 1 | F 2 | F 3 | F 4 | F 5 | F 6 | C.N. |
|---|---|---|---|---|---|---|---|
| Li | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | ⑥ |
| Fe | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 6 |
| Sr | 1/1 (1/1) | 1/1 | 1/1 | 1/1 (1/1) | 1/1 | 1/1 | 6+2 |
| C.N. | 3+1 | 3 | 3 | 3+1 | 3 | 3 | |

c) $LiBaCrF_6$

| | F 1 | F 2 | F 3 | F 4 | F 5 | F 6 | C.N. |
|---|---|---|---|---|---|---|---|
| Li | 1/1 | 1/1 | | 1/1 | 1/1 | | ④ |
| Cr | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 4 |
| Ba | 1/1 1/1 | 1/1 1/1 | 1/1 1/1 1/1 | 1/1 | 1/1 1/1 | 1/1 1/1 | 12 |
| C.N. | 4 | 4 | 4 | 3 | 4 | 3 | |

*Gutmann*[94] pointed out that the term *"order"* used in the crystallographic sense relates to the *arrangement* of particles.

## 2.9. The Madelung Part of the Lattice Energy (MAPLE) for Fluorometalates

If MAPLE is calculated for *fluoro-* or *oxometalates* then experience shows[87] that for well-determined crystal structures this value agrees with the sum of the MAPLE values of the binary components; the difference between them is lower than 1%, often lower than 0.5%. The MAPLE values given in Table 10 demonstrate how remarkable, on the whole this consistency is, if the individual differences in the contribution of the single components are considered.

We frequently use such MAPLE calculations in direct association with our preparative work. They show whether new structural suggestions are commensurable with those known, they indicate peculiarities and allow important structural parameters to be estimated independently from X-ray data, for those substances which have so far only been obtained as a powder. They can be consulted for an indication of the structural principles of still unknown binary metal fluorides.

Table 11 illustrates that a deviation in the MAPLE values may suggest a refinement of the structure, e.g. for *light-pink* $MnAlF_5$[95], and confirms the quality of the structure determination for $Cr^{II}Cr^{III}F_5$[96]. The example of $CaCrF_5$[97] underscores the limitations of the MAPLE concept: If the proposed structures are "adequately" good, then MAPLE cannot help to decide which space-group is present. If on the whole there is a good agreement, but very different single contributions for chemically and functionally equivalent particles appear, (for example: $BaFeF_5$[98]) then MAPLE warns not to trust the structural proposal too much (here: for the "sub-cell") and prompts a check. The "coordination numbers" of typical solid substances can be counted unambiguously only when it is known which one and to what distance a particle can be regarded as a "neighbor". Here, a new concept can be used, "Effective" Coordination Numbers (ECoN), so that such doubt on counting is removed[99]. Table 12 shows, that for *e.g.* $K_2[NiF_6]$, the value for the structure determining parameter $x_F$ derived from *calculations of ECoN* agrees well with that determined by *neutron diffraction*[100] on the powder. Table 13 shows that the analogously obtained values for powders of the mixed crystal series $Cs_2MnF_6$/$Rb_2MnF_6$/$K_2MnF_6$ are consistent; the pertinent MAPLE values give, by subtraction, practically consistent values for *ultramarine* $MnF_4$ whose structure is not yet known.

Table 10. The Madelung portion of the lattice energy (MAPLE) of two typical garnets (all values in kcal/mol).

| Particle | MAPLE(binary) | MAPLE(ternary) | Δ |
|---|---|---|---|
| a) $Ca_3Al_2Si_3O_{12}$ | | | |
| $Ca^{2+}$ | 482.2 | 508.7 | +26.5 (3 × ) |
| $Al^{3+}$ | 1264.6 | 1298.2 | +33.6 (2 × ) |
| $Si^{4+}$ | 2228.5 | 2214.8 | −13.7 (3 × ) |
| $O^{2-}$ | 482.2 (3 × )<br>608.1 (3 × )<br>709.9 (6 × ) | 612.5 | −15.0 (12 × ) |
| Σ | 18191.3 | 18116.6 | −74.4 (0.4%) |
| b) $Na_3Al_2Li_3F_{12}$ | | | |
| $Na^+$ | 125.5 | 126.3 | + 0.8 (3 × ) |
| $Al^{3+}$ | 1146.1<br>1141.1 | 1108.3 | −35.3 (2 × ) |
| $Li^+$ | 144.3 | 160.5 | +16.2 (3 × ) |
| F | 125.5 (3 × )<br>144.3 (3 × )<br>170.6 (6 × ) | 153.7 | + 0.9 (12 × ) |
| Σ | 4930.1 | 4921.6 | − 8.5 (0.2%) |

Table 11. MAPLE-values (kcal/mol) of fluorides of the $A^{II}M^{III}F_5$-type

| | Σbinary | ternary | Δ | Δ (%) |
|---|---|---|---|---|
| $SrRhF_5$ | 2145 | 2133 | −12.7 | −0.6 |
| $BaGaF_5$ | 2184 | 2174 | −10.4 | −0.5 |
| $SrAlF_5$ | 2321 | 2316 | − 5.8 | −0.2 |
| $BaFeF_5$ | 2165 | 2180 | +14.7 | +0.7 |
| $SrFeF_5$ | 2208 | 2180 | −28.2 | −1.3 |
| $MnCrF_5$ | 2308 | 2308 | − 0.5 | 0.0 |
| $CaFeF_5$ | 2249 | 2260 | −10.2 | −0.4 |
| $CaCrF_5$ [a] | 2262 | 2259 | − 3.6 | −0.2 |
| | 2262 | 2262 | − 0.6 | 0.0 |
| $MnAlF_5$ | 2408 | 2378 | −30.1 | −1.3 |
| $Cr^{II}Cr^{III}F_5$ | 2317 | 2320 | + 3.4 | +0.2 |

[a] Two independent structure determinations.

Table 12. Calculation of the structure determining parameter $x_F$ *via* the effective coordination numbers (ECoN) for two sets of different ionic radii of $F^-$ in $K_2[NiF_6]$.

| a)<br>Starting values of the ionic radii Å:<br>$K^+$ 1.64; $Ni^{4+}$ 0.48; $F^-$ 1.40 | | | b)<br>Starting values of the ionic radii Å:<br>$K^+$ 1.64; $Ni^{4+}$ 0.48; $F^-$ 1.33. | | |
|---|---|---|---|---|---|
| | Contribution to ECoN(F/Σ) | | | Contribution to ECoN(F/Σ) | |
| $x_F$ | Ni | K | $x_F$ | Ni | K |
| 0.217 | 0.87 | 4 × 0.80 | 0.214 | 0.92 | 4 × 0.84 |
| 0.2175 | 0.87 | 4 × 0.82 | 0.2145 | 0.91 | 4 × 0.86 |
| 0.218 | 0.87 | 4 × 0.83 | 0.215 | 0.91 | 4 × 0.87 |
| 0.2185 | 0.87 | 4 × 0.84 | 0.2155 | 0.91 | 4 × 0.88 |
| 0.219 | 0.87 | 4 × 0.85 | 0.2160 | 0.90 | 4 × 0.89 |
| *0.2195* | *0.86* | *4 × 0.86* | *0.2165* | *0.90* | *4 × 0.90* |
| 0.220 | 0.86 | 4 × 0.88 | 0.217 | 0.90 | 4 × 0.91 |
| 0.2205 | 0.86 | 4 × 0.89 | 0.2175 | 0.89 | 4 × 0.92 |
| 0.221 | 0.86 | 4 × 0.90 | 0.218 | 0.89 | 4 × 0.93 |
| 0.2215 | 0.85 | 4 × 0.91 | 0.2185 | 0.88 | 4 × 0.94 |
| 0.222 | 0.85 | 4 × 0.92 | | | |

Average value for $x_F$ from ECoN: 0.218→*d*(Ni—F) = 1.768 Å
*Experimental,* from neutron diffraction: 0.219→*d*(Ni—F) = 1.776 Å

Table 13. MAPLE of $A_{2-x}A'_xMnF_6$, $K_2PtCl_6$-type [kcal/mol]. Calculation of $MAPLE(MnF_4)$ from MAPLE-values of cubic fluorides $A_2[MnF_6]$. In each case $x_F$ was calculated using ECoN, as shown in Table 12 for, *e. g.*, $K_2[NiF_6]$.

| Compound | MAPLE | $MAPLE(MnF_4)$ |
|---|---|---|
| $Cs_2MnF_6$ | 2863.9 | 2477.9 |
| $Cs_{1.8}Rb_{0.2}MnF_6$ | 2875.7 | 2487.2 |
| $Cs_{1.6}Rb_{0.4}MnF_6$ | 2876.4 | 2485.4 |
| $Cs_{1.4}Rb_{0.6}MnF_6$ | 2880.1 | 2486.5 |
| $Cs_{1.2}Rb_{0.8}MnF_6$ | 2874.1 | 2478.0 |
| $CsRbMnF_6$ | 2879.7 | 2481.1 |
| $Rb_2MnF_6$ | 2888.1 | 2476.9 |
| $RbKMnF_6$ | 2880.5 | 2458.0 |
| $Rb_{0.8}K_{1.2}MnF_6$ | 2880.0 | 2455.0 |
| $Rb_{0.6}K_{1.4}MnF_6$ | 2877.1 | 2450.1 |
| $Rb_{0.4}K_{1.6}MnF_6$ | 2884.7 | 2455.4 |
| $Rb_{0.2}K_{1.8}MnF_6$ | 2889.9 | 2458.4 |
| $K_2MnF_6$ | 2888.6 | 2454.8 |
| | | $\overline{MAPLE}(MnF_4) = 2470.0$ |

Table 14 shows, for the example of yellow $K_2[MnF_6]$, how older ideas about the Mn—F distance can be revised and remain in agreement with the data obtained for cubic $K_2MnF_6$.

If it is assumed, as experience shows, that the theory of additivity of the MAPLE values of binary fluorides is valid in general for MAPLE values of ternary fluorides, then such

Table 14. MAPLE-values for the hexagonal modification of $K_2[MnF_6]$ with the newly determined lattice constants $a = 5.72_1$, $c = 9.32_4$ Å. From this it follows that $MAPLE(MnF_4) = 2460$ kcal/mol, which is in good agreement with the average $\overline{MAPLE}(MnF_4) = 2470$ kcal/mol (cf. Table 13).

| Ion | **Shortest distance [Å]** | MAPLE |
|---|---|---|
| $Mn^{4+}$ | 1.77, 1.81 | 1818.8 |
| $F1^-$ (3 × ) | 1.77 | 160.0 (3 × ) |
| $F2^-$ (3 × ) | 1.81 | 156.2 (3 × ) |
| K1 | 2.83 | 109.2 |
| K2 | 2.84 | 117.1 |
| | | $\sum = 2994$ |

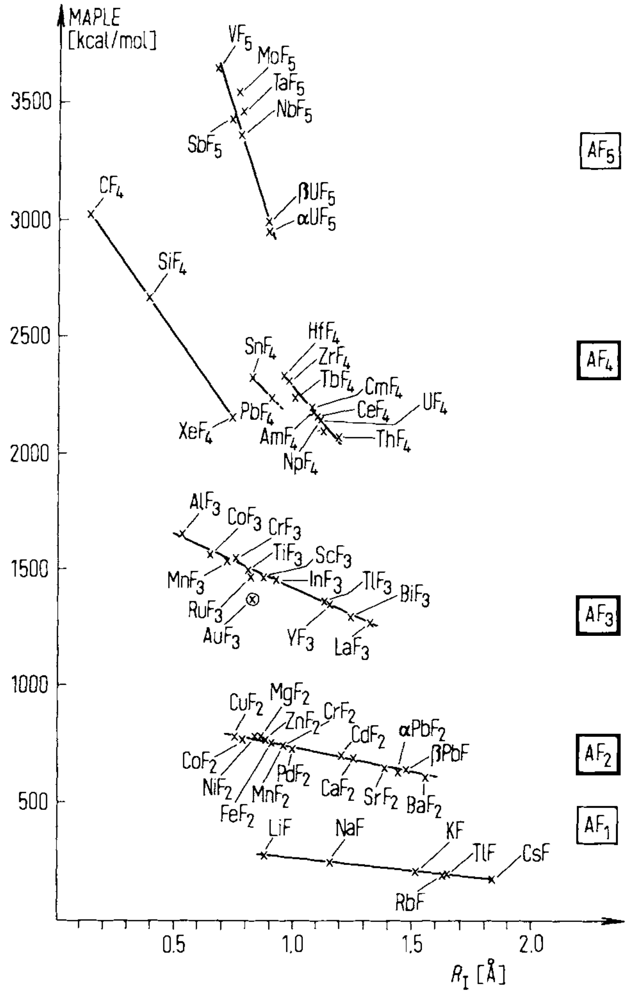


Fig. 8. MAPLE $(MF_n)$ as a function of the ionic radius of $M^{n+}$.

values can be calculated for still unknown fluorides. Figure 8 shows that conclusions can be made for the structural principles of binary fluorides still not investigated crystallographically.

## 2.10. Lattice Constants

Many may be surprised to learn that the lattice constants of even simple substances known for a long time—such as the fluorides LiF to CsF—are not all known with adequate certainty (example: $a$(CsF) = 6.002—6.05 Å[101]). The values for complex compounds vary so much, even in the case of "classic" examples with simple crystal structures ($K_2OsCl_6$: $a = 9.74_9$, $9.79_2$ or 9.82 Å; $K_2PtCl_6$: $a = 9.66$, 9.69, 9.73 or $9.75_5$ Å[101]), that the *"chemical quality"* of the sample must be questioned, even if the difference in precision of older (Debye-Scherrer patterns) and newer determinations (Guinier patterns) are taken into account. Moreover, it is unclear whether differences can be caused by varying content of $OH^-$ instead of $Cl^-$[102], with differing composition (*e.g.* $K_{1.96}[PtCl_{5.96}]$?) or by the orientation *e.g.* of the $[PtCl_6]$-groups not uniformly corresponding to the accepted structure.

Can the lattice constants be *theoretically calculated*? Not yed. Can they be *estimated from the ionic radii*? No, because there are no "rigid" ions. They can by estimated though, from fluorides of the same structural type, as shown in the case of the elpasolites[103].

However, they can be *compared*: Figure 9 shows that for the fluorides $Cs_2[MF_6]$ with M = Ti...Cu, which have the cubic $K_2PtCl_6$-type structure, the lattice constant $a$ decreases linearly with the atomic number. Since, in all known substances $M^{4+}$ has no $e_g$-electrons (with the exception of $Cu^{4+}$) no statement can be made about the still unknown $Cs_2[FeF_6]$ (with $t_{2g}^3e_{2g}^1$ for $Fe^{4+}$). From the values of $Cs_2[CuF_6]$ it is assumed that there could be non-cubic symmetry in the case of $Cs_2[FeF_6]$ too.

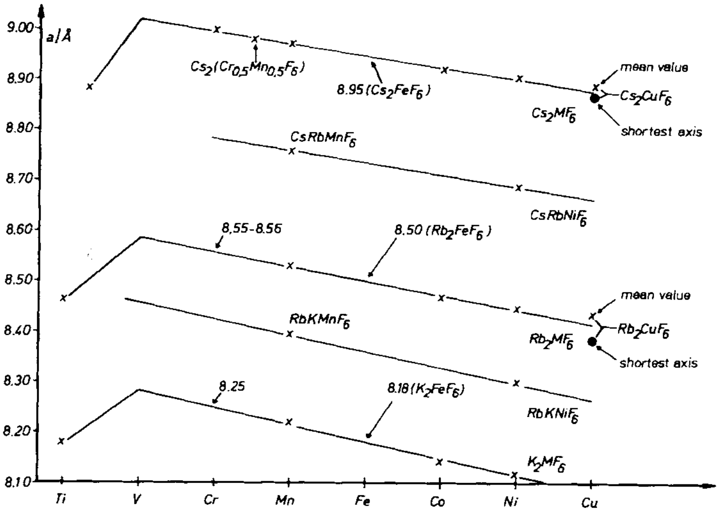


Fig. 9. Trend of the lattice constants of cubic fluorides of the $K_2PtCl_6$-type in the sequence $Ti^{IV}$—$Cu^{IV}$.

The situation is different for the cubic elpasolites $Cs_2K[ScF_6]$—$Cs_2K[CuF_6]$ (see Fig. 10). The lattice constant decreases regularly from the starting member of the series in spite of the addition of the $t_{2g}$-electrons. The jump to the sequence which begins with $Cs_2K[FeF_6]$ is related to the addition of the $e_{2g}$-electrons. Another jump is notable on going from $Cs_2K[NiF_6]$ to $Cs_2K[CuF_6]$; this may be caused by the addition of the second $e_{2g}$-electron.

Mixed crystals such as $CsRb[MnF_6]$ and $Cs_2[Cr_{0.5}Mn_{0.5}F_6]$[104] as well as $Cs_2[Ni_{0.5}Mn_{0.5}F_6]$[66] fit well into the series.

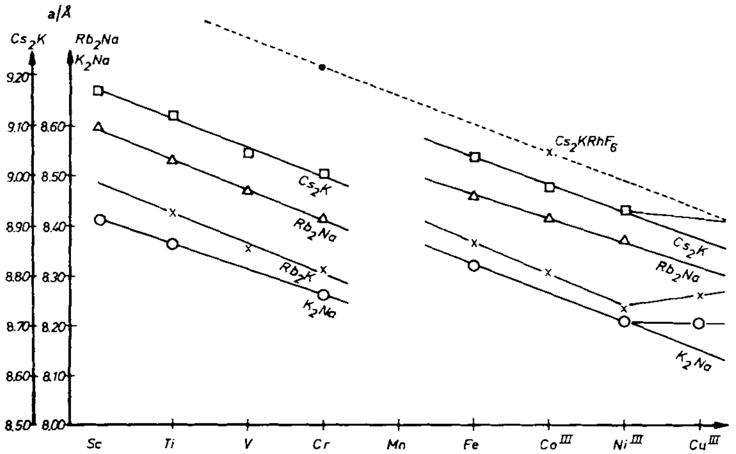


Fig. 10. Trend of the lattice constants of cubic fluorides of the elpasolite-type $A_2B[MF_6]$ in the sequence $Sc^{III}$—$Cu^{III}$.

Analogous linear relationships are found for the tetragonal fluorides of the $(NH_4)_3F[SiF_6]$-type (cf. Fig. 11), as also in the "real" heptafluorometalates of the $(NH_4)_3ZrF_7$-type (Fig. 12).

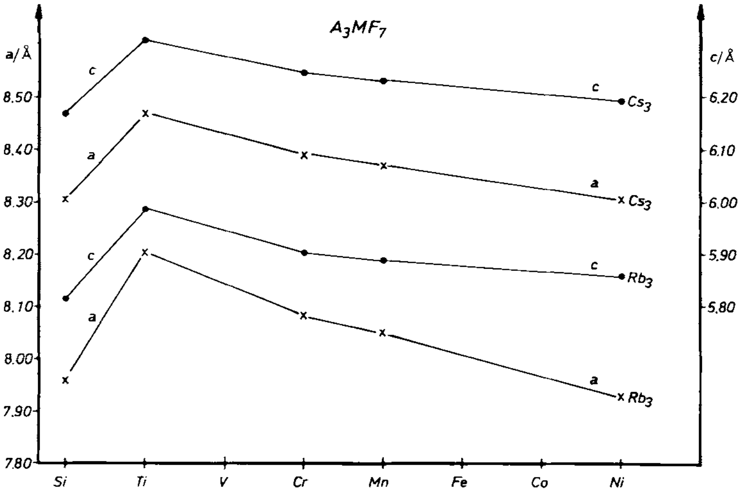


Fig. 11. Trend of the lattice constants *a* and *c* of tetragonal fluorides of the $A^I_3F[M^{IV}F_6]$-type.

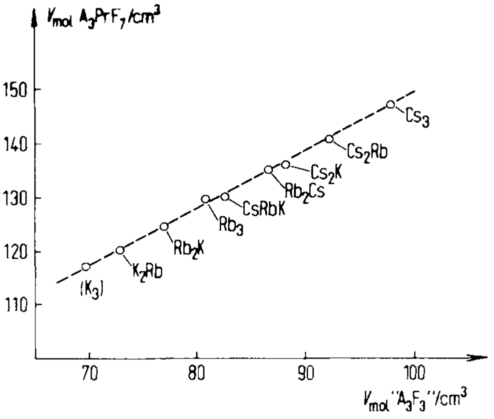


Fig. 12. Molar volumes of the fluorides $A_{3-n-m}A'_nA''_m[PrF_7]$ as a function of the sum of the molar volumes of the alkali-metal fluorides AF, A'F and A"F concerned.

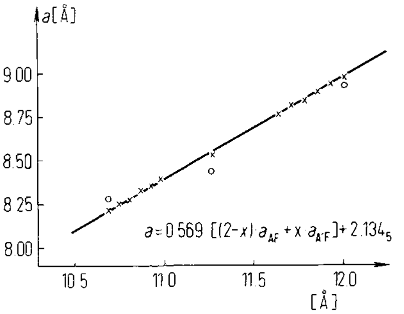


Fig. 13. New lattice constants of $A_{2-n}A'_n[Mn^{IV}F_6]$ as a function of $(2-n)\cdot a(AF)+n\cdot a(A'F)$; here: $K_2MnF_6$...$Rb_2MnF_6$...$Cs_2MnF_6$ (older values: ○).

| Compound | $a_{obs.}$ [Å] | $a_{calc.}$ [Å] | $x_F$ |
|---|---|---|---|
| $Cs_2MnF_6$ | 8.972 | 8.971 | 0.207 |
| $Cs_{1.8}Rb_{0.2}MnF_6$ | 8.935 | 8.930 | 0.207 |
| $Cs_{1.6}Rb_{0.4}MnF_6$ | 8.891 | 8.888 | 0.208 |
| $Cs_{1.4}Rb_{0.6}MnF_6$ | 8.837 | 8.846 | 0.209 |
| $Cs_{1.2}Rb_{0.8}MnF_6$ | 8.815 | 8.804 | 0.210 |
| $CsRbMnF_6$ | 8.757 | 8.762 | 0.211 |
| $Rb_2MnF_6$ | 8.531 | 8.553 | 0.216 |
| $RbKMnF_6$ | 8.397 | 8.386 | 0.220 |
| $Rb_{0.8}K_{1.2}MnF_6$ | 8.360 | 8.353 | 0.221 |
| $Rb_{0.6}K_{1.4}MnF_6$ | 8.330 | 8.320 | 0.222 |
| $Rb_{0.4}K_{1.6}MnF_6$ | 8.270 | 8.286 | 0.223 |
| $Rb_{0.2}K_{1.8}MnF_6$ | 8.255 | 8.253 | 0.223 |
| $K_2MnF_6$ | 8.221 | 8.219 | 0.225 |

Table 15. Elpasolites $Cs_2NaLnF_6$: Agreement between the measured lattice constant and that calculated from a linear relationship between the lattice constant *a* and the mumber *n* of the 4f-electrons.

| Ln | $a_{calc}$ | $a_{abs}$ |
|---|---|---|
| Sm | $9.16_7$ | $9.17_3$ |
| Eu | $9.14_9$ | $9.15_4$ |
| Gd | $9.13_2$ | $9.13_6$ |
| Tb | $9.11_4$ | $9.09_9$ |
| Dy | $9.09_6$ | $9.09_4$ |
| Ho | $9.07_8$ | $9.07_5$ |
| Er | $9.06_0$ | $9.05_8$ |
| Tm | $9.04_2$ | $9.03_9$ |
| Yb | $9.02_5$ | $9.02_8$ |
| Lu | $9.00_7$ | $9.01_4$ |

Our experience shows that: *One* lattice constant is *no* lattice constant. Values obtained from various samples which have been prepared by different methods, and where possible from mixed crystals, should always be checked to see how well they fit together "within themselves". Figure 13 and Table 15 show that the actual precision of the determination in the case of cubic fluorometalates is clearly smaller than the usual standard deviation.

## 2.11. Chemical Properties of Fluorometalates

According to *Ruff*[105], colorless $HgF_2$ is extremely hygroscopic and should even withdraw water from moist $P_2O_5$ to form yellow-red products. Trifluoromercurates(II) such as colorless $Cs[HgF_{6/2}]$[106] are similarly sensitive to traces of moisture. However, sometimes $HgF_2$ is formed during their preparation and sublimes onto the cold end of the reaction tube where it forms *large* (diameter up to 5 mm), clear *colorless* single crystals[107], which are stable for days, even in moist air! This and other observations throw doubt on the frequently described special sensitivity of fluorometalates as a property of the "pure" substance. We assume that traces of HF (*e.g.* as $KHF_2$?) act here as an activator.

Yellow samples of $Cs_2[PdF_6]$[108] decompose quickly in the air to give black-brown hydrolysis products. If, after the actual fluorination of red $Cs_2[PdCl_6]$ (dil. $F_2$, 450 °C, 7d), the samples are annealed for a long time, then they are stable for hours in the air. If the samples are then re-annealed (200 bar $F_2$, 300 °C, 2d) they are again sensitive and decompose in a moment even under an inert gas (due to traces of moisture). Powder patterns show that the core of their black-brown crystallites is unaltered $Cs_2[PdF_6]$[109].

## 2.12. Magnetic Measurements of Fluorometalates

The Curie-Weiss law is valid in general for the complexes discussed here, if diamagnetic ligands "envelope" the paramagnetic central ion and "sufficient" magnetic dilution occurs (see Fig. 14). The occurrence of magnetic interactions in the collective *can* also be absent right to low temperature in linear chains (see Fig. 14).

$K_3[NiF_6]$ and $Cs_2K[NiF_6]$[110] are counter-examples (Fig. 15): Here, deviations occur although the mentioned criteria are fulfilled. They are caused by the influence of the ligand field which alters the energy term sequence of $Ni^{3+}$ from that of the ion in a vacuum; the ground state is now so close to the first excited state (of different multiplicity) that according to Boltzmann statistics, both are occupied. Roughly speaking it is as if there were a "thermal" equilibrium between two states of different multiplicity.

The influence of the ligand field can lead to strong deviations in the magnetic behavior expected according to classical ideas. *Light green* $Cs_2K[PrF_6]$ is *diamagnetic* at low temperatures (other than expected according to *Hund*: $\mu = 3.58\,\mu_B$). Non-diagonal elements in the *secular* determinant imply that there is, in addition, ***temperature independent "weak" paramagnetism***[111]; the ground state of $Pr^{3+}$ is here

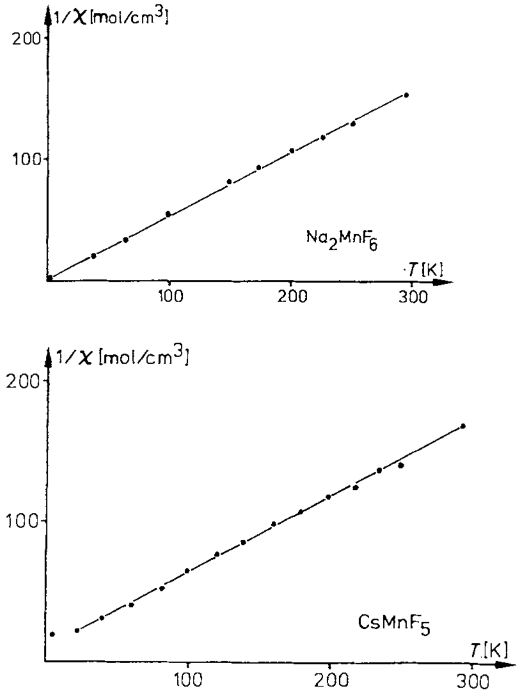


Fig. 14. Magnetic measurements of $Na_2MnF_6$ and $CsMnF_5$ in the range 3—300 K.

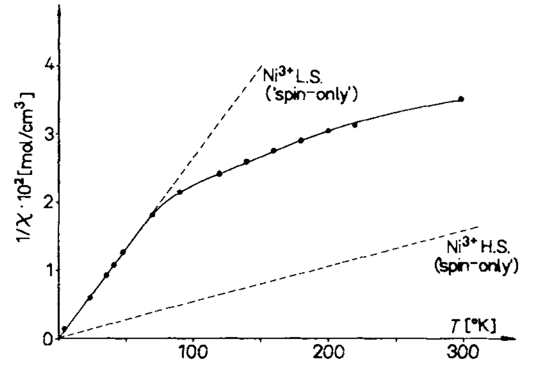


Fig. 15. Magnetic measurements of $Cs_2KNiF_6$ in the range 3—300 K.

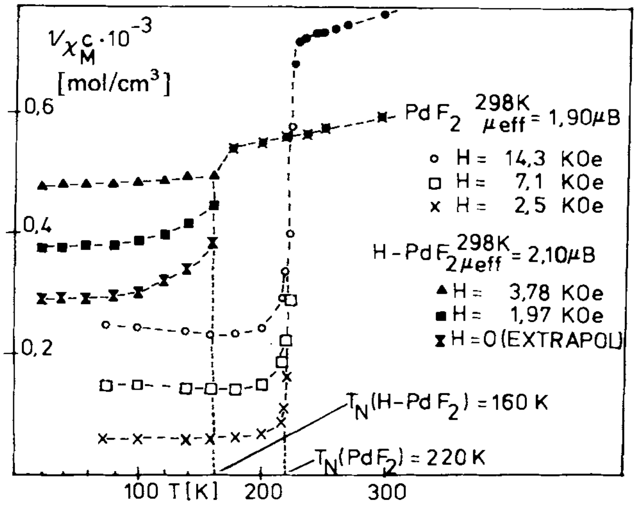


Fig. 16. Magnetic measurements of $PdF_2$.

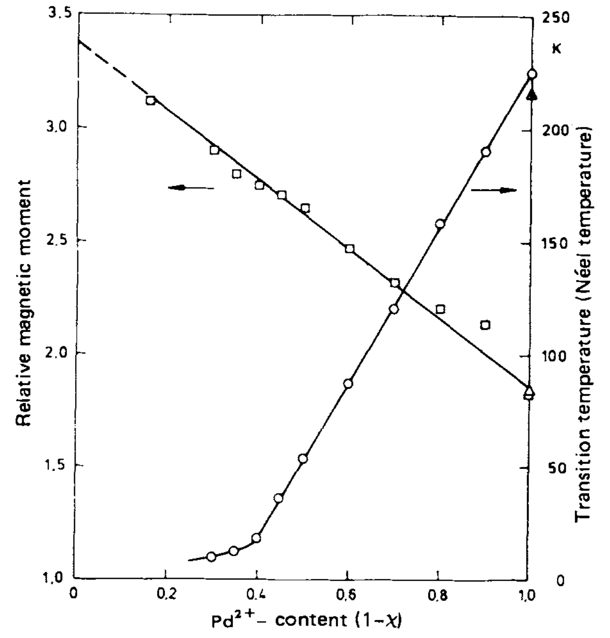


Fig. 17. Magnetic measurements of mixed crystals of $Pd_{1-x}Zn_xF_2$.

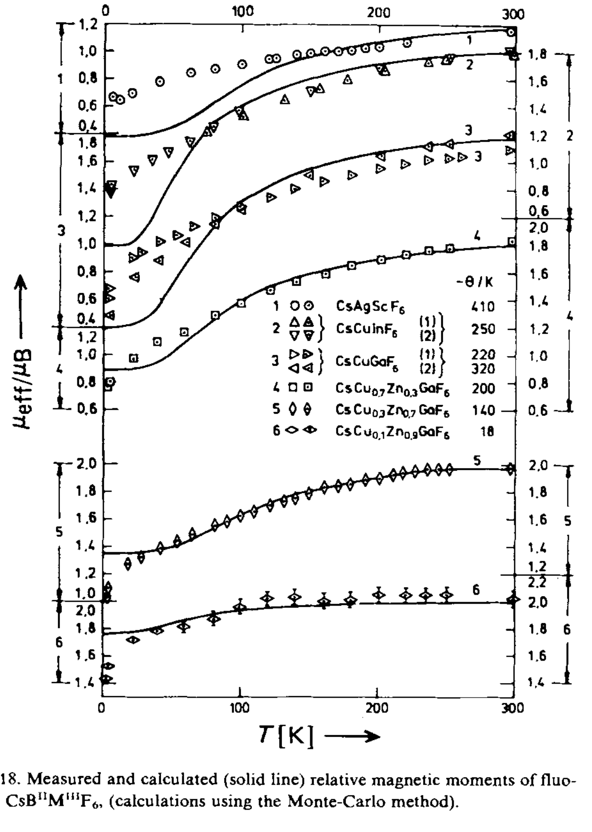


Fig. 18. Measured and calculated (solid line) relative magnetic moments of fluorides $CsB^{II}M^{III}F_6$, (calculations using the Monte-Carlo method).

$\Gamma_1$. $PdF_2$ should also be mentioned[112], it shows *antiferromagnetism* with *"weak" ferromagnetism* which is due to *"canted spins"* (see Fig. 16). Magnetic investigations on the mixed crystals $Pd_{1-x}Zn_xF_2$ gave additional information about the collective interactions[113] (see Fig. 17).

Paramagnetic $Cu^{2+}$ and diamagnetic $Ga^{3+}$ ions are randomly distributed in fluorides such as $CsCuGaF_6$[88], which belong to the $RbNiCrF_6$-type (*cf.* Section 2.8). The probability that mono-, bi- or *n*-nuclear "clusters" of $[CuF_6]$-groups are present, which have mutual bridge-building $F^-$, plays an important role in the interpretation of the magnetic measurements (Fig. 18). We have successfully used the Monte-Carlo method for this example[114].

The magnetic structure was determined for numerous fluorides with "normal" oxidation states (example: $Ba[NiF_4] = Ba[NiF_{4/2}F_{2/1}]$[115]) (see Fig. 19).

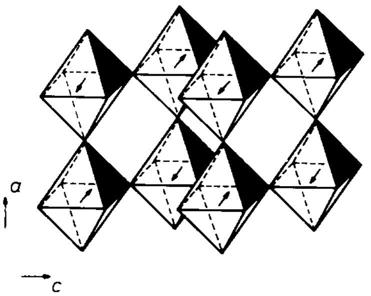


Fig. 19. Magnetic arrangement in $Ba[NiF_4]$ (schematic, only the $[NiF_{2/1}F_{4/2}]$ octahedra are shown).

### 2.13. Fluorometalates with Unusual Cations

The synthesis of xenon fluorides was initiated by two independent investigations: (a) Thermochemical estimations gave a value of *ca.* −30 kcal/mol for $\Delta H^0_{298}(XeF_2)$[116]. (b) Gaseous $PtF_6$ reacts with $O_2$ to form red $O_2^+[PtF_6]^-$[117], therefore the existence of "$XeF^+[PtF_6]^-$" seemed possible.

Since then, fluorides such as $O_2^+[SbF_6]^-$[118] *etc.* (see Table 16) have been prepared. The *bond length of the $O_2^+$-cation* (here 1.10 Å) was determined for the first time from the crystal structure of $O_2^+[Mn_2F_9]^-$[119] using X-rays (see Fig. 20).

Table 16. "Unusual cations" in fluorides of the type $A^+[MF_6]^-$.

$[A]^+ = O_2^+, Cl_2^+, Br_2^+, I_2^+$
$[KrF]^+, [Kr_2F_3]^+$
$[ClF_6]^+, [BrF_6]^+, [IF_6]^+$
$[ClOF_2]^+, [BrOF_2]^+, [NOF_2]^+$
$[XeF_5]^+, [XeF_3]^+, [XeF]^+, [XeOF_3]^+, [XeO_2F]^+$
$[MF_6]^- = [SbF_6]^-, [AuF_6]^-$
$[AsF_6]^-$

For some time it was thought that such "unusual" cations could be advantageously used to "stabilize" still unknown oxidation states of the 3d-metals. This is not the case: For the formation of *e.g.* $A^+[MnF_6]^-$ which contains *pentavalent manganese,* the deciding factor, according to the Born-Haber cycle, is the change of $\Delta H^0_{298}$ for the conversion of AF into $A^+_{gas}$ and $F^-_{gas}$. The following examples show that the "stabilizing" effect of both $O_2^+$ and $NO^+$, and also probably that of other cations such as $XeF_3^+$, presumably does not exceed that of $Cs^+$.

$$\begin{aligned}
&CsF_{solid} \rightarrow Cs^+_{gas} + F^-_{gas}; && \Delta H^0_{298} = +130.6\ \text{kcal/mol}\\
&LiF_{solid} \rightarrow Li^+_{gas} + F^-_{gas}; && \Delta H^0_{298} = +245.6\ \text{kcal/mol}\\
&NOF_{gas} \rightarrow NO^+_{gas} + F^-_{gas}; && \Delta H^0_{298} = +187.6\ \text{kcal/mol}\\
&\text{“}O_2F\text{”}_{gas} \rightarrow O^+_{2\,gas} + F^-_{gas}; && \Delta H^0_{298} = +216.8\ \text{kcal/mol} + \Delta H^0_{298}(O_2F
\end{aligned}$$

However, the addition of $O_2$ to $F_2$ in *high-pressure fluorination* plays an important role. Single crystals of *ultramarine* $MnF_4$[120] and *garnet-red* $MnF_3$[121] were thus obtained for the first time[18].

The formation of *dark red* and *water-clear* single crystals of $O_2^+[Mn_2F_9]^-$ and $(O_2^+)_2[Ti_7F_{30}]^{2-}$, respectively, show how the $O_2$ molecule acts in the "chemical transport" reaction.

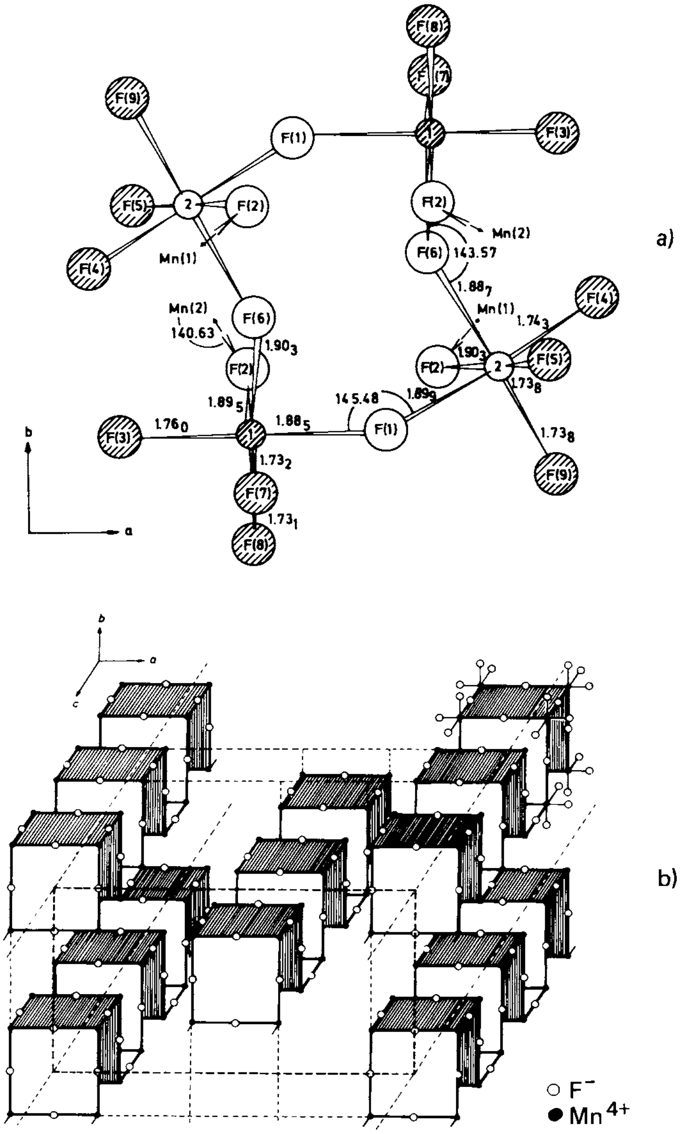


Fig. 20. a) Conformation and bond lengths of the $[Mn_4F_{18}]^{2-}$ group of $O_2^+[Mn_2F_9]^-$; b) Model of the meander-type arrangement of the linked $[Mn_4F_{18}]^{2-}$ groups.

In the first case a *meander-type* linkage of "four-membered ring" analogues of $Ru_4F_{20}$ (Fig. 20) gives a *"Zweier-Vierer" chain*[122], and in the second case[123] one of the few *genuine columnar structures*[124] is present (see Fig. 21).

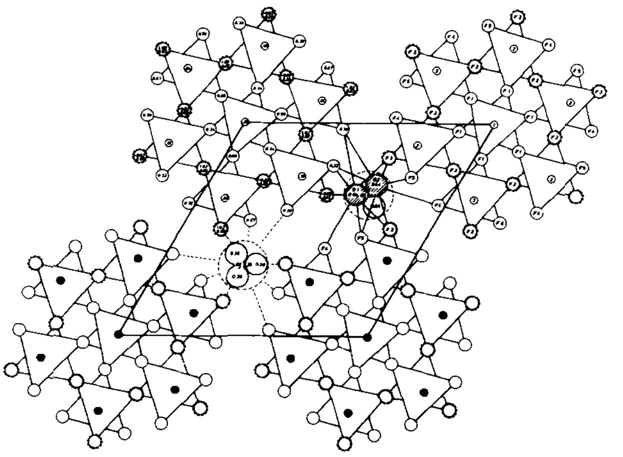


Fig. 21. $(O_2^+)_2[Ti_7F_{30}]^{2-}$ : Projection of the crystal structure along [00.1] (•: $Ti^{4+}$, ·: $F^-$, O: $O^{1/2+}$ at split-positions).

## 2.14. Reactions of Fluorides with Fluorometalates: "Exchange Reactions"

If a mixture of $K_2[MnF_6]+2CsF$ is heated in a welded gold tube, then $Cs_2[MnF_6]+2KF$ is formed smoothly[125]. $K_2[MnF_6]+2LiF$ is produced analogously under corresponding conditions from a mixture of $Li_2[MnF_6]+2KF$. The "exchange" of the "complementary cations" proceeds in accordance with the classical ideas about the complex-stabilizing effect of cations—here with differing ionic radius. In agreement with this, mixtures of $Cs_2[MnF_6]+2KF$ are unaltered by annealing[126]. However, these experiments were carried out under $F_2$ in corundum boats; they must be repeated using Mg-boats (*cf.* Section 2.7) in order to check whether or not $Cs_2KF[MnF_6]$ is formed.

Such exchange reactions proceed quite differently with oxometalates, and are mostly contradictory to classical ideas. Thus, a mixture of $2LiInO_2+Na_2O$ or *also* $2KInO_2+Na_2O$ gives $2NaInO_2$ in both cases as well as $Li_2O$ and $K_2O$, respectively. *Fluorometalates* can react with *oxometalates* to form only *binary* components. Thus, mild tempering (300 °C) of a mixture of $2Na_2[PbO_3]+Na_2[PbF_6]$ will give $6NaF+3$"$PbO_2$"[127]. The sharpness of the powder reflections of the binary component NaF (which has a relatively high melting point), is surprising under such mild conditions.

The frequently described fluorination reactions of organic compounds are also of industrial importance. Our attempts to get fluorometalates such as $Cs_2[NiF_6]$, $Rb_2[MnF_6]$, $K_2[CrF_6]$, $Ba[MnF_6]$, or $K[MnF_5]$ to react with *e.g.* $F_3C—CF{=}CF_2$ in the temperature range between 25 and 300 °C have always been unsuccessful if "pure" samples were used. Even, $AgF_2$ and $TlF_3$ did not detectably react when "dry" (reaction time in each case, 8 h).

## 2.15. Kinetic Influences in the Synthesis of Fluorides

*"Reaction with the surface of the vessel"* are difficult to suppress, especially if there are reactive end products. Sometimes it can be slowed down so that under otherwise optimum conditions, the reaction time is kept as short as possible.

We had to take other types of kinetic influences into account in the synthesis of oxygen-free *bright yellow* $MoF_3$[129] and new fluorides of tetravalent tungsten. If, *e.g.*, for the preparation of $K_2NaWF_7$ the mixture $2KF+NaF+W$ is heated in an autoclave with the stoichiometric amount of previously liquid fluorine, then the formation of *green* $K_2NaWF_7$ competes with that of volatile $WF_5$. The latter than reacts with the surface of the Monel autoclave, inspite of the inlay, to give gray reaction products. The conditions can be optimized by always using the same autoclave and controlling the experimental conditions exactly, especially the temperature control: So much tungsten [(instead of 1 W per 2 KF + 1 NaF, now $(1+\delta)$ W) and fluorine (instead of $2F_2$ per 1 W additional $(5\delta/2)F_2$)] is added so that practically quantitative "$K_2NaWF_7$" along with excess "$WF_5$" is formed within the reaction time. The samples so obtained are subsequently *homogenized* by annealing in a sealed Au-tube[130].

However, fluorides $TlAWF_7$ (A = Cs, Rb, K) are obtained from the mixtures $2TlF_3+AF+W$ by simply annealing in a Au-tube. The tube must be warmed with caution in order to avoid violent deflagration. The unavoidable intermediate formation of gaseous $WF_5$ would inevitably cause the Au-tubes to rupture; this can be prevented by counter-pressure (150 bar Ar) in an autoclave. The glittering *green* fluorides thus produced are cited in Table 17.

Table 17. Cubic fluorides of $(NH_4)_3[ZrF_7]$-type.

| Compound | Color | *a* [Å] |
|---|---|---|
| $Tl_2NaWF_7$ | green | $9.25_8$ |
| $Tl_2KWF_7$ | green | — |
| $K_2NaWF_7$ | gray-green | $8.81_6$ |
| $Rb_2KWF_7$ | green | $9.07_1$ |
| $Rb_2NaWF_7$ | green | $8.89_1$ |

## 2.16. Investigations of the Vibrational Spectra

The importance of the conclusions about structural details obtained from the reflection spectra of such fluorides is known. Only the examples $K_3[NiF_6]$[110] and $Cs_2K[VF_6]$[131] are referred to here.

Raman spectra are useful for the preparative chemist as a "finger-print method": According to Guinier patterns, lanthanoid fluorides such as *colorless* $Cs_3TbF_7$[132] belong to the cubic $(NH_4)_3ZrF_7$-type; the oxidation state of $Tb^{4+}$ has been proved and the Raman spectra are characteristically different (C.N. 7 for $Tb^{4+}$) from similar fluorides with C.N. 6, *e.g.* *colorless* $Cs_2Rb[TbF_6]$[132] (see Fig. 22).

The existence of analogous fluorides with tetravalent *neodymium* and *dysprosium* has been assumed for a long time[133], however, the characterization of the *yellow* samples (*e.g.* of $Cs_3NdF_7$ and $Cs_3DyF_7$) caused difficulties. New preparations of *orange-yellow* *e.g.* $Cs_2RbNdF_7$ and $Cs_2RbDyF_7$[134] produced by high pressure fluorination, exhibit characteristic peaks of $Cs_3CeF_7$ in the Raman spectra and thereby differentiate themselves from *light violet* $Cs_2RbNdF_6$ and *colorless* $Cs_2RbDyF_6$, the cubic elpasolites[135] which have a C.N. 6 for $Nd^{3+}$ and $Dy^{3+}$ as well.

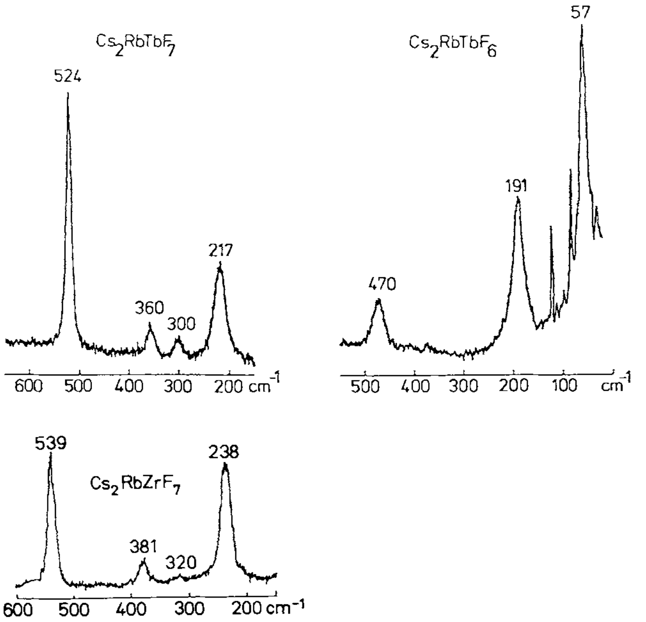


Fig. 22. Comparison of the Raman spectra of $M^{IV}$ fluorides with different coordination numbers.

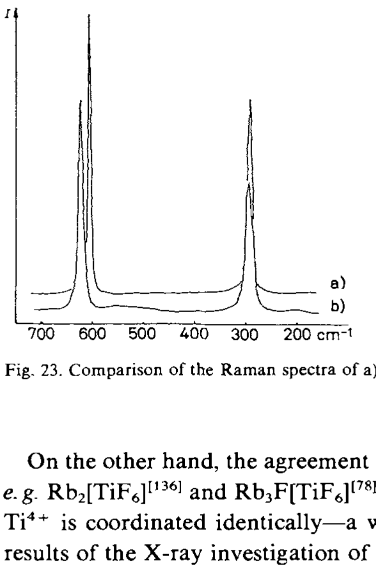


Fig. 23. Comparison of the Raman spectra of a) $Rb_2[TiF_6]$ and b) $Rb_3F[TiF_6]$.

On the other hand, the agreement of the Raman spectra of *e.g.* $Rb_2[TiF_6]$[136] and $Rb_3F[TiF_6]$[78] (see Fig. 23) shows that $Ti^{4+}$ is coordinated identically—a welcome support for the results of the X-ray investigation of the powder samples.

## 3. The Klemm Fluorination

For the preparation of other fluorides in an analogous way to $K_2[NiF_6]$, many factors play a deciding role, mostly only known to insiders. This is illustrated with some examples.

### 3.1. Purity of Fluorine

Fluorine electrolytically evolved on a nickel[137] or graphite[138] electrode—here called $F_2$(I) and $F_2$(II) respectively—always contains hydrogen fluoride and oxygen. Complete purification is difficult (oxygen is trapped *e.g.* as $O_2[SbF_6]$[139]) and for preparative purposes usually unnecessary. HF increases the reactivity. Thus *yellow* $Cs[AgF_4]$ is produced easily with $F_2$(I) but with difficulty using $F_2$(II), from mixtures of $2\,CsCl + Ag_2SO_4$. In contrast, colorless $Cs_2K[YF_6]$[140] is easily obtained with $F_2$(II) but difficult with $F_2$(I), because of the formation of $KHF_2$[*]. If corundum vessels are used for the reactions, then $F_2$(II) permits higher reaction temperatures.

### 3.2. What is Fluorinated?

If possible *compounds* should be fluorinated which already contain the "cations" in the desired ratio *e.g. colorless* $Li_3[Co(CN)_6]$[33] to $Li_3[CoF_6]$. Longer roundabout ways are also worthwhile. $BaPr^{IV}F_6$ and analogues $M^{II}LnF_6$ (M = Ba, Sr; Ln = Pr, Tb)[141] were hitherto only obtained by the following routes:

a) $6\,BaCO_3 + \text{“}Pr_6O_{11}\text{”} \xrightarrow[\text{reptd. evapn.}]{20\%\ HNO_3} 6\,\text{“}BaPr(NO_3)_5\,aq\text{”}$

b) $\text{“}BaPr(NO_3)_5\,aq\text{”} \xrightarrow[500\,^\circ C,\ 12\ h]{\text{HCl-stream}} \text{“}BaPrCl_5\text{”}$

c) $\text{“}BaPrCl_5\text{”} \xrightarrow[350\,^\circ C]{N_2/F_2\ (10:1)} \text{“}BaPrF_x\text{”}$ with $5 \leq x \leq 6$

d) $\text{“}BaPrF_x\text{”} \xrightarrow[500\,^\circ C,\ 12\ h]{F_2\,(500\,bar)} BaPrF_6$

The *molar volume* should decrease during fluorination: *e.g.* $CeF_4$[142] from $CeS_2$, not from $CeO_2$; $ZnF_2$[143] from ZnS or ZnSe, not from ZnO. Homogeneous samples of fluorometalates are only obtainable from *mixtures* if at least one component is "mobile".

### 3.3. How Does the Klemm Fluorination Proceed?

With ACl (A = K, Rb, Cs) as one of the components, the intermediate products are $A[ClF_4]$[144]; and probably $AHF_2$ as well, which leads to "full-fluorination". Little is known about other *intermediate products* of the reaction:

*Light yellow* $Ba[Ni(CN)_4]$ gives first[145] *green* $BaNi(CN)_4F_2$ (or $BaNi(CN)_4(HF)_2$[146]?) of unknown constitution. *Olive-green* "NiO" gives first a *velvet-black* product (NiOF, $NiO_{1+x}$?)[147] with $F_2$ at 300 °C. *Light-yellow* AuCl reacts with $F_2$ at 100 °C to give a *black* product, accompanied by a marked reduction in volume.

Mixtures of $BaCl_2 + NiCl_2$ yield $BaF_2 + NiF_2$ rather than $BaNiF_5$ which is easily produced from $Ba[Ni(CN)_4]$[145]. However, $2\,LiCl$ + "$MnO_2$" gives *bright yellow* $Li_2[MnF_6]$[148], because "volatile" $MnF_4$ is formed as an intermediate. $BaAgF_5$[149] can be produced not only from "$BaAgPO_4$"[150], but also from $BaCO_3 + AgF_2$, although $AgF_2$ (melting point 690 °C) is immobile; probably AgF and/or intermediate products such as *(orange-yellow?)* "$AgAgF_3$"[151] are formed first by partial *reduction in the fluorine stream*; these lower the melting point of $AgF_2$.

The reaction of oxides such as $Na_2PbO_3$[152] with $F_2$ was investigated in more detail: The *yellow* powder first becomes

---

[*] $3\,Cs_2K[YF_6] + 3\,HF = 2\,Cs_3[YF_6] + YF_3 + 3\,KHF_2$.

*black-brown* (200 °C, 2 h) and gives a *mixture* of $2NaF + "PbO_2"$, which also on annealing produces a mixture ($Na_2[PbF_6] + 2Na_2[PbO_3]$) in thermal equilibrium without $F_2$ being formed. Further heating with $F_2$ (300 °C) leads to $Pb_{12}O_{19}$ by reduction[127]. Only then is $Na_2[PbF_6]$ produced[153]. The sharpness of the NaF reflections of samples thus obtained is surprising. $LiInO_2$ and $NaInO_2$[154] analogously afford LiF and NaF, respectively, along with *yellow* $In_2O_3$; $NaTlO_2$ and $Li_2SnO_3$ behave correspondingly. Subsequently, $LiInF_4$, $NaInF_4$, $NaTlF_4$, and $Li_2SnF_6$ are formed[43].

### 3.4. How is Fluorination Carried out Today?

Whenever possible we fluorinate with "stationary" $F_2$ in order to reduce the influence of traces of HF. Local heating can be avoided by dilution (*e.g.* $N_2:F_2 = 10:1$) and lower temperatures at the beginning of the fluorination process.

*High-pressure fluorination* in Monel-autoclaves (up to 4500 bar, 600 °C [short-term], for up to 6 weeks and sealing after the Bridgman principle) offers certain advantages. The starting material must be carefully chosen in order to avoid violent explosions! Additives are necessary for the growth of single crystals, often Ar and $O_2$ are also favorable for still unknown reasons. The autoclave is filled with liquid fluorine, the end pressure can be adjusted *via* this amount (calibrated glass vessel).

### 3.5. Other Synthetic Routes

"Lower" fluorides are produced by annealing suitable mixtures (*e.g.* $2TlF_3 + V$) in a welded noble-metal tube. Redox reactions lead to otherwise inaccessible fluorides such as *deep-orange* $Tl_2VF_6$[155] or *straw-yellow* $Tl_2[MoF_6]$[129].

Oxide fluorides such as *e.g.* colorless $Pb[WO_3F_2]$, isotypic with $Sr[AlF_5]$[156], can be obtained by annealing the binary components. In the case of $Pb[WO_3F_2]$, gray samples are always produced in *new* welded tubes because partial reduction of $WO_3$ is unavoidable. However, if tubes which have already been used and then carefully cleaned are heated in $O_2$, then *colorless* samples are obtained. Probably hair-cracks allow some $O_2$ to penetrate the surface of the vessel and hinder the partial reduction of $WO_3$.

### 3.6. Choice of Vessel Material

The best material is still *sintered corundum.* Nevertheless, there are some fluorides, such as $Cs_3F[MnF_6]$ (cf. Section 2.7) which can only be produced in magnesium boats, previously passivated by $F_2$. Obviously the intermediate $CsHF_2$, formed from HF, reacts here with the corundum.

## *Part B: Oxometalates with d-Metals*

Are oxo- and fluorometalates comparable? Even *Scholder*[1] referred to the classical ideas of complex chemistry, according to which no principal difference in constitution exists between the two. In fact the different charge of $F^-$ and $O^{2-}$ leads to marked differences: For the *same oxidation state* (example: $Ba[MnF_6]$ and $Ba[MnO_3] = Ba[MnO_{6/2}]$[157]) the composition, and therefore the structure (*"isolated"* anions in the former, *3-dimensional giant anions* in the latter) is fundamentally different. For the *same composition* (example: $K[VO_3] = K[VO_{2/1}O_{2/2}]$[158] and $K[VF_3] = K[VF_{6/2}]$[159]) then, *non-commensurable* substances with different structures are present because of the different oxidation states. Tetrahedral groups with high oxidation state are well-known in oxometalates such as *e.g. colorless* $Cs_2[MoO_4]$[160] (isotypic with $\beta$-$K_2SO_4$). In the case of fluorometalates, so far only fluoroberylates such as $K_2[BeF_4]$[161] (related to olivine $Mg_2[SiO_4]$) are known. For $Cs[LiF_2] = Cs[LiF_{4/2}]$ and $RbLiF_2$[162] there is no analogy to silicates (here to "stuffed" framework structures of the $SiO_2$-type) but a characteristic *layer structure* determined by "double tetrahedra" *i.e.* $Cs^2_\infty[F_{2/2}LiF_2LiF_{2/2}]$ occurs.

*Remarkable differences* between both groups of compounds result from the fact that there are *"cation-rich" oxides* $A_2O$ (A = Li—Cs, Cu, Ag, Tl) which form numerous derivatives, however the fluoride analogs are missing; the unique sub-fluoride $Ag_2F$[163] is "without chemistry".

The plethora of the new investigations compels a limitation: Only *"genuine" oxometalates* with *"small" anions* of the d-metals are considered here.

## 1. What is an Oxometalate?

I do not know a generally applicable definition.

If a ternary metal oxide *e.g.* $KMnO_4$, dissolves in water without decomposing and thereby dissociates into ions, here $K^+$ and $[MnO_4]^-$, then an *oxometalate* is undoubtedly present. But the overwhelming majority of the compounds regarded as "oxometalates" are hydrolytically decomposed by water; in most cases other solvents are unknown. If *e.g.* $Na_6[ZnO_4]$[164] is dissolved in concentrated sodium hydroxide to give a clear solution, then nothing is known about the ions present in solution. If solid phases are formed *e.g.* $Na[Zn(OH)_3]$[165], then they crystallize as the phase with the lowest solubility under the reaction conditions. It is still not known to what extent they are involved in an equilibrium in solution.

The frequently used arguments derived from the geometry of the atomic positions are of doubtful value. I ask again: Does a shorter distance always represent also a stronger chemical bond?

An example might arouse further doubt: $Li_2SiO_3$ has been known for a long time. If, as in all previously known silicates, one assumes the C.N. 4 for $Si^{4+}$ relative to $O^{2-}$, then a structure of the type $[SiO_{2/1}O_{2/2}]$ must occur which contains $O^{2-}$-bridges. This means that it has either an *infinite chain* or a finite ring (found for the first time for alkali metal silicates with $K_6[O_{2/1}SiO_{2/2}]_3$[166], see Fig. 24) as a structural characteristic. But C.N. 4 is also to be expected for $Li^+$!

If we assume (in agreement with the known crystal structure of $Li_2SiO_3$[167]) that a (here: hexagonal) closest-packing of $O^{2-}$ is present and $Li^+$ and $Si^{4+}$ occupy tetrahedral inter-

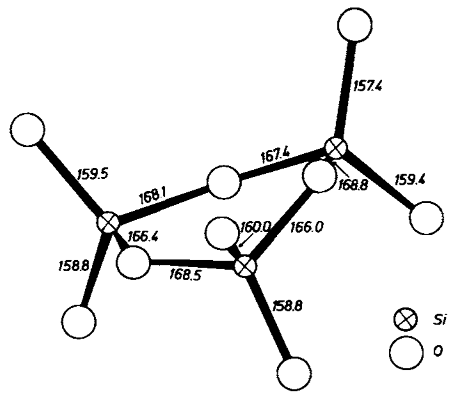


Fig. 24. $[Si_3O_9]^{6-}$ group of $K_6[Si_3O_9]$; bond lengths in pm.

stices in a regular fashion, then the cations are arranged themselves in a close-packed manner. Assuming that, for energetic reasons, the $Si^{4+}$ have the greatest possible distance from one another, then, according to Figure 25, there is only one possibility, to arrange $Li^+$ and $Si^{4+}$ electrostatically favorably within *each* layer. If these layers are stacked along [00.1] due to a closest packing, then $[O_{2/2}SiO_{2/2}]$ chains are automatically built in this direction; this is found in the case of $Li_2SiO_3$.

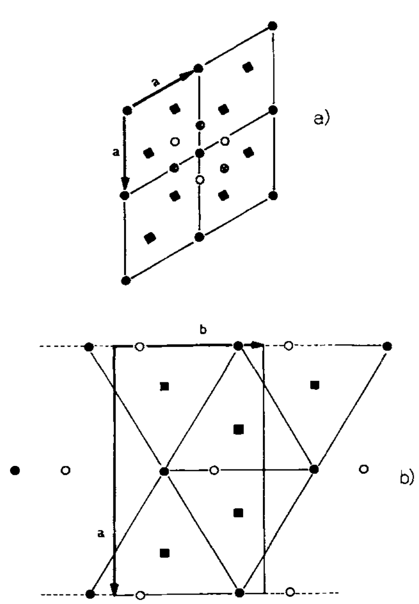


Fig. 25. a) $Li_2SiO_3$: ● $Si^{4+}$, ■ $Li^+$ within a layer; ○ and ⊗ possible positions of $Si^{4+}$ in the next layer (in projection). b) Arrangement of ● $Si^{4+}$, □ $Li^+$ in a layer, ○ $Si^{4+}$ in the neighboring layer.

Resumé: If $Li_2SiO_3$, according to $Li_{0.67}Si_{0.33}O$ is an *ordered variety* of the ZnO family, then the *composition* already determines the formation of $[SiO_{2/1}O_{2/2}]$ "chains". And if so can these then be regarded as "characteristic"?

## 2. Oxometalates with "Isolated" Anions

Thirty years ago one learnt for examinations that "isolated" oxo-complexes such as $[MnO_4]^-$ only exist if the oxidation state is "high", but also *e.g.* $[MnO_4]^{2-}$ in *green* $K_2MnO_4$[168] or the phosphate ion analog $[MnO_4]^{3-}$ in *blue* $Na_3[MnO_4]\cdot 10H_2O$[169] may be possible.

The new syntheses of numerous ternary and multi-component oxides containing metals in lower oxidation states confirmed this concept over many years: "Highly-polymeric" anions were found not only on typical double oxides *e.g.* the perovskites such as $CaTiO_3$, or the spinels of the $MgAl_2O_4$ type[170], but also in those compounds which correspond to *anhydrous* derivatives of amphoteric hydroxides (cf. Table 18).

Table 18. Order variants of the NaCl-type in oxides $AMO_2$.

| Compound | Type | Color | $a$ [Å] | $c$ [Å] | $c/a$ |
|---|---|---|---|---|---|
| $LiCrO_2$ | α-$NaFeO_2$ hex. $R\bar{3}m$ | olive-green | 289.9 | 1442 | 4.974 |
| $LiVO_2$ |  | black | 283.8 | 1480 | 5.215 |
| $NaAlO_2$ |  | colorless | 286.8 | 1588 | 5.54 |
| α-$NaFeO_2$ |  | black | 301.9 | 1593.4 | 5.28 |
| $NaYO_2$ |  | colorless | 338.6 | 1643 | 4.85 |
| $KInO_2$ |  | colorless | 329.6 | 1829 | 5.55 |
| $KTbO_2$ |  | colorless | 349 | 1860 | 5.33 |
| $KRhO_2$ |  | red | 317.5 | 1721 | 5.42 |
| $RbTlO_2$ |  | colorless | 345.3 | 1914.8 | 5.54 |
| $RbHoO_2$ |  | colorless | 346 | 1940 | 5.61 |
| $RbLuO_2$ |  | colorless | 340 | 1915 | 5.63 |
| $CsTlO_2$ |  | colorless | 338.8 | 2077 | 6.13 |
| α-$LiFeO_2$ | α-$LiFeO_2$ tetr. $I4_1/amd$ | black | 405.7 | 875.9 | 2.16 |
| $LiTmO_2$ |  | colorless | 440.5 | 1015 | 2.30 |

There are *"ordered variants"* of simple structural types here (NaCl, ZnS, also $Na_2O$ *etc.*). Surprisingly, "cation-rich" oxides also comply with this picture if the distances $d(A^I—O)$ and $d(M^{III}—O)$ are of about the same length *e.g. colorless* $Li_5AlO_4$[171] or *yellow* $Na_5TlO_4$[172]. Vacancies appear not only in the *cationic part* (*i.e.* $Li_5Al_2\square_1O_4 \triangleq Li_8O_4$), but also (though more rarely) in the *anionic part* (example: *red* $Na_4Mn_2O_5$[173] $= Na_4Mn_2O_5\square_1 \triangleq Na_6Cl_6$, derivative of the rock salt type) if cations and anions are not present in the same quantities.

In addition, even the crystal structure of $Na_3[AgO_2] \triangleq [Na_4O_2]$ (colorless single crystals) is a somewhat similar example[174]. In contrast to $K_2[HgO_2]$, the [O—Ag—O] dumbbells are not all arranged the same, but in two alternating directions (cf. Fig. 26).

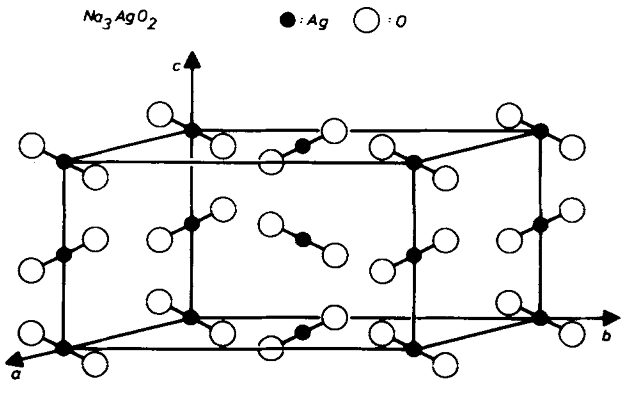


Fig. 26. Crystal structure of $Na_3[AgO_2]$, arrangement of the $[AgO_2]$ dumbbells in the unit cell.

There was a surprise with *colorless,* transparent single crystals of KAgO[175]. Because of the diagonal relationship of $Ag^+$ to $Hg^{2+}$ in the periodic table, a $[AgO_{2/2}]$ "chain" of ..O—Ag—O.. dumbbells, as with HgO[176], would be "normal". However, a "ring", *i.e.* an almost square planar unit of the type $K_4[(AgO_{2/2})_4]$[177] was observed. Would this point to the existence of further oxides with "small anions" having low oxidation states? Today we can answer this question with a Yes. Such "cation-rich" oxides are reported in the following Section.

## 3. Oxometalates with "Mononuclear" Groups

An unsolved, but current question concerning these metal oxides is whether groups with a single ligand exist, *i.e.* compounds of Cs[MO]-type, like Cs[ClO].

### 3.1. Mononuclear Groups with Only One Ligand

Three separate questions may be raised:

a) Intermediate phases appear in the system $Li_2O$/$Cs_2O$[43,178]. Would the "isolated" group [LiO] be capable of existence in (the still hypothetical) CsLiO, or would it polymerize according to $[LiO_{2/2}]$ or $[LiO_{4/4}]$?

b) Could a [:Tl—O]-type dumbbell with a *lone pair* as an "invisible" ligand occur in oxothallates(I) A[TlO], where $A^+$ is *extremely large,* larger than $Cs^+$!)?; colorless K[TlO] is, *e.g.* well known[179]).

c) Which structures do KAgO analogues have? Is the tetrameric "ring" (see Fig. 27) always formed? The structural elucidation of water-clear, *colorless* single crystals of recently obtained CsCuO[180] show that here, as in the case of *red* HgO[176], there is a chain built of *linear dumbbells* of OCuO (Cu—O—Cu angle = 89°). Contrary to our hopes, the *d*(Cu—O) distances within the dumbbell are of the same length.

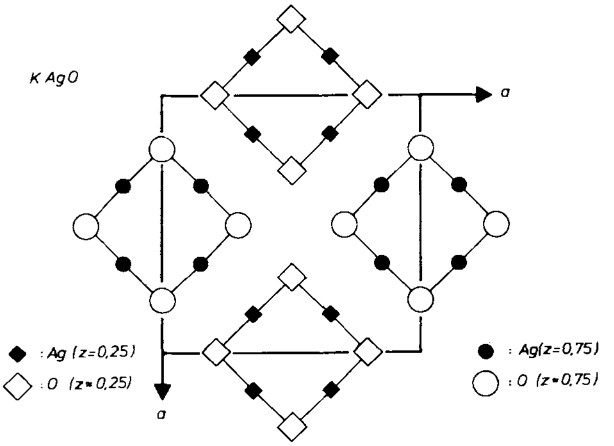


Fig. 27. Crystal structure of $K_4[Ag_4O_4]$, arrangement of the $[Ag_4O_4]$ rings in projection along [001].

Can oxides such as *e.g.* $(Ph_4As)[CuO]$ be prepared? Are perhaps the mentioned differences of the O...Cu—O distance present here?

*Yellow* CsAuO[182] follows $K_4[Ag_4O_4]$ corresponding to $Cs_4[Au_4O_4]$. It is the first defined oxoaurate(I) and was obtained by direct oxidation of *green* CsAu[183].

### 3.2. Mononuclear Groups with Two Ligands

These groups are very rare for metal oxides, two examples are known:

a) We had already obtained oxomercurates(II), such as $K_2[HgO_2]$[184], in the form of *colorless* single crystals. For this it was important that the reacting mixture (*e.g.* $K_2O + HgO$) was annealed in a sealed vessel. It has one of the rare *"stuffed" molecular structures* (see Fig. 28). The arrangement of the [O—Hg—O] dumbbells corresponds to the structure[185] of $XeF_2$[116].

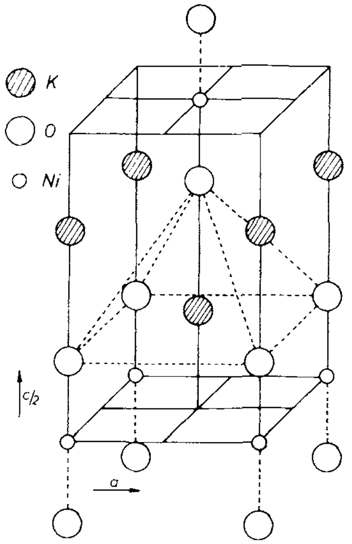


Fig. 28. The tetragonal $K_2[HgO_2]$-type, for example $K_2[NiO_2]$; only half of the unit cell is reproduced. The arrangement of the [ONiO] dumbbells corresponds to the $XeF_2$-type.

b) Little is known about the system K/Ni/O. For years many[186] experiments, including our own[187], remained unsuccessful. Finally we heated the mixture (*e.g.* $K_2O + NiO$) in a sealed Ni-tube and used the otherwise dreaded "reaction with the surface" in order to hinder the partial oxidation of $Ni^{II}$ to $Ni^{III}$, caused by unavoidable traces of $O_2$. This resulted in strongly dichroic (red/green), *lustrous dark red* single crystals of $K_2[NiO_2]$, which, like $Rb_2NiO_2$ and $Cs_2NiO_2$, is isotypic with the oxomercurates(II)[188].

It is fascinating that inspite of the unusually short $d(Ni—O) = 1.68$ Å distance in the linear dumbbells, the samples are paramagnetic and the Curie-Weiss law is obeyed with $\mu = 3.0\mu_B$, $\theta = -30$ K (as expected by *Klemm*[189]). Nothing is known about the bonding behavior.

### 3.3. Mononuclear Groups with Three Ligands

In contrast to oxides of non-metals ($BO_3^{3-}$, $CO_3^{2-}$, $NO_3^-$, $SO_3^{2-}$ *etc.*), these groups are rare in the case of metal oxides!

a) Although "FeO" is of great industrial importance and has been thoroughly investigated, oxoferrates(II) remained unknown for a long time, since unavoidable traces of $O_2$ effected oxidation of $Fe^{II}$ to $Fe^{III}$ when appropriate mixtures were annealed (*e.g.* BaO + FeO). Again, the "reaction with the vessel surface" (here: a Ni-bomb with Fe-lining) led for the first time to garnet-red single crystals of $Na_4[FeO_3]$[190] (see Fig. 29 and Table 19).

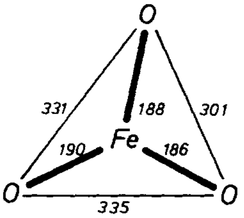


Fig. 29. The $[FeO_3]^{4-}$ group in $Na_4[FeO_3]$, distances in pm.

Table 19. Motifs of mutual adjunction in $Na_4FeO_3$; distances [pm] are given in addition to the Mo. A.

| | O1 | O2 | O3 | C.N. |
|---|---|---|---|---|
| Na 1 | 1/1<br>238 | 2/2<br>233 235 | 1/1<br>242 | 4 |
| Na 2 | 2/2<br>237 243 | 1/1<br>236 | 1/1<br>261 | 4 |
| Na 3 | 1/1<br>228 | 1/1<br>229 | 1/1<br>220 | 3 |
| Na 4 | 1/1<br>228 | 264 | 2/2<br>232 236 | 4 |
| Fe | 1/1<br>183 | 1/1<br>186 | 1/1<br>188 | |
| C.N. | 6 | 6 | 6 | |

*Carbonate-like*, almost planar $[FeO_3]^{4-}$ groups, exist. This finding confirms our concept, which had been developed to deal with the occurrence of such remarkable groups. The C.N. of the 3d-metal is so low here because of the numerous counter-cations which also have an affinity to coordinate to $O^{2-}$ and because of the tendency of $O^{2-}$ not to coordinate to more than a total of six cations.

This *experimental* finding obliged us to check the usual conceptions about "oxometalates". Contrary to all classical ideas, here the coordination number of the *ligand* has much more influence on the structure than does the nature of the central ion. In addition, there is the influence of the "ligands" on the crystal structure. Apparently, this latter mentioned influence (cf. [83]) is responsible for the individual components exhibiting unexpected coordination numbers in the structure of even "classical" examples of complex chemistry such as $K_2[PtCl_6]$ (here; 12 for $K^+$ with respect to $Cl^-$, instead of 6 as in KCl). The interplay of various influences which lead to the formation of this or that crystal structure is best surveyed if the "motifs of mutual adjunction" are considered (see *e.g.* Table 19).

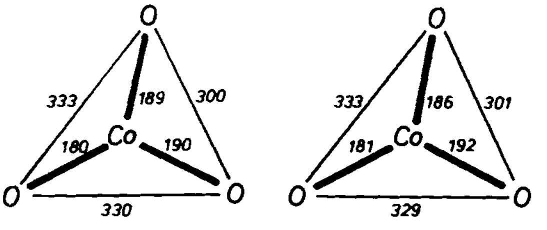


Fig. 30. The two crystallographically independent $[CoO_3]^{4-}$ groups in $Na_4[CoO_3]$, distances in pm.

b) From mixtures of $2Na_2O$ + "CoO" we obtained *deep red* single crystals of the analogous oxocobaltate(II) $Na_4[CoO_3]$[191]; it also contains carbonate-like groups (see Fig. 30).

c) In the search for the still unknown $K_4[NiO_3]$, we obtained *black* single crystals of $K_9[Ni^{II}O_3][Ni^{III}O_4]$[192], a *mixed valence* oxoniccolate(II,III) (see Fig. 31 and Table 20). In addition to the *paramagnetic* $[Ni^{III}O_4]^{5-}$ groups, there are *diamagnetic* planar $[NiO_3]^{4-}$ groups, like those occurring in the two previously cited oxides.

### 3.4. Mononuclear Groups with Four Ligands

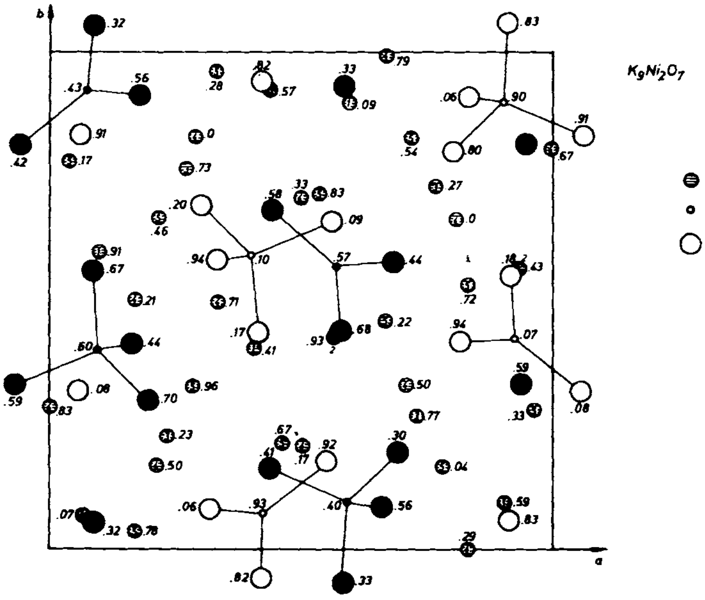


Fig. 31. Crystal structure of cubic $K_9[Ni^{II}O_3][Ni^{III}O_4]$, unit cells in projection along [001].

Table 20. Motifs of mutual adjunction in $K_9Ni_2O_7$; distances [pm] are given in addition to the Mo. A.

| | O1 | O2 | O3 | C.N. |
|---|---|---|---|---|
| K/1 | 3(1<br>268 | | | 3 |
| K 2 | 3/1<br>304 | 3/1<br>273 | | 6 |
| K 3 | 3/1<br>310 | 3/1<br>276 | | 6 |
| K 4 | 2/2<br>263<br>288 | 2/2<br>277<br>278 | 1/3<br>262 | 5 |
| K 5 | 2/2<br>284<br>285 | 2/2<br>286<br>293 | 1/3<br>307 | 5 |
| Ni 1 | 3/1<br>189 | | 1/1<br>196 | 4 |
| Ni 2 | | 3/1<br>180 | | 3 |
| C.N. | 8 | 7 | 7 | |

Such groups have only recently become known in lower oxidation state oxometalates. Sulfate-analogous groups were found to be present in the *colorless* oxides $Na_5[GaO_4]$, and $Na_6[ZnO_4]$[193]. In the meantime the oxomagnesate $K_6[MgO_4]$[194], which is isotypic with $Na_6[ZnO_4]$, has been obtained, so it would now seem that $Cs_7[LiO_4]$ should also be accessible. Single crystals of $Na_5[FeO_4]$[195] are *yellow*, those of $Na_5[CoO_4]$[196] are *violet*, and those of $Na_5[NiO_4]$[197] are *steel gray*; all are isotypic with colorless $Na_5[GaO_4]$. The recently prepared red-brown $Na_5[MnO_4]$ also belongs to this group.

*Oxometalates with "single" $O^{2-}$* are hardly known. To our surprise $Li_4[SiO_4]$ is not the Li-richest silicate, rather it reacts with excess $Li_2O$ to form $Li_8O_2[SiO_4] = (OLi_4)_2[SiO_4]$[198]. We obtained this silicate by a directed synthesis after we had successfully prepared *lustrous-red* single crystals of $Li_8O_2[CoO_4]$, the first compound of this type among the oxometalates of the d-metals[199] (see Fig. 32).

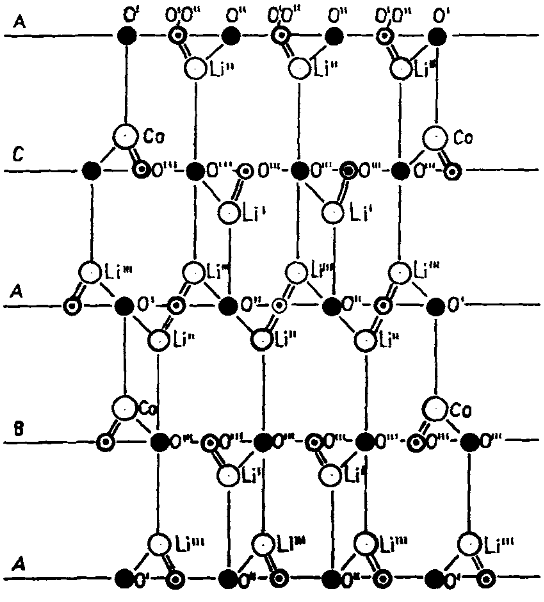


Fig. 32. Structural principle of $Li_8O_2[CoO_4]$, sequence of the layers of $O^{2-}$ along [00.1] with $Co^{2+}$ and $Li^+$ incorporated in the tetrahedral interstices.

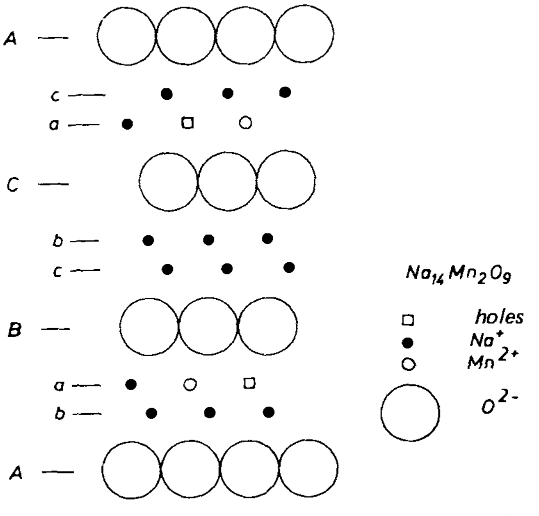


Fig. 33. Occupation of the tetrahedral interstices by $Na^+$ and $Mn^{2+}$ (with holes) in the cubic closed packing of $O^{2-}$ in $Na_{14}Mn_2O_9$; sequence stacking along [001].

The oxometalate $Na_{14}O[MnO_4]_2$, which shows the highest content of alkali oxide should be mentioned here. It is the first oxomanganate(II)[200] and forms *pale red* single crystals. The crystal structure is illustrated in Fig. 33.

*Oxometalates with "solitary" $O^{2-}$* (cf. Section *A* 2.7) are still unknown.

## 4. Oxometalates with Binuclear Groups

These groups, which have been known for a long time in oxochromates(VI) such as $K_2[Cr_2O_7]$, are present in only a few compounds of "cation-rich" metal oxides.

### 4.1. Binuclear Groups with a Total of Two Ligands

There are no examples known. A hypothetical example would be the $[:TlO_2Tl:]^{2-}$ group, in which the "lone pairs" act as "extra ligands" and could form bridges to the complementary cations, as has been found in *yellow* $K_4[Pb_2O_4]$[181] (*cf.* Fig. 34) and *orange-yellow* $K_2[Sn_2O_3]$[201].

Binuclear groups *with three ligands* are still unknown.

### 4.2. Binuclear Groups with Four Ligands

To date these are also unknown in the case of metal oxides of the d-metals; only two examples of such groups are known:

a) *light-yellow* $K_4[OPbO_2PbO]$ (see Fig. 34), in which each $Pb^{2+}$ has a "lone pair" as the fourth, invisible ligand[181].

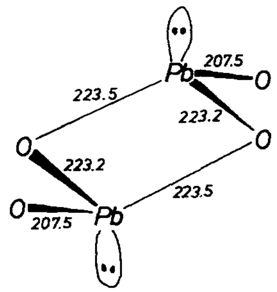


Fig. 34. $K_4[Pb_2O_4]$: The $[Pb_2O_4]$ group in perspective, bond lengths in pm.

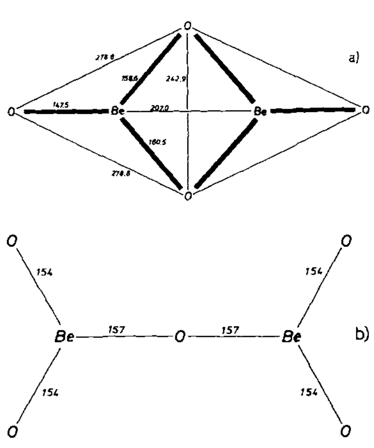


Fig. 35. a) Planar $[Be_2O_4]$ group in $K_4[Be_2O_4]$, distances in pm.—b) "butterfly" $[Be_2O_5]$ groups in $Na_6[Be_2O_5]$, distances in pm.

b) *colorless* $K_4[OBeO_2BeO]$[202] (see Fig. 35a), which contains two triangular groups linked *via* a common edge. The anion exhibits the *shortest Be—Be distance* known so far, *i. e.* *d*(Be—Be) = 2.07 å (in metallic Be: 2.23 Å). MAPLE, however, does not reveal any unusual energetic features.

### 4.3. Binuclear Groups with Five Ligands

There are no examples known for the d-metals, and only *one* such metal oxide has been prepared, namely $Na_6[O_2BeOBeO_2]$[203], which contains a "butterfly-like" anion (cf. Fig. 35b).

### 4.4. Binuclear Groups with Six Ligands

There are two examples; $K_6[Fe_2O_6]$ and $K_6[Mn_2O_6]$[204] (cf. Fig. 36). Unexpectedly, the groups contain edge-to-edge-linked tetrahedra. It is also unusual that the C.N. of part of the $O^{2-}$ exceeds the usual limiting value of 6. This grouping was recently found in $Na_6[Fe_2S_6]$ and $Rb_6[In_2S_6]$[205].

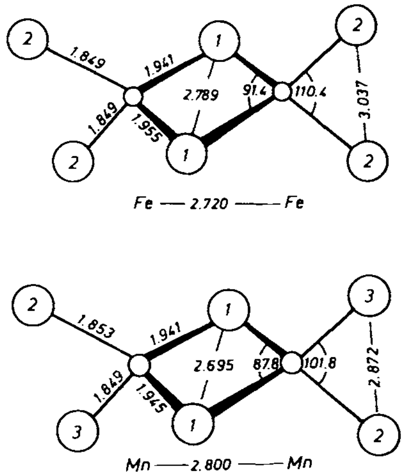


Fig. 36. $[M_2O_6]$ groups with M = Fe, Mn (double tetrahedra) of $K_6[M_2O_6]$; distances in Å.

In $Na_6[Au_2O_6]$[206], *pale-yellow* transparent single crystals, $Au^{3+}$ has a planar environment (cf. Fig. 37).

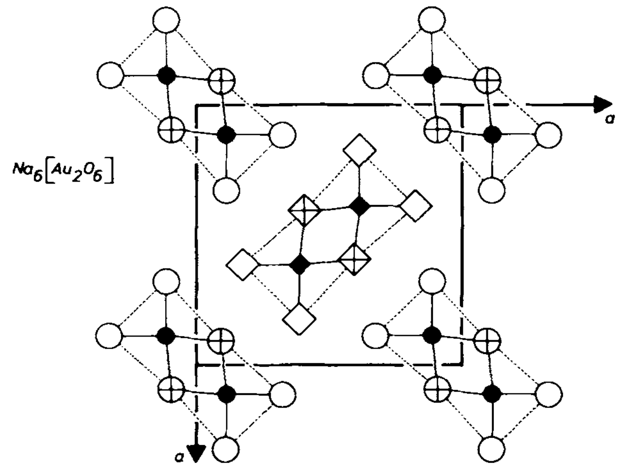


Fig. 37. $Na_6[Au_2O_6]$; arrangement of the planar $[Au_2O_6]$ group in the tetragonal unit cell, projection along [001].

### 4.5. Binuclear Groups with Seven Ligands

These are well known in oxometalates of higher oxidation states, such as *red* $Rb_2[Cr_2O_7]$[207] and its analogues. Generally, but by all means not always, all $[O_3M—O—MO_3]$ groups of such an oxide have the same conformation. However, in *red* $Sr[Cr_2O_7]$[208], two groups of different conformation are present in the ratio 1 : 1 (cf. Fig. 38).

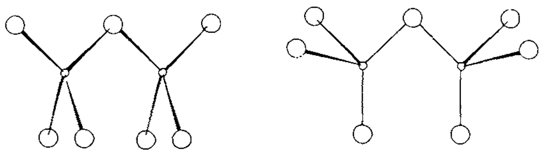


Fig. 38. Conformation of the two different $[Cr_2O_7]^{2-}$ groups in $Sr[Cr_2O_7]$.

In connection with the structure determination of *thortveitite* $Sc_2[Si_2O_7]$[209], the following questions arise. When does the valence angle M—O—M reach the value 180° within this group? When does the bridging $O^{2-}$ lie at a center of symmetry, and when not? Why does the bridging angle vary so much? Experimental findings are listed in Table 21.

Table 21. Bond angles M—O—M of some $Si_2O_7^{6-}$-groups.

| Compound | M—O—M [°] |
|---|---|
| $Sc_2Si_2O_7$ | 180 |
| $Y_2Si_2O_7$ | 134 |
| $Li_6Si_2O_7$ | 136 |
| $Rb_2Be_2Si_2O_7$ | 171 |

Only two examples are known for d-metals in *lower* oxidation states, and they are remarkably different: The *yellow, transparant* single crystals of $Na_8[Fe_2O_7]$[210] are isotypic with $Na_8[Ga_2O_7]$[211] and have the smallest M—O—M valence angle of 119.7° hitherto found in such $[M_2O_7]$ groups. Whereas with $K_6[Co_2O_7]$, which contains the *isoelectronic anion,* this angle widens to 180° and, moreover, the bridges are found at a center of symmetry! We obtained $K_6[Co_2O_7]$ in the form of *permanganate-colored* single crystals[212]. The enormous difference in the valence angle at the bridging $O^{2-}$ in the case of these two isoelectronic anions shows that attempts to interpret such differences of structure using ideas which are confined to the bonding situation inside the "closed" groups and perhaps include the "hybrid orbitals", are fundamentally insufficient. The influence of the "completing" cations is clearly seen; in one case eight smaller ($Na^+$) and in the other six larger ($K^+$) decidedly influence the *crystal structure* and with it the *configuration* of the anion.

## 5. Oxometalates with Tri- or Multinuclear Groups

Illustrative examples are known with d-metals in polyacids, above all of the elements of groups Va and VIa of the periodic table. While attempting to synthesize $Na_4[CoO_3]$—cf. Section *B* 3.3—we found *dark red* single crystals of $Na_{10}[Co_4O_9]$[213], the first example of an analogous *lower valence oxide* of the d-metals. The anion, which corresponds to the still unknown tetracarbonates such as $K_2[C_4O_9]$, has a conformation (see Fig. 39) which leads to *one* especially short Co—Co distance.

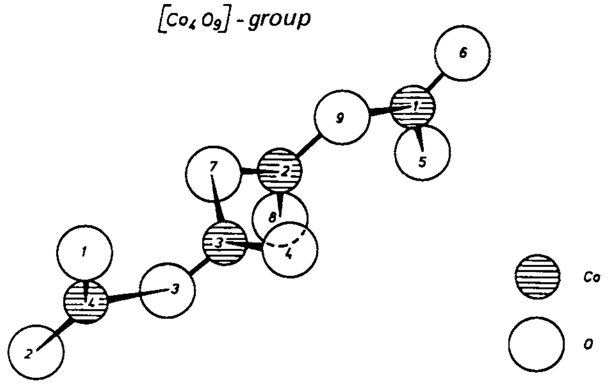


Fig. 39. $[Co_4O_9]$ group in $Na_{10}[Co_4O_9]$, conformation in perspective.

*Bright red* $Ag_{10}[Si_4O_{13}]$[214] was obtained as the first oxosilicate with a tetranuclear anion, and recently $Na_{14}[Al_4O_{13}]$[215] was obtained in the form of *clear, colorless* single crystals and is the first oligooxoaluminate.

## 6. On the Syntheses of New Oxides

When we started preparing "cation-rich" *oxoferrates(III)*, the system $Na_2O/Fe_2O_3$ was considered to have been essentially investigated. The crystal structures of the different forms of $NaFeO_2$ (ordered variety of the NaCl-type, and in the case of β-$NaFeO_2$ the ZnS-type) were known. Surprisingly, we then obtained $Na_5FeO_4$[216] and $Na_8[Fe_2O_7]$[210] with an *island structure,* $Na_{14}[Fe_6O_{16}]$[216] with a *chain structure* (see Fig. 40a), and $Na_4[Fe_2O_5]$[217] with a *sheet structure* (Fig. 40b). There is probably at least one further phase present in "$Na_3FeO_3$". It is assumed that these advances materialized because in each case mixtures of $Na_2O$ and "active" $Fe_2O_3$ were used, whereas previously $Na_2CO_3$ instead of $Na_2O$ was often used along with "normal" $Fe_2O_3$.

However, here, as with the syntheses of practically all other ternary or multicomponent metal oxides, the reactants are the *binary* components. We consider this type of reaction control to be improvable, even if especially "active" forms are introduced, and have already made some progress in this direction which will now be briefly reported here:

a) The *oxidation of intermetallic phases* has not been investigated in sufficient detail. The amount of moisture in the $O_2$ used proved to be important for the course of the reaction *e.g.* for NaTl. We obtained whisker-like, efflorescent single crystals of $LiSbO_3$ from the melt of LiSb under similar conditions.

b) Ternary oxides of the noble metals are obtained only with difficulty in the form of single crystals, since thermal decomposition usually occurs before the single crystals grow. We succeeded, however, in preparing glass clear, well formed single crystals of $Na_3[AgO_2]$[174], again by using the "reaction with the surface", and by exploiting a side reaction:
An oxide with a new type of formula results from the *exchange reaction* of $NaNiO_2$[218] and $K_2O$: $K_3[Ni^{II}Ni^{III}O_4]$[219] is formed by the partial reduction of $Ni^{III}$ to $Ni^{II}$, and in addition $Na_2O$. Apparently it is this "$Na_2O$" in *statu nascendi,* which with nascent $O_2$ enables the formation of single crystals *in situ* which cannot otherwise be prepared at temperatures as low as 300 °C.

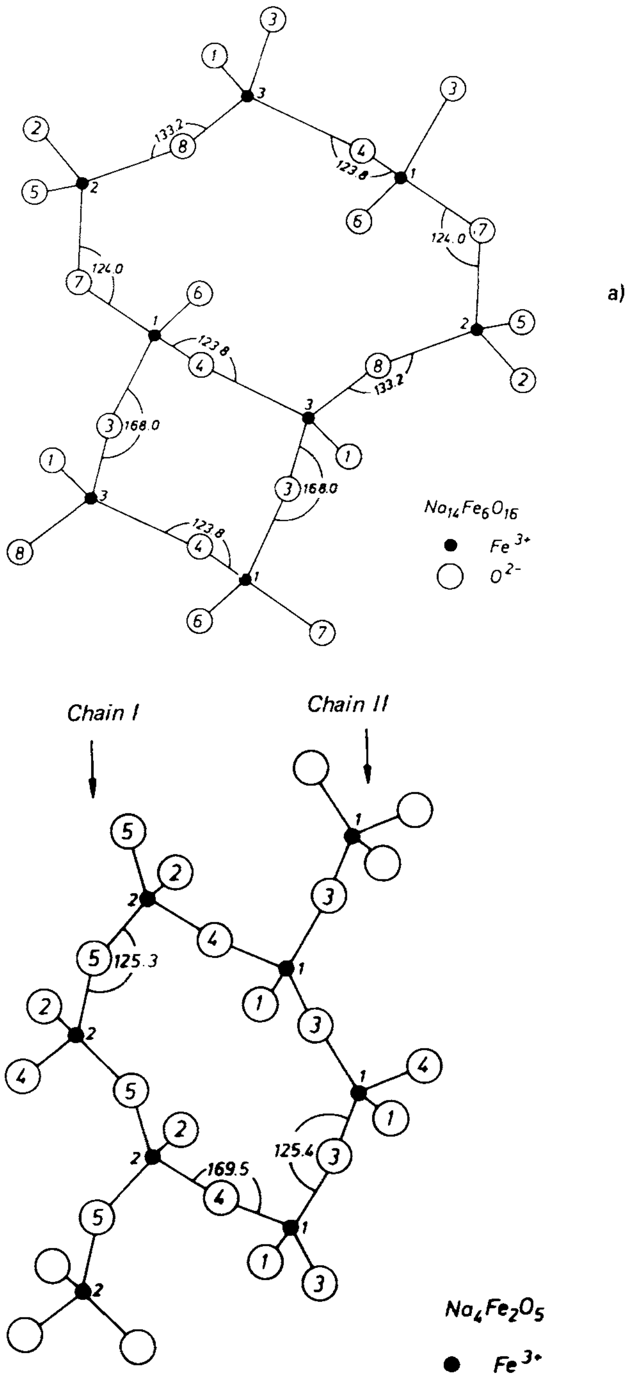


Fig. 40. a) Repeat unit of two rings in the "band structure" of $Na_{14}[Fe_6O_{16}]$.—b) Section from the $[Fe_4O_{10}]$ layer of $Na_4[Fe_2O_5]$.

c) From suitably chosen exchange reactions, *e.g.*

$$2\,LiInO_2 + Na_2O \rightarrow 2\,NaInO_2 + Li_2O$$
$$2\,KInO_2 + Na_2O \rightarrow 2\,NaInO_2 + K_2O$$

the change of $\Delta H^0_{298}$ is estimated to be only small (±2 kcal/mol). Such reactions are therefore especially sensitive to changes of $T$ because finally $\Delta G_T$ decides their fate.
Keeping this in mind, we have more closely investigated the reaction between *yellow* $K_2PbO_3$[220], an oxoplumbate which has the remarkable C.N. 5 for $Pb^{4+}$, and excess

$Li_2O$. We obtained *glass clear, colorless* single crystals of $K_2Li_{14}[Pb_3O_{14}]$[221], the first *oligooxoplumbate* with previously unobserved *triple-octahedra* groups (see Fig. 41).

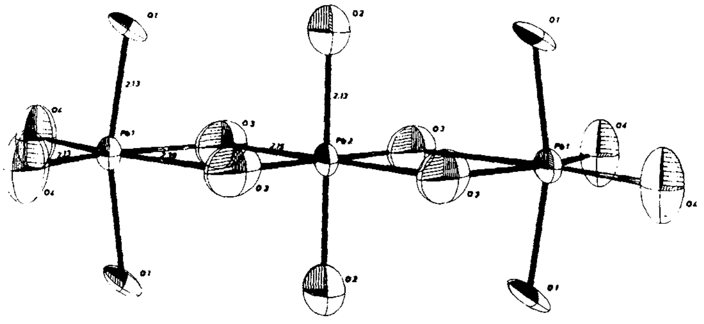


Fig. 41. The $[Pb_3O_{14}]$ triple octahedra of $K_2Li_{14}[Pb_3O_{14}]$ in perspective.

Further results of these investigations also reveal that other *lead oxides* for which similar unsuccessful searches had been made can also be grown at relatively low temperatures.

### *Part C: Synopsis*

From the plethora of new results which can hardly be surveyed by a single person, those chosen for this progress report originated from the investigations of *Wilhelm Klemm*, or were prompted by his questioning.

Our knowledge of the fluoro- and oxometalates has without doubt not only broadened, if the number of new substances and elucidated crystal structures can be called simply broadening, but also deepened, because:

- New synthetic routes have been discovered, of which the *high-pressure synthesis of novel fluorides and oxides* should be forcefully emphasized[222]. From known thermodynamic relationships it follows that even $F_2$- or $O_2$-pressures of 5 kbar do not open up a "new world of phenomena". Nevertheless, under such conditions substances whose existence was only hinted at or even overlooked in experiments performed under normal pressure, can be prepared in the form of well characterized compounds, and, if the conditions are chemically favorale, single crystals of *e.g.* "active fluorine" compounds can then be obtained.
- Exploitation of the "reaction with the surface" for the preparation of oxides (and fluorides?) which otherwise cannot be prepared or cannot be obtained as single crystals, undoubtedly constitutes a most invaluable extension to the normal preparative methods that are available.
- The "cation-rich" oxides, which (still) have no parallel in the fluorometalates, show a previously unexpected wealth of new compounds, some with "exotic" structures or component groups.
- Not only magnetic investigations and identification of "magnetic structures" by neutron diffraction, but also the interpretation of vibrational spectroscopic measurements, measurements of the electrical resistance or those made by electron spectroscopy, as have been carried out on *e.g.* suboxides of the alkali metals[233], promise to yield more detailed information about chemical bonding in the solid state.

But the new results not only help to broaden and deepen our knowledge, they also reveal even more clearly than before our inability to understand and interpret some of the profound peculiarities within the periodic table:

- What actually enables the *coinage metals* to break the normal rules of the periodic system of elements to such an extraordinary degree, and to form stable, "producible" compounds of the oxidation states +2, +3 and even +4 and +5?
- Has a yawning gap not developed after the synthesis of the noble gas fluorides, which brought a long and overdue harmoniously balanced confirmation of the periodic system? Does this gap extend up to the chemistry of the elements of the second sub-group zinc, cadmium and mercury, as many suppose and try to confirm through hitherto unsuccessful experiments?
- Are there possibly other still unknown gaps in the periodic system, which on critical and purposeful research would reveal further cracks in the trusted architecture of the system?

What is the situation in the field of solid state chemistry, where an abundance of metastable phases largely die latent in the shady gray of superficial knowledge? What revolutionary changes in our "solid" ideas would be brought about if new experimental techniques were to allow the growth of single crystals from metastable phases.

Why and to which end are the metal fluorides and oxides still being studied?

- If there are substances of simple composition, with "small" formulas and which can be regarded as being built up of ions, *i.e.* are accessible by simple calculations—they are to be found here.
- If the search for the *"vis vitalis"* fans out into a dendritic labyrinth of ever more complicated substances and reactions, and "progress" suggests we would understand the ocean of complications more and more, is it not necessary then to prove with such simple substances how difficult the interpretation of the known is, and how uncertain prophesies about the comparatively unknown remain? Is it not salutary to realize how hopeless it is, even with supposed elementary nature, to predict what could be captured by casting a line or net into the sea of the unknown?

We study them further in order to learn how difficult it is to acquire knowledge and how almost hopeless the perception of elementary nature is.

*My thanks go to my revered teacher Wilhelm Klemm who knows how to spice friendship with criticism and stimulating agreement. How little he, how little all those professors to whom I feel indebted—Otto Ruff, who answered all the schoolboy questions about the colors of metal fluorides, Walter Hückel who supplied "organic epistles" to he who had tried futilely for years to study; Werner Heisenberg, who activated Osenberg; Otto Diels, who even as a Nobel prize-winner could still become so wonderfully excited over the incomprehensible properties of oxalic acid; Hans Martin, to whom it was worth a night to discuss the fluorouranates(VI) of the alkali metals—how little they all resemble that caricature of the German professor—outlined as an object of ridicule by inadmissable generalization of some regrettable single cases, and which still dis-*

*turbs the human trust between the already experienced elder and the striving young student.*

*Without my co-workers only a fraction of the fruits of this research would have been harvested. I thank them for their more than enthusiastic assistance with the experiments.*

Received: October 7, 1980 [A 348 IE]
German version: Angew. Chem. *93*, 64 (1981)

---

[1] *R. Scholder, W. Klemm,* Angew. Chem. *66*, 461 (1954).

[2] After *F. Schiller,* inaugural lecture, "What is universal history, and to which end is it studied?", Jena Universität Jena 1789.

[3] $CrF_2$ should be colorless like $CrCl_2$; however it has been described as blue-green to deep green; lustrous mother-of-pearlish crystals; c.f. *K. H. Jack, R. Maitland,* Proc. Chem. Soc. London *1957*, 232; *J. W. Cable, M. K. Wilkinson, E. O. Wollau,* Phys. Rev. *118*, 950 (1960); *J. W. Tracy et al.*, Acta Crystallogr. *14*, 927 (1961).

[4] *M. Jansen,* Z. Naturforsch. *B 34*, 10 (1979).

[5] *G. Maier, S. Pfriem, U. Schäfer, R. Matusch,* Angew. Chem. *90*, 552 (1978); Angew. Chem. Int. Ed. Engl. *17*, 520 (1978).

[6] *W. Klemm, E. Huss,* Z. Anorg. Allg. Chem. *258*, 221 (1949).

[7] *W. Klemm,* Angew. Chem. *63*, 396 (1951).

[8] *A. G. Sharpe,* J. Chem. Soc. *1949*, 2901.

[9] *H. Moissan,* Ann. Chim. Phys., Ser. 6, *24*, 224 (1891).

[10] From weakly gray-blue-violet $TiF_3$ [according to *P. Ehrlich, G. Pietzka,* Z. Anorg. Allg. Chem. *275*, 121 (1954)] we obtained lustrous, deep blue crystals by sublimation ($10^{-3}$ Torr, 880 °C, Ni-crucible); cf. *E. Alter, R. Hoppe,* Z. Anorg. Allg. Chem. *403*, 127 (1974).

[11] *R. H. Odenthal, R. Hoppe,* Z. Anorg. Allg. Chem. *384*, 104 (1971).

[12] *R. Domesle, R. Hoppe,* 9. Int. Fluor-Symp., Avignon 1979; Z. Anorg. Allg. Chem., in press.

[13] *J. L. Howard,* J. Am. Chem. Soc. *61*, 1252 (1939); *G. M. Brown, L. A. Walker,* Acta Crystallogr. *20*, 220 (1966).

[14] *H. G. von Schnering, R. Hoppe,* unpublished (1962).

[15] *G. Siebert, R. Hoppe,* Z. Anorg. Allg. Chem. *391*, 117 (1972).

[16] *R. Hoppe, K. Blinne,* Z. Anorg. Allg. Chem. *291*, 269 (1957).

[17] *H. Schäfer,* Angew. Chem. *73*, 11 (1961).

[18] *B. G. Müller,* 6. Eur. Fluor-Symp., Dortmund 1977.

[19] *E. Alter, R. Hoppe,* Z. Anorg. Allg. Chem. *405*, 167 (1974).

[20] *D. Paus, R. Hoppe,* Z. Anorg. Allg. Chem. *431*, 207 (1977); cf. Dissertation *D. Paus,* Universität Giessen 1976.

[21] *W. Harnischmacher, R. Hoppe,* Angew. Chem. *85*, 590 (1973); Angew. Chem. Int. Ed. Engl. *12*, 582 (1973).

[22] *T. Fleischer, R. Hoppe,* unpublished; cf. Dissertation *T. Fleischer,* Universität Giessen 1981.

[23] *B. N. Figgis:* Introduction to Ligand Field Theory. Wiley, New York 1966, S. 159 ff.

[24] *B. G. Müller, R. Hoppe,* unpublished (1974); private communication to Prof. *N. Bartlett,* Berkeley (1974).

[25] *P. Sorbe, J. Grannec, J. Portier, P. Hagenmuller,* 6. Eur. Fluor-Symp., Dortmund 1977.

[26] *P. Sorbe, J. Grannec, J. Portier, P. Hagenmuller,* C. R. Acad. Sci. *C 284*, 231 (1977).

[27] *R. Hoppe, W. Klemm,* Z. Anorg. Allg. Chem. *268*, 364 (1952); *R. Hoppe, R. Homann,* ibid. *379*, 163 (1970).

[28] *N. Bartlett, K. Leary,* Rev. Chim. Miner. *13*, 82 (1976).

[29] *M. J. Wasile, T. J. Richardson, F. A. Stevie, W. E. Falconer,* J. Chem. Soc. Dalton Trans. *1976*, 351; *J. H. Holloway, G. J. Schrobilgen,* J. Chem. Soc. Chem. Commun. *1975*, 623.

[30] *B. G. Müller,* unpublished.

[31] *W. A. Sunder, A. L. Wayda, B. Distefano, W. E. Falconer, J. E. Griffiths,* J. Fluorine Chem. *14*, 299 (1979).

[32] *E. Huss, W. Klemm,* Z. Anorg. Allg. Chem. *262*, 25 (1950).

[33] *R. Hoppe,* Recl. Trav. Chim. Pays-Bas *75*, 569 (1956).

[34] *W. Klemm, W. Brandt, R. Hoppe,* Z. Anorg. Allg. Chem. *308*, 179 (1961); *J. W. Quail, G. A. Rivett,* Can. J. Chem. *50*, 2447 (1972); cf. also [33].

[35] *J. W. Quail, G. A. Rivett,* Can. J. Chem. *50*, 2447 (1972).

[36] *W. Harnischmacher, R. Hoppe,* 5. Eur. Fluor-Symp. Aviemore 1974.

[37] *B. Hoffmann, R. Hoppe,* Z. Anorg. Allg. Chem. *458*, 151 (1979).

[38] *R. Hoppe, H. Mattauch,* unpublished; cf. Dissertation *H. Mattauch,* Universität Münster 1962.

[39] *R. Hoppe,* Z. Anorg. Allg. Chem. *292*, 28 (1957).

[40] *R. Hoppe, R. Homann,* Z. Anorg. Allg. Chem. *379*, 193 (1970).

[41] *R. Hoppe, R. Homann,* Naturwissenschaften *53*, 501 (1966).

[42] *T. Fleischer, R. Hoppe,* Z. Anorg. Allg. Chem., in press.

[43] *R. Hoppe et al.*, unpublished (1954–1980).

[44] *A. Werner,* Z. Anorg. Allg. Chem. *3*, 267 (1893).

[45] *R. Hoppe,* Z. Anorg. Allg. Chem. *294*, 135 (1958).

[46] *N. Bartlett, P. R. Rao,* Proc. Chem. Soc. London *1964*, 393.

[47] *R. E. Thoma, C. F. Weaver, H. A. Friedmann, H. Insley, L. A. Harris, H. A. Yakel,* J. Phys. Chem. *65*, 1096 (1961).

[48] *K. Feldner, R. Hoppe,* Z. Anorg. Allg. Chem., *471*, 131 (1980).

[49] NBS Tech. Note (U. S.) *270, 271* (1968); *O. Kubaschewski, C. B. Alcock:* Metallurgical Thermochemistry, 5th Edit. Pergamon, Oxford 1979.

[50] *H. Henkel, R. Hoppe, G. C. Allen,* J. Inorg. Nucl. Chem. *31*, 3855 (1969).

[51] *T. Fleischer, R. Hoppe,* Z. Anorg. Allg. Chem., in press.

[52] *T. Fleischer, R. Hoppe,* J. Fluorine Chem. *11*, 251 (1978).

[53] *G. Siebert, R. Hoppe,* Naturwissenschaften *58*, 95 (1971); Z. Anorg. Allg. Chem. *391*, 126 (1972).

[54] *J. Grannec,* J. Fluorine Chem. *6*, 267 (1975).

[55] *H. G. von Schnering, P. Bleckmann,* Naturwissenschaften *55*, 342 (1968).

[56] *K. Knox,* Acta Crystallogr. *14*, 583 (1961).

[57] *D. Baltz, K. Plieth,* Z. Elektrochem. *59*, 545 (1955).

[58] *H. G. von Schnering,* Z. Anorg. Allg. Chem. *353*, 13 (1967).

[59] *B. G. Müller, R. Hoppe,* Naturwissenschaften *58*, 268 (1971); Mater. Res. Bull. *7*, 1297 (1972); *E. Alter, R. Hoppe,* Z. Anorg. Allg. Chem. *408*, 115 (1974).

[60] *R. H. Odenthal, R. Hoppe,* Naturwissenschaften *57*, 305 (1970); Monatsh. Chem. *102*, 1340 (1971); *R. H. Odenthal, D. Paus, R. Hoppe,* Z. Anorg. Allg. Chem. *407*, 151 (1974).

[61] *B. G. Müller,* unpublished.

[62] *G. Gafner, G. J. Kruger,* Acta Crystallogr. *B 30*, 250 (1974).

[63] *D. McKee, A. Zalkin, N. Bartlett,* Inorg. Chem. *12*, 1713 (1973).

[64] *E. Alter, R. Hoppe,* Z. Anorg. Allg. Chem. *412*, 110 (1975).

[65] *R. Domesle, R. Hoppe,* 9. Int. Fluor-Symp., Avignon 1979; Dissertation *R. Domesle,* Universität Giessen 1980.

[66] *T. Fleischer, R. Hoppe,* unpublished.

[67] *R. Hoppe, W. Liebe, W. Dähne,* Z. Anorg. Allg. Chem. *307*, 276 (1961).

[68] *F. Wall, G. Pausewang, D. Babel,* J. Less Common Met. *25*, 257 (1971).

[69] *D. Babel,* Z. Naturforsch. *A 20*, 165 (1965); *M. Steiner, W. Krüger, D. Babel,* Solid State Commun. *9*, 227 (1971).

[70] *R. Domesle, R. Hoppe,* Angew. Chem. *92*, 499 (1980); Angew. Chem. Int. Ed. Engl. *19*, 489 (1980).

[71] *S. J. Mitchell, J. H. Holloway,* J. Chem. Soc. *A 1971*, 2789.

[72] *B. K. Morrell, A. Zalkin, A. Tressaud, N. Bartlett,* Inorg. Chem. *12*, 2640 (1973).

[73] *R. M. Herak, S. S. Malčić, L. M. Manojlović,* Acta Crystallogr. *18*, 520 (1965).

[74] *E. Huss, W. Klemm,* Z. Anorg. Allg. Chem. *262*, 25 (1950).

[75] *J. L. Howard, M. B. Williams,* J. Am. Chem. Soc. *64*, 633 (1942); *D. L. Deadmore, W. F. Bradl,* Acta Crystallogr. *15*, 186 (1962).

[76] *V. E. Bratishko, E. G. Rakov, V. E. Selznev, B. N. Sudarikov,* Zh. Neorg. Khim. *14*, 3177 (1969).

[77] *W. Klemm,* Z. Anorg. Allg. Chem. *184*, 345 (1929).

[78] *B. Hoffmann, R. Hoppe,* Z. Anorg. Allg. Chem. *458*, 151 (1979).

[79] *H. J. Hurst, J. C. Taylor,* Acta Crystallogr. *B 26*, 417, 2136 (1970).

[80] *R. Domesle, R. Hoppe,* Z. Anorg. Allg. Chem., in press.

[81] *W. H. Zachariasen,* J. Am. Chem. Soc. *70*, 2147 (1948); Acta Crystallogr. *2*, 388 (1949).

[82] *R. Hoppe, B. Mehlhorn,* Z. Anorg. Allg. Chem. *425*, 200 (1976).

[83] Vgl. *R. Hoppe,* Angew. Chem. *92*, 106 (1980); Angew. Chem. Int. Ed. Engl. *19*, 110 (1980).

[84] *R. R. Ryan, R. A. Penneman, A. Rosenzweig,* Acta Crystallogr. *B 25*, 1958 (1969).

[85] *R. R. Ryan, P. A. Penneman,* Acta Crystallogr. *B 27*, 829 (1971); *G. Brunton, ibid. B 27*, 2290 (1971).

[86] *D. Babel,* Z. Anorg. Allg. Chem. *387*, 161 (1972); cf. also *R. Hoppe, R. Jesse, ibid. 403*, 143 (1974).

[87] *R. Hoppe,* Angew. Chem. *78*, 52 (1966); *82*, 7 (1970); Angew. Chem. Int. Ed. Engl. *5*, 95 (1966); *9*, 25 (1970); Adv. Fluorine Chem. *6*, 387 (1970); Izvj. Yugoslav. Centr. Krist. (Zagreb) *8*, 21 (1973); Vorträge aus dem Gebiet der Festkörperforschung 1971 (Münster 1973); in *C. J. M. Rooymans, A. Rabenau:* Crystal Structure and Chemical Bonding in Inorganic Chemistry. Elsevier, Amsterdam 1975.

[88] *R. Hoppe, R. Jesse,* Z. Anorg. Allg. Chem. *402*, 29 (1973); *403*, 143 (1974); *R. Hoppe,* ibid. *402*, 39 (1973).

[89] *B. G. Müller, R. Hoppe,* Z. Anorg. Allg. Chem. *395*, 239 (1973).

[90] *B. G. Müller,* J. Fluorine Chem., in press.

[91] *T. Fleischer, R. Hoppe,* 9. Int. Fluor-Symp., Avignon 1979.

[92] *W. Viebahn,* Z. Anorg. Allg. Chem. *386*, 335 (1971).

[93] *D. Babel,* Z. Anorg. Allg. Chem. *406*, 23 (1974).

[94] *V. Gutmann, G. Resch,* Rev. Inorg. Chem., in press.

[95] *A. Tressaud, J. M. Parentheau, J. M. Dance, J. Portier, P. Hagenmuller,* Mater. Res. Bull. *8*, 565 (1973); *J. M. Dance, A. Tressaud,* Solid State Commun. *17*, 185 (1975).

[96] *H. Steinfink,* Acta Crystallogr. *17*, 823 (1964).

[97] *D. Dumora, R. von Der Mühll, J. Ravez,* Mater. Res. Bull. *6*, 561 (1971); *Kang Kun Wu, I. D. Brown,* ibid. *8*, 593 (1973).

[98] *R. von Der Mühll, S. Andersson, J. Galy,* Acta Crystallogr. *B 27*, 2345 (1971).

[99] *R. Hoppe,* Angew. Chem. *82*, 7 (1970); Angew. Chem. Int. Ed. Engl. *9*, 25 (1970); Z. Kristallogr. *150*, 23 (1979).

[100] *J. C. Taylor, P. W. Wilson,* J. Inorg. Nucl. Chem. *36*, 1561 (1974).

[101] Cf. Landolt-Börnstein, Neue Serie, Vol. *7*, Teil a. Springer-Verlag, Berlin 1973.

[102] *W. Preetz, U. Dietl,* Z. Anorg. Allg. Chem. *438*, 160 (1978).

[103] *D. Babel*, private communication (1980).

[104] *B. Hofmann, R. Hoppe*, Z. Anorg. Allg. Chem. *436*, 65 (1977).

[105] *O. Ruff*, Ber. Dtsch. Chem. Ges. *A 69*, 181 (1936).

[106] *R. Hoppe, R. Homann*, Z. Anorg. Allg. Chem. *369*, 212 (1969).

[107] *R. Hoppe, R. Homann*, unpublished.

[108] *R. Hoppe, W. Klemm*, Z. Anorg. Allg. Chem. *268*, 364 (1952).

[109] *R. Hoppe, L. Grosse*, unpublished; cf. Diplomarbeit *L. Grosse*, Universität Giessen 1980.

[110] *E. Alter, R. Hoppe*, Z. Anorg. Allg. Chem. *405*, 167 (1974).

[111] *W. Urland, K. Feldner, R. Hoppe*, Z. Anorg. Allg. Chem. *465*, 7 (1980).

[112] *O. Ruff, E. Ascher*, Z. Anorg. Allg. Chem. *183*, 204 (1929); *N. Bartlett, R. Maitland*, Acta Crystallogr. *11*, 747 (1958); *B. G. Müller, R. Hoppe*, Mater. Res. Bull. *7*, 1297 (1972).

[113] *D. Paus, R. Hoppe*, Z. Anorg. Allg. Chem. *431*, 207 (1977).

[114] *D. Paus, R. Hoppe*, Z. Anorg. Allg. Chem. *426*, 83 (1976).

[115] *H. G. von Schnering, P. Bleckmann*, Naturwissenschaften *55*, 342 (1968); *D. E. Cox et al.*, J. Appl. Phys. *41*, 943 (1970).

[116] *R. Hoppe, W. Dähne, H. Mattauch, K. M. Rödder*, Angew. Chem. *74*, 903 (1962); Angew. Chem. Int. Ed. Engl. *1*, 599 (1962); *N. Bartlett, D. H. Lohmann*, Proc. Chem. Soc. London *1962*, 115.

[117] *F. O. Sladky, P. A. Bulliner, N. Bartlett*, J. Chem. Soc. *A 1969*, 2179.

[118] *I. J. Solomon, R. I. Brabets, R. K. Wenishi, J. N. Keith, J. M. McDonough*, Inorg. Chem. *3*, 457 (1964).

[119] *B. G. Müller*, J. Fluorine Chem., in press.

[120] *R. Hoppe, W. Dähne, W. Klemm*, Naturwissenschaften *48*, 429 (1961).

[121] *M. A. Hepworth, K. A. Jack*, Acta Crystallogr. *10*, 345 (1957).

[122] *F. Liebau* in: Handbook of Geochemistry, Vol. II/3. Springer-Verlag, Berlin 1972.

[123] *B. G. Müller*, J. Fluorine Chem., in press.

[124] Many "columnar structures" are actually "stacks", because the linkage forces within the stacked units is markedly stronger than between them. Here, as with $Cs_3[Al_3F_{12}]$ it is different; cf. *R. Lösch, C. Hebecker*, Z. Naturforsch. *B 34*, 131 (1979); *D. Babel, G. Knoke*, Z. Anorg. Allg. Chem. *442*, 151 (1978).

[125] Such "exchange reactions" have been investigated by us on other compounds: *R. Hoppe et al.*, unpublished.

[126] *B. Hofmann, R. Hoppe*, unpublished; cf. Dissertation *B. Hofmann*, Universität Giessen 1979.

[127] Cf. *R. Hoppe, C. Hebecker*, unpublished; Dissertation *C. Hebecker*, Universität Münster 1967. A special case of exchange reactions occur if redox reactions appear at the same time, *e.g.* according to $4NaNiO_2 + 9K_2O \rightarrow 2\,K_9[Ni_2O_7] + 2\,Na_2O + 1/2\,O_2$.

[128] *B. Hofmann, R. Hoppe*, unpublished.

[129] *R. Hoppe, K. Lehr*, Z. Anorg. Allg. Chem. *416*, 240 (1975).

[130] Cf. Dissertation *K. Lehr*, Universität Giessen 1975.

[131] *E. Alter, R. Hoppe*, Z. Anorg. Allg. Chem. *412*, 110 (1975).

[132] *K. Feldner, R. Hoppe*, 9. Int. Fluor-Symp., Avignon 1979; Z. Anorg. Allg. Chem., in press.

[133] *R. Hoppe*, Angew. Chem. *73*, 30 (1961).

[134] *K. Feldner, R. Hoppe*, 9. Int. Fluor-Symp., Avignon 1979; Z. Anorg. Allg. Chem., in press.

[135] *R. Hoppe, I. Siddiqi*, Z. Anorg. Allg. Chem. *374*, 225 (1970).

[136] *B. Cox, A. G. Sharpe*, J. Chem. Soc. *1953*, 1783.

[137] *H. von Wartenberg*, Z. Anorg. Allg. Chem. *244*, 337 (1940).

[138] Cf. *E. Weise* in *Winnacker-Küchler:* Chemische Technologie, Vol. I. Hanser Verlag, München 1970.

[139] *A. Šmalc, K. Lutar, J. Slivnik*, J. Fluorine Chem. *6*, 257 (1975).

[140] *R. Hoppe, S. Schneider*, Z. Anorg. Allg. Chem. *361*, 113 (1968); *R. Hoppe* in: 20 Jahre Fonds der Chemischen Industrie. VCI, Frankfurt 1970, p. 15.

[141] *K. Feldner, R. Hoppe*, unpublished; cf. Dissertation *K. Feldner*, Universität Giessen 1980.

[142] *W. Klemm, P. Henkel*, Z. Anorg. Allg. Chem. *220*, 180 (1934).

[143] *R. Hoppe, H. G. von Schnering*, unpublished (1960).

[144] Cf. *e.g. D. H. Kelly, P. Post, R. W. Mason*, J. Am. Chem. Soc. *85*, 307 (1963).

[145] *R. Hoppe*, Recl. Trav. Chim. Pays-Bas *75*, 569 (1956).

[146] *R. Hoppe, H. Henkel*, unpublished; cf. Dissertation *H. Henkel*, Universität Giessen 1968.

[147] *R. Hoppe*, unpublished (1952).

[148] *R. Hoppe, W. Liebe, W. Dähne*, Z. Anorg. Allg. Chem. *307*, 276 (1961).

[149] *R. Hoppe*, Z. Anorg. Allg. Chem. *292*, 28 (1957).

[150] Preparation of samples by heating the mixture $2BaHPO_4 + Ag_2O$ at $10^{-3}$ Torr.

[151] *R. Hoppe, W. Harnischmacher, B. Mehlhorn*, unpublished.

[152] *C. Hebecker, R. Hoppe, G. Kreuzburg*, Z. Anorg. Allg. Chem. *375*, 270 (1970).

[153] *C. Hebecker, R. Hoppe*, Naturwissenschaften *53*, 106 (1966).

[154] *R. Hoppe, B. Schepers*, Z. Anorg. Allg. Chem. *295*, 233 (1958).

[155] *K. Lehr, R. Hoppe*, unpublished.

[156] *R. Domesle, R. Hoppe*, Z. Anorg. Allg. Chem., in press.

[157] *A. Hardy*, Acta Crystallogr. *15*, 179 (1962).

[158] *H. T. Evans Jr.*, Z. Kristallogr. *114*, 257 (1960).

[159] *M. W. Shafer*, Mater. Res. Bull. *4*, 905 (1969).

[160] *W. Gonschorek, Th. Hahn*, Z. Kristallogr. *138*, 167 (1973).

[161] *N. M. Mustafaev, V. V. Iljukhin, N. V. Belov*, Sov. Phys. Crystallogr. *10*, 676 (1965).

[162] *J. H. Burns, W. R. Busing*, Inorg. Chem. *4*, 1510 (1965).

[163] *G. Argay, I. Náray-Szabó*, Acta Chim. Acad. Sci. Hung. *49*, 329 (1966).

[164] *P. Kastner, R. Hoppe*, Z. Anorg. Allg. Chem. *409*, 69 (1974).

[165] *H. G. von Schnering*, Naturwissenschaften *48*, 665 (1961).

[166] *R. Werthmann, R. Hoppe*, unpublished.

[167] *K. F. Hesse*, Acta Crystallogr. *B 33*, 901 (1977).

[168] *G. J. Palenik*, Inorg. Chem. *6*, 507 (1967).

[169] *R. Scholder, D. Fischer*, Z. Anorg. Allg. Chem. *277*, 234 (1954).

[170] *O. Muller, R. Roy*, The Major Ternary Structural Families, in: Crystal Chemistry of Non-Metallic Materials, Vol. 4. Springer-Verlag, Berlin 1974.

[171] *R. Hoppe, H. König*, Z. Anorg. Allg. Chem. *430*, 211 (1977).

[172] *R. Hoppe, D. Fink*, Z. Anorg. Allg. Chem. *443*, 193 (1978).

[173] *G. Brachtel, R. Hoppe*, Naturwissenschaften *64*, 272 (1977).

[174] *H. Klassen, R. Hoppe*, unpublished; cf. *R. Hoppe, F. Schenck*, Naturwissenschaften *56*, 414 (1969).

[175] *H. Sabrowsky, R. Hoppe*, Z. Anorg. Allg. Chem. *358*, 241 (1968).

[176] *R. W. G. Wyckoff:* Crystal Structures, 2. Ed., Vol. 1. Wiley, New York 1965.

[177] *H. Klassen, R. Hoppe*, Z. Anorg. Allg. Chem., in press.

[178] *R. Hoppe, P. Kastner*, unpublished (1973).

[179] *H. Sabrowsky*, Z. Anorg. Allg. Chem. *438*, 213 (1978).

[180] *H. Klassen, R. Hoppe*, unpublished.

[181] *K. P. Martens, R. Hoppe*, Z. Anorg. Allg. Chem. *440*, 81 (1978).

[182] *H. D. Wasel-Nielen, R. Hoppe*, Z. Anorg. Allg. Chem. *359*, 36 (1968).

[183] *G. Kienast, J. Verma, W. Klemm*, Z. Anorg. Allg. Chem. *310*, 143 (1961).

[184] *R. Hoppe, H. J. Röhrborn*, Z. Anorg. Allg. Chem. *329*, 110 (1964).

[185] *S. Siegel, E. Gebert*, J. Am. Chem. Soc. *85*, 240 (1963); *H. A. Levy, P. A. Agron, ibid. 85*, 241 (1963).

[186] *W. Bronger, H. Bode, W. Klemm*, Z. Anorg. Allg. Chem. *333*, 188 (1964).

[187] *R. Hoppe, H. Rieck*, unpublished; cf. Diplomarbeit *H. Rieck*, Universität Gießen 1974.

[188] *H. Rieck, R. Hoppe*, Z. Anorg. Allg. Chem. *400*, 311 (1973).

[189] *W. Klemm*, persönliche Mitteilung (1972).

[190] *R. Hoppe, H. Rieck*, Z. Anorg. Allg. Chem. *437*, 95 (1977).

[191] *W. Burow, R. Hoppe*, Z. Anorg. Allg. Chem. *459*, 59 (1979).

[192] *H. Zentgraf, R. Hoppe*, Z. Anorg. Allg. Chem. *462*, 80 (1980).

[193] *D. Fink, R. Hoppe*, Z. Anorg. Allg. Chem. *414*, 193 (1975); *P. Kastner, R. Hoppe, ibid. 409*, 69 (1974).

[194] *B. Darriet, M. Devalette, F. Roulleau, A. Avallet*, Acta Crystallogr. *B 30*, 2667 (1974).

[195] *G. Brachtel, R. Hoppe*, Naturwissenschaften *62*, 138 (1975).

[196] *W. Burow, R. Hoppe*, Naturwissenschaften *67*, 192 (1980).

[197] *H. Zentgraf, R. Hoppe*, Z. Anorg. Allg. Chem. *462*, 61 (1980).

[198] *W. Schartau, R. Hoppe*, Naturwissenschaften *60*, 256 (1973).

[199] *M. Jansen, R. Hoppe*, Z. Anorg. Allg. Chem. *398*, 54 (1973).

[200] *G. Brachtel, R. Hoppe*, Z. Anorg. Allg. Chem. *438*, 97 (1978).

[201] *R. M. Braun, R. Hoppe*, Angew. Chem. *90*, 475 (1978); Angew. Chem. Int. Ed. Engl. *17*, 449 (1978).

[202] *P. Kastner, R. Hoppe*, Naturwissenschaften *61*, 79 (1974).

[203] *M. Jansen*, Naturwissenschaften *62*, 236 (1975).

[204] *H. Rieck, R. Hoppe*, Angew. Chem. *85*, 587 (1973); Angew. Chem. Int. Ed. Engl. *12*, 673 (1973); Z. Anorg. Allg. Chem. *408*, 151 (1974); *G. Brachtel, R. Hoppe*, Naturwissenschaften *63*, 339 (1976); Z. Anorg. Allg. Chem. *446*, 64 (1978).

[205] *W. Bronger et al.*, Jahrestagung GDCh-Fachgruppe Festkörperchemie, Stuttgart 1980; *P. Müller, W. Bronger*, Z. Naturforsch. *B 34*, 1264 (1979); *H. J. Deiseroth, ibid. B 35*, 953 (1980).

[206] *H. Klassen, R. Hoppe*, Naturwissenschaften *63*, 387 (1976); Z. Anorg. Allg. Chem., in press.

[207] *P. Loefgren, K. Waltersson*, Acta Chem. Scand. *25*, 35 (1971).

[208] *K. A. Wilhelmi*, Ark. Kemi *26*, 149 (1967).

[209] *J. I. Smolin, J. F. Shepelev*, Sov. Phys. Crystallogr. *17*, 749 (1973).

[210] *G. Brachtel, R. Hoppe*, Z. Anorg. Allg. Chem. *438*, 15 (1978).

[211] *D. Fink, R. Hoppe*, Z. Anorg. Allg. Chem. *422*, 1 (1976).

[212] *M. Jansen, R. Hoppe*, Z. Anorg. Allg. Chem. *409*, 152 (1974).

[213] *W. Burow, R. Hoppe*, Angew. Chem. *91*, 71 (1979); Angew. Chem. Int. Ed. Engl. *18*, 61 (1979); Z. Anorg. Allg. Chem. *467*, 158 (1980).

[214] *M. Jansen, H. Keller*, Angew. Chem. *91*, 500 (1979); Angew. Chem. Int. Ed. Engl. *18*, 464 (1979).

[215] *F. Griesfeller, R. Hoppe*, unpublished.

[216] *G. Brachtel, R. Hoppe*, Z. Anorg. Allg. Chem. *446*, 87 (1978).

[217] *G. Brachtel, R. Hoppe*, Z. Anorg. Allg. Chem. *446*, 97 (1978).

[218] *M. Dodero, C. Déportes*, C. R. Acad. Sci. Paris *C 242*, 2939 (1956).

[219] *H. Zentgraf, K. Claes, R. Hoppe*, Z. Anorg. Allg. Chem. *462*, 92 (1980).

[220] *R. Hoppe, H. J. Röhrborn, H. Walker*, Naturwissenschaften *51*, 86 (1964).

[221] *B. Brazel, R. Hoppe*, Jahrestagung der Arbeitsgemeinschaft Kristallographie und der Deutschen Mineralogischen Gesellschaft, Göttingen 1980.

[222] These special autoclaves were constructed from plans by *R. Juza*. We thank Prof. *Juza*, Kiel, for his support.

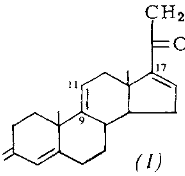
[223] *A. Simon*, Struct. Bonding (Berlin) *36*, 81 (1979).

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

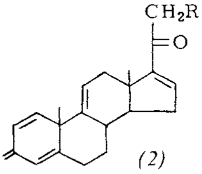
## A Novel Entry to Corticoids

By *Ulrich Kerb, Manfred Stahnke, Paul-Eberhard Schulze,* and *Rudolf Wiechert*[*]

Compounds of type *(1)* and *(2)* are key substances for the synthesis of highly active corticoids[1] such as dexamethasone, betamethasone and triamcinolone. The usual methods for their technical production are based on microbiological hydroxylation at $C_{11}$ and dehydration with cleavage of the 11- and 17$\alpha$-hydroxy groups.



*(1)*



*(2)*

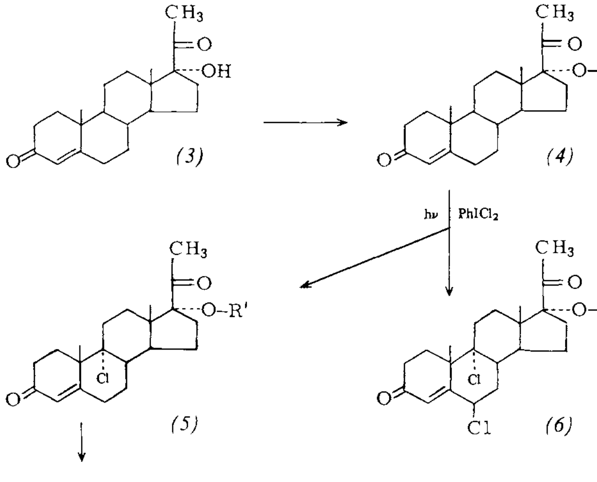
*(a)*, R = H; *(b)*, R = Acyl

A remarkable alternative to the enzymatic functionalizations at $C_{11}$—the radical relay chlorination was discovered by *Breslow et al.*[2]. They demonstrated, specifically on the example of 17-epitestosterone *m*-iodobenzoate, a regiospecific 9$\alpha$-chlorination.

We have investigated this reaction on numerous steroids and developed a technically useful method for the production of corticoid precursors. The esterification of the sterically hindered 17$\alpha$-hydroxy group on 17$\alpha$-hydroxyprogesterone *(3)* was accomplished in high yields with *m*-iodobenzoic anhydride and 4-(dimethylamino)pyridine[3].

The long-wave UV-light induced chlorination of the ester *(4)* with (dichloroiodo)benzene afforded the 9$\alpha$-chloro compound *(5)* as major product and the 6,9-dichloro compound *(6)* as by-product. By addition of the HCl-scavenger potassium acetate it was possible to completely suppress the allylchlorination to *(6)* and to isolate *(5)* in quantitative yield.

For the elimination of HCl and *m*-iodobenzoic acid a method was developed for thermolysis in high-boiling aromatic hydrocarbons. At 200—220 °C only HCl is cleaved off to give the 4,9(11)-diene; at 240—260 °C the desired triene *(1a)* is formed in very high yields. The tetraene *(2a)* was prepared in an analogous sequence.



*(1a)*

R' = $m$-$IC_6H_4$–CO

### Procedure

*(4):* A mixture of *(3)* (33.05 g, 100 mmol), 4-(dimethylamino)pyridine (48.87 g, 400 mmol) and *m*-iodobenzoic anhydride (95.6 g, 200 mmol) in toluene (300 cm$^3$) is stirred in a closed flask for 18 h at 50 °C (bath temperature). For workup the mixture is diluted with 800 cm$^3$ $CH_2Cl_2$ and successively washed with water, 1 N HCl, 5% $NaHCO_3$ solution, and once again with water. After drying over sodium sulfate and evaporating down in a vacuum, 57.4 g of crude product is obtained. Recrystallization from acetone affords 53.46 g (95%) pure *(4)*, m.p. 187—193 °C.

*(5):* A mixture of *(4)* (33.62 g, 60 mmol) and potassium acetate (60 g, previously dried over $P_2O_5$) in distilled $CH_2Cl_2$ (3.6 dm$^3$) is stirred under argon in a 4-liter Quickfit flask and after treatment with (dichloroiodo)benzene (19.8 g) is irradiated for 5 mins with a water-cooled Hanau TQ 150 immersion lamp. For workup the mixture is washed successively with 5% $NaHSO_3$ solution, 5% $NaHCO_3$ solution, and water and then evaporated down in a vacuum. The crude product is rubbed with pentane and filtered; yield 35.7 g *(5)*, m.p. 208—210 °C (dec.).

*(1a):* *(5)* (35.7 g) is added to preheated Dowtherm A (300 cm$^3$)[4] (oil-bath temperature 280 °C) and the mixture stirred for 25 min under argon at 250 °C internal temperature. After cooling in a stream of argon the mixture is diluted with $CH_2Cl_2$, washed with 5% $Na_2CO_3$ solution and water, evaporated down, and steam distilled. The residue after distillation is dried in a vacuum and recrystallized from methanol. 15.82 g of 4,9(11),16-pregnatriene-3,20-dione *(1a)* [m.p. 199.5—201 °C (199—201 °C[5]); $\lambda_{max} = 239$ nm ($\varepsilon = 25200$)] is obtained. Yield of the photochlorination and thermolysis 85%.

Received: July 14, 1980 [Z 646 IE]
German version: Angew. Chem. 93, 89 (1980)

CAS Registry numbers:
*(1a)*, 21590-20-5; *(2a)*, 75863-26-2; *(3)*, 68-96-2; *(4)*, 74176-91-3; *(5)*, 74176-92-4; *(6)*, 75863-27-3; *m*-iodobenzoic anhydride 75863-28-4

---

[*] Prof. Dr. R. Wiechert, Dr. U. Kerb, M. Stahnke, Dr. P. E. Schulze
Forschungslaboratorien der Schering AG Berlin/Bergkamen
Müllerstr. 170—178, D-1000 Berlin 65 (Germany)

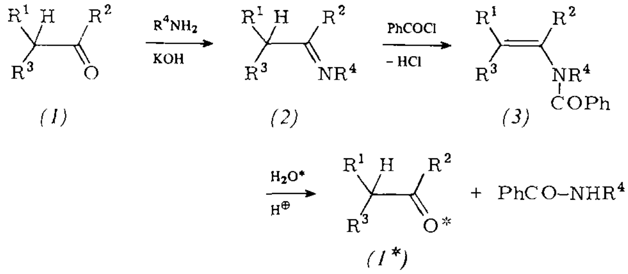
[1] Ullmanns Encyklopädie der technischen Chemie. 4th edit. Verlag Chemie, Weinheim 1977. Vol. 13, p. 55ff.

[2] *R. Breslow, R. J. Corcoran, B. B. Snider, R. J. Doll, P. L. Khanna, R. Kaleya,* J. Am. Chem. Soc. *99,* 905 (1977).
[3] *G. Höfle, W. Steglich,* Synthesis *1972,* 619.
[4] Eutectic mixture of biphenyl and dibenzofuran.
[5] *S. A. Szpilfogel, V. Gerris,* Recl. Trav. Chim. Pays-Bas *74,* 1462 (1955).

## Preparation of Labeled Aldehydes and Ketones from Enamides[**]

By *Bernard T. Golding* and *Ah Kee Wong*[*]

Full exploitation of $^{17}$O-NMR spectroscopy[1] in mechanistic organic chemistry requires efficient, simple methods for the synthesis of $^{17}$O-labeled compounds. The classical method for labeling aldehydes and ketones with $^{17}$O or $^{18}$O is based on their reversible hydration[2]. However, to obtain by this method aldehydes or ketones with the atom percentage of labeled oxygen approaching that of the water used, either a large excess of labeled water or repeated exchange is required. Several methods have been described in which an aldehyde or ketone is converted into a derivative which can be hydrolyzed with a stoichiometric amount of water. Suitable derivatives are acetals[3], dithioketals[4], and aminals[5].



| | R¹ | R² | R³ | R⁴ | Educt *(1)* |
|---|---|---|---|---|---|
| *a* | Pr | H | H | Et | pentanal |
| *b* | H | H | H | Et | acetaldehyde |
| *c* | —(CH$_2$)$_3$— | | H | Et | cyclopentanone |
| *d* | —(CH$_2$)$_4$— | | H | PhCH$_2$ | cyclohexanone |
| *e* [a] | Et | Me | H | PhCH$_2$ | 2-pentanone |
| | H | Pr | H | PhCH$_2$ | |

[a] *(3e)* is a mixture of *(3e')* top row and *(3e'')* (bottom row).

We have found a convenient, efficient method for preparing oxygen-labeled aldehydes and ketones based on the hydrolysis of enamides *(3)*. *N*-alkylideneethylamines (obtained by treating an aldehyde or ketone with EtNH$_2$/KOH)[6] or *N*-alkylidenebenzylamines *(2d), (2e)* (from ketone + benzylamine/3A sieves in CH$_2$Cl$_2$)[7] are allowed to react with benzoyl chloride/triethylamine[8] in ether *[(2a)—(2c)]* or haloalkanes[9] to give enamides *(3a)—(3e)*. These derivatives are quantitatively hydrolyzed to their parent aldehydes or ketones *(1)* and *N*-ethyl(or *N*-benzyl)benzamide by one equivalent of water in ether or haloalkane containing 0.05 mol-% HCl. The use of [$^{17}$O]- or [$^{18}$O]water in this procedure with *(1a)* and *(1c)* gives unlabeled *N*-ethylbenzamide (analysis by mass spectrometry) and labeled pentanal *(1a*)* or cyclopentanone *(1c*)*. The extent of labeling of the aldehyde or ketone was shown to be equivalent to that of the water used (IR spectroscopy as well as reduction with LiAlH$_4$ and derivatization with $\alpha$-C$_{10}$H$_7$NCO to an $\alpha$-naphthylurea that was examined by mass spectrometry).

The advantages of this method for synthesizing labeled aldehydes and ketones are that the precursor enamides *(3)* are easy to prepare[9] and can be stored (under N$_2$, $-20\,^{\circ}$C) until hydrolysis is effected; the by-product of hydrolysis, *N*-ethyl(or *N*-benzyl)benzamide, is easy to separate and does not catalyze further reactions of the aldehyde or ketone[10]; pure aldehyde or ketone is readily obtained in acceptable yield; if desired, oxygen-labeled alcohols (*e.g.* [$^{18}$O]-1-pentanol) can be obtained by addition of LiAlH$_4$ to the solution of *(1*)* in ether, after filtration of *N*-ethylbenzamide.

Benzaldehyde reacts with EtNH$_2$/KOH to give *N*-benzylidene-ethylamine, which with benzoyl chloride gives the adduct PhCHCl—N(Et)—COPH. This adduct was directly hydrolyzed with 1 equivalent [$^{18}$O]water (23 atom-% $^{18}$O) to benzaldehyde and *N*-ethylbenzamide. Extraction of benzaldehyde with ether and final purification by Kugelrohr distillation gave 23 atom-% [$^{18}$O]benzaldehyde (86%).

### *Procedure*

To *(3a)* in dry ether (2 cm$^3$/10$^{-3}$ mol) was added 1 mol equiv. 31 atom-% [$^{17}$O]water (BOC Ltd. Prochem) and 0.05 mol equiv. HCl (soln. in ether). The hydrolysis was followed by TLC and after 2 h/room temperature, diisopropylaminomethyl polystyrene (2 g/mmol HCl) was added. Filtration and partial evaporation caused crystallization of *N*-ethylbenzamide which was filtered off. The filtrate was concentrated and processed by preparative GLC (20% DEGS/chromosorb WHP, 130 °C) to give [$^{17}$O]pentanal *(1a*)* (52%); IR: $\nu = 1697$ (C=$^{18}$O), 1711 (C=O$^{17}$) and 1720 cm$^{-1}$ (rel. int. *ca.* 5:3:2); 54.24-MHz $^{17}$O-NMR (CDCl$_3$): $\delta = 582.9$ (relative to external 1:1 H$_2$O-D$_2$O).

Received: September 8, 1980 [Z 650 IE]
German version: Angew. Chem. *93*, 93 (1981)

CAS Registry numbers:
*(1a)*, 110-62-3; *(1b)*, 75-07-0; *(1c)*, 120-92-3; *(1d)*, 108-94-1; *(1e)*, 591-78-6; *(1a)** ($^{17}$O), 75961-85-2; *(1a)** ($^{18}$O), 75961-86-3; *(1b)** ($^{17}$O), 1632-96-8; *(1b)** ($^{18}$O), 3752-37-2; *(1c)** ($^{17}$O), 75961-87-4; *(1c)** ($^{18}$O), 27491-23-2; *(1d)** ($^{17}$O), 75961-88-5; *(1d)** ($^{18}$O), 73007-69-9; (1e)* ($^{17}$O), 75961-89-6; *(1e)** ($^{18}$O), 75961-90-9; *(2a)*, 10599-76-5; *(2b)*, 1190-79-0; *(2c)*, 54966-05-1; *(2d)*, 4471-09-4; *(2e)*, 63459-02-9; *(3a)*, 75961-91-0; *(3b)*, 75961-92-1; *(3c)*, 75961-93-2; *(3d)*, 30312-24-4; *(3e)*, 75961-94-3; *N*-ethylbenzamide, 614-17-5; *N*-benzylbenzamide, 1485-70-7; benzoylchloride, 98-88-4; ethylamine, 75-04-7; benzylamine, 100-46-9

---

[*] Dr. B. T. Golding, Mr. A. K. Wong
Department of Chemistry and Molecular Sciences
University of Warwick
Coventry, CV4 7AL (England)

[**] We thank the British Council for an award to A. K. W. Thanks are also due to Dr. *J. Schreiber*, ETH Zürich for a gift of diisopropylaminomethylpolystyrene.

---

[1] *W. G. Klemperer,* Angew. Chem. *90,* 258 (1978); Angew. Chem. Int. Ed. Engl. *17,* 246 (1978); *J. K. Crandall, M. A. Centeno, S. Børresen, J. Org. Chem. 44,* 1184 (1979).

[2] *M. Cohn, H. C. Urey,* J. Am. Chem. Soc. *60,* 679 (1938); *H. Dahn, H.-P. Schlunke, J. Temler,* Helv. Chim. Acta *55,* 907 (1972).

[3] *C. B. Sawyer,* J. Org. Chem. *37,* 4225 (1972); *D. P. Higley, R. W. Murray,* J. Am. Chem. Soc. *98,* 4526 (1976).

[4] *M. Hojo, R. Masuda, K. Hakotani,* Tetrahedron Lett. *1978,* 1121.

[5] *Yu. A. Strepikheev, L. V. Kovalenko, A. B. Batalina,* Zh. Obshch. Khim. *46,* 2468 (1976).

[6] *A. I. Fetell, H. Feuer,* J. Org. Chem. *43,* 497 (1978); *A. O. Bedenbaugh, J. H. Bedenbaugh, J. D. Adkins, W. A. Bergin, ibid. 35,* 543 (1970).

[7] Cf. *K. Taguchi, F. H. Westheimer,* J. Org. Chem. *36,* 1570 (1971).

[8] *H. Breederveld,* Recl. Trav. Chim. Pays-Bas *79,* 1197 (1960).

[9] Formation of enamides *(3a)—(3c)* takes place rapidly on addition of benzoyl chloride in ether to a mixture of *(2a)—(2c)* + triethylamine in ice-cold ether. After filtration of triethylammonium chloride, the filtrate is concentrated and distilled to give *(3a)—(3c)* as colorless/pale yellow oils, which were characterized by their $^{1}$H-NMR spectra, mass spectra and by combustion analyses. The formation of *(3d)* and *(3e)* from *(2d)* and *(2e)* was followed in an NMR tube (solvent CDCl$_3$ or CCl$_4$).

[10] We have investigated the hydrolysis of *(2)* with 1 equivalent each of water and HCl as a route to labeled aldehydes and ketones. For aldehydes (*e.g.* pentanal) this method is unsatisfactory because of competing aldol condensation. However, the *N*-ethyliminium hydrochloride of camphor is a satisfactory precursor of oxygen-labeled camphors.—The *N*-ethylimine of camphor does not react with benzoyl chloride/$Et_3N$ in $CHCl_3$ at room temperature over several days.

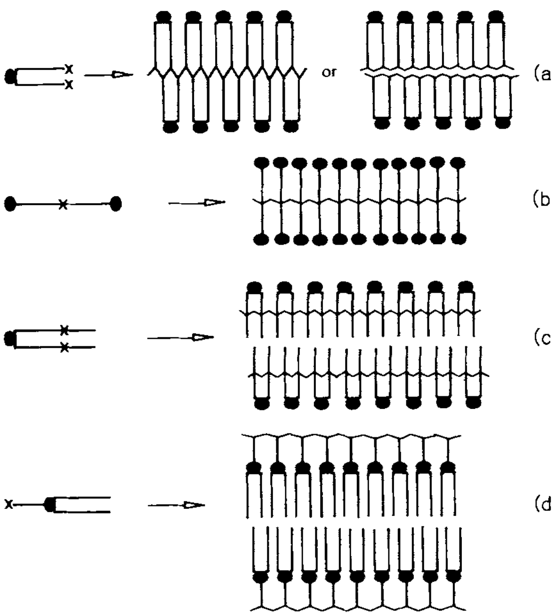
---

## Polymer Model Membranes[**]

By *Akira Akimoto, Klaus Dorn, Leo Gros,*
*Helmut Ringsdorf,* and *Hans Schupp*[*]

The synthesis of stable model membranes which can be used to study biological processes, for instance cell recognition or cell-cell-interaction, has been a scientific goal for a long time[1]. Especially liposomes—artificial, spherical particles with a bimolecular membrane and an aqueous interior—serve as models for biological membranes; however, they show a significantly decreased stability[2].

To stabilize synthetic double layers *Khorana et al.*[3] synthesized lipids carrying photoreactive groups and could prove a crosslinking of membrane components. Another method to stabilize model membranes providing an even broader scope of possible applications is the polymerization of lipid-analogous systems[4a] (Scheme 1).



Scheme 1. Possible preparation of polymer model membranes (x = polymerizable group). (a—c): polymerization preserving head-group properties; d: polymerization preserving chain mobility (Monomer examples, see Table 1).

All four possibilities in Scheme 1, however, alter the physical properties of the membrane: polymerization in the hydrophobic part of the monomers (examples a—c) especially influences the phase transition temperature, while polymerization in the hydrophilic moiety changes the headgroup properties. Nevertheless, in our opinion, the properties of biological membrane systems can be thoroughly achieved by making the right choice of polymerizable groups. Furthermore, by adding natural phospholipids the properties of biological membranes can be imitated to an even greater extent.

The different possibilities shown in Scheme 1 have all been realized. So far only a few contributions have appeared in the literature: acrylate and diacetylene systems have already been described by us[4b] and by *Regen et al.*[5a], *Chapman et al.*[5b], and *O'Brien*[5c]. Due to the conjugated double bonds of the polymer chain resulting in a rather rigid conformation in poly(diacetylene) compounds no phase transition temperature can be observed, in contrast to biological membranes[4b,5b]. New monomer systems for the polymerization according to Scheme 1 are collected in Table 1.

Table 1. Polymerizable and liposome forming lipid analogues Type (a)—(d), cf. Scheme 1. $R = CH_2{=}C(CH_3){-}CO$.

| Type | Compound | | M.p. [°C] |
|---|---|---|---|
| (a) | $R{-}NH{-}(CH_2)_{10}{-}CO{-}O{-}(CH_2)_2\diagdown\ \diagup CH_3$<br>$\overset{\oplus}{N}\qquad Br^{\ominus}$<br>$R{-}NH{-}(CH_2)_{10}{-}CO{-}O{-}(CH_2)_2\diagup\ \diagdown CH_3$ | *(1)* | 99 |
| (b) | $HOOC{-}(CH_2)_8C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}COOH$ | *(2)* | 119 [15] |
| (c) | $H_3C{-}(CH_2)_{12}{-}CH{=}CH{-}CH{=}CH{-}CO{-}O\diagdown$<br>$X$<br>$H_3C{-}(CH_2)_{12}{-}CH{=}CH{-}CH{=}CH{-}CO{-}O\diagup$ | | |
| | $X = {-}(CH_2)_2{-}N(CH_3){-}(CH_2)_2{-}$ | *(3)* | 36 |
| | $X = {-}(CH_2)_2{-}\overset{\oplus}{N}(CH_3)_2{-}(CH_2)_2{-}\ \ Br^{\ominus}$ | *(4)* | 94 |
| | $X = {-}CH_2{-}\overset{\vert}{C}H{-}CH_2OH$ | *(5)* | 59 |
| | $X = {-}CH_2{-}\overset{\vert}{C}H{-}CH_2{-}O{-}\underset{O^{\ominus}}{\overset{O}{\overset{\Vert}{P}}}{-}O{-}(CH_2)_2{-}\overset{\oplus}{N}(CH_3)_3$ | *(6)* | 220 |
| (d) | $H_3C{-}(CH_2)_{14}{-}CO{-}O{-}CH_2$<br>$H_3C{-}(CH_2)_{14}{-}CO{-}O{-}CH$<br>$CH_2{-}O{-}R$ | *(7)* | 51 |
| | $H_3C{-}(CH_2)_{17}{-}O{-}CH_2$<br>$H_3C{-}(CH_2)_{17}{-}O{-}CH$<br>$CH_2{-}O{-}Y$ | | |
| | $Y = CO{-}(CH_2)_5{-}NH{-}R$ | *(8)* | 54 |
| | $Y = R$ | *(9)* | 36 |
| | $H_3C{-}(CH_2)_n\diagdown$<br>$N{-}Y$<br>$H_3C{-}(CH_2)_n\diagup$ | | |
| | $n = 11,\ Y = R$ | *(10)* | – |
| | $n = 17,\ Y = R$ | *(11)* | 36-38 |
| | $n = 11,\ Y = (CH_2)_3{-}NH{-}R$ | *(12)* | – |
| | $n = 17,\ Y = (CH_2)_3{-}NH{-}R$ | *(13)* | 35-36 |
| | $H_3C{-}(CH_2)_{17}{-}O{-}CO$<br>$CH_2$<br>$^{*}CH{-}NH{-}Y$<br>$H_3C{-}(CH_2)_{17}{-}O{-}CO$ | | |
| | $Y = R$ | *(14)* | 64-68 |
| | $Y = CO{-}(CH_2)_5{-}NH{-}R$ | *(15)* | 78 |

The spreading and polymerization behavior of the monomers were investigated at the gas-water interface. The pressure-area diagrams of compounds *(3)* and *(4)* qualitatively resemble those of the corresponding diacetylene derivatives[6a]. However, they already show a liquid-analogous phase at substantially lower temperatures. The pressure-area diagram of *(5)* shows a solid-analogous phase at 2 °C, and a liquid-analogous film with transition to a solid phase at 25 °C (Fig. 1a).

In contrast to the diacetylenes, which react only topochemically[6b], the butadiene and acrylic derivatives can be polymerized by UV light at any temperature in the solid-analogous as well as in the liquid-analogous phase. The polymerization can be followed by measuring the contraction of the film. The pressure-area diagrams of the polymers show a steeper slope corresponding to the closer packing of the monomer units. This is shown for the butadiene derivative *(5)* (Fig. 1a) and the acrylic system *(13)* (Fig. 1b).

---

[*] Prof. Dr. H. Ringsdorf, Dr. A. Akimoto, Dipl.-Chem. K. Dorn, Dipl.-Chem. L. Gros, Dipl.-Chem. H. Schupp
Institut für Organische Chemie der Universität
J.-J.-Becher-Weg 18—20, D-6500 Mainz 1 (Germany)

[**] Polyreactions in Oriented Systems, Part 23.—Part 22: *H. Koch, H. Ringsdorf,* Makromolek. Chem. Commun., in press.

These high packing densities together with the increased stability of the monolayers provide a basis for the use of these polymer systems as model membranes.

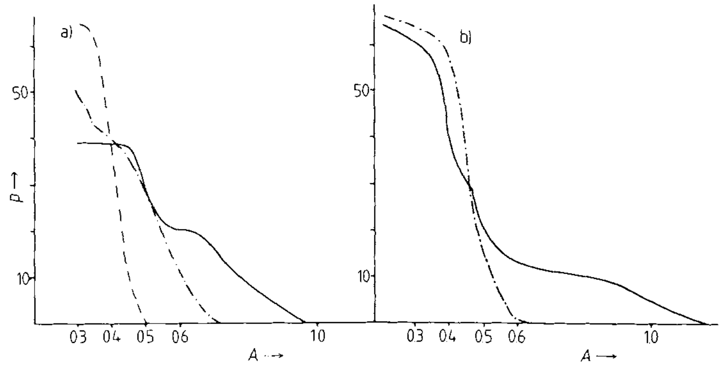


Fig. 1. a) Surface-pressure-area diagram of *(5)* at 2 °C (-----) and 25 °C (——) and of polymeric *(5)* at 25 °C (–·–·–). b) Surface-pressure-area diagram of *(13)* (——) and of polymeric *(13)* (–·–·–), each at 25 °C. $p$ = surface pressure (mN/m); $A$ = area (nm$^2$/molecule).

Liposomes, *i.e.* cell models with bimolecular membranes, were prepared by sonicating aqueous dispersions[2c] of the monomers at *ca.* 40 °C. On filtration through a 8-μm Millipore-filter, clear or slightly opaque solutions are obtained, which turn turbid after some days.

The polymerization of these monomer vesicles is carried out by UV-irradiation of the aqueous solutions. The polyreaction of the butadiene derivatives *(3)—(6)* in liposomes can be followed by the decreasing monomer absorption at 265 nm. The polymerization of the acryl derivatives *(7)—(9)* was proved by freeze-drying the aqueous solutions followed by gel-filtration. In contrast to the monomers the polymer vesicle solutions are stable for weeks.

It could be shown by electron microscopy that the vesicle structure is preserved during the polymerization. This is consistent with results obtained on polymerizing diacetylene vesicles[4b].

Compounds *(14)* and *(15)* were synthesized in order to study the influence of chiral membrane components on model reactions. In addition, mixed systems of polymerizable lipid analogues, natural phospholipids, and proteins are under current investigation. For investigations on cell recognition, monolayers and polymer liposomes consisting of glycolipids have been prepared (cf. [6c]).

### *Procedure*

*(1):* 11-(*N*-Methacryloylamino)undecanoic acid[7] is esterified with *N*-methyliminodiethanol in the presence of dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine and quaternized using methyl bromide[8].

*(3):* 2,4-Octadecadienoic acid[9] is esterified with *N*-methyliminodiethanol adding DCC/4-(dimethylamino)pyridine [8].

*(4):* Monomer *(3)* is allowed to react with methyl bromide in acetone.

*(5)* and *(6)* are synthesized *via* conventional lipid chemistry methods[10].

*(7)—(11), (14), (15):* The corresponding 1,2-diglycerine ester [*(7)*][11], 1,2-diglycerine ethers [*(8), (9)*][12], dialkylamines [*(10), (11)*] (Fluka, Eastman) or L-aspartic acid dioctadecyl esters [*(14), (15)*][13] are allowed to react with methacryloyl chloride or 6-(*N*-methacryloylamino)hexanoic acid [*(15)*] and DCC.

*(12), (13):* The corresponding dialkylamines are added to acrylonitrile, reduced with $LiAlH_4$[14], and then allowed to react with methacryloyl chloride.

Received: November 24, 1980 [Z 652a IE]
German version: Angew. Chem. *93*, 108 (1981)

---

[1] *J. H. Fendler*, Acc. Chem. Res. *13*, 7 (1980).

[2] a) *E. Sackmann*, Ber. Bunsenges. Phys. Chem. *82*, 891 (1978); b) *D. A. Tyrell, T. D. Heath, C. M. Colley, B. E. Ryman*, Biochim. Biophys. Acta *457*, 259 (1976); c) *C.-H. Huang*, Biochemistry *8*, 344 (1969); d) *T. Kunitake*, J. Macromol. Sci. Chem. *A 13*, 587 (1979); e) *G. Scherphof, F. Roerdink, D. Hoekstra, J. Zborowski, E. Wisse* in *G. Gregoriadis:* Liposomes in Biological Systems. Wiley, New York 1980, p. 179.

[3] *C. M. Gupta, C. E. Costello, H. G. Khorana*, Proc. Natl. Acad. Sci. USA *76*, 3139 (1979).

[4] a) *H.-H. Hub, B. Hupfer, H. Ringsdorf*, Am. Chem. Soc., Org. Coatings Plastics Chem. Div. Prepr. *42*, 2 (1980); cf. Nachr. Chem. Tech. Lab. *28*, 215 (1980); b) *H.-H. Hub, B. Hupfer, H. Koch, H. Ringsdorf*, Angew. Chem. *92*, 962 (1980); Angew. Chem. Int. Ed. Engl. *19*, 938 (1980).

[5] a) *S. L. Regen, B. Czech, A. Sing*, J. Am. Chem. Soc. *102*, 6638 (1980); b) *D. S. Johnston, S. Sanghera, M. Pons, D. Chapman*, Biochim. Biophys. Acta *602*, 57 (1980); c) *D. O'Brien*, private communication.

[6] a) *D. Day, H.-H. Hub, H. Ringsdorf*, Isr. J. Chem. *18*, 325 (1979); b) *D. Day, H. Ringsdorf*, J. Polym. Sci. Lett. *16*, 205 (1978); c) *H. Bader, H. Ringsdorf, J. Skura*, Angew. Chem. *93*, 109 (1981); Angew. Chem. Int. Ed. Engl. *20*, Nr. 1 (1981).

[7] *H. G. Batz, J. Koldehoff*, Makromol. Chem. *177*, 683 (1976).

[8] *B. Neises, W. Steglich*, Angew. Chem. *90*, 556 (1978); Angew. Chem. Int. Ed. Engl. *17*, 522 (1978).

[9] *H. Ringsdorf, H. Schupp*, Am. Chem. Soc., Org. Coatings Plastics Chem. Div. Prepr. *42*, 379 (1980).

[10] *H. Eibl, D. Arnold, H. U. Weltzien, O. Westphal*, Justus Liebigs Ann. Chem. *709*, 226 (1967).

[11] *F. R. Pfeiffer, C. K. Miao, J. A. Weisbach*, J. Org. Chem. *35*, 221 (1970).

[12] *A. F. Rosenthal*, J. Chem. Soc. *1965*, 7345.

[13] *L. Gros*, Dissertation, Universität Mainz, planned for 1981.

[14] *Cronin et al.* US-Pat. 4034040 (1977).

[15] *A. Scher*, Justus Liebigs Ann. Chem. *589*, 234 (1954).

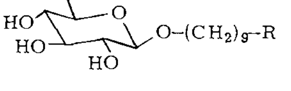
---

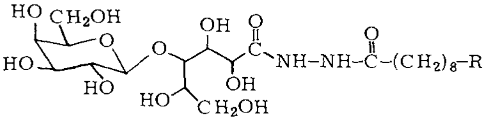
## Liposomes from Polymerizable Glycolipids[**]

By *Hubert Bader, Helmut Ringsdorf,* and *Josef Skura*[*]

Polymerizable analogues of cell membrane components, *e.g.* phospholipids and lysophospholipids bearing acryl-, butadiene-, and diyne groups[1] in the hydrophobic parts of the molecules have already been synthesized and investigated in monolayers and liposomes[2].

In this connexion glycolipids are of particular interest, since they exhibit vital functions and properties in the natural cell membrane such as cell recognition, antigenicity, histocompatibility, and lectin affinity. Especially their properties as lectin receptors make glycolipids useful tools for studying specific interactions between lectins (sugar recognizing proteins) and saccharide bearing liposomes[3]. We report here on the first glycolipids with the diyne group [*(1)* and *(2)*], their behavior in monomolecular films, their poly-


*(1)*


*(2)*

$R = C{\equiv}C{-}C{\equiv}C{-}(CH_2)_{12}{-}CH_3$

---

[*] Prof. Dr. H. Ringsdorf, H. Bader, Dr. J. Skura
Institut für Organische Chemie der Universität
J.-J.-Becher-Weg 18—20, D-6500 Mainz 1 (Germany)

[**] Polyreactions in Oriented Systems, Part 24.—Part 23: [1].

merization in monolayers and liposomes, as well as their interactions with the lectin Concanavalin A (Con A).

The glycolipids *(1)* and *(2)* (see Procedure) were spread as monomolecular layers at the gas-water interphase on a Langmuir film balance. Figure 1 shows the corresponding surface-pressure-area isotherms.

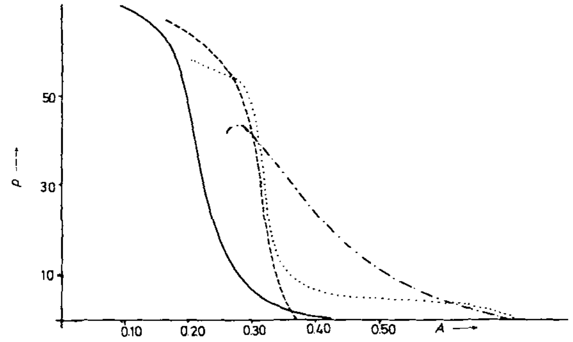


Fig. 1. Surface pressure-area isotherms of *(1)* at 20 °C (-·-·-) and 1 °C (·····), of *(2)* at 20 °C (——), and of polymer *(1)* at 1 °C (-----). $p$ = surface pressure (in mN/m), $A$ = area (in $nm^2$/molecule).

While *(1)* is only in a liquid expanded phase at 20 °C with a collapse point of 0.29 $nm^2$/molecule and 43 mN/m, at 1 °C it shows a liquid expanded phase up to about 0.45 $nm^2$/molecule and 8 mN/m followed by the solid-analogous phase with a collapse point of 0.31 $nm^2$/molecule and 51 mN/m. The high area value at the collapse point evidences the large area occupied by the glucopyranose ring bound directly to the diyne alcohol.

The glycolipid *(2)* has a solid phase in the whole temperature range investigated from 20 °C to 40 °C (collapse point 0.18 $nm^2$/molecule and 63 mN/m). The head-group of *(2)* occupies a smaller area than that of *(1)*; the reason for this is the hydrophilic spacer between galactopyranose and diynoic acid which permits a deeper penetration of the sugar moiety into the subphase.

When a monomolecular film of *(1)* is UV irradiated at 1 °C and a surface pressure higher than 10 mN/m, the typical polymerization of the diyne group takes place. The colorless monomer film turns blue and then red[4]. As expected the polymerized film does not exhibit a liquid expanded phase any more. The occupied area at the collapse point is only insignificantly smaller than in the monomer film.

The monomolecular film of *(2)* also yields a blue polymer film when irradiated at 20 °C and 35 mN/m, but does not show the color change to red caused by change of the polymer conformation even after 30 min of irradiation. As in the case of *(1)*, the contraction of the film during the polymerization is very small. When an aqueous suspension of *(1)* is sonicated for 15 min at 50 °C, a clear colorless solution is obtained, which is polymerized in a quartz cuvette at 0 °C by UV irradiation. As in monolayers, during the polyreaction the color change *via* blue to red takes place, as had already been observed in the case of different liposome forming diacetylene compounds[1]. In contrast, no liposomes are formed by *(2)* when sonicated for longer periods (up to 30 min) and at higher temperatures (up to 80 °C). Only a crystalline suspension is formed. Its filtrate turns faintly blue on irradiation. The strong tendency of the hydrazide linkages to form hydrogen bonds make glycolipid (2) excessively rigid and poorly dispersible in water, which is also confirmed by the missing liquid expanded phase in the monolayer.

The interaction of *(1)* with the lectin Con A was investigated in monolayers and with monomer and polymer liposomes. When a con A solution in phosphate buffer (pH 7.4) is injected under a monomolecular film of *(1)* on the same buffer at a constant surface pressure of 10 mN/m, a considerable expansion of the film can be observed due to strong interaction of the lectin with the monolayer.

Solutions of monomer and polymer liposomes of glycolipid *(1)* react with Con A solution by agglutination and precipitation within a short period of time. This effect could not be observed with different polymer liposomes not bearing saccharide moieties.

### *Procedure*

The glucose derivative *(1)* was obtained as a colorless solid (m.p. 73—75 °C)[6] when acetobromoglucose and 10,12-hexacosadiyne-1-ol in dry ether were allowed to react in the presence of silver 4-hydroxyvaleriate (Koenigs-Knorr reaction[5]), followed by the cleavage of the protective groups with sodium methoxide.

The lactobionic acid derivative *(2)* could be synthesized from lactobiono-1,5-lactone[7] *via* its hydrazide, followed by coupling with 10,12-hexacosadiynoic acid *via* its mixed anhydride with ethyl chloroformate (m.p. 114 °C)[6].

Received: November 26, 1980 [Z 652b IE]
German version: Angew. Chem. *93*, 109 (1981)

CAS Registry numbers:
*(1)*, 76024-88-9; *(2)*, 76036-52-7; acetobromoglucose, 572-09-8; hexacosa-10,12-diyn-1-ol, 75495-26-0; hexacosa-10,12-diynoic acid, 73510-21-1; lactobionolactone hydrazide, 76024-89-0

---

[1] *A. Akimoto, K. Dorn, L. Gros, H. Ringsdorf, H. Schupp*, Angew. Chem. *93*, 108 (1981); Angew. Chem. Int. Ed. Engl. *20*, 90 (1981).

[2] *H.-H. Hub, B. Hupfer, H. Koch, H. Ringsdorf*, Angew. Chem. *92*, 962 (1980); Angew. Chem. Int. Ed. Engl. *19*, 938 (1980); *D. S. Johnston, S. Sanghera, M. Pons, D. Chapman*, Biochim. Biophys. Acta *602*, 57 (1980).

[3] *G. A. Orr, R. R. Rando, F. W. Bangerter*, J. Biol. Chem. *254*, 4721 (1979). *R. Y. Hampton, R. W. Holz, I. J. Goldstein*, *ibid. 255*, 6766 (1980).

[4] *D. R. Day, H. Ringsdorf*, Makromol. Chem. *180*, 1059 (1979).

[5] *G. Wulff, W. Krüger, G. Röhle*, Chem. Ber. *104*, 1387 (1971); *G. Wulff, G. Röhle, W. Krüger*, *ibid. 105*, 1097 (1972).

[6] The IR and NMR spectra are wholly in accord with the assigned structures.

[7] *T. J. Williams, N. R. Plessas, I. J. Goldstein, J. Lönngren*, Arch. Biochem. Biophys. *195*, 145 (1979).

## Palladium-Catalyzed Reduction of Multiple Bonds with Mg/$CH_3OH$[**]

By *George A. Olah, G. K. Surya Prakash, Massoud Arvanaghi*, and *Mark R. Bruce*[*]

It has long been known that magnesium in methanol (or in ethyl or isopropyl alcohol) can been used for the reduction of carbon-heteroatom double bonds[1] and *N*-oxides[2]; more recently, the selective reduction of $\alpha$,$\beta$-unsaturated nitriles[3a] and aryl-substituted ethylenes has also been achieved in this way[3b]. In all these reactions, however, isolated, nonactivated double or triple bonds were found unaffected by the reducing system. We now wish to report that addition of catalytic palladium metal on carbon to the Mg/$CH_3OH$ reagent dramatically enhances its reactivity, thus allowing rapid

---

[*] Prof. Dr. G. A. Olah, Dr. G. K. S. Prakash, M. Arvanaghi,
Dr. M. R. Bruce
Hydrocarbon Research Institute and Department of Chemistry
University of Southern California
Los Angeles, California 90007 (USA)

[**] Synthetic Methods and Reactions, Part 94. This work was supported by the National Science Foundation and the National Institutes of Health.—Part 93; *G. A. Olah, S. C. Narang, L. D. Field, G. F. Salem*. J. Org. Chem. *45*, 4792 (1980).

and facile reduction of nonactivated multiple bonds (Table 1).

Table 1. Reduction of multiple bonds with $Mg/CH_3OH/Pd—C$.

| Substrate | Product [a] | Yield [b] [%] | B.p. [°C/torr] M.p. [°C] |
|---|---|---|---|
| Bicyclo[2.2.2]octene | Bicyclo[2.2.2]octane | 96 | 169–170 |
| 2-Octene | *n*-Octane | 89 | 122–123/760 |
| 1-Methyl-1-cycloheptene | Methylcycloheptane | 92 | 131/760 |
| Ethynylcyclohexane | Ethylcyclohexane | 82 | 132/760 |
| 1-Nonene | *n*-Nonane | 86 | 35/10 |
| Cyclododecene | Cyclododecane | 85 | 60 |
| 2-Cyclopentenylacetic acid | Cyclopentylacetic acid | 93 | 125/17 |
| 5-Norbornene-2-carbonitrile | 2-Norbornane-carbonitrile [c] | 91 | 62/7 |
| 5-Norbornen-2-yl acetate | 2-Norbornyl acetate [c] | 96 | 95/15 |
| 3-Cyclohexenol | Cyclohexanol | 66 | 160–161/760 |
| Ethyl-3-cyclohexene-carboxylate | Ethylcyclohexane-carboxylate | 91 | 81–83/12 |
| 1-Ethynylcyclopentanol | 1-Ethylcyclopentanol | 90 | 170–171/760 |
| 2-Cyclopropyl-3-buten-2-ol | 2-Cyclopropyl-2-butanol | 78 | 162–163/760 |
| 2-(3-Cyclohexenyl)ethanol | 2-Cyclohexylethanol | 87 | 102/17 |
| 2-Butynol | 2,2,3,3-Tetradeuterio-1-butanol [d] | 69 | 118/760 |
| *trans*-Stilbene | 1,2-Dideuterio-1,2-diphenylethane [d] | 89 | 49–50 |
| Diphenylacetylene | 1,1,2,2-Tetradeuterio-1,2-diphenylethane [d] | 86 | 50–51 |

[a] All products were characterized by elemental analysis, and $^1H$-NMR and IR spectra. [b] Yield of isolated product. [c] Mixture of *exo* and *endo* derivatives. [d] Reduction with $CH_3O[^2H]$.

The present reducing system has distinct advantages over the conventional catalytic hydrogenation procedures[4]: cyclopropyl groups are not reduced by the system and also benzylic ethers and alcohols remain unaffected under the reaction conditions. On the other hand, the deuteration of multiple bonds is readily achieved in good yields with the use of $CH_3O[^2H]$. The system $Mg/CH_3OH/Pd—C$ thus serves as a useful convenient alternative procedure for catalytic hydrogenation or deuteration.

*Procedure:*

To the well stirred mixture of the corresponding unsaturated compound (10 mmol) and 50 mg of 10% Pd/C in methanol (30 cm$^3$) in a 250 ml round bottom flask at room temperature is added magnesium turnings (five equivalents of Mg per double bond). After a sluggish induction period the reaction starts with brisk evolution of hydrogen gas. After all the magnesium metal has dissolved, the mixture is poured with vigorous stirring into 30 cm$^3$ of an ice-cold 3 N HCl solution and extracted with ether (3 × 100 cm$^3$). The ethereal layer is washed twice with saturated brine solution (2 × 100 cm$^3$) and dried over $MgSO_4$. The solvent is removed by evaporation and the residue purified by distillation or recrystallization.—The reduction with $CH_3O[^2H]$ is carried out under a dry argon atmosphere.

Received: June 18, 1980 [Z 654 IE]
German version: Angew. Chem. 93, 107 (1981)

---

[1] a) *L. Zechmeister, P. Romm,* Justus Liebigs Ann. Chem. *468,* 117 (1929); b) *V. Hahn, R. Hansal, I. Markovcic, D. Vargazon,* Ark. Kemi *26,* 21 (1954); Chem. Abstr. *50,* 2927 (1956); c) *R. Hansal, D. Vargazon, V. Hahn, ibid. 27,* 33 (1955); Chem. Abstr. *50,* 4894i (1956).

[2] *C. P. Joshua, P. K. Ramadas,* Synthesis *1974,* 873.

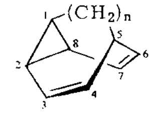
[3] a) *J. A. Profitt, D. S. Watt, E. J. Corey,* J. Org. Chem. *40,* 127 (1975); b) *J. A. Profitt, H. H. Ong, ibid. 44,* 3972 (1979).

[4] *P. N. Rylander:* Catalytic Hydrogenation in Organic Syntheses. Academic Press, New York 1979.

## 2,6-Barbaralane Dicarbonitrile: A Probe for Dewar-Hoffmann-Type Homoaromatic Molecules[**]

By *Helmut Quast, Yvonne Görlach,* and *Josef Stawitz*[*]

The originally postulated existence of neutral homoaromatic molecules through cyclic homoconjugative interaction of $(4n+2)$ $\pi$-electrons, which are located in *even* $\pi$-electron parts of the molecule, meets apparently unsurmountable energy barriers[1]. By extrapolating structural effects on the energy barrier of the degenerate Cope-rearrangement, *Dewar* and *Hoffmann* postulated a novel type of homoaromatic molecules, which is characterized by cyclic homoconjugative interaction of *uneven* $\pi$-electron parts of the molecule[2]. Indeed, by structural modifications, the energy barrier of the degenerate Cope-rearrangement may be drastically lowered, which leads to fluxional molecules, *e.g.* semibullvalene *(1a)* [$\Delta G^{\ddagger}_{133} = 23$ kJ/mol] and barbaralane *(1b)* [$\Delta G^{\ddagger}_{196} = 33$ kJ/mol][3]. Reducing the energy barrier further might result in stable molecules with a homoaromatic ground state. This has been predicted to be effected by azasubstitution at positions 2 and 6 or, alternatively, 3 and 7 of semibullvalene *(1a)* or by donor substituents at C-1 and C-5 and acceptor substituents at C-2, C-4, C-6, and C-8[2]. So far, no such compound is known. We now report a simple synthesis of 2,6-barbaralane dicarbonitrile *(6)*, which should allow an experimental investigation of the above predictions.



*(1a)*, n = 0
*(1b)*, n = 1

The readily available bicyclononanedione *(2)*[4] was converted quantitatively with trimethylsilyl cyanide and zinc iodide in dichloromethane[5] into the *O,O'*-bis(trimethylsilyl)biscyanohydrin (m.p. 97—99 °C), which apparently exists as one stereoisomer ($^1H$-NMR spectrum). By refluxing for 1.5 h in methanol and concentrated hydrochloric acid (1 : 1), the trimethylsilyl derivative was hydrolyzed to the biscyanohydrin. Without purification, this intermediate was allowed to react with 12 moles of trichlorophosphane oxide (per mol of biscyanohydrin) in boiling pyridine (2 h) and thereby converted in 53% yield [based on *(2)*] into the unsaturated dicarbonitrile *(3)*, which was sublimed at 110–125 °C/4 × $10^{-6}$ torr.

The bromination of *(3)* with *N*-bromosuccinimide in tetrachloromethane proceeds smoothly and completely diastereoselectively. However, even in other solvents, the bromination cannot be stopped at the stage of the bromodicarbonitrile *(4)*. Instead, with one mol of *N*-bromosuccinimide in boiling tetrachloromethane after 2 h, one obtains a mixture of 0.51 mol *(4)* and 0.22 mol dibromodicarbonitrile *(5)*, which can be easily separated by preparative layer chromato-

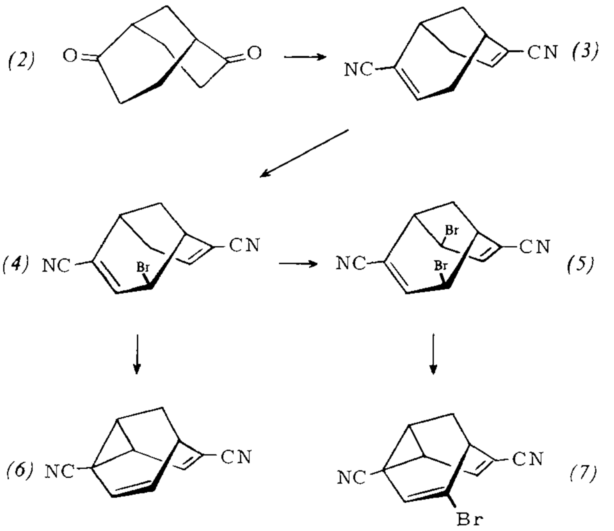
---

[*] Prof. Dr. H. Quast, Dipl.-Chem. Y. Görlach, Dr. J. Stawitz
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. The results have been taken from the Diplomarbeit of *Y. G.*, University of Würzburg 1980.

graphy (silica, ether/tetrachloromethane 1:1). According to the NMR spectra (Table 1), *(4)* and *(5)* form only one stereoisomer. Because of the C$_2$ symmetry of *(5)* its bromine atoms are homotopic.

The ring closure of the bicyclo[3.3.1]nonane to the barbaralane system has already been accomplished in different ways[6]. In the case of *(4)* and *(5)*, it is achieved extremely rapidly with alkoxides in alcohols. Thus, with sodium [D$_3$]methoxide in [D$_4$]methanol, immediate quantitative ring-closure occurs to give the (bromo-)barbaralane dicarbonitrile instead of H/D exchange. In preparative runs using 1.15 moles of sodium methoxide in methanol/benzene per mol of *(4)* and *(5)*, 77% *(6)* and 95% *(7)*, respectively, are obtained as crystalline products.



The assigned structures *(3)*—*(7)* are based on elemental analyses and IR, NMR, and mass spectra. X-ray structure determinations have been performed on *(3)*, *(4)*, *(5)*, and *(7)* which provide unequivocal proof of structure[7]. In particular, they establish the *exo* position of the bromine atoms of the bromodicarbonitriles *(4)* and *(5)* inferred already on the basis of steric arguments. The IR spectra of the bicyclononadiene dicarbonitriles *(3)*, *(4)*, and *(5)* show only one C$\equiv$N frequency arising from $\alpha,\beta$-unsaturated nitrile groups. In contrast, the IR spectra of the barbaralane dicarbonitriles *(6)* and *(7)* display two nitrile bands. An analogous situation is found for the C=C frequencies.

While the $^{13}$C-NMR spectra can be easily interpreted, long-range couplings complicate the 90-MHz $^1$H-NMR spectra in most cases (Table 1). The reported coupling constants were assigned with the aid of decoupling experiments under the simplifying assumption of first order spectra. The $^1$H-NMR data are in harmony with those of the parent hydrocarbons, *viz.* bicyclo[3.3.1]nona-2,6-diene[8] and barbaralane *(1b)*[9], respectively. Like barbaralane *(1b)*, *(6)* exhibits averaged NMR spectra at ambient temperature. In the 50-MHz $^{13}$C-NMR spectrum of *(6)* in [D$_2$]dichloromethane, the signal of C-2/C-6 as well as that of C-4/C-8 begins to broaden only at −60 °C[10]. That is, at −60 °C the degenerate Cope rearrangement of *(6)* still occurs rapidly on the $^{13}$C-NMR time scala; on the IR time scala, however, it is slow at +30 °C.

The $^1$H-NMR spectrum of the bromobarbaralane dicarbonitrile shows the signals of *two* vinyl protons and *two* cyclopropane protons. As anticipated, the compound prefers the structure *(7)* and hence may serve as a model for a static (non-fluxional) system.—Our approach offers a possible synthetic route to the hypothetical homoaromatic semibullvalenes of *Dewar* and *Hoffmann*[2].

Received: October 28, 1980 [Z 656 IE]
German version: Angew. Chem. 93, 96 (1981)

CAS Registry numbers:
*(1a)*, 6909-37-1; *(1b)*, 14693-11-9; *(2)*, 16473-11-3; *(2)* *O,O*-bis(trimethylsilyl)biscyanhydrin, 75993-72-5; *(3)*, 76010-12-3; *(4)*, 75993-73-6; *(5)*, 75993-74-7; *(6)*, 75993-75-8; *(7)*, 75993-76-9

---

[1] *K. N. Houk, R. W. Gandour, R. W. Strozier, N. G. Rondan, L. A. Paquette,* J. Am. Chem. Soc. *101*, 6797 (1979).

[2] *R. Hoffmann, W.-D. Stohrer,* J. Am. Chem. Soc. *93*, 6941 (1971); *M. J. S. Dewar, D. H. Lo, ibid. 93*, 7201 (1971); *M. J. S. Dewar, Z. Náhlovská, B. D. Náhlovský,* Chem. Commun. *1971*, 1377.

[3] *A. K. Cheng, F. A. L. Anet, J. Mioduski, J. Meinwald,* J. Am. Chem. Soc. *96*, 2887 (1974).

[4] *J. A. Peters,* Synthesis *1979*, 321.

[5] *P. G. Gassman, J. J. Talley,* Tetrahedron Lett. *1978*, 3773; *M. Oda, A. Yamamuro, T. Watabe,* Chem. Lett. *1979*, 1427.

[6] *G. Schröder, J. F. M. Oth,* Angew. Chem. *79*, 458 (1967); Angew. Chem. Int. Ed. Engl. *6*, 414 (1967); summary of the literature: *H. Quast, B. Müller,* Chem. Ber. *113*, 2959 (1980).

[7] *K. Peters, H. G. von Schnering,* unpublished results.

[8] *R. Bishop, W. Parker, I. Watt,* Tetrahedron Lett. *1977*, 4345.

[9] *W. von E. Doering, B. M. Ferrier, E. T. Fossel, J. H. Hartenstein, M. Jones, Jr., G. Klumpp, R. M. Rubin, M. Saunders,* Tetrahedron *23*, 3943 (1967); *U. Biethan, W. Fauth, H. Musso,* Chem. Ber. *110*, 3636 (1977); *H. Tsuruta, K. Kurabayashi, T. Mukai,* Tetrahedron Lett. *1967*, 3775; *M. J. Goldstein, B. G. Odell,* J. Am. Chem. Soc. *89*, 6356 (1967).

[10] *L. M. Jackman,* unpublished results.

Table 1. Melting points, IR frequencies (KBr), and NMR data (in [D]chloroform, $\delta$ values, $J$ [Hz]) of the bicyclo[3.3.1]nona-2,6-diene-2,6-dicarbonitriles *(3)*—*(5)* and the 2,6-barbaralane dicarbonitriles *(6)* and *(7)*. The assignments of the $^{13}$C-NMR signals of *(4)* and *(5)* were supported by off-resonance decoupled spectra.

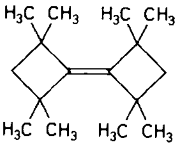
| | | | | | | $^1$H-NMR | | | | | | $^{13}$C-NMR | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cpd.<br>M.p. [°C] | IR [cm$^{-1}$]<br>—C$\equiv$N | <br>C=C | 1-H<br>5-H | 3-H<br>7-H | 4-H<br>8-H | 9-H | $J_{1,8}$<br>$J_{4,5}$ | $J_{1,9}$<br>$J_{5,9}$ | $J_{3,4}$<br>$J_{7,8}$ | C-1<br>C-5 | C-2<br>C-6 | C-3<br>C-7 | C-4<br>C-8 | C-9 | C—N |
| *(3)*<br>189—190 | 2212 | 1631 | 2.85 | 6.62 | 2.52 | 1.90 | | 3.2 | 3.7 | 28.7 | 115.9 | 142.4 | 30.7 | 26.3 | 118.3 |
| *(4)* [a]<br>154—155 | 2218 | 1630 | 0.84<br>2.52 | 5.93<br>5.70 | 4.22<br>1.86 | 1.49 | ?<br>1.9 | 3.6 | 5.1<br>3.8 | 28.8<br>37.0 | 113.3<br>116.4 | 144.0 [b]<br>140.2 [b] | 41.9<br>30.6 | 22.0 | 117.5<br>117.2 |
| *(5)*<br>216—217 | 2225 | 1623 | 3.08 | 6.65 | 4.60 | 2.34 | 1.7 | 3.2 | 5.2 | 37.1 | 113.7 | 141.5 | 40.9 | 17.8 | 116.6 |
| *(6)* [c]<br>93—94 | 2240<br>2215 | 1628<br>1610 | 2.95 | 6.14 | 4.50 | 1.32 | 7.3 | 2.6 | 8.2 | 28.3 | 66.9 | 126.9 | 78.8 | 15.5 | 119.3 |
| *(7)* [d]<br>163—164 | 2240<br>2215 | 1618<br>1606 | 1.46<br>3.24 | 6.12<br>6.66 | —<br>1.66 | 2.96 | 13.7<br>— | | | 23.1<br>40.9 | 30.7<br>112.0 | 119.9<br>135.8 | 116.1<br>25.1 | 17.9 | 116.9<br>119.5 |

[a] $^1$H-NMR. spectrum in [D$_6$]benzene; $J_{1,3}=J_{3,5}=0.8$ Hz; $J_{1,7}=J_{5,7}=0.7$ Hz; W-coupling: $^4J_{4,9}=1.3$ Hz. [b] The assignment may be exchanged. [c] Weak C=C bands at 1628 cm$^{-1}$ $^{13}$C-NMR spectrum in [D$_6$]benzene. [d] $J_{1,3}=?$, $J_{3,5}=1.4$ Hz.

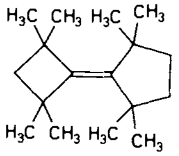
## Radical Cations of Sterically Hindered Bicycloalkylidenes: An Experimental Contribution Concerning the Planarity of the Ethylene Radical Cation[**]

By *Fabian Gerson, Javier Lopez, Adolf Krebs,*
and *Wolfgang Rüger*[*]

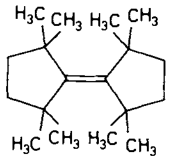
Experimentally derived information on the geometry of the ethylene radical cation is scarce[1]. Most semiempirical[2] and *ab initio* MO calculations[3] predict a planar arrangement of the atoms in this one-π-electron system, but the potential curve for the twisting of the $CH_2$-groups is expected to be extremely flat. Deviations from planarity should thus easily be brought about by bulky substituents. Investigations on the radical cations of 2,2,2′,2′,4,4,4′,4′-octamethylbicyclobutylidene *(1)*[4], 1,1,3,3-tetramethyl-2-(2,2,4,4-tetramethylcyclobutylidene)cyclopentane *(2)*[4] and 2,2,2′,2′,5,5,5′,5′-octamethylbicyclopentylidene *(3)*[5] ought to verify this statement.



*(1)*



*(2)*



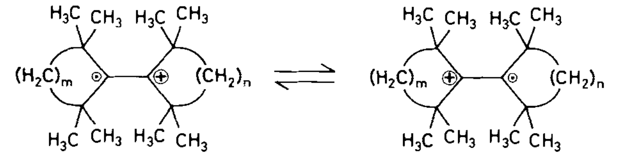
*(3)*

As shown by cyclic voltammetry[6], the first oxidation wave of the three compounds is reversible; in each case, one electron is released and taken up again. The relevant potential is substantially lower for *(3)* (+1.37 V *vs.* SCE) than for *(1)* (+1.81 V) and *(2)* (+1.65 V). Moreover, the dependence of the cyclic voltammograms on the scanning speed would point to the radical cation *(3)*$^{\cdot+}$ having a longer lifetime than *(1)*$^{\cdot+}$ and *(2)*$^{\cdot+}$.

The ease of formation of *(3)*$^{\cdot+}$ under a variety of conditions (reaction with $AlCl_3$ in $CH_2Cl_2$; electrolysis in $CH_2Cl_2$, $CH_2Cl_2/CF_3COOH/(CF_3CO)_2O$ or $CH_3CN$) and its remarkable stability (persistence) are consistent with these findings. Thus, the concentration of *(3)*$^{\cdot+}$ remains almost unchanged for weeks, when a solution of the radical cation is allowed to stand at room temperature with exclusion of air. Even upon the addition of water, the concentration decreases only gradually. In the temperature range 183—313 K, the ESR spectrum of *(3)*$^{\cdot+}$ exhibits the coupling constants $a(12\,H) = 0.203$ and $a(4\,H) = 0.028$ mT for the methyl and methylene protons, respectively, of *only one* cyclopentylidene moiety ($g = 2.0026$)[7].

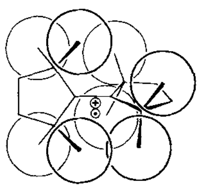
The radical cations *(1)*$^{\cdot+}$ and *(2)*$^{\cdot+}$ are less easily generated than *(3)*$^{\cdot+}$ and their persistence is substantially lower. Electrolytic oxidation of *(1)* and *(2)* in $CH_2Cl_2/CF_3COOH/(CF_3CO)_2O$ (volume ratio 10:1:1)[8] proved to be the best method of preparation of the corresponding radical cations. In the range 193—293 K, *(1)*$^{\cdot+}$ shows a hyperfine interaction with the methyl and methylene protons of *both* cyclobutylidene moieties: $a(24\,H) = 0.123$ and $a(4\,H) = 0.049$ mT, respectively ($g = 2.0027$). The ESR spectrum of *(2)*$^{\cdot+}$ recorded in the same solvent mixture ($g = 2.0026_5$) is strongly temperature dependent with strikingly varying line-widths of the individual hyperfine components. Computer simulations are consistent with the assumption that this behavior is due to electron exchange between the cyclobutylidene and cyclopentylidene moieties of *(2)*$^{\cdot+}$. An exact analysis is difficult, however, in the investigated temperature interval, whose lower (193 K) and upper (263 K) limits are determined by the freezing point of the solvent mixture and by the persistence of the radical cation, respectively. This is because neither the range of the "slow" nor that of the "fast" exchange is attained. The analysis is made all the more difficult by the fact that, in contrast to *(1)*$^{\cdot+}$ and *(3)*$^{\cdot+}$, the two cycloalkylidene moieties in *(2)*$^{\cdot+}$ are not equivalent.

From the ESR spectra of the three radical cations, it is possible to estimate the frequency of the electron exchange.



Whereas for *(2)*$^{\cdot+}$ ($m = 1$; $n = 2$) this frequency is evidently of the same order of magnitude as the hyperfine time-scale ($10^7$—$10^8$ $s^{-1}$), it must be substantially lower ($< 10^6$ $s^{-1}$) for *(3)*$^{\cdot+}$ ($m = n = 2$), and considerably higher ($> 10^9$ $s^{-1}$) for *(1)*$^{\cdot+}$ ($m = n = 1$).

The frequency of the electron exchange depends on the overlap between the $2p_z$ AO's at the two $sp^2$-hybridized carbon atoms and therefore on the extent of the coplanarity of the π-system. Hence, the experimental result implies that the energy required to approach coplanarity increases in the order *(1)*$^{\cdot+}$ < *(2)*$^{\cdot+}$ < *(3)*$^{\cdot+}$. This conclusion bears out the expectation that the planar arrangement is more difficult the larger the size of the cycloalkylidene moieties, because of the enhanced steric hindrance by the alkyl substituents. The same sequence should also hold for the trend of the moieties to twist about the central C—C bond. The high persistence of *(3)*$^{\cdot+}$ could then be rationalized by a nearly perpendicular arrangement of the five-membered rings, which offers an optimal protection of the radical and cationic centers by the methyl groups.



Finally, it should be mentioned that the structural parameters of the neutral molecules *(1)*, *(2)*, and *(3)* have not yet been determined. At present, merely results of calculations by the force-field method are available[9], according to which there should be no appreciable twist about the double bond, even in *(3)*. Presumably, the twist comes about only when the neutral two-π-electron system changes into the one-π-electron system of the radical cation.

Received: July 29, 1980 [Z 658 IE]
German version: Angew. Chem. 93, 106 (1981)

---

[*] Prof. Dr. F. Gerson [+] and Dipl.-Chem. J. Lopez
Physikalisch-Chemisches Institut der Universität Basel
Klingelbergstrasse 80, CH-4056 Basel (Switzerland)
Prof. Dr. A. Krebs and Dipl.-Chem. W. Rüger
Institut für Organische Chemie und Biochemie der Universität Hamburg
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Swiss National Foundation (Project 2.209.79) and the Deutsche Forschungsgemeinschaft. Financial assistance by the Fonds der Chemischen Industrie, Ciba-Geigy SA, Sandoz SA and F. Hoffmann-La Roche & Cie. SA is also gratefully acknowledged. We thank Mr. *A. Metzger* and Dr. *G. Plattner* for recording the cyclic voltammograms and for computer simulation of the temperature dependent ESR spectrum of *(2)*$^{\cdot+}$, respectively.

CAS Registry numbers:
*(1)*, 75993-80-5; *(1)* radical cation, 75993-81-6; *(2)*, 75993-82-7; *(2)* radical cation, 75993-83-8; *(3)*, 71691-01-5; *(3)* radical cation, 75993-84-9

---

[1] For the structurally related Rydberg-state of the neutral ethylene, a twist by 25 ± 1° of the $CH_2$-groups was derived from the electronic spectrum: *A. J. Merer, L. Schoonveld*, Can. J. Phys. *47*, 1731 (1969).

[2] See, *e.g.*, *W. A. Lathan, W. J. Hehre, J. A. Pople*, J. Am. Chem. Soc. *93*, 808 (1971).

[3] See, *e.g.*, *W. Rodwell, M. F. Guest, D. T. Clark, D. Shuttleworth*, Chem. Phys. Lett. *45*, 50 (1977).

[4] The compounds *(1)* and *(2)* were synthesized analogously to *(3)*; cf. [5].

[5] *A. Krebs, W. Rüger*, Tetrahedron Lett. *1979*, 1305.

[6] Working electrode: Pt; reference electrode: Ag/0.1 M $AgNO_3/CH_3CN$; Solvent: $CH_3CN$; supporting salt: $LiClO_4$.

[7] Limits of error: ±0.001 mT for *a* and ±0.0001 for *g*. ENDOR signals for $(3)^{\ddagger}$ in $CH_2Cl_2$ at 193 K: 10.96 s, 13.42 w, 14.19 w, and 16.64 s MHz; frequency of the free proton: 13.80 MHz.

[8] *H. Ohya-Nishiguchi*, Bull. Chem. Soc. Jpn. *52*, 2064 (1979).

[9] *U. Burkert*, Tetrahedron, in press; *D. Lenoir, H. Dauner, R. M. Frank*, Chem. Ber. *113*, 2636 (1980)

## NMR Spectroscopic Investigation of Intercalation Compounds of Organic Molecules and Sheet Silicates—*p*-Xylene-Hectorite and Related Systems[*]

By *Colin A. Fyfe, John M. Thomas*, and
*James R. Lyerla*[*]

Many categories of sheet silicates are known to be capable of taking up, within their interlamellar spaces, a wide range of organic compounds[1,2a]. The majority of these "organic" intercalates break down upon heat-treatment simply to yield the separate parent materials, but it has of late become increasingly apparent that several, highly selective chemical conversions[1a,2-4] can be carried out through the agency of such intercalates. In elucidating the nature of the microenvironment to which the organic molecule is exposed in the interlamellar region little use has so far been made of NMR spectroscopy, even though this technique has already proved illuminating in probing the properties of clay:water systems[5], and also in clarifying the nature of adsorbed organic molecules at exterior surfaces (of ZnO for example[6a]), of organic clathrates[6b] and of small organic molecules, such as methanol, in zeolites and silica gel[5a].

We here report how, using a commercially available pulsed FT-NMR spectrometer, it is possible to assess (i) the degree of molecular freedom, (ii) the composition of mixtures and (iii) the keto-enol equilibrium of certain organic species retained in the interlamellar spaces of a synthetic hectorite—idealized formula $Na_{0.67}Si_8(Mg_{5.33}Li_{0.67})O_{20}(OH)_4$.

Experimental methods for preparing a range of room-temperature stable intercalates of hectorites (and of montmorillonites) are given elsewhere[7]. X-Ray diffractometry and TGA readily reveal the degree of uptake and extent of *c*-axis expansion that accompanies the formation of these intercalates. High-resolution $^1H$- and $^{13}C$-NMR spectra were obtained using a conventional Varian CFT-20 spectrometer at 80 MHz and 20 MHz, respectively. Both proton and carbon spectra were obtained using a spinning sample. The proton spectral widths were such that no extra proton decoupling power in addition to the 3 kHz available from the basic spectrometer was necessary to obtain $^{13}C$ spectra at ambient temperature.

Typical spectra of powdered specimens of the organic intercalates at 30 °C are shown in Figures 1 and 2. Although the proton peaks are rather broad they are much narrower than would be obtained from solid *p*-xylene or solid γ-butyrolactone, indicating that these organic molecules have considerable freedom of motion in the interlamellar region. The

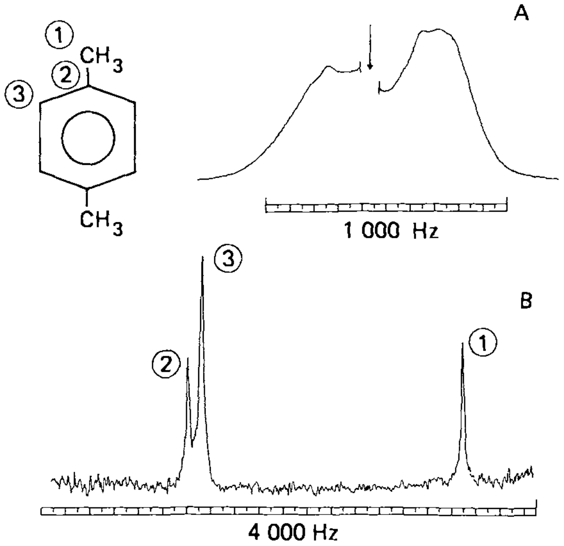


Fig. 1. A) $^1H$-NMR spectrum of the *p*-xylene-hectorite intercalate at 80 MHz (50 pulses). The vertical arrow indicates the position of a small, sharp peak arising from HOD impurity in the $D_2O$ lock reference which has been deleted for clarity (see also Fig. 2A). B) $^{13}C$-NMR spectrum of the same intercalate at 20 MHz (4000 pulses).

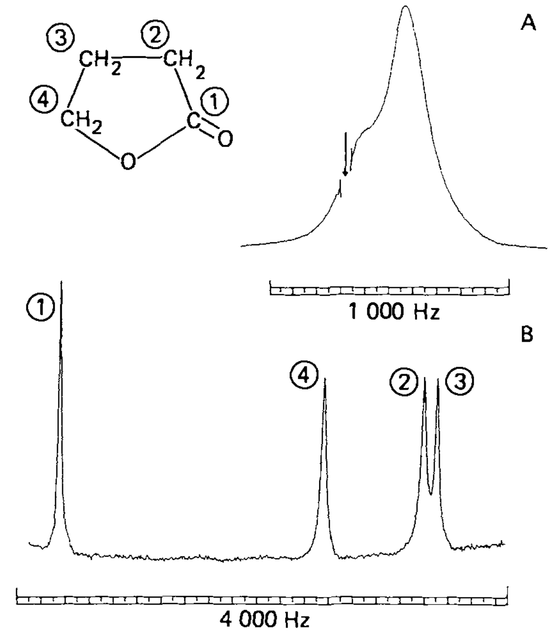


Fig. 2. A) $^1H$-NMR spectrum of the γ-butyrolactone intercalate of hectorite at 80 MHz (15 pulses). B) $^{13}C$-NMR spectrum of the same intercalate recorded at 20 MHz (16000 pulses).

---

[*] Prof. C. A. Fyfe
Guelph-Waterloo Centre for Graduate Work in Chemistry
University of Guelph
Guelph, Ontario N1G 2W1 (Canada)
Prof. J. M. Thomas
Dept. of Physical Chemistry, University of Cambridge
Lensfield Road, Cambridge CB2 1EP (England)
Dr. J. R. Lyerla
IBM Research Laboratories
Monterey & Cottle Roads, San Jose, California 95193 (USA)

[**] This work was initiated when two of us (*J. M. T.* and *C. A. F.*) were visiting scientists at IBM, San Jose. We are grateful to IBM and particularly to Dr. G. Castro for their hospitality and support, and also to the Science Research Council (U. K.) and the Natural Sciences and Engineering Research Council of Canada for their support.

two proton peaks for the xylene intercalate have relative intensities of 2:3 and the chemical shifts are very similar to the aromatic and methyl resonances in the high-resolution solution spectrum. The $^{13}C$-NMR spectrum shows separate sharp absorptions for each of the three different types of carbon in the molecule (linewidth *ca.* 25 Hz); and the relative chemical shifts [$\delta = 0.0$ ①, $-114.0$ ② and $-108.5$ ③] are identical to those of the pure liquid, again indicating that the molecules are motionally relatively free. The $^{13}C$-NMR spectrum of γ-butyrolactone (Fig. 2) shows four distinct peaks; and good quality, readily interpretable, NMR spectra are obtained from hectorite intercalates of several other organic molecules including tetrahydrofuran, ethylbenzene and 1,3-pentanedione.

The composition of ethylbenzene/*p*-xylene mixed intercalates could readily be deduced from the $^{13}C$-NMR spectra of the powdered solid. Moreover, the keto-enol equilibrium of 1,3-pentanedione in the interlamellar space is seen, by *in situ* NMR measurement, to be displaced in favor of the enol form.

It proved readily possible with these systems to measure, by standard methods, $^{13}C$ spin-lattice relaxation times. For the *p*-xylene intercalate the values are: (C1) 490, (C2) 430 and C3 480 ms, essentially indistinguishable from one another within the accuracy of the experiment. (Compare the corresponding values of 11.8, 13.5, and 44.7 s for the pure *p*-xylene as liquid.) These differences again point to the integration of the xylene guest into the sheet-silicate host. We have also shown, and shall describe more fully elsewhere, that magic-angle spinning, as expected[8], enhances the resolution of both the proton and the carbon spectra of these intercalates.

Received: June 25, 1980 [Z 664 IE]
German version: Angew. Chem. 93, 104 (1981)

---

[1] a) *A. Weiss* in *G. Eglington, M. T. J. Murphy:* Organic Geochemistry. Springer, Berlin 1969; b) *R. M. Barrer* in *L. Mandelcorn:* Non-Stoichiometric Compounds. Academic Press, New York 1964, p. 309; c) *B. K. G. Theng:* The Chemistry of Clay-Organic Reactions. Adam Hilger, London 1974. *J. M. Thomas* in: Intercalation Chemistry (ed. *A. J. Jackson* and *M. S. Whittingham*). Academic Press, New York 1981 (in press).

[2] a) *J. M. Thomas, J. M. Adams, S. H. Graham, D. T. B. Tennakoon,* Adv. Chem. Ser. *163*, 298 (1977); b) *D. T. B. Tennakoon, J. M. Thomas, M. J. Tricker, S. H. Graham,* J. Chem. Soc. Chem. Commun. *1974*, 124; c) *J. M. Adams, S. H. Graham, P. I. Reid, J. M. Thomas, ibid. 1977*, 67.

[3] *T. J. Pinnavaia, P. K. Weltz,* J. Am. Chem. Soc. 97, 3819 (1975).

[4] a) *J. M. Adams, J. A. Ballantine, S. H. Graham, R. J. Laub, J. H. Purnell, P. I. Reid, W. Y. M. Shaman, J. M. Thomas,* Angew. Chem. 90, 290 (1978); Angew. Chem. Int. Ed. Engl. *17*, 282 (1978); J. Catal. *58*, 238 (1979); c) *J. M. Thomas,* Pure Appl. Chem. *51*, 1065 (1979).

[5] a) *R. Fouillaux, P. Salvador, C. Vandermeersche, J. J. Fripiat,* Isr. J. Chem. *6*, 337 (1968); b) *A. M. Hecht, E. Geissler,* J. Colloid Interface Sci. *34*, 32 (1970); c) *J. J. Fripiat, ibid. 58*, 511 (1977).

[6] a) *A. G. Whitney, I. D. Gay,* J. Catal. *25*, 176 (1972); b) *J. P. McTague,* J. Chem. Phys. *50*, 47 (1969).

[7] a) *J. M. Adams, J. M. Thomas, M. J. Walters,* J. Chem. Soc. Dalton Trans. *1975*, 1459; b) *J. M. Adams, S. E. Davies, S. H. Graham, J. M. Thomas,* J. Chem. Soc. Chem. Commun. *1978*, 930; *1979*, 527.

[8] *J. R. Lyerla, C. A. Fyfe, C. S. Yannoni,* J. Am. Chem. Soc. *101*, 1351 (1979).

---

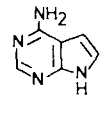
## Selective 7-Glycosylation of 4-Amino-7*H*-pyrrolo[2,3-*d*]pyrimidine to Ara-Tubercidin and Its α-Anomer

By *Frank Seela* and *Heinz-Dieter Winkeler*[*]

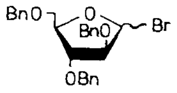
4-Amino-7-(β-D-arabinofuranosyl)pyrrolo[2,3-*d*]pyrimidine (ara-tubercidin) *(4b)*, like its aza analogue ara A[1], has antiviral properties; however, it is not deaminated by adenosine deaminase[2] and is therefore not deactivated.

Whereas ribonucleosides are only biologically accepted as β-anomers, the α-anomers of arabinonucleosides are also of interest since their 2′-hydroxy group is *trans* to the nucleobase and therefore several enzymes recognize α-D-arabinonucleosides like β-D-ribonucleosides[3].

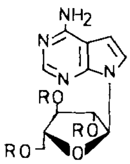
Ara-tubercidin *(4b)* can be obtained either semisynthetically from tubercidin[4] or by total synthesis *via* glycosylation of 4-chloro-2-methylthio-7*H*-pyrrolo[2,3-*d*]pyrimidine[2]. A selective 7-glycosylation of the aglycone *(1)* has hitherto not been described, since an exclusive activation of the pyrrole nitrogen avoiding the *N*-glycosylation of the pyrimidine nitrogens was not possible.



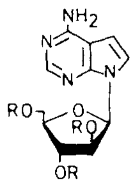
*(1)*



*(2)*



*(3a)*, R=Benzyl
*(3b)*, R=H



*(4a)*, R=Benzyl
*(4b)*, R=H

We were able to couple *(1)*[2,5] with the halogenose *(2)*[6] selectively at N-7 without protecting the 4-amino group under the conditions of phase-transfer catalysis[7]. A 1:1 mixture ($^{1}H$-NMR) of the anomers *(3a)* and *(4a)* is obtained in 57% yield, which, however, is difficult to separate on a preparative scale. Debenzylation of the mixture is accomplished by hydrogenation in the presence of palladium on charcoal and the reaction product is separated on an ionexchange column[8] yielding ara-tubercidin *(4b)*[2,4] and its α-anomer *(3b)*.

### *Procedure*

2,3,5-Tri-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-D-arabinofuranose[6] (2.55 g, 4.4 mmol) is converted into the yellowish, viscous halogenose according to the procedure given in Ref. [7b] *(2)*. A suspension of pulverized *(1)* (0.5 g, 3.7 mmol)[2,5] in dichloromethane (10 cm$^3$) and dimethoxyethane (5 cm$^3$) is stirred with benzyltriethylammonium chloride (0.15 g, 0.55 mmol) and 50% aqueous NaOH (15 cm$^3$) for 5 min in a vibromixer.—The halo sugar is added dropwise to the emulsion and mixing of the layers is continued for a further 30 min. The organic layer is separated off, extracted with water, dried over sodium sulfate, filtered, and evaporated. The oily residue is dissolved in a small amount of chloroform/methanol (99:1) and chromatographed in the same solvent on silica gel (Lobar pre-packed column, size C, Merck). The main zone is separated and the solvent removed; 1.12 g (57%) of a yellowish, viscous mixture of the anomers *(3a)* and *(4a)* (1:1) is obtained. TLC ($CHCl_3/CH_3OH$ 98:2): $R_f = 0.3$; UV ($CH_3OH$): $\lambda_{max} = 270$ nm ($\varepsilon = 11\,400$).

The mixture *(3a)*/*(4a)* (1.0 g, 1.9 mmol) dissolved in methanol (100 cm$^3$) is hydrogenated at room temperature under normal pressure with 10% palladium on charcoal as catalyst. After filtration of the catalyst and evaporation of the solvent a colorless, oily crude product is obtained which is applied on a 2.5 × 30 cm ion-exchange column (Dowex 1 × 2, $OH^-$

---

[*] Prof. Dr. F. Seela, Dipl.-Chem. H.-D. Winkeler
Universität Paderborn—Gesamthochschule
Fachbereich 13 (Organische Chemie)
Warburger Str. 100, D-4790 Paderborn (Germany)

form)[8]. Water elutes a byproduct, methanol/water (2:3) elutes compound *(3b)* (25%) followed by *(4b)* (34%)[9].

Received: February 13, 1980 [Z 665 IE]
German version: Angew. Chem. *93*, 105 (1981)

---

[1] *E. De Clercq, P. F. Torrence*, J. Carbohydr. Nucleosides Nucleotides *5*, 187 (1978).

[2] *H.-D. Winkeler, F. Seela*, Chem. Ber. *113*, 2069 (1980).

[3] *L. L. Bennet, Jr., W. M. Shannon, P. W. Allan, G. Arnett*, Ann. N. Y. Acad. Sci. *255*, 342 (1975).

[4] *M. J. Robins, Y. Fouron, W. H. Muhs*, Can. J. Chem. *55*, 1260 (1977).

[5] *J. Davoll*, J. Chem. Soc. *1960*, 131.

[6] *R. Barker, H. J. Fletcher, Jr.*, J. Org. Chem. *26*, 4605 (1961).

[7] a) *E. V. Dehmlow*, Angew. Chem. *86*, 187 (1974); *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *13*, 170 (1974); *16*, 493 (1977); b) *F. Seela, D. Winkeler*, *ibid. 91*, 570 (1979) and *18*, 536 (1979).

[8] *C. A. Dekker*, J. Am. Chem. Soc. *87*, 4027 (1965).

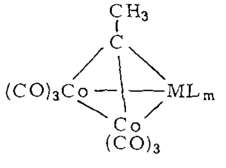
[9] *(3b)*: m.p. 233—235 °C; TLC (silica gel, $CHCl_3/CH_3OH$ 8:2): $R_f = 0.42$; UV ($CH_3OH$): $\lambda_{max} = 271$ nm ($\varepsilon = 11600$); $^1H$-NMR ([D$_6$]DMSO): $\delta = 3.67$ (m, 5'-H), 4.2—5.2 (m, 2',3',4'-H, 3 × HO), 6.07 (d, 1'-H, $J = 5$ Hz), 6.68 (d, 5-H, $J = 3$ Hz), 7.23 (s, $NH_2$), 7.45 (d, 6-H, $J = 3$ Hz), 8.17 (s, 2-H); *(4b)*: m.p. (hydrate) 115—117 °C; TLC (silica gel, $CHCl_3/CH_3OH$ 8:2): $R_f = 0.35$.

## Direct Metal Exchange in Carbonylcobalt Clusters[**]

By *Harald Beurich* and *Heinrich Vahrenkamp*[*]

Experience so far indicates that it should be extremely difficult to devise a directed synthesis of a tetrahedral framework structure consisting of heteroatoms, since each corner of the tetrahedron must be bonded to the remaining three corner units. It is therefore all the more astonishing that tetrahedral heteroatom clusters can be fromed indirectly in one-step[1] or in multi-step addition and substitution reactions by the systematic addition and incorporation of organometallic units[2,3]. We now wish to report that these types of organometallic expansion reactions can be performed by a still simpler direct metal exchange process. In this connection, carbonyl cobalt clusters were reacted with simple binuclear carbonyl (cyclopentadienyl) metallic compounds *(1)* which are present in equilibrium with their mononuclear radical moieties[4]. The latter species are able to attack the clusters and substitute the $Co(CO)_3$-units by organometallic groups. The binuclear complexes *(1)* and $CH_3CCo_3(CO)_9$ react to produce the hetero clusters *(2)*, of which we had already obtained *(2a)* and *(2b)* by the Co—As-elimination method. The reactions are accelarated by thermal and photochemical stimuli and proceed in low yield in the case of *(1c)* and in high yield with an excess of *(1d)*.

$L_nM{-}ML_n$

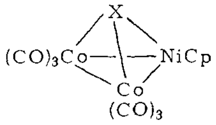


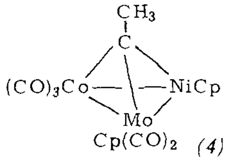
*(1a)*, $ML_n$ = $MoCp(CO)_3$
*(1b)*, $ML_n$ = $WCp(CO)_3$
*(1c)*, $ML_n$ = $FeCp(CO)_2$
*(1d)*, $ML_n$ = NiCpCO

*(2a)*, $ML_m$ = $MoCp(CO)_2$
*(2b)*, $ML_m$ = $WCp(CO)_2$
*(2c)*, $ML_m$ = FeCpCO
*(2d)*, $ML_m$ = NiCp

When *(1d)* was reacted with other cobalt clusters, similar products were obtained *e.g.* with $XCo_3(CO)_9$ (X = CF, $CC_6H_5$) the clusters *(3a)* and *(3b)* were formed, and the $NiCo_3$-cluster *(3c)* was formed from $Co_4(CO)_{12}$ and *(1d)* in at least twice the yield (50—90%) of the previously described process[5]. Table 1 gives the most important spectroscopic data of the new compounds.

*(3a)*, X = CF
*(3b)*, X = $CC_6H_5$
*(3c)*, X = $Co(CO)_3$





*(4)*

Table 1. Important spectroscopic data of the new hetero-cluster compounds. $^1H$-NMR in $C_6D_6$, TMS int. std., δ-values. IR in cyclohexane, ν(Co) [cm$^{-1}$].

| Cmpd. | $^1H$-NMR | IR |
|---|---|---|
| *(2c)* | 3.98, 3.76 | 2073 s, 2030 vs, 2020 vs, 1996 m, 1988 w, 1920 m |
| *(2d)* | 4.76, 3.43 | 2078 m, 2038 vs, 2020 vs, 2009 m, 1994 w |
| *(3a)* | 4.79 | 2085 s, 2048 vs, 2030 vs, 2021 m, 2011 w |
| *(3b)* | 4.78 | 2078 s, 2040 vs, 2020 vs, 2012 m, 1998 w |
| *(4)* | 4.84, 4.68, 3.70 | 2053 m, 2034 s, 2005 m, 1990 vs, 1976 s, 1968 st, 1947 vw, 1934 m, 1916 w, 1898 vw, 1870 vw |

The chiral trimetal cluster *(4)* was obtained from $CH_3CCo(CO)_9$ by a stepwise double metal exchange which proceeds *via (2a)* or *(2d)*. Compound *(4)* spontaneously forms optically active crystals, a structural analysis of which was carried out (Fig. 1)[6]; we have endeavored to obtain larger single crystals of *(4)* so that a separation of them into their enantiomers by manual selection can be carried out. Furthermore, since the cluster compound *(4)* can readily be prepared, it would be a suitable species with which to examine the process of optical induction in cluster catalysis reactions. This species should also provide definite proof that cluster compounds, viewed as a structural whole, can be catalytically active[7].

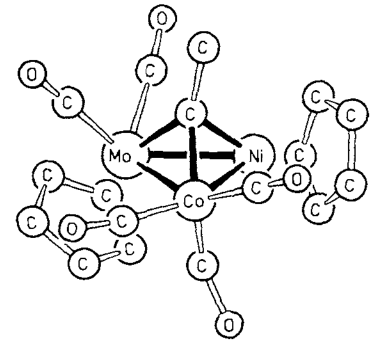


Fig. 1. Structure of *(4)*. The most important bond lengths are as follows; Co—Mo 265.1 (4), Mo—Ni 255.7 (3), Ni—Co 233.6 (4), Co—C 187 (2), Mo—C 208 (2), Ni—C 188 (2) pm [6].

### *Experimental*

A solution of *(2a)* (100 mg, 0.21 mmol) and *(1d)* (190 mg, 0.63 mmol) in 15 cm$^3$ benzene was stirred for 5 d at 60 °C. Chromatography on a silica gel column (3 × 30 cm) using a hexane/benzene eluent (9:1) produced firstly *(2a)* (green), secondly *(1d)* (red), and *(4)* (brown) as the third fraction. Recrystallization from hexane gave 20 mg (19%) of *(4)* as dark brown crystals (19%) (m.p. = 152 °C).

Received: May 30, 1980 [Z 680 IE]
German version: Angew. Chem. *93*, 128 (1981)

---

[*] Prof. Dr. H. Vahrenkamp, Dipl.-Chem. H. Beurich
Chemisches Laboratorium der Universität
Albertstrasse 31, D-7800 Freiburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and by the Rechenzentrum der Universität Freiburg. We thank Dr. *P. Merbach*, Erlangen, for the mass spectra.

*0570-0833/81/0101-0098 $ 02.50/0*

CAS Registry numbers:
*(1c)*, 12154-95-9; *(1d)*, 12193-98-5; *(2a)*, 68185-42-2; *(2c)*, 76206-95-6; *(2d)*, 76206-96-7; *(3a)*, 76206-97-8; *(3b)*, 76206-98-9; *(4)*, 76206-99-0; $CH_3CCo_3(CO)_9$, 13682-04-7; $CC_6H_5Co_3(CO)_9$, 13682-03-6; $CFCo_3(CO)_9$, 18433-91-5

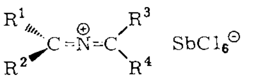
---

[1] *S. A. Khattab, L. Markó, G. Bor, B. Markó*, J. Organomet. Chem. *1*, 373 (1964).
[2] *P. C. Steinhardt, W. L. Gladfelter, D. Harley, J. R. Fox, G. L. Geoffroy*, Inorg. Chem. *19*, 332 (1980).
[3] *H. Beurich, H. Vahrenkamp*, Angew. Chem. *90*, 915 (1978); Angew. Chem. Int. Ed. Engl. *17*, 863 (1978).
[4] *Th. Madach, H. Vahrenkamp*, Chem. Ber. *113*, 2675 (1980), and references cited therein.
[5] *A. T. T. Hsieh, J. Knight*, J. Organomet. Chem. *26*, 125 (1971).
[6] Orthorhombic, $P2_12_12_1$, $Z=4$, $a=1194.8(4)$, $b=1705.2(2)$, $c=908.9(4)$ pm; 1343 Reflections, $R=0.065$.
[7] *A. Agapiou, S. E. Pedersen, L. A. Zyzyck, J. R. Norton*, J. Chem. Soc. Chem. Commun. *1977*, 393.

## Phenyl-Substituted Dimethyleneammonium Salts: 2-Aza-allenium Derivatives[**]

By *Ernst-Ulrich Würthwein*[*]

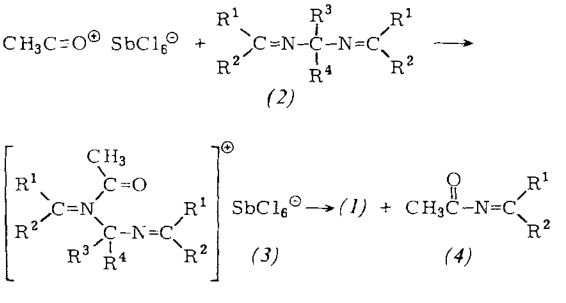
Dimethyleneammonium salts *(1)* have been postulated as intermediates[1a,b] and were observed in mass spectrometric fragmentations[1c], but little is known about their synthesis and reactivity[2]. These linear 2-aza-allenium salts, which have the topology and electronic structure of cumulenes, are of considerable theoretical interest. They are novel examples for the influence of positively charged, sp-hybridized nitrogen on charge distribution and structural preference. For organic synthesis the salts *(1)* can be used as highly reactive C—N—C synthons ("double" methyleneammonium or iminium salts), *e.g.* as electrophiles, dienophiles and as stable precursors for nitrile ylides[1b].



*(1a)*, $R^1, R^2, R^3, R^4$ = Ph
*(1b)*, $R^1, R^2, R^3$ = Ph; $R^4$ = H
*(1c)*, $R^1, R^3$ = Ph; $R^2, R^4$ = H

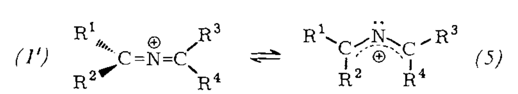
We report here a simple method for the synthesis of substituted dimethyleneammonium salts *(1)* which is applicable not only to the known tetraphenyl derivative *(1a)*[2a], but also to the tri- and diphenyl derivatives *(1b)*, *(1c)* and others. *(1c)* is the first chiral representative of this class of compounds.

Starting materials are the easily accessible *N,N'*-bisalkylidenediaminomethanes *(2)* ("iminals")[3], of which "hydrobenzamide" *(2c)*[3b] is the best known. Acylium salts, powerful acylation reagents[4], attack *(2)* at nitrogen and lead directly to *(1)*. The *N*-acyliminium salts *(3)* could not be detected as intermediates. *(1a)* and *(1c)* are isolated as crystalline solids when the reaction is performed in $CHCl_3$ or $CHCl_3/CCl_4$ (1:1), respectively, whereas *(1b)* is obtained as an oil, which does not crystallize easily from $CHCl_3/CCl_4$ (cf. *Procedure*).



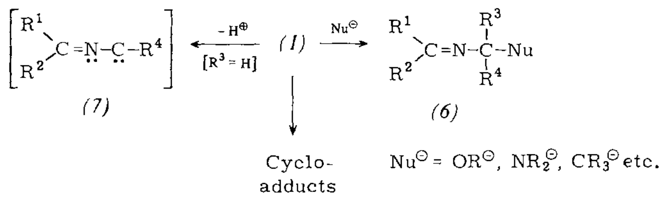
Apart from *(1)*, the cleavage of *(3)* yields the *N*-alkylideneacetamides *(4)*, which are of theoretical and synthetic interest as reactive dienes[5a] and 1,4-dipoles[5b]. The driving force which facilitates the formation of the highly reactive dimethyleneammonium salts *(1)* is the strong acyl-imine bonding in *(4)*[6].

The linear allene-like structure of *(1)* is especially evident from the very intense cumulene-stretching bands in the IR-spectrum, [$\nu=1870$ *(1a)*, 1890 *(1b)*, and 1910 $cm^{-1}$ *(1c)*] whose frequencies are similar to the corresponding absorptions in the allene spectrum. The planar, bent 2-azaallyl cation structure, *(5)*, can therefore be ruled out as a valence isomer of the cation *(1')* for *(1a)*, *(1b)* and *(1c)*. Compounds with amino-substituents in the 1- and 3-positions prefer the allyl form *(5)*, however, because of the formation of the electronically favorable amidinium fragments[7,8].



The ¹H-NMR signals for the cumulene protons in *(1b)* and *(1c)* occurs, as expected for methyleneammonium salts, at low field: $\delta=9.8$ *(1b)* and 9.4 *(1c)*. The $^{13}C$-NMR spectrum of *(1c)* ($CD_3NO_2$, 70 °C) exhibits a triplet at $\delta=145.3$ for C-1 and C-3 with an unusually large $^{13}C$-$^{14}N$ coupling constant ($^1J_{^{13}C\text{-}^{14}N}=16.3$ Hz); comparable methyleneammonium salts absorb at $\delta\approx170$ ppm, and the corresponding allenes at $\delta=80$—100.

Dimethyleneammonium salts *(1)* are valuable C—N—C synthons in organic synthesis; they react rapidly and under mild conditions with nucleophiles to give substituted *N*-methylimine derivatives *(6)*, which in turn can be subjected to a second, specific, nucleophilic attack at the imine group. The salts *(1)* can be used as ene-partner in cycloadditions; deprotonation of the derivatives *(1b)* and *(1c)* with strong, non-nucleophilic bases leads to the nitrile ylides *(7)*[9], which cannot be isolated, but give trapping products typical for this type of 1,3-dipole.



### *Experimental*

All operations were performed under a nitrogen atmosphere.

*(1c)*: A solution of *(2c)*[3b] (1.5 g, 5.0 mmol) in 20 $cm^3$ dry chloroform is treated with 0.4 g (5.0 mmol) acetyl chloride at room temperature with stirring. The reaction mixture is cooled to 0 °C and a solution of 1.5 g (5.0 mmol) antimony pentachloride in 20 ml $CHCl_3$ is added dropwise. When the addition is nearly complete a colorless precipitate forms. This solid is filtered off under nitrogen after 3 h stirring in the dark and is washed twice with 10 ml portions of $CHCl_3$. 2.0 g (76%) of the white, microcrystalline, extremely mois-

---

[*] Dr. E.-U. Würthwein
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie. I thank Prof. Dr. *P. von R. Schleyer* for discussions and *R. Kupfer*, *R. Neufert* and *R. Bauer* for valuable experimental assistance.

ture-sensitive salt *(1c)* is obtained after vacuum drying; m.p. 201-202 °C (decomposition above *ca.* 190 °C).

Received: May 20, 1980 [Z 661 IE]
Supplemented: December 19, 1980
German version: Angew. Chem. *93*, 110 (1981)

CAS Registry numbers:
*(1a)*, 20055-29-2; *(1b)*, 76058-05-4; *(1c)*, 76058-07-6

---

[1] a) *P. G. Gassman, I. Nishiguchi, H.-A. Yamamoto*, J. Am. Chem. Soc. *97*, 1600 (1975), and ref. therein; b) *K. Bunge, R. Huisgen, R. Raab*, Chem. Ber. *105*, 1296 (1972); c) *H. Schwarz, C. Köppel* in *S. Patai:* The Chemistry of Ketenes, Allenes and Related Compounds. Wiley, New York 1980, 189.

[2] a) *B. Samuel, K. Wade*, J. Chem. Soc. *A 1969*, 1742; b) *A. Schmidt*, Chem. Ber. *105*, 3050 (1972); c) *M. T. Reetz, W. F. Maier*, unpublished results; *W. F. Maier*, Diplomarbeit, Universität Marburg 1975; d) *D. H. R. Barton, R. D. Bracho, A. A. L. Gunatilaka, D. A. Widdowson*, J. Chem. Soc. Perkin I *1975*, 579.

[3] a) *H. Böhme, A. Ingendoh*, Justus Liebigs Ann. Chem. *1978*, 1928; b) *O. Baier* in *Houben-Weyl:* Methoden der Organischen Chemie, Vol. VII/1, Thieme, Stuttgart 1954, 407.

[4] Cleavages of ethers and aminals are analogous: a) *H. Meerwein, H. Maier-Hüser*, J. Prakt. Chem. *134*, 51 (1932); b) *H. Böhme, K. Hartke*, Chem. Ber. *93*, 1305 (1960); *H. Böhme, A. Sickmüller, ibid. 110*, 208 (1977) and references cited therein.

[5] a) *R. R. Schmidt*, Synthesis *1972*, 333; b) *R. Huisgen* in *R. N. Castle:* Topics in Heterocyclic Chemistry. Wiley, New York 1969, 223.

[6] *E.-U. Würthwein*, unpublished experiments and calculations.

[7] *Z. Janousek, H. G. Viehe* in *H. Böhme, H. G. Viehe:* Iminium Salts in Organic Chemistry, Wiley, New York 1976, Vol. I, 400; *H. Gold*, Angew. Chem. *72*, 956 (1960); *R. Gompper, C. S. Schneider*, Synthesis *1979*, 215.

[8] MNDO calculations indicate that, for the equilibrium *(1')*$\rightleftarrows$*(5)* the valence isomer *(5)* should be the more stable for the 1,1- and 1,3 diamino derivatives, but that *(1')* is preferred for the monoamino, phenyl and chloro derivatives; *E.-U. Würthwein*, unpublished results.

[9] *R. Huisgen, H. Stangl, H. J. Sturm, R. Raab, K. Bunge*, Chem. Ber. *105*, 1258 (1972) and the following publications.

---

## Crystal Structure of $P_4O_7$[**]

By *Martin Jansen* and *Marlen Voss*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

$P_4O_6$ opens up several preparatively interesting possibilities, which, however, have hitherto remained largely unexploited. The reason for this appears to be coupled with the problematical isolation of pure $P_4O_6$[1] and the complexity of the $P_4O_6/P_4O_{10}$ system[2].

We report here on the reaction of $P_4O_6$ with alkali metal oxides $A_2O$ ($A = K$, Rb, Cs), which proves to be unexpectedly difficult: whereas no reaction occurs at low temperature (20—50 °C), increasing decomposition of $P_4O_6$ is observed with increasing temperature above 50 °C. In the temperature range 120—180 °C violent and uncontrolled reactions take place. On sublimation of the heterogeneous solid reaction products pure $P_4O_7$ separates in the form of translucent, strongly refracting crystals in the warm zone 120—130 °C of the temperature gradient (170→25 °C).

Owing to its extreme sensitivity towards moisture and oxidation the compound was prepared under argon for the X-ray crystallographic and vibration spectroscopic investigations. The structure determination[3] shows that $P_4O_7$ molecular units are present (cf. Fig. 1)[4]. The anisotropy of the temperature factors can be ascribed to librational motion of the rigid $P_4O_7$ groups (almost about the baricenter); the intramolecular distances quoted take into account this effect[5].

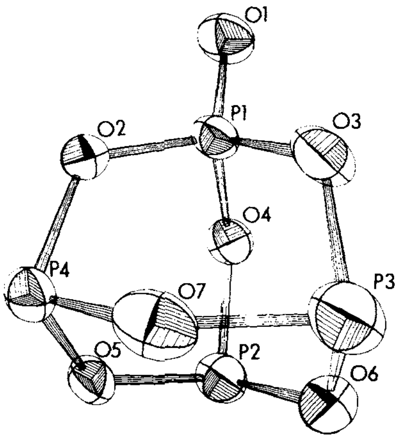


Fig. 1. Perspective representation of a $P_4O_7$ molecule. Bond lengths [pm] and angles [°] in $P_4O_7$ (maximum standard deviations: 0.7 pm and 0.3°, respectively): P1—O1 (O2; O3; O4) = 145.0 (159.7; 158.9; 159.5); P2—O4 (O5; O6) = 168.2 (164.2; 164.7); P3—O3 (O6; O7) = 168.9 (166.2; 164.4); P4—O2 (O5; O7) = 168.2 (164.2; 163.7); O1—P1—O2 (O3; O4) = 114.5 (115.3; 115.0); O3—P1—O2 (O4) = 103.8 (103.4); O2—P1—O4 = 103.2; O4—P2—O5 (O6) = 99.1 (97.9); O5—P2—O6 = 99.5; O3—P3—O6 (O7) = 97.1 (98.6); O6—P3—O7 = 100.3; O2—P4—O5 (O7) = 98.9 (98.1); O5—P4—O7 = 100.2; intermolecular: O3—O5 = 300.5; P2—O2 = 319.7.

Despite the low positional symmetry 1 in the crystalline state $P_4O_7$ has, within the limits of error of the structure determination, the $C_{3v}$ symmetry to be expected for the free molecule. One can clearly distinguish between pentavalent (P1) and trivalent (P2, P3, P4) phosphorus by virtue of the atomic environment (coordination number, P—O distances). However, the concept based on models that such molecules are made up of $P_4O_{10}$ and $P_4O_6$ moieties with retention of the P—O bond lengths is reconcilable only to a limited extent with the structural data found here. Thus, for example, the distance from P1 to the terminal O1 (145.0 pm) in $P_4O_7$ is significantly longer than the corresponding distances in $P_4O_{10}$ (139.0—142.9 pm)[6]. This observation points to a certain reduction in the "pentavalent character" of P1, which could be caused by a shift of electrons from the trivalent P2, P3 and P4 atoms linked by oxygen bridges. The marked difference in lengths of P—O bonds from P2, P3 and P4 undoubtedly follows from the stronger interaction of O2, O3 and O4 with P1. The shortest intermolecular contacts exist between bridging oxygen atoms and correspond exactly to the sum of the respective van der Waals radii.

Indications of a deviation from the ideal composition, as have been described in the case of $P_4O_{\approx 8}$[2b], have not been observed in the case of $P_4O_7$.

Received: September 4, 1980 [Z 679 IE]
German version: Angew. Chem. *93*, 120 (1981)

CAS Registry number:
$P_4O_7$, 55230-51-8

---

[*] Priv.-Doz. Dr. M. Jansen, Dipl.-Chem. M. Voss
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and Hoechst AG (sample of $P_4O_6$).

[1] *D. Heinz*, Z. Anorg. Allg. Chem. *347*, 167 (1966).

[2] a) *D. Heinz, H. Rienitz, D. Radeck*, Z. Anorg. Allg. Chem. *383*, 120 (1971); *B. Beagley, D. W. J. Cruickshank, T. G. Hewitt, K. H. Jost*, Trans. Faraday Soc. *65*, 1219 (1969); b) *K. H. Jost*, Acta Crystallogr. *21*, 34 (1966); *17*, 1593 (1964).

[3] A complete set of photographs indicate the space group $P2_1/n$; $a = 981.7$, $b = 995.4$, $c = 685.8$ pm, $\beta = 96.8°$; $Z = 4$; 1772 observed intensities (four-circle diffractometer PW 1100, $Mo_{K\alpha}$); $R = 0.056$.

[4] Raman spectrum of $P_4O_7$ [cm$^{-1}$ (rel. int.)]: 270 (1.5); 310 (2.0); 335 (0.2); 398 (2.1); 433 (2.0); 535 (1.9); 614 (0.8); 630 (10); 660 (1.5); 685 (0.2); 715 (0.4); 1333 (1.3); 1345 (0.5).

[5] *V. Schomaker, K. N. Trueblood*, Acta Crystallogr. *B 24*, 63 (1968).

*0570-0833/81/0101-0100 $ 02.50/0*

[6] *D. W. J. Cruickshank*, Acta Crystallogr. *17*, 677, 679 (1964); *B. Beagley, D. W. J. Cruickshank, T. G. Hewitt, A. Haaland*, Trans. Faraday Soc. *63*, 836 (1967). The possibility of a comparison is impaired by the fact that in the case of the dimensions of $P_4O_{10}$ determined by electron diffraction the influence of intermolecular interactions is practically missing and that the structure determinations on solid $P_4O_{10}$ are relatively inaccurate and have furnished controversial results.

## Electrochemical Processes in Supercritical Phases[**]

By *Giuseppe Silvestri, Salvatore Gambino, Giuseppe Filardo, Carmelo Cuccia'*, and *Enrico Guarino'*[*]

*Dedicated to the memory of Professor Raffaele Ercoli*

Substances in the supercritical state, *i. e.* at temperatures and pressures above their critical point, exhibit unusual solvent properties towards many organic and inorganic compounds[1]. The conductivity of supercritical steam containing various dissolved salts has been the object of considerable attention both for basic studies on the thermodynamic properties of such systems, and for the investigation of the corrosion processes taking place in power plants[2]. To our knowledge, nothing has been done to examine substances other than water as media for electrochemical processes in the supercritical state, although the combination of the solvent properties and fluid dynamic characteristics of such systems make them an interesting area to explore. In this communication we report our preliminary results concerning the use of carbon dioxide, bromotrifluoromethane, hydrogen chloride, and ammonia as supercritical solvents for electrochemical processes. Precise conductivity measurements were not the intention of this research, which was rather an initial evaluation of the synthetic possibilities opened by these systems[3].

Among the substances tested, a correlation between the conductivity of the liquid phase and that under supercritical conditions was observed *e. g.* a solution of tetrabutylammonium iodide in $CO_2$ was a poor conductor in the liquid, as well as in the supercritical state. Bromotrifluoromethane, in which electrolytes are practically insoluble, also proved to be a very poor conductor. $CO_2$ and $CF_3Br$ are consequently unsuitable as solvents for preparative electrolyses in the supercritical state, and were therefore not considered further.

Ammonia and hydrogen chloride, have high dielectric constants and also appreciable solvent properties even in supercritical conditions (see Table 1). In a series of preliminary experiments in sealed glass capillary tubes[3], it was observed that at 50 °C NaCl was relatively insoluble in $NH_3$ and that the meniscus disappeared at 129 °C; preparative scale electrolyses on this system with similar electrolyte concentration, were therefore performed at temperatures above 129 °C. The variation of the conductivity of the cell with temperature, for the system: Ag/$NH_3$, NaCl/Ag, is plotted in Fig. 1.

Table 1. Conductivity of electrochemical systems in supercritical condition [a].

| Solvent | *p* [bar] | | *T* [°C] | | *I* [mA] | *U* [V] |
|---|---|---|---|---|---|---|
| | exp. | crit. | exp. | crit. | | |
| $CO_2$ | 177 | 73.8 | 83 | 31 | 1.37 | 300 |
| $CF_3Br$ | 97.5 | 50.8 | 85 | 67 | 0.2 | 80 |
| HCl | 103.4 | 83.0 | 80 | 51.4 | 4.1 | 57 |
| $NH_3$ [b] | 171 | 113.8 | 155 | 132.5 | 25 | 47 |

[a] Conducting salt: $nBu_4NI$. [b] Conducting salt: NaCl.

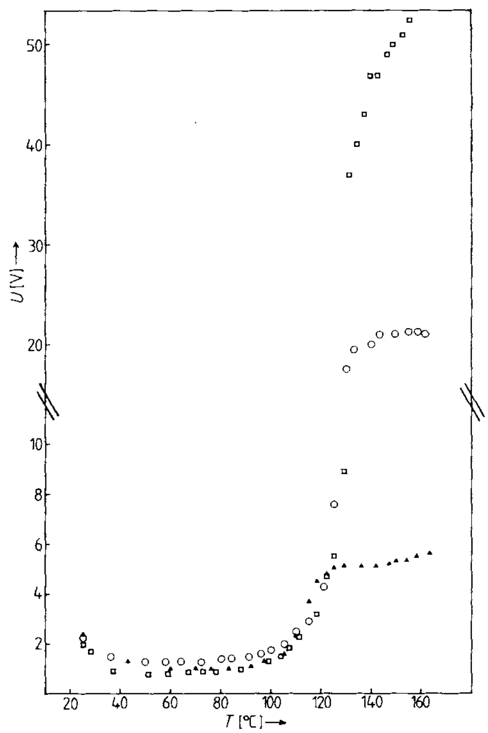


Fig. 1. The voltage of the $NH_3$/NaCl system at a constant current (5 mA) as a function of temperature. Measurements were carried out in a cylindrical stainless steel autoclave (206 $cm^3$). Silver foil (surface area of inner and outer cylinders 8.478 and 20.41 $cm^2$ resp.; electrode separation 0.8 cm) served as the electrodes which were held in Teflon frames and insulated from the autoclave jacket.

▲: 77.48 g/$NH_3$, 154 mg NaCl, $\rho$ = 387 g/$dm^3$

○: 64.5 g/$NH_3$, 154 mg NaCl, $\rho$ = 313 g/$dm^3$

□: 57.63 g/$NH_3$, 154 mg NaCl, $\rho$ = 280 g/$dm^3$

It was determinant, for the conductivity of the medium, that the supercritical system should have a high density (280—390 g/$dm^3$) ($\rho$ at the critical point 235 g/$dm^3$).

The curves show that the dependence of the conductivity with temperature beyond the critical point is approximately inversely proportional to the specific weight of the supercritical phase. Electrolyses were also performed over long periods of time, in which up to 4000 Coulombs were passed through the cell; it was observed that the conductivity of the system remains substantially unchanged during electrolysis. The data on electrolyses involving the above mentioned system, as well as the Fe/NaCl, $NH_3$/Fe system, are summarized in Table 2.

Table. 2. Preparative scale electrolyses in supercritical ammonia (Q = quantity of charge transported).

| Anode | *p* [bar] | *T* [°C] | $\rho$ [g/$dm^3$] | *Q* [C] | Anodic current efficiency [%] |
|---|---|---|---|---|---|
| Ag | 207 | 141 | 336.7 | 78.5 | 95 |
| Ag | 171 | 155 | 359.2 | 1177 | 82 |
| Fe | 161 | 146 | 368 | 4093 | 45 |

The anodic dissolution of silver takes place with very good current yields. Reduction of the silver ions at the cathode resulted in a deposit of fine silver powder on all the internal surfaces of the cell. In the case of iron, the anodic process of dissolution of the metal accounts for only 45% of the charge

---

[*] Prof. Dr. G. Silvestri, Dr. S. Gambino, Dr. G. Filardo, C. Cuccia, E. Guarino
Instituto di Ingegneria Chimica, Viale delle Sienze, Palermo (Italy)

[**] The content of this publication is part of a dissertation by C. C. and E. G.

passed, assuming that Fe(III) is produced at the anode. Hydrogen was also produced, in a quantity corresponding to 48% of the charge passed. The formation of hydrogen can be explained by assuming that, in addition to the oxidation of iron, the anodic reaction involves the well known oxidation of ammonia to nitrogen and ammonium ions: ($4NH_3 \rightarrow 1/2N_2 + 3NH_4^{\oplus} + 3e$), and the ammonium ions so formed are reduced at the cathode, producing molecular hydrogen. Electrochemical reactions in liquid ammonia behave in a similar way[4].

The use of hydrogen chloride as electrolytic medium is also of interest, but experiments with this solvent were difficult due to its high corrosive action. The experimental data obtained up to now confirm that hydrogen chloride containing dissolved potassium iodide gives rise to an increase in the cell resistance similar to that observed for the systems with ammonia. Electrolysis of the supercritical HCl/KI system produced elementary iodine at the anode.

The transition of a system from the liquid to the supercritical state results, as seen in these experiments, in an increase in resistance by one to two orders of magnitude (also Fig. 2). Looking at the possible use of these systems for synthetic purposes, the results obtained so far show that it is possible to obtain good conductivities when cells having a narrow gap between the electrodes are used with supercritical phases of high density.

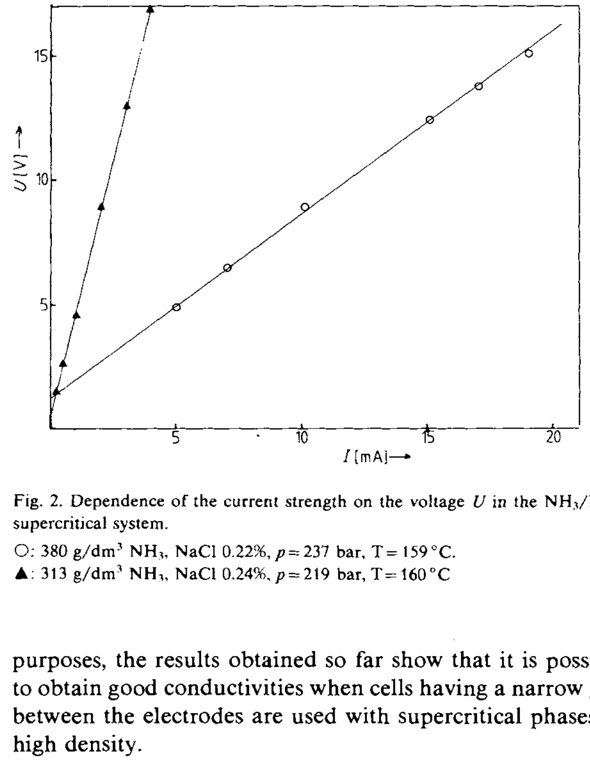


Fig. 2. Dependence of the current strength on the voltage $U$ in the $NH_3$/NaCl supercritical system.

○: 380 g/dm³ $NH_3$, NaCl 0.22%, $p$ = 237 bar, T = 159 °C.

▲: 313 g/dm³ $NH_3$, NaCl 0.24%, $p$ = 219 bar, T = 160 °C

Received: October 8, 1980 [Z 663 IE]
German version: Angew. Chem. 93, 131 (1981)

CAS Registry numbers:
$CO_2$, 124-38-9; $CF_3Br$, 75-63-8; HCl, 7647-01-0; $NH_3$, 7664-41-7; $n$-$Bu_4NI$, 311-28-4; NaCl, 7647-14-5; Ag, 7440-22-4; Fe, 7439-89-6

---

[1] *K. Zosel*, Angew. Chem. *90*, 748 (1978); Angew. Chem. Int. Ed. Engl. *17*, 702 (1978).

[2] High Temperature High Pressure Electrochemistry in Aqueous Solutions, International Corrosion Conference Series—NACE—*4* (1976).

[3] Preliminary experiments were carried out in small pyrex reaction vessels (inner and outer diameters; 1—2 and 8—14 mm respectively) to determine whether at the reaction temperature of the preparative electrolysis the supercritical state had been reached; see also *C. P. Hicks, C. L. Young*, Chem. Rev. *75*, 119 (1975).

[4] *O. R. Brow* in Electrochemistry, Specialist Periodical Rep., Vol. 4, Chem. Soc., London 1974, pages 55 and 77.

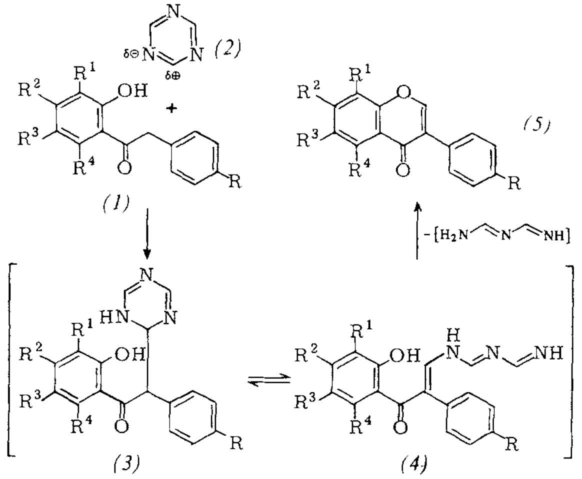
---

# Isoflavone Synthesis with 1,3,5-Triazine

By *Hem Chandra Jha, Fritz Zilliken*, and
*Eberhard Breitmaier*[*]

*Dedicated to Professor Rudolf Tschesche on the occasion of his 75th birthday*

The isoflavones *(5)*, which are of interest as antioxidants[1], fungicides[2] and anticontraceptives[3], are usually obtained by formylation of *o*-hydroxydeoxybenzoins *(1)* and subsequent cyclocondensation. Hitherto the systems formic acid and orthoformate/base[4a], zinc cyanide/hydrochloric acid[4b], dimethylformamide (DMF)/phosphorus oxide chloride[4c] and DMF/boron trifluoride/methanesulfonic acid[4d] have been used as formylating reagents. However, with exception of the latter method the yields are frequently poor and many by-products are obtained.



Since 1,3,5-triazine *(2)*, as a carbonyl-analogous electrophile, is attacked by CH-acidic compounds[5a] and is effective as a formylating agent[5b] we have tested it as a possible $C_1$-synthon in the synthesis of isoflavone. *(2)* reacts with *o*-hydroxydeoxybenzoins *(1)* in the presence of boron trifluoride ether in glacial acetic acid to give the corresponding isoflavones *(5)*. The advantages of this method are: good yields (up to 90%), short reaction times (2—3 h), mild conditions, and the simplicity of the technique and workup (Table 1).

The ring closure can be accomplished *via* the formyldeoxybenzoin formed from 1,3,5-triazine *(2)* and deoxybenzoin *(1)* in the sense of the Gattermann aldehyde synthesis[5b]. In analogy to earlier formylations[5a] the cyclization could also start with a nucleophilic addition of the acidic methylene group of *(1)* to the electrophilic carbon of *(2)*. The isoflavone *(5)* can be formed from the open-chain tautomer *(4)* of the primary adduct *(3)* with cleavage of the further reactive 1-amino-2,4-diaza-1,3-butadiene.

## *Procedure*

A solution of *(1)* (0.05 mmol) and *(2)* (0.1 mmol) in glacial acetic acid (1 cm³) is treated with 0.1 cm³ each of boron trifluoride ether (50% in diethyl ether) and acetic anhydride.

---

[*] Prof. Dr. F. Zilliken [+], Dr. H. Ch. Jha
Institut für Physiologische Chemie der Universität
Nussallee 11, D-5300 Bonn 1 (Germany)
Prof. Dr. E. Breitmaier
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Str. 1, D-5300 Bonn 1 (Germany)

[+] Author to whom correspondence should be addressed.

Table 1. Isoflavones from *o*-hydroxydeoxybenzoins *(1)* and 1,3,5-triazine *(2)*.

| Cpd. | R | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Yield [%] | M.p. [°C] | Ref. |
|---|---|---|---|---|---|---|---|---|
| *(5a)* | $OCH_3$ | H | $OCH_3$ | $OCH_3$ | H | 95 | 174—175 | [6] |
| *(5b)* | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | H | 92 | 151 | [7] |
| *(5c)* | OH | H | OH | H | H | 72 | 320—321 (dec.) | [8] |
| *(5d)* | $OCH_3$ | H | OH | H | H | 91 | 257—258 | [8] |
| *(5e)* | OH | H | OH | H | OH | 78 | 295—296 (dec.) | [8] |
| *(5f)* | $OCH_3$ | H | OH | H | OH | 81 | 212 | [8] |
| *(5g)* | OH | H | OH | OH | H | 58 | 320—321 (dec.) | [6] |
| *(5h)* | $OCH_3$ | H | OH | $OCH_3$ | H | 90 | 228—229 | [6] |
| *(5i)* | $OCH_3$ | H | OH | OH | H | 60 | 291—292 | [9] |

The mixture is boiled gently under reflux for 2—3 h, then cooled and poured into ice-water (20 $cm^3$). The precipitated isoflavone *(5)* is filtered off and purified by column chromatography (silica gel 60, particle size 0.063—0.200 mm; eluant benzene with increasing amounts of methanol) and recrystallization from methanol. The identities of the isoflavones thus obtained (Table 1) were confirmed by comparison with authentic samples (thin layer chromatography, melting points, IR and $^{13}C$-NMR spectra).

Received: May 19, 1980 [Z 673 IE]
German version: Angew. Chem. *93*, 129 (1981)

CAS Registry numbers:
*(1a)*, 5128-49-4; *(1b)*, 3606-32-4; *(1c)*, 17720-60-4; *(1d)*, 487-49-0; *(1e)*, 15485-65-1; *(1f)*, 15485-66-2; *(1g)*, 76095-37-9; *(1h)*, 5128-54-1; *(1i)*, 76095-38-0; *(2)*, 290-87-9; *(5a)*, 798-61-8; *(5b)*, 37816-21-0; *(5c)*, 486-66-8; *(5d)*, 485-72-3; *(5e)*, 446-72-0; *(5f)*, 491-80-5; *(5g)*, 17817-31-1; *(5h)*, 550-79-8; *(5i)*, 897-46-1

---

[1] *P. György, K. Murata, H. Ikehata*, Nature *203*, 870 (1964).

[2] *H. Fukami, M. Nakajima* in *M. Jacobsen, G. W. Crosby:* Naturally Occurring Insecticides. Marcel Dekker, New York 1971, p. 71—97.

[3] *J. D. Biggers* in *J. W. Fairbairn:* The Pharmacology of Plant-Phenolics. Academic Press, New York 1969, p. 51—69.

[4] a) *H. S. Mahal, H. S. Rai, K. Venkataraman*, J. Chem. Soc. *1934*, 1120; *S. A. Kagal, S. S. Karamarkar, K. Venkataraman*, Proc. Indian Acad. Sci. *A 44*, 36 (1956); b) *L. Farkas*, Chem. Ber. *90*, 2940 (1957); *L. Farkas, A. Major, L. Pallos, J. Várady, ibid. 91*, 2858 (1958); *S. A. Kagal, P. M. Nair, K. Venkataraman*, Tetrahedron Lett. *1962*, 593; *R. J. Bass*, J. Chem. Soc. Chem. Commun. *1976*, 78.

[5] a) *Ch. Grundmann*, Angew. Chem. *75*, 393 (1963); Angew. Chem. Int. Ed. Engl. *2*, 309 (1963); b) *A. Kreutzberger, ibid. 79*, 978 (1967) and *6*, 940 (1967), resp.

[6] *S. K. Arora, A. C. Jain, T. H. Seshadri*, J. Indian Chem. Soc. *38*, 61 (1961).

[7] *L. Jurd, K. Stevens, G. Manners*, Phytochemistry *11*, 2149 (1972).

[8] *W. Baker, J. Chadderton, J. B. Harborne, W. D. Ollis*, J. Chem. Soc. *1953*, 1852.

[9] *S. F. Dyke, W. D. Ollis, M. Sainsbury, J. S. D. Schwarz*, Tetrahedron *20*, 1331 (1964).

---

# $(NH_4)_4[P_4S_8]\cdot 2H_2O$, the Salt of a "Square" Phosphoric Acid[**]

By *Hans Falius, Werner Krause*, and *William S. Sheldrick*[*]

We have obtained a series of previously unknown phosphates upon oxidation of elemental phosphorus with polysulfidic sulfur[1]. Two of these, which were prepared from red phosphorus, display an identical composition, namely $M^IPS_2$ (without water of crystallization). They were shown to be *cyclo*-thiophosphates(III) with respective ring sizes of five and six members.

We have now succeeded in synthesizing a further thiophosphate with the same composition, in this case by the reaction of white phosphorus with polysulfides in a nonaqueous medium. This reaction is very rapid at room temperature and leads to a mixture of different thiophosphate anions, one of which, however, predominates proportionally. It could be isolated as the moderately soluble ammonium salt.

From the analytical and spectroscopic findings ($NH_4:P:S = 1:1:2$, oxidation number of phosphorus: +3, $^{31}P$-NMR: only one singlet) it was reasonable to assume that this salt was once again a cyclic thiophosphate(III). Furthermore, since the compound had been prepared from white phosphorus, it could be concluded that it contained a four-membered ring. This supposition was confirmed by the X-ray analysis[2] (Fig. 1).

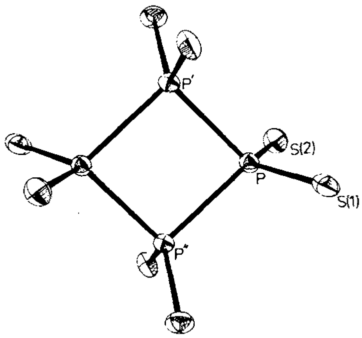


Fig. 1. Structure of the anion $[P_4S_8]^{4-}$. Bond lengths and angles: P—S1 197.6(1), P—S2 198.0(1), P—P' 228.0(1), P—P'' 228.7(1) pm; S1—P—S2 118.6(1), S1—P—P' 121.7(1), S1—P—P'' 111.8(1), S2—P—P' 119.7(1), S2—P—P'' 110.7(1)°.

The triethylammonium salt formed by the reaction (a) was converted into the sodium salt with sodium hydroxide, without having been first isolated. Addition of $NH_4NO_3$ to an aqueous solution of this readily soluble salt led to the crystallization of the less soluble ammonium octathiocyclotetraphosphate(III), $(NH_4)_4[P_4S_8]\cdot 2H_2O$ *(1)*. Similarly, use of a readily soluble potassium salt, such as potassium acetate, instead of $NH_4NO_3$, yielded a precipitate of the less soluble $K_4[P_4S_8]\cdot 2H_2O$ *(2)*.

$$P_4 + 4[Et_3NH]HS_{2.5} \rightarrow [Et_3NH]_4[P_4S_8] + 2H_2S \tag{a}$$

*(1)* forms shiny flaky platelets. Its $^{31}P$-NMR spectrum ($H_2O$) displays a singlet at $\delta = 121$ (85% $H_3PO_4$, external). The aqueous solution of this salt of a monobasic polyvalent acid has, as expected, a pH of 7; the anion is remarkably stable. Alkaline hydrolysis at boiling heat leads to thiomonophosphates(III): $[PHOS_2]^{2-}$ (high yield), $[PHO_2S]^{2-}$ (low yield), $[PHS_3]^{2-}$ (very low yield). On acid hydrolysis $[PO_4]^{3-}$ and $[PH_2O_2]^-$ are formed in addition to the previously mentioned phosphates(III). Precipitates are formed for the *cyclo*-thiophosphate with the following cations: $Pb^{II}$ (red-brown), $Sn^{II}$ (orange), Bi (brown-black), $Cu^{II}$ (yellow-brown), Cd (white), $Hg^{II}$ (bright yellow), Ag (yellow, slowly becoming brown and then black).

---

[*] Prof. Dr. H. Falius and Dr. W. Krause
Institut für Anorganische Chemie der TU
Pockelsstrasse 14, D-3300 Braunschweig (Germany)
Priv.-Doz. Dr. W. S. Sheldrick
Gesellschaft für Biotechnologische Forschung
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

The anion of *(1)* is the first known homocycle consisting of four tetracoordinated phosphorus atoms. It represents, thereby, an ionic analogue to *cyclo*butane.

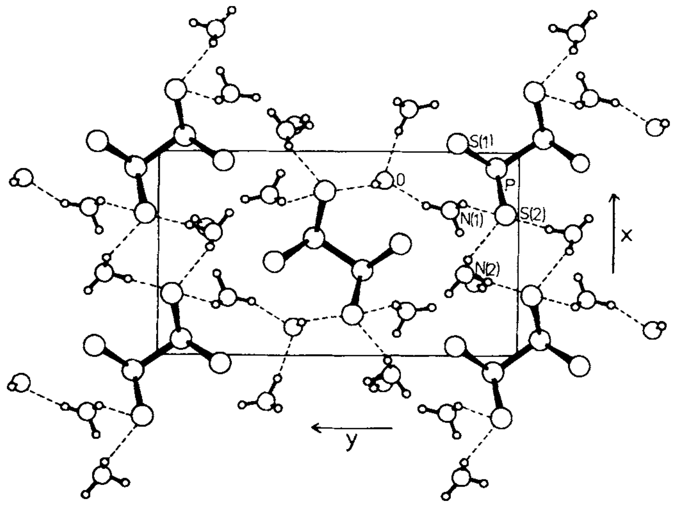


Fig. 2. Projection of the crystal lattice of *(1)* perpendicular to [001].

The crystal structure of *(1)* is stabilized by a network of N—H···S and O—H···S hydrogen bonds to S2, and N—H···O hydrogen bonds between N1 and the water of crystallization. N1 and the water oxygen lie in the mirror plane at z = 0.5, N2 in the mirror plane at z = 0. $[P_4S_8]^{4-}$ has crystallographic $C_{2h}$-symmetry, P′ being related by a $C_2$-axis and P″ by a mirror plane to P. The four-membered ring must, therefore, be exactly planar with angles of 90° at phosphorus. The P—P distances of respectively 228.0(1) and 228.7(1) pm are significantly longer than those which are normally observed (218—222 pm), independent of oxidation state and the nature of the substituents. Longer P—P bonds have been observed in caged phosphorus sulfides, namely 235 pm in $P_4S_7$[4] and 236 pm in α-$P_4S_4$[5].

*Experimental*

Solvents and $H_2S$ are dry. A mixture of $Et_3N$ (14 cm$^3$, 0.1 mol) and $CHCl_3$ (50 cm$^3$) is saturated with $H_2S$. 3.2 g (0.1 mol) of sulfur is added in portions, with stirring and further introduction of $H_2S$. After the sulfur has dissolved, the gas stream is strongly reduced and a solution of phosphorus (1.5 g, 0.05 mol) in $CS_2$ (5 cm$^3$) is added dropwise (water cooling). After stirring for a further hour the reaction mixture is shaken with 50 cm$^3$ of ice-cooled 10% NaOH. A mixture of sodium salts is exhaustively precipitated with ethanol from the upper aqueous phase. This is dissolved in 90 cm$^3$ of water and 10 cm$^3$ 25% $NH_3$ and $NH_4NO_3$ (15 g) are added with stirring. The *cyclo*-thiophosphate begins to crystallize during this addition. Yield 3 g (50%).—If recrystallization is necessary, *(1)* is dissolved in the required quantity of 10% NaOH and added to the described solution of water, 25% $NH_3$ and $NH_4NO_3$.

Received: June 11, 1980 [Z 681 IE]
German version: Angew. Chem. *93*, 121 (1981)

---

[1] *W. Krause*, Dissertation, Technische Universität Braunschweig 1978.

[2] *(1)* crystallizes orthorhombically (Pbam) with $a = 807.9(1)$, $b = 1433.7(4)$, $c = 868.1(1)$ pm, $Z = 2$, $\rho_{calc} = 1.61$, $\rho_{obs} = 1.58$ g·cm$^{-3}$. The structure was refined to $R = 0.037$, $R_w = 0.031$ for 1325 reflexions (Syntex $P2_1$-diffractometer, $\theta$'$2\theta$ mode, $2\theta \leqslant 60°$, $F^2 \geqslant 1.5\sigma(F^2)$, Mo-K$_\alpha$ radiation). A refinement in the non-centrosymmetric space group $Pba2_1$ did not lead to a significant improvement of the *R*-factor.

[3] *A. H. Cowley*, Chem. Rev. *65*, 617 (1965); *D. C. Corbridge:* The Structural Chemistry of Phosphorus, Elsevier, London 1974.

[4] *A. Vos, R. Olthof, F. van Bolhuis, R. Botterweg*, Acta Crystallogr. *19*, 864 (1965).

[5] *A. M. Griffin, P. C. Minshall, G. M. Sheldrick*, J. Chem. Soc. Chem. Commun. *1976*, 809.

---

## Oxidation of Alcohols with Benzyl(triethyl)ammonium Permanganate

By *H.-Jürgen Schmidt* and *Hans J. Schäfer*[*]

Benzyl(triethyl)ammonium permanganate, which is safe to handle below 50 °C[1], can be used for the oxidation of hydrocarbons to alcohols or ketones[2a] and of ethers to esters[2b]. We report here on the oxidation of primary and secondary alcohols with this reagent (Table 1).

Table 1. Products of the oxidation of alcohols with benzyl(triethyl)ammonium permanganate.

| Alcohol [a] | Oxidation products (yield isolated [%]) |
|---|---|
| Benzyl alcohol | Methylene dibenzoate (62), chloromethyl benzoate (11), Benzoic acid (18) |
| 1-Heptanol | Methylene diheptanoate (70), chloromethyl heptanoate (9), heptanoic acid (15) [b] |
| 1-Decanol | Methylene didecanoate (71), chloromethyl decanoate (13), Decanoic acid (15) [c] |
| 2-Octanol | 2-Octanone (89), hexanoic acid (10) [d] |
| D,L-1-Phenylethanol | Acetophenone (78), benzoic acid (19) |
| Benzhydrol | Benzophenone (95), benzoic acid (3) |

[a] General reaction conditions: 5 mmol alcohol, 10 mmol benzyl(triethyl)ammonium permanganate in 75 cm$^3$ dichloromethane, 1—2 d at 5 to 40 °C. [b] Mixture of 94% $C_7$-, 5% $C_6$-, and 1% $C_5$-acids. [c] Mixture of 88% $C_{10}$, 7% $C_9$-, and 4% $C_8$-acids. [d] Mixture of 70% $C_6$-, 5% $C_7$-, and 20% $C_6$-acids.

The main products of the primary alcohols are the methylene diesters, which are presumably formed by nucleophilic attack of the carboxylates on the solvent dichloromethane[3]. While the carboxylic acids formed as byproducts contain shorter chain homologs—apparently by oxidative follow-up reactions—the diesters are uniform. Secondary alcohols furnish high yields of ketones, accompanied by the carboxylic acids formed by α-cleavage.

While benzyl alcohol and benzhydrol are oxidized with tetrabutylammonium permanganate in pyridine in yields of the same order[4], in the potassium permanganate-oxidation in water or glacial acetic acid the yields of the alcohol oxidation are distinctly lower[5]. In the oxidation of primary alcohols the title reagent is superior to solid carriers such as molecular sieves[6a], copper sulfate[6b] and aluminum oxide[6c] impregnated with potassium permanganate.

Received: July 9, 1980 [Z 670a IE]
German version: Angew. Chem. *93*, 124 (1981)

CAS Registry numbers:
Benzyl alcohol, 100-51-6; 1-heptanol, 111-70-6; 1-decanol, 112-30-1; 2-Octanol, 123-96-6; D,L-1-phenylethanol, 13323-81-4; benzhydrol, 91-01-0; benzyl(triethyl)ammonium permanganate, 68844-25-7; methylene dibenzoate, 5342-31-4; Chloromethyl benzoate, 5335-05-7; benzoic acid, 65-85-0; methylene diheptanoate, 20177-68-8; Chlormethyl heptanoate, 76068-79-6; methylene didecanoate, 76068-80-9; Chlormethyl decanoate, 67317-62-8; 2-Octanone, 111-13-7; acetophenone, 98-86-2; benzophenone, 119-61-9

---

[1] *H.-J. Schmidt, H. J. Schäfer*, Angew. Chem. *91*, 852 (1979); Angew. Chem. Int. Ed. Engl. *18*, 787 (1979); *H. H. Jäger, J. Lütolf, M. W. Meyer, ibid. 91*, 852 (1979) and *18*, 786 (1979) resp.

[2] a) *H.-J. Schmidt, H. J. Schäfer*, Angew. Chem. *91*, 77 (1979); Angew. Chem. Int. Ed. Engl. *18*, 68 (1979); b) *ibid. 91*, 78 (1979) and *18*, 69 (1979) resp.

[3] *K. Holmberg, B. Hansen*, Tetrahedron Lett. *1975*, 2303.

[4] *T. Sala, M. V. Sargent*, J. Chem. Soc. Chem. Commun. *1978*, 253.

[5] *K. B. Wiberg:* Oxidation in Organic Chemistry. Part A. Academic Press, New York 1965.

[6] a) *S. L. Regen, C. Koteel*, J. Am. Chem. Soc. *99*, 3837 (1977); b) *F. M. Menger, C. Lee*, J. Org. Chem. *44*, 3446 (1979); c) *S. Quici, S. L. Regen, ibid. 44*, 3436 (1979).

---

[*] Prof. Dr. H. J. Schäfer, Dipl.-Chem. H.-J. Schmidt
Organisch-Chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

## Oxidation of Amines with Benzyl(triethyl)ammonium Permanganate

By *H.-Jürgen Schmidt* and *Hans J. Schäfer*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

Tertiary amines can be heterogeneously oxidized with potassium permanganate only with difficulty, and even then to a mixture of products of little preparative use[1]. In contrast, the homogeneous oxidation with benzyl(triethyl)ammonium permanganate in dichloromethane affords an *N,N*-dialkylamide as single product in high yield. In the case of secondary and primary amines the oxidation is less selective (see Table 1).

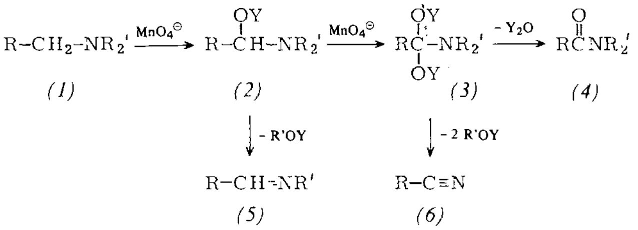
Table 1. Products of the oxidation of amines with benzyl(triethyl)ammonium permanganate.

| Amine [a] | Oxidation products (yield isolated [%]) |
|---|---|
| *n*-Decylamine [b] | Decanonitrile (11), decanamide (6), decanoic *N*-decylamide (35) |
| *n*-Decylamine [c] | Decanonitrile (54), decanamide (13), *N*-decylformamide (4), decanoic *N*-decylamide (15), decanoic acid (10) [d] |
| Di(*n*-butyl)amine | Butyric *N*-butylamide (44), methylene dibutyrate (14), butyric acid (30) [e] |
| Di(*n*-octyl)amine | Octanoic *N*-octylamide (49), methylene dioctanoate (11), octanoic acid (20) [f] |
| Dibenzylamine | *N*-Benzylbenzamide (36), dibenzamide (6), benzamide (20), benzaldehyde (7), benzoic acid (25) |
| *N*-Methylbenzylamine | *N*-Methylbenzamide (36), benzaldehyde (33), benzoic acid (27) |
| *N*-Methylaniline | *N*-Phenylformamide (<10) |
| *N*-Ethylaniline | *N*-Phenylacetamide (<10) |
| Tributylamine | *N,N*-Dibutylbutyramide (93), butyric acid (5) |
| *N,N*-Dimethylaniline | *N*-Methyl-*N*-phenylformamide (78) |
| *N,N*-Diethylaniline | *N*-Ethyl-*N*-phenylacetamide (63) |
| *N,N*-Dimethyldodecylamine | *N,N*-Dimethyldodecanoylamide (30), *N*-dodecyl-*N*-methylformamide (42) |
| *N*-Methyl-*N,N*-dioctylamine | *N*-Methyl-*N*-octyl-octanoylamide (51), *N,N*-dioctylformamide (21) |
| *N,N*-Dimethylbenzylamine | *N,N*-Dimethylbenzamide (70), *N*-benzyl-*N*-methylformamide (7), benzaldehyde (3), benzoic acid (14) |
| *N*-Ethylpiperidine | 1-Ethyl-2-piperidone (72), *N*-acetylpiperidine (13) |

[a] General reaction conditions: 5 mmol amine, 10 mmol benzyl(triethyl)ammonium permanganate in 75 cm$^3$ dichloromethane, 0.5 to 2 d at 0 to 40 °C; isolation of the product: HPLC separation. [b] At 20 °C and 1 equiv. benzyl(triethyl)ammonium permanganate. [c] At 40 °C and 2 equiv. benzyl(triethyl)ammonium permanganate. [d] Additional lower homologs. [e] Mixture of 80% $C_4$-, 20% $C_3$-acids. [f] Mixture of 75% $C_8$-, 20% $C_7$-, and 5% $C_6$-acids.

The formation of the products can be explained (in part analogously to [2]) according to Scheme 1.

The amine *(1)* is oxidized with permanganate to *(2)* or *(3)*. For example, *n*-decylamine reacts (i) *via (2)* to give the imine *(5)*, which with decylamine and after secondary oxidation yields decanoic *N*-decylamide, or (ii) *via (3)* to give the nitrile *(6)*; under milder reaction conditions the former pathway predominates, on more rapid oxidation the latter. Secondary amines furnish the amides *(4)* in yields between 35—50%. Side reactions are markedly reduced in comparison to the oxidation of primary amines; secondary amines give carboxylic acids and esters, presumably by oxidation of the imine *(5)*. Tertiary amines afford the amides *(4)* in 75—98% yield, practically without formation of byproducts. The different CH bonds react with about the following chemoselectivities: benzyl:$CH_2$:$CH_3$ = 24:2:1.



$$R{-}CH_2{-}NR_2' \xrightarrow{MnO_4^{\ominus}} R{-}\overset{OY}{\overset{|}{C}}H{-}NR_2' \xrightarrow{MnO_4^{\ominus}} R\underset{OY}{\overset{OY}{C}}{-}NR_2' \xrightarrow{-Y_2O} R\overset{O}{\overset{\|}{C}}NR_2'$$

$$R{-}CH{=}NR' \qquad R{-}C{\equiv}N$$

R = Phenyl, Alkyl; R' = H, Alkyl; Y = H, $MnO_3H^{\ominus}$

Scheme 1.

There are only few preparatively useful methods for the conversion of secondary and tertiary amines into amides. *N*-Methylamines form formamides on oxidation with oxygen on platinum[3]; *N*-methylanilines are oxidized with manganese dioxide to *N*-phenylformamides, while in anilines with longer-chain alkyl groups one residue is decomposed to formamide[4]. Other oxidizing agents such as benzoyl peroxide[5], bromine[6], *N*-bromosuccinimide[7] lead, similarly to aqueous permanganate solution[2], to aldehydes. Benzyl(triethyl)ammonium permanganate extends these possibilities, in particular, to the oxidation of tertiary amines.

Received: July 9, 1980 [Z 670b IE]
German version: Angew. Chem. *93*, 124 (1981)

CAS Registry numbers:
Decylamine, 2016-57-1; di(*n*-butyl)amine, 111-92-2; di(*n*-octyl)amine, 1120-48-5; dibenzylamine, 103-49-1; *N*-methylbenzylamine, 103-67-3; *N*-methyl-*N*-ethylaniline, 613-97-8; tributylamine, 102-82-9; *N,N*-dimethylaniline, 121-69-7; *N,N*-diethylaniline, 91-66-7; *N,N*-dimethyldodecylamine, 112-18-5; *N*-methyl-*N,N*-dioctylamine, 4455-26-9; *N,N*-dimethylbenzylamine, 103-83-3; *N*-ethylpiperidine, 766-09-6; decanonitrile, 1975-78-6; decanoamide, 2319-29-1; decanoic-*N*-decylamide, 33598-69-5; *N*-decylformamide, 42414-94-8; decanoic acid, 334-48-5; butyro-*N*-butylamide, 10264-16-1; methylene dibutyrate, 55696-44-1; butyric acid, 107-92-6; octanoic-*N*-octylamide, 42886-89-5; methylene dioctanoate, 76058-01-0; octanoic acid, 112-05-0; *N*-benzylbenzamide, 1485-70-7; dibenzamide, 614-28-8; benzamide, 55-21-0; benzaldehyde, 100-52-7; benzoic acid, 65-85-0; *N*-methylbenzamide, 613-93-4; *N*-phenylformamide, 103-70-8; *N*-phenylacetamide, 103-84-4; *N,N*-dibutylbutyramide, 14287-95-7; *N*-methyl-*N*-phenylformamide, 93-61-8; *N*-ethyl-*N*-phenylacetamide, 5461-49-4; *N,N*-dimethyldodecanoylamide, 3007-53-2; *N*-dodecyl-*N*-methylformamide, 76058-02-1; *N*-methyl-*N*-octyloctanoylamide, 76058-03-2; *N,N*-dioctylformamide, 6280-57-5; *N,N*-dimethylbenzamide, 611-74-5; *N*-benzyl-*N*-methylformamide, 17105-71-4; 1-ethyl-2-piperidone, 4789-07-5; *N*-acetylpiperidine, 618-42-8; benzyl(triethyl)ammonium permanganate, 68844-25-7

---

[1] *H. Shechter, S. S. Rawalay*, J. Am. Chem. Soc. *86*, 1706 (1964).
[2] *H. Shechter, S. S. Rawalay, M. Tubis*, J. Am. Chem. Soc. *86*, 1701 (1964); *M.-M. Wei, R. Stewart, ibid. 88*, 1974 (1966); *S. S. Rawalay, H. Shechter*, J. Org. Chem. *32*, 3129 (1967).
[3] *G. T. Davis, D. H. Rosenblatt*, Tetrahedron Lett. *1968*, 4085.
[4] *H. B. Henbest, A. Thomas*, J. Chem. Soc. *1957*, 3032.
[5] *D. Buckley, S. Dunstan, H. B. Henbest*, J. Chem. Soc. *1957*, 4901.
[6] *N. C. Deno, R. E. Fruit, Jr.*, J. Am. Chem. Soc. *90*, 3502 (1968).
[7] *S. Dunstan, H. B. Henbest*, J. Chem. Soc. *1957*, 4905.

---

[*] Prof. Dr. H. J. Schäfer, Dipl.-Chem. H.-J. Schmidt
Organisch-Chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

## Topotactic Electron/Proton Transfer Reactions of Transition Metal Complexes with Columnar and Cluster Structures

By *Robert Schöllhorn, Klaus Wagner*, and *Hermann Jonke*[*]

Considerable work has been devoted in recent years to the investigation of reversible topotactic redox reactions, at ambient temperature, of electronically conducting solids with layer, chain and framework structures of the host lattice ma-

---

[*] Prof. Dr. R. Schöllhorn, K. Wagner, H. Jonke
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

trix[1]. There are no comparable reports, however, on this type of reaction in the case of molecular solids which is obviously a consequence of low electronic conductivities and of modest lattice energies which usually prevent topotactic processes. Favorable conditions should be expected in case of (*i*) extensive intermolecular delocalization of electrons, *e.g.* *via* charge transfer or metal d-orbital interaction, (*ii*) small guest ion size, *i.e.* minor steric perturbation of the host lattice, and (*iii*) appropriate intracrystalline transport pathways for guest ions with low activation energy. Since protons are the smallest guest ions available, we decided to start a systematic investigation on reversible topotactic electron/proton transfer reactions [eq. (1)] in molecular solids and report here on electrochemical and structural studies of transition metal complexes with metal/metal bonding.

$$xH^+ + xe + Z \rightleftarrows H_x^+[Z]^{x-} \quad (Z = \text{host lattice matrix}) \qquad (1)$$

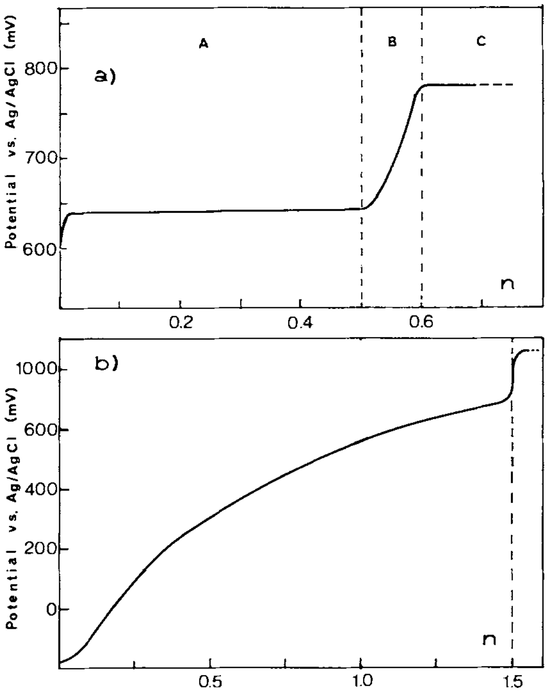


Fig. 1. Potential/charge transfer curve for anodic oxidation of (a) Magnus Green Salt $[Pt(NH_3)_4][PtCl_4]$ in 50% aqueous $H_2SO_4$ electrolyte, $n$ = e/formula unit; (b) $[Ta_6Cl_{14}](H_2O)_8$ in aqueous 1 M HCl/1 M NaCl electrolyte, $n$ = e/formula unit. Current density 100 μA cm$^{-2}$ (see text).

The heterogeneous oxidation of Magnus's Green Salt (MGS) $[Pt(NH_3)_4]^{2+}[PtCl_4]^{2-}$—whose structure is characterized by stacks of planar $PtX_4$ complex ions[2]—has been described by *Tschugajeff*[3]. The crystals obtained on $H_2SO_4/O_2$ oxidation behave as one-dimensional metallic conductors[4]; two different structure models have been proposed suggesting either Pt—Pt chains with coordinated $HSO_4$-ligands[5] or chlorine bridged ··X—Pt—X—Pt·· chain polymers[6]. We observed on galvanostatic anodic oxidation of single crystal or polycrystalline electrodes of MGS in aqueous $H_2SO_4$ electrolyte (40—70 wt-%; 300 K) quantitative oxidation with the formation of bright copper-red needles. The potential/charge transfer curve for this process is given in Fig. 1a. X-Ray studies and analytical investigations showed that the potential plateau of region A corresponds to a two phase region MGS/oxidized product. At low current densities the reaction in the two phase region is fully reversible and MGS is obtained quantitatively on cathodic reduction. The long axes of the crystal needles of the oxidized phase are oriented parallel to the original MGS crystals. Tetragonal symmetry was found with the lattice parameters $a = 946.4$, $c = 572.7$ pm. Charge transfer values, X-ray results and analytical data are consistent with the formula $[Pt(NH_3)_4PtCl_4]^{0.5+}[H_{1.5}SO_4]^{0.5-}(H_2O)_y$. The structure can be described as consisting of partially oxidized MGS type chains with metal/metal bonding and a Pt—Pt distance $d = c/2 = 286$ pm; the excess positive charge of the chain matrix is compensated by hydrated $HSO_4^-$ anions in the interchain space (Fig. 2). Further oxidation (region B, Fig. 1a) corresponds in agreement with the continuous rise in potential to a nonstoichiometric phase region and represents a reversible topotactic redox reaction by electron/proton transfer with very small changes in lattice parameters [eq. (2)]. Since the redox range

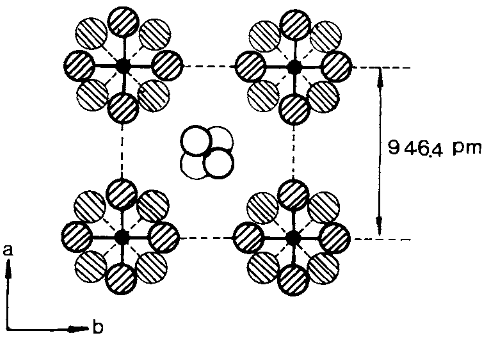


Fig. 2. Structure scheme of tetragonal $[Pt(NH_3)_4PtCl_4]^{0.5+}(H_{1.5}SO_4)^{0.5}(H_2O)_y$ with partially oxidized $PtX_4$ chains and hydrated interchain anions ($H_2O$ molecules not indicated). ● = Pt, ○ = O, ▨ = Cl, ▧ = $NH_3$.

$$\begin{aligned}&[Pt(NH_3)_4PtCl_4]^{0.5+}[H_{1.5}SO_4]^{0.5-}(H_2O)_y \rightleftarrows \\ &[Pt(NH_3)_4PtCl_4]^{(0.5+x)+}[H_{1.5-x}SO_4]^{(0.5+x)-}(H_2O)_y + xH^+ + xe\end{aligned} \qquad (2)$$

corresponds to $0 \leqslant x \leqslant 0.1$, the average oxidation state of Pt in the nonstoichiometric region varies between +2.25 and +2.3. The electron transport path is provided by the Pt metal chain, while hydrogen transport must proceed via the intracrystalline $HSO_4^-/H_2O$ electrolyte phase. A two phase range is found on further oxidation (region C, Fig. 1a), which is presently under investigation. On anodic oxidation of MGS in acid electrolytes with other tetrahedral anions, *e.g.* $HClO_4$, $H_3PO_4$, $HBF_4$, similar reactions and products are observed. The perchlorate compound is isomorphous with the sulfate and undergoes partial dehydration at 300 K/10$^{-3}$ torr; tetragonal lattice parameters of the dehydrated phase are $a = 747.5$, $c = 572.1$, $d$(Pt—Pt) = 286 pm. A series of platinum complexes related to MGS were found to exhibit analogous nonstoichiometric phase ranges on anodic oxidation, *e.g.* *cis*-$PtCl_2(NH_3)_2$ which yields reversibly a sulfate with columnar structure and an intrachain Pt—Pt distance of 295 pm.

Redox and exchange reactions of $M_6$-cluster halides (M *e.g.* Nb, Ta, Mo) are well known from studies in homogeneous solution[7]. We have now found that $Ta_6Cl_{14} \cdot 8H_2O$ is able to undergo reversible oxidation by topotactic electron/proton transfer in the solid state [eq. (3), Fig. 1b]. The structure of this cluster halide consists of $Ta_6Cl_{14} \cdot 4H_2O$ molecular units which are arranged in sheets *via* hydrogen bonding; the remaining four $H_2O$ are located between these layers[8]. The accessible redox range [eq. (3)] of $0 \leqslant x \leqslant 1.5$ is equivalent to a

$$[Ta_6Cl_{14}](H_2O)_8 \rightleftarrows [Ta_6Cl_{14}]^{x+}(OH^-)_x(H_2O)_{8-x} + xe + xH^+ \qquad (3)$$

change in Ta average oxidation state from +2.33 to +2.58. The hexagonal lattice parameters vary between $a=936.7$, $c=2600.5$ pm (reduced state, dark green) and $a=938.0$, $c=2589.6$ pm (fully oxidized state, dark brown). It is assumed for electrostatic reasons that the deprotonation takes place at $H_2O$ molecules coordinated directly to the $Ta_6$-cluster. $Nb_6Cl_{14}\cdot 8H_2O$ electrodes may be oxidized similarly; cathodic reduction is, however, kinetically hindered.

Electrochemical studies on quinoliniumtetracyanoquinodimethane $(QH^+)[(TCNQ)_2]^-$—which behaves as a one-dimensional electronic conductor[9]— revealed reversible electron/proton transfer according to eq. (4) (electrolyte 0.1 N $H_2SO_4/K_2SO_4$, two phase region at 150 mV *vs* Ag/AgCl with $x=2$). The protons are assumed to be bound to the —C≡N groups.

$$(QH^+)[(TCNQ)_2]^- + xH^+ + xe \rightleftarrows (QH^+)(H^+)_x[(TCNQ)_2]^{(1+x)-} \qquad (4)$$

The results presented demonstrate that under appropriate conditions reversible topotactic redox reactions may be observed readily also for molecular inorganic and organic solids which is of interest with respect to synthetic aspects (preparation of novel metastable phases), to the modification of physical properties of molecular solids and to potential technical use of these systems, *e.g.* as electrode materials in secondary batteries, nonemissive electrochromic devices, heterogeneous catalysts *etc.*

Received: June 13, 1980 [Z 676 IE]
German version: Angew. Chem. *93*, 122 (1981)

CAS Registry numbers:
$[Pt(NH_3)_4][PtCl_4]$, 13820-46-7; $Ta_6Cl_{14}$, 12133-85-6

---

[1] *R. Schöllhorn*, Angew. Chem. *92*, 1015 (1980); Angew. Chem. Int. Ed. Engl. *19*, 983 (1980).

[2] *M. Atoji, J. W. Richardson, R. E. Rundle*, J. Am. Chem. Soc. *79*, 3017 (1957).

[3] *L. Tschugajeff, J. Tschernjajeff*, Z. Anorg. Allg. Chem. *182*, 159 (1929).

[4] *I. Tsujikawa, R. Kubota, T. Enoki, S. Miyajima, H. Kobayashi*, J. Phys. Soc. Jpn. *43*, 1459 (1977).

[5] *W. Gitzel, H. Keller, H. H. Rupp, K. Seibold*, Z. Naturforsch. *B 27*, 365 (1972).

[6] *G. C. Papavassiliou, T. Theophanides*, Z. Naturforsch. *B 34*, 986 (1979).

[7] *H. Schäfer, H. G. von Schnering*, Angew. Chem. *76*, 833 (1964); *R. E. McCarley, B. G. Hughes, F. A. Cotton, R. Zimmermann*, Inorg. Chem. *10*, 1491 (1965); *B. Spreckelmayer, H. Schäfer*, J. Less-Common Met. *13*, 122, 127 (1967).

[8] *R. D. Burbank*, Inorg. Chem. *5*, 1491 (1966).

[9] *G. Mihaly, R. Ritvay-Emandity, G. Grüner*, J. Phys. *C 8*, L 361 (1975).

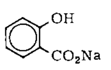
## Negative Ion Field Desorption Mass Spectrometry (NFD-MS) of Salts[**]

By *Karl H. Ott, Franz W. Röllgen, Jan J. Zwinselman, Roel H. Fokkens,* and *Nico M. M. Nibbering*[*]

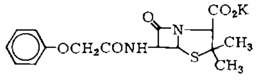
The low field-strength required for field electron emission from metals and semiconductors and secondary effects such as cathode sputtering and gas discharges prevented in the past the development of field desorption mass spectrometry of negative ions (NFD-MS). However, more recently we were able to show that field desorption of negative ions is possible if the samples are admixed with polymers such as polyethylene oxides[1]. The viscous polymers reduce the field strength necessary to desolvate negative ions from the condensed phase below the threshold field strength for field electron emission.

With this method the compound to be investigated and polyethylene oxide 4000 (mixing ratio 1:1) is dissolved in water and deposited onto a 10-μm tungsten wire emitter. Thereafter the wire covered with the mixture is introduced into the FD source of a conventional mass spectrometer. After applying a voltage of −4 kV to the emitter, a mass spectrum of negative ions can be recorded in the usual way by heating the emitter wire.

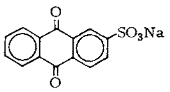
Table 1. Negative ions in the NFD mass spectra of some salts. $M$ = salt molecule.



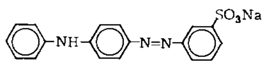
*(1)*



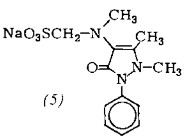
*(2)*



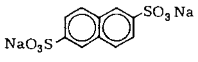
*(3)*



*(4)*



*(5)*



*(6)*

| Salt | Ions | Salt | Ions |
|---|---|---|---|
| NaCl | $Cl^-$, $NaCl_2^-$,<br>$Na_2Cl_3^-$ | $(CH_3)_4PI$ | $I^-$, $(CH_3)_4PI_2^-$ |
| $CaCl_2$ | $Cl^-$ | $(CH_3)_3SI$ | $I^-$, $(CH_3)_3SI_2^-$ |
| $NaNO_3$ | $NO_3^-$, $H(NO_3)_2^-$,<br>$Na(NO_3)_2^-$ | $NaB(C_6H_5)_4$ | $B(C_6H_5)_4^-$ |
| $Ca(NO_3)_2$ | $NO_3^-$ | $Na(CH_3CO_2)$ | $(CH_3CO_2)^-$,<br>$H(CH_3CO_2)_2^-$,<br>$Na(CH_3CO_2)_2^-$ |
| $MgSO_4$ | $HSO_4^-$ | $Ca(CH_3CO_2)_2$ | $(CH_3CO_2)^-$ |
| NaCN | $CN^-$, $Na(CN)_2^-$ | $CH_3(CH_2)_{16}CO_2Na$ | $(M-Na)$ |
| KSCN | $SCN^-$, $K(SCN)_2^-$ | *(1)* | $(M-Na)$ |
| $NaH_2PO_4$ | $H_2PO_4^-$ | *(2)* [b] | $(M-K)$ |
| $K_2Cr_2O_7$ | $HCr_2O_7^-$, $KCr_2O_7^-$ | *(3)* | $(M-Na)$ |
| $KMnO_4$ | $MnO_4^-$ | *(4)* [c] | $(M-Na)$ |
| $K_4Fe(CN)_6$ | $K_3Fe(CN)_6^-$ [a] | *(5)* [d] | $(M-Na)^-$ |
| $NH_4Cl$ | $Cl^-$, $NH_4Cl_2^-$ | *(6)* | $(M-Na)$ |
| $(C_2H_5)_4NI$ | $I^-$, $(C_2H_5)_4NI_2^-$ | | |

[a] Very weak signal. [b] Potassium salt of penicillin V. [c] Metanil yellow orange. [d] Novalgin.

We have employed the new ionization method for the analysis of a number of inorganic and organic salts. A selection of the salts together with the characteristic ions observed in the NFD mass spectra are listed in Table 1. The spectra are very simple and do not exhibit fragment ions. The cluster ions which appear at higher salt concentrations and higher emitter temperatures allow the mass of the cation to be determined[2]. Doubly charged anions have not been detected so far. Additional ion signals resulting from fragmentation of the matrix have been observed with fluorides, hydroxides and strong oxidizing agents such as $KMnO_4$.

Comparing the widely used field desorption mass spectrometry of positive ions (FD-MS) with NFD-MS there are a

---

[*] Prof. Dr. F. W. Röllgen [+], Dipl.-Chem. K. H. Ott
Institut für Physikalische Chemie der Universität
Wegelerstraße 12, D-5300 Bonn (Germany)

Prof. Dr. N. M. M. Nibbering [+], J. J. Zwinselman, R. H. Fokkens
Laboratory of Organic Chemistry, University of Amsterdam
Nieuwe Achtergracht 129, NL-1018-WS Amsterdam (Holland)

[**] This work was supported by the Wissenschaftsministerium des Landes Nordrhein-Westfalen. The authors thank *F. A. Pinkse* for technical assistance.

[+] Authors to whom correspondence should be addressed.

Table 2. Negative ions in the NFD mass spectrum of a soap.

| Ion | Rel. int. [%] | Ion | Rel. int. [%] |
|---|---|---|---|
| $CH_3(CH_2)_{16}CO_2^-$ | 52 | $CH_3(CH_2)_{10}CO_2^-$ | 100 |
| $CH_3(CH_2)_{14}CO_2^-$ | 42 | $CH_3(CH_2)_8CO_2^-$ | 20 |
| $CH_3(CH_2)_{12}CO_2^-$ | 48 | $CH_3(CH_2)_6CO_2^-$ | 18 |

few points to be emphasized. 1. The detection sensitivity for anions of salts is significantly higher with NFD-MS; for the analytically important salts of sulfonic acids by at least one order of magnitude (with FD-MS information about the anion is provided by the cluster ions). 2. Without the exchange of cations no useful spectrum is obtained by FD-MS from salts such as $MgSO_4$, $CaCO_3$ and $Ca(CH_3CO_2)_2$. Particularly difficult to analyze are also salts of disulfonic acids such as *(6)*. 3. Anions of salts can selectively be detected from technical and biological mixtures without further preparation. In general this is not possible with FD-MS. As an example the mass spectrum obtained by NFD-MS of a soap containing potassium salts of fatty acids is listed in Table 2. For recording this spectrum it was not necessary to admix polyethylene oxide. The results demonstrate that NFD-MS opens up new possibilities for the analysis of salts.

Received: September 17, 1980 [Z 655 IE]
German version: Angew. Chem. 93, 96 (1981)

---

[1] *K. H. Ott, F. W. Röllgen, J. J. Zwinselman, R. H. Fokkens, N. M. M. Nibbering*, Org. Mass Spectrom. *15*, 419 (1980).

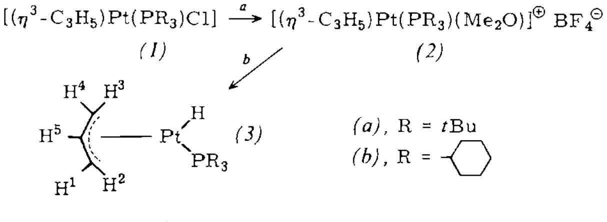
[2] *H.-R. Schulten, F. W. Röllgen*, Angew. Chem. *87*, 544 (1975); Angew. Chem. Int. Ed. Engl. *14*, 561 (1975); *H. J. Veith*, Org. Mass Spectrom. *11*, 629 (1976); *G. W. Wood, E. J. Oldenburg, P. Y. Lau*, Can. J. Chem. *56*, 2750 (1978).

## $\eta^3$-Allyl(hydrido)phosphaneplatinum(II) Complexes

By *Giovanni Carturan, Alberto Scrivanti,* and *Franco Morandini*[*]

We recently reported that allylpalladium(II) complexes are effective catalysts in the selective hydrogenation of dienes to monoolefins[1]; the understanding of the mechanistic facets of this reaction were in part speculative because of the impossibility of detecting the intermediate active species. Within a $d^8$—$d^{10}$ metal system, the process accounting for selective hydrogenation might involve as a fundamental step the equilibrium between allyl (hydrido)-$d^8$ and olefin-$d^{10}$ species. Indeed, this equilibrium, although frequently invoked in a variety of homogeneously catalyzed reactions, has been recognized only for a limited number of organometallic complexes[2,3].

Our current interest prompted us to prepare novel allyl (hydrido)platinum(II) complexes *(3)* as outlined in Scheme 1. Complexes *(1)* react in dimethyl ether with $AgBF_4$ to give the solvated species *(2)*, which on treatment with $NaBH_4$ form complexes *(3)* at −70 °C in good yield. The new complexes have been fully characterized by their $^1H$- and $^{31}P$-NMR spectra (Table 1).



Scheme 1. Synthesis of complexes *(3)*. Reaction conditions: *a)* $AgBF_4$, −40 °C, 6 h, $Me_2O$; *b)* $NaBH_4$, −60 °C, 48 h, THF; after THF evaporation in *vacuo*, *(3)* was extracted with toluene and crystallized by addition of pentane at −70 °C.

In analogy to the allyl(hydro)nickel(II) complexes[2], but at variance with the usual allylplatinum(II) complexes[4], compounds *(3)* display a dynamic behavior in the $^1H$-NMR spectrum even at low temperature. The presence of the strongly electron perturbing action of the hydride ligand may account for this fact; indeed, for compounds *(3)*—as for the nickel complexes—a substantial reduction of the coupling constant $J_{Pt-P}$ (of about 500 Hz) and a general upfield shift of the allylic proton signals with respect to those of the parent chloro complexes *(1)* was observed[4].

Compounds *(3)* are very unstable and decompose above −30 °C with propene evolution, even in the solid state. This instability is expected, for the behavior of alkyl(hydrido)platinum(II) derivatives suggests that the reductive elimination of $CH_2{=}CH{-}CH_2{-}H$ should be favored in allyl(hydrido)platinum(II) complexes[5]. This elimination reaction leads, in the case of allyl(hydrido)-complexes of $d^8$-metals, to extremely labile 14 electron species, a fact upon which the versatility and the large catalytic application of these compounds is based[6].

Received: April 8, 1980 [Z 660 IE]
German version: Angew. Chem. 93, 103 (1981)

Table 1. NMR data of allyl(hydrido)(tri-*tert*-butylphosphane)platinum(II) *(3a)* and allyl(hydrido)(tricyclohexylphosphane)platinum(II) *(3b)* (δ values, coupling constants in Hz). $^1H$-NMR in $CD_2Cl_2$ at −73 °C; $^{31}P\{^1H\}$ in toluene/$C_6D_6$ at −69 °C. The allyl-H atoms are numbered as in Scheme 1.

| Cpd. | Nucleus | Hydride | $H^1$ | $H^2$ | $H^3$ | $H^4$ | $H^5$ | Phosphane |
|---|---|---|---|---|---|---|---|---|
| *(3a)* | $^1H$ | −7.01<br>$J_{H-P}=27$, $J_{H-Pt}=1548$ | 3.61 |  | 2.22<br>$J_{3,5}=14$, $J_{H-Pt}=72$ | 3.78<br>$J_{4,5}=8$ | 4.13 | 1.35; $J_{H-P}=13$ |
|  | $^{31}P$ |  |  |  |  |  |  | +89.3; $J_{Pt-P}=3859$ |
| *(3b)* | $^1H$ | −6.25<br>$J_{H-P}=28$, $J_{H-Pt}=1505$ | 3.66 |  |  |  | 3.92 | 1.9—1.1 |
|  | $^{31}P$ |  |  |  |  |  |  | +43.5; $J_{Pt-P}=3782$ |

---

[*] Dr. G. Carturan [+], Dr. A. Scrivanti
Centro di Chimica Metallorganica del C.N.R.
Via Marzolo 9, I-35100 Padova (Italy)

Dr. F. Morandini
Centro di Chimica dei Composti di Coordinazione del C.N.R.
Via Marzolo 1, I-35100 Padova (Italy)

CAS Registry numbers:
*(1a)*, 70602-41-4; *(1b)*, 71035-50-2; *(2a)*, 76173-86-9; *(2b)*, 76173-88-1; *(3a)*, 76173-89-2; *(3b)*, 76173-90-5

---

[1] *G. Carturan, G. Strukul*, J. Organomet. Chem. *157*, 475 (1978); *G. Strukul, G. Carturan*, Inorg. Chim. Acta *35*, 99 (1979).

0570-0833/81/0101-0112 $ 02.50/0

[2] *H. Bönnemann*, Angew. Chem. *82*, 699 (1970); Angew. Chem. Int. Ed. Engl. 9, 736 (1970).

[3] *E. O. Sherman, P. R. Schreiner*, J. Chem. Soc. Chem. Commun. *1978*, 223; *J. F. Nixon, B. J. Wilkins*, J. Organomet. Chem. *80*, 129 (1974); *J. W. Byrne, H. U. Blaser, J. A. Osborn*, J. Am. Chem. Soc. *97*, 3871 (1975); *T. H. Tulip, J. A. Ibers, ibid. 101*, 4201 (1979); *E. L. Muetterties, J. R. Bleeke*, Acc. Chem. Res. *12*, 324 (1979).

[4] *G. Carturan, A. Scrivanti, B. Longato, F. Morandini*, J. Organomet. Chem. *172*, 91 (1979).

[5] *L. Abis, A. Sen, J. Halpern*, J. Am. Chem. Soc. *100*, 2915 (1978).

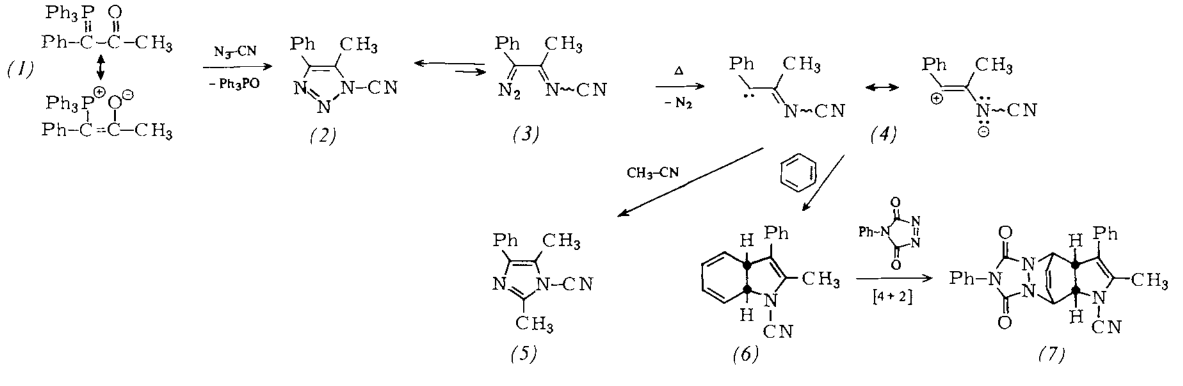
[6] *P. W. Jolly, G. Wilke:* The Organic Chemistry of Nickel. Vol. I and II. Academic Press, New York 1974 and 1975, respectively.

## Pronounced 1,3-Dipolar Cycloaddition Behavior of an α-Cyanimino Carbene[**]

By *Daniel Danion, Bernhard Arnold*, and *Manfred Regitz*[*]

Open-chain α-oxocarbenes such as benzoylmethyl or acetylmethyl carbene readily undergo Wolff rearrangement to ketenes, and only reluctantly undergo 1,3-dipolar cycloadditions—for instance, with acetonitrile—the yields of which are minimal and can be increased to a maximum of 17% only by addition of copper or copper compounds[1]. By way of contrast the α-cyanimino carbene *(4)* shows a pronounced readiness to undergo such cycloadditions.

A suitable starting material for the generation of *(4)* is the triazole-1-carbonitrile *(2)*, obtained in 90% yield by reaction of the methylenephosphorane *(1)* with cyanazide in dichloromethane/acetonitrile at 20 °C with concomitant formation of triphenylphosphane oxide [m.p. 140 °C; IR (KBr): $\nu_{C\equiv N} = 2260\ cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 2.65$ ($CH_3$)][2]. In spite of the pronounced tendency of 1,2,3-triazole-1-carbonitrile to undergo ring-opening[2], no α-diazoimine *(3)* can be detected alongside *(2)* in the equilibrium (no $C=N_2$ absorption in the IR spectrum ($CDCl_3$) at 20 °C); nevertheless, *(4)* is presumably formed under thermal conditions *via* a small equilibrium concentration of *(3)*.



When a solution of *(2)* in acetonitrile is heated under reflux for 10 h, 2,5-dimethyl-4-phenylimidazole-1-carbonitrile *(5)* is formed by [3+2]-cycloaddition of *(4)* to the solvent [yield 75%; m.p. 158 °C; IR (KBr): $\nu_{C\equiv N} = 2222\ cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 2.48, 2.58$ (each $CH_3$)]; the nitrile group in *(5)* can be readily cleaved by treatment with potassium hydroxide in ethanol[3]. *(4)* even adds to benzene (12 h reflux) with formation of 2-methyl-3-phenyl-3a,7a-dihydroindole-1-carbonitrile *(6)* as the sole reaction product [yield 80% m.p. 93 °C; IR (KBr): $\nu_{C\equiv N} = 2219$, $\nu_{C=C} = 1662\ cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 4.18$ (broad d, $^3J_{H\text{-}3a,H\text{-}7a} = 14.5$ Hz, H-7a), 4.90 (dd, $^3J_{H\text{-}3a,H\text{-}7a} = 14.5$ Hz, $^3J_{H\text{-}7,H\text{-}3a} = 4$ Hz, H-3a), 5.50, 6.18 (each m, H-4, H-7), 5.85 (m, H-5/H-6)][4].

As a 1,3-diene, *(6)* reacts with 1-phenyl-1,3,4-triazoline-2,5-dione (dichloromethane, 20 °C) in a [4+2]-cycloaddition to give *(7)* (m.p. 268 °C) in 86% yield. On heating with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone in benzene *(6)* is dehydrogenated to 2-methyl-3-phenylindole-1-carbonitrile (yield 70%; 89 °C); $^1H$-NMR ($CDCl_3$): $\delta = 2.54$ ($CH_3$), 7.0—7.6 (aromatic H).

The ketenimine rearrangement of *(4)* involving a 1,2-methyl shift[5], which is observed alongside OH insertion (ratio 25:75) in the photochemical decomposition of *(2)* in methanol, does not occur in the presence of the dipolarophile.

Received: August 22, 1980 [Z 671 IE]
German version: Angew. Chem. *93*, 118 (1981)

CAS Registry numbers:
*(1)*, 76068-72-9; *(2)*, 76068-73-0; *(3)*, 76068-74-1; *(5)*, 76068-75-2; *cis-(6)*, 76068-76-3; *(7)*, 76068-77-4; cyanazide, 764-05-6; 1-phenyl-1,3,4-triazoline-2,5-dione, 4233-33-4; 2-methyl-3-phenylindole-1-carbonitrile, 76068-78-5

---

[1] *R. Huisgen, G. Binsch, L. Ghosez*, Chem. Ber. *97*, 2228 (1964).

[2] For the method see *B. Arnold, M. Regitz*, Tetrahedron Lett. *1980*, 909.

[3] This leads to formation of 2,5-dimethyl-4-phenylimidazole: *A. Novelli, A. de Santis*, Tetrahedron Lett. *1967*, 265.

[4] It cannot be totally ruled out that *(4)* forms [2+1]-cycloadducts with the dipolarophiles, which subsequently isomerize to *(5)* and *(6)*, respectively.

[5] Cf. *B. Arnold, M. Regitz*, Angew. Chem. *91*, 337 (1979); Angew. Chem. Int. Ed. Engl. *18*, 320 (1979).

---

[*] Prof. Dr. M. Regitz, Dr. B. Arnold
Fachbereich Chemie der Universität
Paul-Ehrlich-Strasse, D-6750 Kaiserslautern (Germany)
Dr. D. Danion
Groupe de Recherches de Physicochimie Structurale
Faculté des Sciences de l'Université, B.P. 25 A,
F-35042 Rennes (France)

[**] Carbenes, Part 24. This work was supported by the Fonds der Chemischen Industrie.—Part 23: *M. Regnitz, H. Eckes*, Tetrahedron *37* (1981), in press.

## *anti*-[4+4]-Dicyclopentadiene

By *Wolfram Grimme, Lothar Schumachers, Rolf Gleiter*, and *Klaus Gubernator*[*]

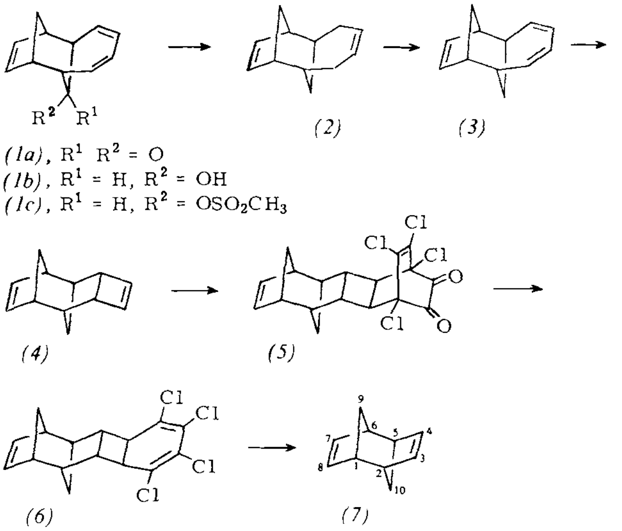
The [4+4]cycloadducts of conjugated carbocycles are more strained than their [2+2] and [2+4] structural isomers and are not directly accessible by thermal, photochemical or metal-catalyzed routes. Their high energy content and the interaction between the central σ-bonds, and the flanking double bonds, make this class of compounds of interest for ther-

---

[*] Dr. W. Grimme[+], Dipl.-Chem. L. Schumachers
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)
Prof. Dr. R. Gleiter, Dipl.-Chem. K. Gubernator
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[+] Author to whom correspondence should be addressed.

mal studies and photoelectron spectroscopic investigations. The *syn* stereoisomer of the title compound could be prepared[1] by partial ring opening of an appropriate cage compound in the key step. However, in the synthesis of the *anti*-[4+4]-cyclodimer of cyclopentadiene *(7)* we used an alternative procedure: ring contraction of its readily available tropone [4+6]-cycloadduct *(1a)*[2a].



*(1a)*, $R^1$ $R^2$ = O
*(1b)*, $R^1$ = H, $R^2$ = OH
*(1c)*, $R^1$ = H, $R^2$ = $OSO_2CH_3$

Table 1. Physical data for compounds *(2)* to *(7)*. $^1$H-NMR spectra were recorded at 90 MHz in $CCl_4$ [*(3)* in $CDCl_3$]; He(I)-PE spectra were recorded on a PS 18 spectrometer (Perkin-Elmer).

*(2)*, M.p. = 37 °C; $^1$H-NMR: $\delta = 6.02$ (m, 2H), 5.45 (m, 2H), 2.4 (m, 6H), 1.8 (m, 3H), 1.3 (m, 3H); $^{13}$C-NMR: $\delta = 135.08$, 128.48, 47.54, 38.02, 34.74, 30.50, 27.13

*(3)*, $^1$H-NMR: $\delta = 6.07$ (m, 4H), 5.96 (m, 2H), 2.77 (m, 2H), 2.43 (m, 2H), 1.65 (AB, $\Delta\nu = 100$ Hz, $J = 12.5$ Hz, part A split into triplets), 1.45 (AB, $\Delta\nu = 51$ Hz, $J = 10.5$ Hz, part B split into triplets); $^{13}$C-NMR: $\delta = 140.51$, 133.44, 126.30, 47.63, 35.49, 34.42, 25.36; MS: $m/e = 158$ ($M^+$), 92 ($M^+ - C_5H_6$, 100%), 91 ($C_7H_7^+$, 98%), 66 ($C_5H_6^+$); UV: $\lambda_{max} = 241$ ($\varepsilon = 5800$) sh, 250 (7100), 259 (7500), 269 nm (4800); PE: 8.25, 8.75, 10.3, 10.7 eV

*(4)*, $^1$H-NMR: $\delta = 6.02$ (m, 2H), 5.93 (s, 2H), 3.23 (s, 2H), 2.33 (m, 2H), 1.75 (m, 2H), 1.73 (AB, $\Delta\nu = 96$ Hz, $J = 10.5$ Hz, part B further split), 1.47 (m, 2H); MS: $m/e = 158$ ($M^+$), 92 ($M^+ - C_5H_6$, 85%), 91 ($C_7H_7^+$, 100%), 66 ($C_5H_6^+$)

*(5)*, dissociation temp. = 240 °C; MS: $m/e = 404$ ($M^+$), 378 ($M^+ - C_2H_2$), 322 ($M^+ - 2CO - C_2H_2$), 216 ($C_6H_2Cl_4^+$), 132 ($C_{10}H_{12}^+$), 106 ($C_8H_{10}^+$), 91 ($C_7H_7^+$), 78 ($C_6H_6^+$), 66 ($C_5H_6^+$); UV (acetonitrile): $\lambda_{max} = 235$ ($\varepsilon = 3000$) sh, 278 (1400), 435 nm (200)

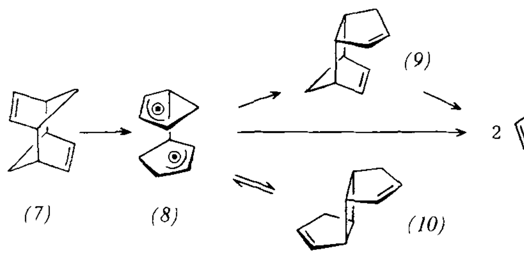
*(6)*, M.p. = 133 °C; $^1$H-NMR: $\delta = 5.94$ (s, 2H), 2.97 (s, 2H), 2.87 (m, 2H), 2.48 (m, 2H), 2.0—1.0 (m, 6H); MS: $m/e = 348$ ($M^+$), 216 ($C_6H_2Cl_4^+$), 132 ($C_{10}H_{12}^+$), 106 ($C_8H_{10}^+$), 91 ($C_7H_7^+$), 78 ($C_6H_6^+$), 66 ($C_5H_6^+$, 100%); UV (dioxane): $\lambda_{max} = 272$ ($\varepsilon = 2700$) sh, 287 (4000) sh, 297 (4800), 310 (4100) sh, 327 nm (1600) sh

*(7)*, M.p. = 135 °C in fused glass capilliary tube; $^1$H-NMR: $\delta = 6.08$ (s, 4H), 2.12 (m, 4H), 1.83 (AB, $\Delta\nu = 22.3$ Hz, $J = 9.0$ Hz, part B further split); $^{13}$C-NMR: $\delta = 134.81$ (C-3,4,7,8), 47.36 (C-9,10), 36.56 (C-1,2,5,6); MS: $m/e = 132$ ($M^+$, 3%), 66 ($C_5H_6^+$, 100%); UV (hexane): $\lambda_{max} = 211$ nm ($\varepsilon = 4500$); PE: 8.2, 9.8 eV

The *syn* alcohol *(1b)*, obtained by reduction of *(1a)* by diisobutylalane in dichloromethane, is transformed by treatment with methanesulfonyl chloride in ether/triethylamine into the ester *(1c)* (m.p. = 99 °C) in 82% yield; *(1c)* is then reduced to the hydrocarbon *(2)* (44%, for physical data see Table 1) by sodium in liquid $NH_3$/THF. Reaction of *(2)* with dichlorodicyano-*p*-benzoquinone in boiling $CCl_4$ gives *(3)* (55%), which in ether solution cyclizes to the four-membered ring compound *(4)* in 72% yield when photolyzed at 0 °C (Hanau Hg low-pressure lamp NK 6/20) through quartz. The assignment of the *exo* configuration to the photoproduct *(4)* follows from the absence of coupling between the aliphatic protons of the four-membered ring and the bridgehead protons, and from the small change in the chemical shift difference ($\Delta\delta = 1.06$ ppm) between the methylene protons of the norbornene part in going from *(3)* to *(4)*. The cyclobutene ring in *(4)* is degraded using the method of *Warrener et al.*[3], by first forming the cycloadduct *(5)* (74%)[4] with *o*-chloranil in $CCl_4$ (70 °C). Irradiation of a solution of *(5)* in dichloromethane with an incandescent lamp (Osram Bellaphot, 400 W) through Solidex gives the *bis* decarbonylated product *(6)* (69%). Compound *(6)* dissociates into a mixture of *anti*-tricyclo[4.2.1.1$^{2,5}$]deca-3,7-diene *(7)* and tetrachlorobenzene when photolyzed under similar conditions using a Hg high-pressure lamp (Philips HPK 125)[5]. The title compound *(7)* is separated from tetrachlorobenzene by column chromatography (silica gel, pentane) and from residual eluent by gas chromatography (10% DEGS, 0.5 m, 30 °C); it forms colorless crystals (38%) which have a high vapor pressure and a penetrating smell.

The PE spectrum of *(7)* is characterized by two broad bands of equal intensity at 8.2 and 9.8 eV; the large splitting ($\Delta IP = 1.6$ eV) of the vertical π-ionization potential is caused by the strong interaction between the double bonds and the central single bonds[6a]. This same electronic effect also manifests itself in the UV spectrum of *(7)*, the absorption maximum of which occurs at $\lambda = 211$ nm ($\varepsilon = 4500$); an unusually long wavelength for an unconjugated diene[6b].

The [4+4]-dicyclopentadiene *(7)* dissociates to the monomer at 180 °C by a [4+4]retrocyclization, which according to the rules of conservation of orbital symmetry[7] must proceed *via* the diradical *(8)*. Its intermediary is indeed indicated by small amounts of *endo*-[2+4]-dicyclopentadiene *(9)* and *anti-cis*-[2+2]-dicyclopentadiene *(10)*, products of recyclization, which under the reaction conditions also dissociate to the monomer[9,10].



The thermal behaviour of *anti*-[4+4]-dicyclopentadiene differs significantly from that of the *syn* stereoisomer[1], which at 58 °C forms *syn-cis*-[2+2]-dicyclopentadiene *via* a synchronous Cope rearrangement without giving the products of a radical process.

Received: August 14, 1980 [Z 657 IE]
German version: Angew. Chem. *93*, 98 (1980)

CAS Registry numbers:
*(1b)*, 68926-88-5; *(1c)*, 75993-66-7; *(2)*, 75993-67-8; *(3)*, 76024-05-0; *(4)*, 75993-68-9; *(5)*, 75993-69-0; *(6)*, 75993-70-3; *(7)*, 76024-06-1; *(9)*, 1755-01-7; *(10)*, 76024-07-2; *(11)*, 35522-50-0; *(12)*, 75993-71-4; *o*-chloranil, 2435-53-2

---

[1] *C. W. Doecke, G. Klein, L. A. Paquette*, J. Am. Chem. Soc. *100*, 1596 (1978); *101*, 7599 (1979).

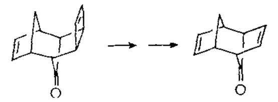
[2] a) *R. C. Cookson, B. V. Drake, J. Hudec, A. Morrison*, Chem. Commun. *1966*, 15; *S. Itô, Y. Fujise, T. Okuda, Y. Inoue*, Bull. Chem. Soc. Jpn. *39*, 1351 (1966); b) *S. Itô, I. Itoh, Y. Fujise, T. Nakatsu, C. A. Senkler, P. v. R. Schleyer*, *ibid. 51*, 2379 (1978).

[3] *E. E. Nunn, W. S. Wilson, R. N. Warrener*, Tetrahedron Lett. *1972*, 175.

[4] In addition to *(5)* a 2:1 adduct, caused by a second addition to the norbornene double bond, is formed.

[5] In the analogous degradation of the photoketone *(11)* (M.p. = 38 °C; *T. Mukai, Y. Akasaki, T. Hagiwara,* J. Am. Chem. Soc. *94*, 675 (1972)) was formed the *anti*-tricyclo[4.2.1.$1^{2,5}$]deca-3,7-dien-9-one *(12)* (dissociation temp. = 152 °C): *W. Mauer,* Dissertation, Köln 1978.

*(11)*



*(12)*

[6] a) MINDO/3 result [eV]: 8.61 ($a_g(\pi)$); 9.90 ($b_u(\pi)$); b) CNDO/S-CI result [nm]: 221.4, f = 0.000, $\pi^*(b_u) \leftarrow \pi(a_g)$; 210.0, f = 0.146, $\pi^*(a_g) \leftarrow \pi(a_g)$.

[7] *R. B. Woodward, R. Hoffmann,* Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).

[8] *G. S. Hammond, N. J. Turro, R. S. H. Liu,* J. Org. Chem. *28*, 3297 (1963).

[9] In the thermolysis of *anti*-[4+4]-dicyclopentadienone the corresponding recyclization products of the intermediate radical are formed: *U. Klinsmann, J. Gauthier, K. Schaffner, M. Pasternak, B. Fuchs,* Helv. Chim. Acta *55*, 2643 (1972).

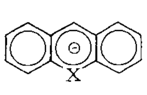
[10] The kinetic analysis of the dissociation of *(7)* has been carried out by Prof. *W. R. Roth,* Universität Bochum, and will be published separately.

---

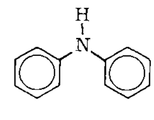
## Generation and NMR Spectroscopic Investigation of Diheteroanthracenide Ions: Stable 4nπ Systems[**]

By *A. G. Anastassiou, H. S. Kasmai,* and *M. R. Saadein*[*]

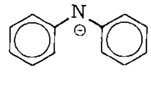
The three potentially antiaromatic 4*n*π systems *(1a)*—*(1c)* were recently prepared and analyzed (NMR) in our laboratories[1] to reveal, at least in the case of the first-row variants *(1a)*[1a] and *(1b)*[1b], the presence of well-developed molecular paratropicity. In an effort to assess the possible effect that increased π-frame electronegativity may have on the magnitude and/or nature of this ring current effect we next focussed our attention on a group of direct diheteroatomic relatives of *(1)*, namely the amide ions *(5)* and wish to briefly elaborate on our findings in the area.



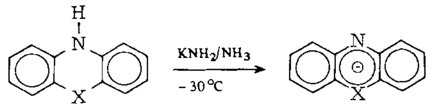
*(1)*



*(2)*



*(3)*



*(4)* → *(5)*

*(a)*, X = NMe
*(b)*, X = O
*(c)*, X = S

The desired diheteroanthracenide ions *(5a)*—*(5c)* were prepared as deeply colored, thermally stable solutions[2] by deprotonation of the amines *(4a)*—*(4c)* with $KNH_2$ in $NH_3$ at *ca.* −30 °C. For purposes of direct comparison the $^1$H-NMR spectra of the *N*-methyl-5,10-dihydrophenazine anion *(5a)* and phenooxazine anion *(5b)* are reproduced in Figure 1. As expected, the $^1$H-NMR spectrum of the phenothiazine anion *(5c)* is similarly patterned [δ = 5.7—6.2 (m, 6 H), 6.41 (dt, 2 H)], while that of the diphenylamide ion *(3)* is markedly different [δ = 6.0—6.4 (m, 2 H) and 6.7—7.1 (m, 8 H)]. The $^{13}$C-NMR data of the compounds described are collected in Table 1.

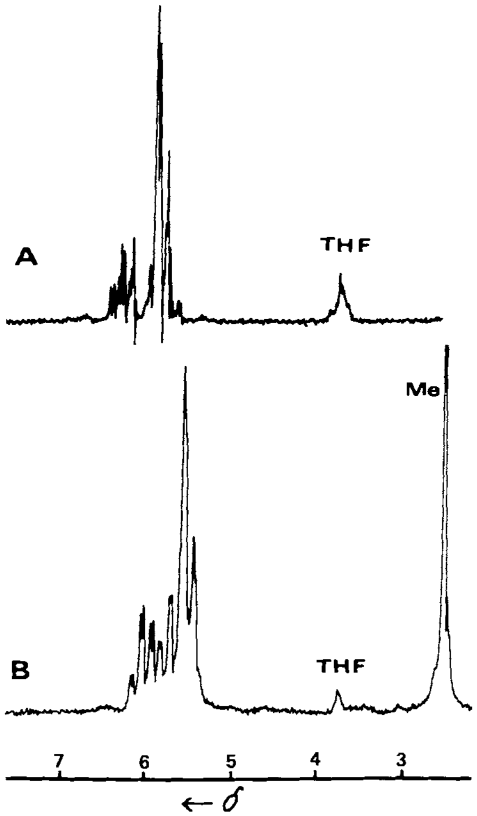


Fig. 1. 60-MHz $^1$H-NMR spectrum (A) of the phenoxazene anion *(5b)* and (B) of the N-methyl-9,10-dihydrophenazine anion *(5a)* in liquid ammonia (THF as internal standard) at *ca.* 34 °C.

Table 1. $^{13}$C-NMR data [a] of compounds *(2)*, *(3)*, *(4b)*, *(4c)*, *(5a)*—*(5c)*. The instability of 5,10-dihydrophenazine *(4a)* in liquid ammonia precludes the recording of a $^{13}$C-NMR spectrum.

| Cpd. | Chemical Shift [b]<br>tert. C-atoms | <br>quat. C-atoms |
|---|---|---|
| *(5a)* [c] | 40.51, 45.15, 45.74, 55.25 | 72.99, 86.62 [d] |
| *(5b)* | 44.02, 44.99, 48.31, 57.09 | 80.28, 82.72 [d] |
| *(5c)* | 47.00, 50.55, 57.74, 60.35 | 49.27, 89.05 [d] |
| *(4b)* | 46.49, 48.47, 53.48, 57.04 | 76.86, 66.64 |
| *(4c)* | 46.77, 54.20, 58.92, 59.96 | 49.75, 75.66 |
| *(2)* | 50.63, 53.11, 62.46 | 77.78 |
| *(3)* | 43.57, 50.86, 62.00 | 91.62 |

[a] The spectra were recorded at 60 MHz and *ca.* 30 °C in liquid ammonia containing *ca.* $10^{-1}$ cm$^3$ [D$_8$]tetrahydrofuran as standard. [b] δ values, referred to the central signal of the low-field multiplet of [D$_8$]THF ($\delta_{TMS} = -67.9$). [c] δ = −36.33 ($CH_3$). [d] C-9a.

Direct comparison of the $^1$H-NMR data of the anions *(5)* with those of the conjugate acids *(4)*, all of which exhibit bands in a region (δ = 6.5—7.0) normally reserved for mesomerically enriched benzenoid moieties, clearly reveals the "4*n*"-π diheteroanions *(5)* to be endowed with elements of molecular paratropicity. Additionally, internal comparison along these lines between *(5a)*, *(5b)*, and *(5c)* appears to establish the magnitude of the induced ring current to be largest in the former and smallest in the latter[3]. Interestingly, this interpretation gains credence from an analysis of the $^{13}$C-NMR data (Table 1) which appears to also offer a reasonable explanation as to why sulfur is less effective than either oxygen or nitrogen (NMe) in contributing its lone pair to the development of π delocalization in *(5)*. Specifically, one notes that whereas the signals of the tertiary carbons of

---

[*] Prof. Dr. A. G. Anastassiou [+], M. R. Saadein
Department of Chemistry, Syracuse University
Syracuse, New York 13210 (USA)
Prof. Dr. H. S. Kasmai
Department of Chemistry, Shiraz University, Shiraz (Iran)

[**] This work was supported by the National Science Foundation.

[+] Author to whom correspondence should be addressed.

*(5)* appear at increasingly high field on passing from *(5c)* to *(5b)* to *(5a)*, as required for increased $\pi$ participation of the system's two heteroatomic lone pairs, the degree of *overall* delocalization of the nitrogen-centered negative charge as assessed by the increasingly *downfield* shift of the directly adjacent quaternary carbon unit, *i. e.*, C-9a[4], is seen to implicate the existence of an alternate sequence namely *(5b)* ($\delta = 82.72$) < *(5a)* ($\delta = 86.62$) < *(5c)* ($\delta = 89.05$)!

We are thus faced with an interesting situation whereby the effectiveness of X in mobilizing the nitrogen-centered negative charge increases in the order S < O < NMe for extended delocalization into the benzenoid moieties and in the order O < NMe < S for *overall* but spacially limited participation. This apparent discrepancy, which was recently also shown to obtain in the case of the related monoheterocarbanions *(1)*[1], is best reasoned by the second-row nature of sulfur and its consequent ability to stabilize an adjacent negative charge be it inductively or *via* direct expansion of its "octet".

Finally, it is notable that whereas the data presented in this report relating to the "benzenoid" chemical shifts of *(5)* clearly implicate, at least in the case of the diaza derivative *(5a)*, the presence of a substantially delocalized distinctly paratropic molecular periphery, the effect does not appear to be as extensive as was recently observed with the monohetero carbanionic relatives *(1)*[1]. For obvious reasons the increased electronegativity of the negatively charged center on passing from *(1)* to *(5)* is believed to account for much of the observed differences.

Received: July 10, 1980 [Z 662 IE]
German version: Angew. Chem. *93*, 111 (1981)

CAS Registry numbers:
*(2)*, 122-39-4; *(3)*, 61057-05-4; *(4a)*, 20057-16-3; *(4b)*, 135-67-1; *(4c)*, 92-84-2; *(5a)*, 76069-02-8; *(5b)*, 76069-03-9; *(5c)* 76069-04-0

---

[1] a) *A. G. Anastassiou, H. S. Kasmai*, Angew. Chem. *92*, 53 (1980); Angew. Chem. Int. Ed. Engl. *19*, 43 (1980); b) *A. G. Anastassiou, H. S. Kasmai, M. R. Saadein*, Tetrahedron Lett. *1980*, 3743.

[2] The sample remained qualitatively and quantitatively unchanged (NMR) after 10 h exposure to ambient temperature.

[3] The centers of both major and minor absorption manifolds consistently undergo 0.2 to 0.25 ppm upfield shifts on passing from *(5c)* to *(5b)* to *(5a)*.

[4] An increase in the degree of amide ion delocalization ought to enhance the double bond character of the link connecting $-\overset{\ominus}{N}-$ to C-9a with consequent deshielding of the carbon center. Hence one's expectation that increased amide ion delocalization should lead to a downfield shift of the C-9a resonance.

---

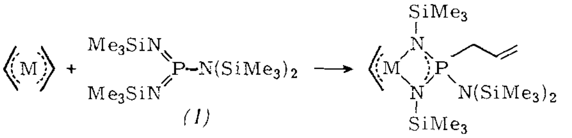
## Novel Nickel- and Palladium-Complexes with Aminobis(imino)phosphorane Ligands for the Polymerization of Ethylene[**]

By *Wilhelm Keim, Rolf Appel, Arnold Storeck, Carl Krüger*, and *Richard Goddard*[*]

Few investigations have been carried out on the influence of chelate ligands in homogeneous catalysis with transition metal compounds. As we discovered earlier, remarkable stereoselective effects can be achieved with bidentate ligands[1]. We report here on novel nickel- and palladium-complexes containing an aminobis(imino)phosphorane as chelate ligand.

The *in-situ* reaction of bis(1,5-cyclooctadiene)nickel or bis($\eta^3$-allyl)nickel with the aminobis(imino)phosphorane *(1)* in toluene yields a catalyst which polymerizes ethylene to polyethylene at 70 °C and 50 bar. Activities of 1000 mol ethylene per mol of nickel are achieved. The physical properties of the short-chain branched polymer lie between those of high-pressure polyethylene and "EPDM". Catalysts of this type are of interest because of their potential for the production of high-pressure polyethylenes.

In the stoichiometric reaction of bis($\eta^3$-allyl)nickel with *(1)* we isolated the complex *(2)*, whose structure followed from spectroscopic data ($^1$H-, $^{13}$C-, and $^{31}$P-NMR, IR), the mass spectrum ($M^+$ with the expected isotopic ratio) and the comparison of these data with those of the analogous palladium compound *(3)*. The formation of *(2)* proceeds *via* an unexpected allyl rearrangement, which leads to a P-bonded $\sigma$-allyl group.



*(2)*, M = Ni; *(3)*, M = Pd

The complex *(2)* contains a four-membered ring made up of two nitrogen atoms, the nickel atom, and the phosphorus atom. Four-membered rings of aminobis(imino)phosphoranes are well known[2], but so far not in combination with transition metals. With respect to electron distribution and bonding there exist resemblances to the phosphoniobis(methanide) derivatives described by *Schmidbaur*[3]. A sulfur analog of *(1)* could recently be complexed as "P=S side-on" ligand to platinum[4].

In analogy to the synthesis of *(2)* we also reacted bis($\eta^3$-allyl)palladium with *(1)* to give the remarkably stable complex

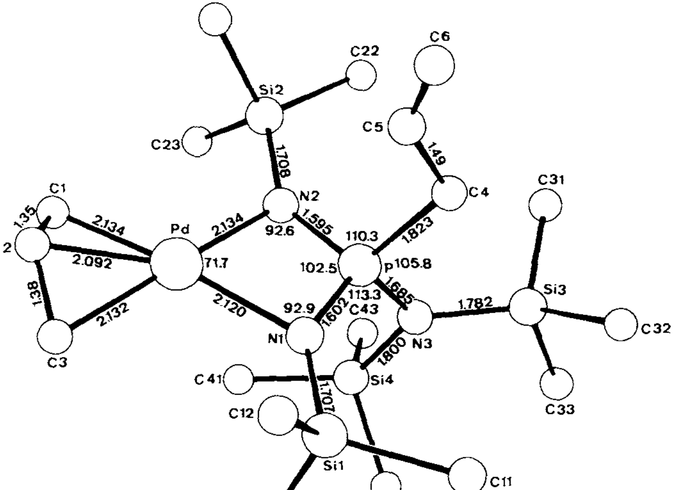


Fig. 1 Molecular structure of complex *(3)* in the crystal. Cell data: $a = 9.174$ (1), $b = 17.745$ (2), $c = 18.900$ (2) Å, $\beta = 104.610$ (7)°, space group $P2_1/c$, $Z = 4$ with $\rho_{calc} = 1.24$ gcm$^{-3}$, $R = 0.037$, $R_w = 0.04$.

---

[*] Prof. Dr. W. Keim [+], Dipl.-Chem. A. Storeck
Institut für Technische Chemie und Petrochemie
der Technischen Hochschule
Worringer Weg 1, D-5100 Aachen (Germany)
Prof. Dr. R. Appel
Anorganisch-chemisches Institut der Universität
D-5300 Bonn 1 (Germany)
Priv.-Doz. Dr. C. Krüger, Dr. R. Goddard
Max-Planck-Institut für Kohlenforschung
D-4330 Mülheim-Ruhr 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

[+] Author to whom correspondence should be addressed.

*(3)*. The $^1H$-, $^{13}C$-, and $^{31}P$-NMR spectra as well as the IR spectrum corresponded to those of *(2)*. The mass spectrum shows the molecular ion with the expected ratio of isotopes.

A crystal structure analysis was carried out on *(3)* (Fig. 1). The primary skeleton of the molecule is characterized by its near $C_s$(m) symmetry, the mirror plane running through N3, P, Pd and C2 perpendicular to a planar ($\pm 0.03$ Å) four-membered ring formed from Pd, P, N1 and N2. Only the arrangement of the trimethylsilyl groups at N1 and N2 do not correspond to this symmetry. The terminal atom C6 of the allyl group is disordered. The phosphorus atom has approximate tetrahedral configuration. Like the Si—N bonds the P—N bonds are of varying length. Thus, in the strained four-membered ring[5] we find on average P—N = 1.598 Å, and thus high multibonding character. The length of the exocyclic P—N bond (1.685 Å) in comparison with the sum of the covalent radii of the two atoms (1.84 Å) is likewise indicative of multibonding character, albeit to a lesser extent. As complex ligand the R—N—$PR_2$—N—R group, like the isoelectronic phosphoniobis(methide) group ($H_2C$—$PR_2$—$CH_2$)[6], is to be regarded as a three-electron donor with analogous geometry and bonding. Thus a 15-electron configuration is present at the central palladium, like in the educt bis($\eta^3$-allyl)palladium.

The palladium complex *(3)* cannot catalyze the polymerization of ethylene. Dry *(3)* is air-stable for several days at room temperature, but decomposes within hours at 50 °C.

### *Procedure*

All operations must be carried out under argon.

*(2)*: A solution of *(1)*[8] (6.8 g, 0.019 mol) in toluene (15 $cm^3$) was added dropwise within 30 min at −78 °C to a stirred suspension of bis($\eta^3$-allyl)nickel[7] (2.5 g, 0.018 mol) in toluene (10 $cm^3$). A reddish brown solution was formed. After standing for several days at −78 °C, red-brown crystals separated out (1.17 g); on concentration of the mother-liquor and addition of a small amount of dichloromethane a further 3.1 g could be isolated. Total yield 4.27 g (47%) of *(2)*, m.p. 135 °C (dec.).

*(3)*: *(1)* (5.5 g, 0.015 mol) was added dropwise within 3 min at −20 °C into a solution of bis($\eta^3$-allyl)palladium[9] (2.8 g, 0.015 ml) in toluene (20 $cm^3$). After *ca.* 12 hours' stirring at room temperature the solvent was removed in an oil-pump vacuum and the residue taken up in 10 ml dichloromethane: Yellowish-green crystals precipitated at −15 °C. Yield: 3.53 g (43%) *(3)*, m.p. 95—96 °C (dec.).

Received: July 14, 1980 [Z 649 IE]
German version: Angew. Chem. *93*, 91 (1980)

CAS Registry numbers:
*(1)*, 52111-28-1; *(2)*, 75949-58-5; *(3)*, 75949-59-6; bis($\eta^3$-allyl)nickel, 12077-85-9; bis($\eta^3$-allyl)palladium, 12240-87-8

---

[1] a) *W. Keim, F. H. Kowaldt, R. Goddard, C. Krüger*, Angew. Chem. *90*, 493 (1978); Angew. Chem. Int. Ed. Engl. *17*, 466 (1978); b) *W. Keim, B. Hoffmann, R. Lodewick, M. Peuckert, G. Schmitt*, J. Mol. Catal. *6*, 79 (1979).

[2] a) *R. Appel, M. Halstenberg, F. Knoll*, Z. Naturforsch. *B 32*, 1030 (1977); b) *O. J. Scherer, W. Glässel*, Chem. Ber. *110*, 3874 (1977).

[3] *H. Schmidbaur*, Acc. Chem. Res. *8*, 62 (1975).

[4] *O. J. Scherer, H. Jungmann*, Angew. Chem. *91*, 1020 (1979); Angew. Chem. Int. Ed. Engl. *18*, 953 (1979).

[5] *E. Niecke, W. Flick, S. Pohl*, Angew. Chem. *88*, 305 (1976); Angew. Chem. Int. Ed. Engl. *15*, 309 (1976).

[6] a) *H. H. Karsch, H. Schmidbaur*, Chem. Ber. *107*, 3684 (1974); b) *H. H. Karsch, H.-F. Klein, C. G. Kreiter, H. Schmidbaur, ibid. 107*, 3692 (1974); c) *D. J. Brauer, C. Krüger, P. J. Roberts, Y.-H. Tsay, ibid. 107*, 3706 (1974).

[7] a) *B. Bogdanović*, Dissertation, Technische Hochschule Aachen 1962; b) *G. Wilke, B. Bogdanović*, Angew. Chem. *73*, 756 (1961).

[8] *O. J. Scherer, N. Kuhn*, Chem. Ber. *107*, 2123 (1974).

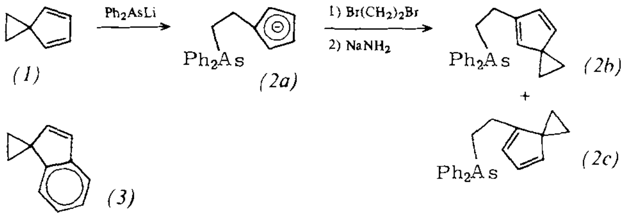
[9] a) *W. Keim*, Dissertation, Technische Hochschule Aachen 1963; b) *G. Wilke, B. Bogdanović, P. Hardt, P. Heimbach, W. Keim, M. Kröner, W. Oberkirch, K. Tanaka, E. Steinrücke, D. Walter, H. Zimmermann*, Angew. Chem. *78*, 157 (1966); Angew. Chem. Int. Ed. Engl. *5*, 151 (1966).

## Synthesis of Multielectron Ligands for Transition Metals *via* Spiro[cyclopropane-1,1′-indene][**]

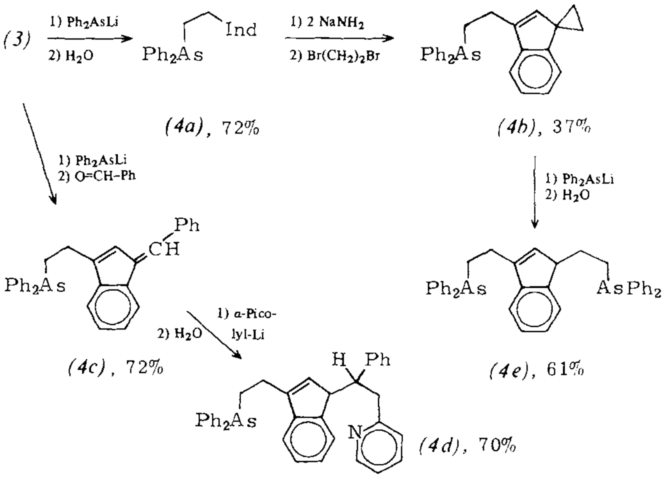
By *Karlheinz Berghus, Angelika Hamsen, Alfons Rensing, Annegret Woltermann* and *Thomas Kauffmann*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

We have recently shown that spiro[2.4]hepta-4,6-diene *(1)* is highly suitable for the synthesis of multielectron ligands for transition metals[1]. As anticipated, analogous ligands *e.g.* *(4a)*, *(5a)*, *(6a)*, and *(6b)* (Ind = 3-indenyl) can be prepared from spiro[cyclopropane-1,1′-indene] *(3)* by similar transformations[2].



Attempts to extend the donor capability of the compounds obtained by addition of a cyclopentadienyl- or indenyl group as five-electron donor[3] demonstrated the expected superiority of indene derivatives for this purpose. Thus, while the reaction of *(2a)*[1] with 1,2-dibromoethane and sodamide led to an (as yet) inseparable mixture of the isomers *(2b)* and *(2c)*, the corresponding reaction of the indene derivative *(4a)*→*(4b)* and the comparable reactions *(3)*→*(4c)* and *(5a)*→*(5b)* gave single products.



*(4b)* and *(4c)* were coupled with a further 2-electron donor group and by this means the potential 9-electron ligands *(4e)* and *(4d)*[4] respectively, were obtained.

---

[*] Prof. Dr. Th. Kauffmann, K. Berghus, A. Hamsen, Dipl.-Chem. A. Rensing, A. Woltermann
Organisch-Chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

[**] Multielectron Ligands, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Part 1: [1].

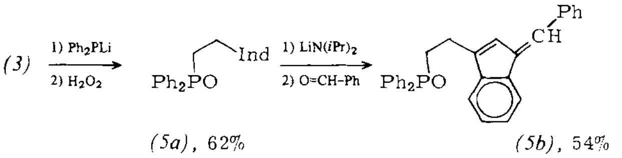
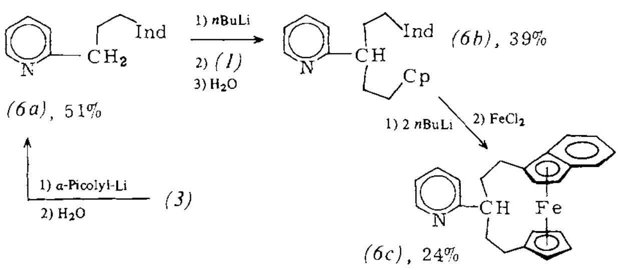


Table 1. Physical Data of the cited compounds. $^1$H-NMR; δ values rel. to TMS in CDCl$_3$; Mass spectra 70 eV, *m/e*.

| Compound | M.p. or *n* | $^1$H-NMR | MS |
|---|---|---|---|
| *(4a)* | 71 °C (Ethanol) | 2.2—2.9 (m; 4 H, As—CH$_2$—CH$_2$), 3.2 (mc; 2 H, C*H*$_2$—CH=), 6.15 (mc; 1 H, =CH—), 7.0—7.65 (m; 14 H, aromatic H) | 372 (6%, *M*$^+$), 229 (24), 227 (51), 219 (45), 152 (100), 143 (26), 128 (48), 115 (34) |
| *(4b)* | $n_D^{30}$ = 1.6495 | 1.51 (s; 4 H, CH$_2$—CH$_2$—C), 2.2—2.9 (m; 4 H, As—CH$_2$—CH$_2$), 5.92 (s; 1 H, =CH—), 7.0—7.6 (m; 14 H, aromatic H) | 398 (69%, *M*$^+$), 229 (63), 227 (75), 169 (100), 141 (88), 129 (31), 115 (31) |
| *(4c)* | 134 °C (Toluene) | 2.2—3.1 (m; 4 H, As—CH$_2$—CH$_2$), 6.83 (s; 1 H, =C—CH=), 7.1—7.8 (m; 20 H, Ph—C*H*, aromatic H) | 460 (39%, *M*$^+$), 432 (2), 307 (61), 231 (100), 229 (61), 227 (67), 115 (24) |
| *(4d)* | $n_D^{20}$ = 1.6259 | 1.9—2.8 (m; 4 H, As—CH$_2$—CH$_2$), 3.1—4.1 (m; 4 H, C*H*$_2$—C*H*PhC*H*), 6.3 (mc; =CH—), 6.7—7.6 (m; 22 H, aromatic H), 8.3—8.6 (m; 1 H, N—CH) | 553 (19%, *M*$^+$), 461 (18), 324 (3), 229 (16), 227 (16), 182 (18), 93 (100) |
| *(4e)* | $n_D^{30}$ = 1.6551 | 1.6—2.8 (m; 8 H, As—CH$_2$—CH$_2$), 3.3—3.5 (m; 1 H, CH—), 6.15 (mc; 1 H, =CH—), 6.9—7.5 (m; 24 H, aromatic H) | 628 (38%, *M*$^+$), 399 (19), 229 (43), 227 (43), 149 (100), 128 (24), 115 (13) |
| *(5a)* | 155—156 °C (Ligroin) | 2.4—3.0 (m; 4 H, P—CH$_2$—CH$_2$), 3.25 (mc; 2 H, C*H*$_2$—CH=), 6.2 (mc; 1 H, =CH—), 7.0—7.9 (m; 14 H, aromatic H) | 344 (65%, *M*$^+$), 215 (100), 202 (71), 201 (30), 155 (10), 115 (9) |
| *(5b)* | 200—201 °C (Toluene) | 2.5—3.15 (m; 4 H, P—CH$_2$—CH$_2$), 6.72 (s; 1 H, =CH—C=), 7.5—7.9 (m; 20 H, Ph—C*H*=, aromatic H) | 432 (54%, *M*$^+$), 344 (10), 230 (100), 215 (67), 202 (57), 155 (13), 115 (8) |
| *(6a)* | $n_D^{20}$ = 1.5849 | 1.95—3.0 (m; 6 H, (CH$_2$)$_3$), 3.3 (mc; 2 H, =CH—C*H*$_2$), 6.2 (mc; 1 H, =CH—), 6.9—7.6 (m; 7 H, aromatic H), 8.35—8.6 (m; 1 H, N—CH) | 235 (21%, *M*$^+$), 141 (7), 128 (12), 115 (10), 106 (13), 93 (100) |
| *(6b)* | $n_D^{20}$ = 1.5798 | 1.8—2.6 (m; 8 H, CH$_2$—CH$_2$), 2.85, 2.95 (2 mc; 2 H, =CH—C*H*$_2$[Cp]), 2.85—2.95 (m; 1 H, >CH—), 3.3 (mc; 2 H, (=CH—C*H*$_2$[Ind]), 5.95—6.4 (m; 4 H, =CH—), 6.9—7.7 (m; 7 H, aromatic H), 8.5—8.7 (m; 1 H, N—CH) | 327 (4%, *M*$^+$), 235 (7), 185 (6), 128 (10), 115 (5), 106 (100) |
| *(6c)* | $n_D^{20}$ = 1.6434 | in C$_6$D$_6$: 2.0—2.7 (m; 8 H, CH$_2$—CH$_2$), 2.95 (m; 2 H [Cp]), 3.7 (mc; 1 H [Cp]), 3.98 (d; 1 H [Ind]), 4.4 (mc; 1 H [Cp]), 4.5—4.8 (m; 1 H, CH—), 4.85 (d; 1 H [Ind]), 6.65—7.6 (m; 7 H, aromatic H), 8.6 (m; 1 H, N—CH) | 381 (47%, *M*$^+$), 276 (14), 142 (6), 115 (11), 106 (9), 84 (100) |

The ligands with the indenyl group have the distinctive feature, not shown by the cyclopentadienyl analogues, that they endow their transition metal complexes with chirality; the stable iron complex *(6c)*[4] was prepared by us and illustrates this capability. This feature could be useful in the development of asymmetric homogeneous catalysts.



The structures of the products have been determined by mass- and NMR-spectroscopy and elemental analysis (see Table 1).

Received: March 24, 1980 [Z 668a IE]
German version: Angew. Chem. 93, 116 (1981)

CAS Registry numbers:
*(1)*, 765-46-8; *(3)*, 19770-38-8; *(4a)*, 76124-28-2; *(4b)*, 76124-29-3; *(4c)*, 76124-30-6; *(4d)*, 76124-31-7; *(4e)*, 76124-32-8; *(5a)*, 76124-33-9; *(5b)*, 76124-34-0; *(6a)*, 76124-35-1; *(6b)*, 76124-36-2; *(6c)*, 76137-11-6; Ph$_2$AsLi, 19061-48-4; Ph$_2$PLi, 4541-02-0; O=CH—Ph, 100-52-7; α-picolyl-Li, 1749-29-7; Br(CH$_2$)$_2$Br, 106-93-4;

---

[1] *Th. Kauffmann, J. Ennen, H. Lhotak, A. Rensing, F. Steinseifer, A. Woltermann,* Angew. Chem. *92*, 321 (1980); Angew. Chem. Int. Ed. Engl. *19*, 328 (1980).

[2] In the absence of synthetic details [*S. W. Staley, M. A. Fox, T. K. Hirzel,* J. Am. Chem. Soc. *98*, 3910 (1976)] we obtained a 58% yield by reacting a solution of indene in THF with 2 equivalents NaNH$_2$ and 1 equivalent 1,2-dibromoethane.

[3] Conventional count of electrons in donor ligand with transition metals.

[4] The position of the CC double bond in the five-membered ring of the indene residue of *(4d)* is not clear. The compound *(6b)* consists of a mixture of the isomers with Cp = 1,3- or 1,4-cyclopentadienyl respectively. It should be possible to separate *(6c)* into two diastereomers, but to date this has been unsuccessful.

## Crown Arsanes; Air-Stable Multielectron Ligands for Transition Metals[**]

By *Johann Ennen* and *Thomas Kauffmann*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

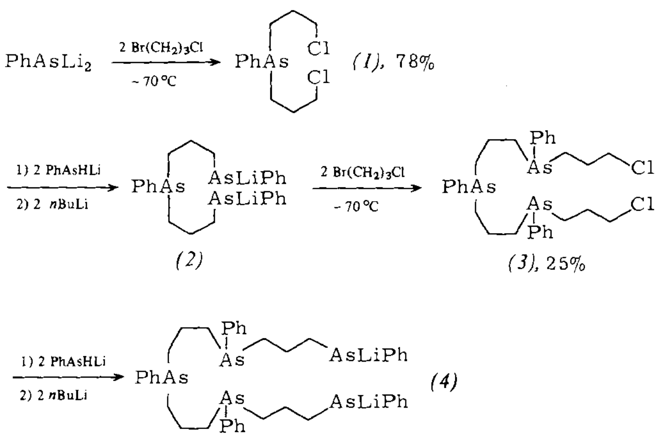
Many of the transition metal reagents and catalysts used in organic synthesis contain ligands which do not participate directly in the reaction ("passive ligands"[2]) and which are often not optimal (low stability of bonding to the metal, easily attacked by nucleophiles, or toxic ligands such as CO or NO). We have therefore synthesized polydentate multi, electron ligands[1,2] and now wish to describe macrocyclic polyarsanes. These "crown arsanes" are air stable and are therefore considerably easier to handle and store than the highly air sensitive macrocyclic polyphosphanes[3]. Both types of compounds suffer from the disadvantage however that the isolation of pure chiral products is difficult. To our knowledge crown arsanes were not known[4], although open chain polyarsanes have already frequently been used to complex with transition metal elements.

The starting materials *(1)*, *(2)*, *(3)*, and *(4)*, which are not described in the literature, were synthesized (reactions were

---

[*] Prof. Dr. Th. Kauffmann, Dipl.-Chem. J. Ennen
Organisch-Chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

[**] Multielectron Ligands, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft. Part 2: [1].



carried out in THF at 20 °C unless otherwise stated)[5]. Of these, only the electrophiles *(1)* and *(3)* were isolated [*(3)*; yield 25% relative to *(1)*]. In this connection it was advantageous that the arsane group reacted with alkyl halides much less readily than the phosphane group.

Using the principle of dilution (all reactions carried out at 20 °C in THF) oily fractions of the crown arsanes *(5)—(7)*[6] were obtained from the starting materials and were cleaned by passing through a chromatographic column (SiO$_2$: diethylether/pet. ether 1:20) and isolated by chromatography. Stereoisomeric mixtures were obtained; this also applied to *(3)*.

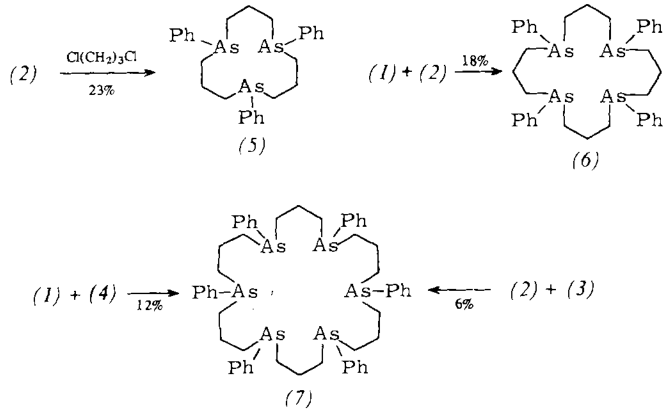


Table 1. Physical data of the compounds obtained. $^1$H-NMR; δ-values rel. TMS in CDCl$_3$. Mass spectra; 70 eV, *m/e* [a]

| Cpd. | M.p. or *n* | $^1$H-N.M.R. | MS |
|---|---|---|---|
| *(1)* | $n_D^{20}$ = 1.5691 | 7.23—7.68 (m; 5H),<br>3.33—3.71 (m; 4H),<br>1.75—2.12 (m; 8H) | 306 ($M^+$, 4.2%), 229 (15), 189 (25), 187 (100), 153 (19), 151 (19), 78 (19) |
| *(3)* | Oil [b] | 7.12—7.68 (m; 15H),<br>3.34—3.65 (m; 4H),<br>1.53—2.12 (m; 20H) | 617 ($M^+$ −78, 37%), 425 (37), 423 (98), 311 (92), 227 (54), 187 (100), 119 (56), 117 (60) |
| *(5)* | Oil [b] | 7.07—7.71 (m; 15H),<br>1.82—2.14 (m; 18H) | 581 ($M^+$ − 1, 2%), 539 (45), 505 (48), 463 (100), 346 (51), 311 (75), 227 (84) |
| *(6)* | 106.5 °C [c] | 7.18—7.63 (m; 20H),<br>1.51—2.11 (m; 24H) | 775 ($M^+$ − 1, 2%), 733 (29), 699 (17), 463 (30), 423 (33), 346 (74), 311 (71), 227 (100), 187 (48), 153 (76) |
| *(7)* | Oil [b] | 7.13—7.53 (m; 30H),<br>1.35—2.17 (m; 36H) | 1164 ($M^+$, 0.2%), 1122 (1), 969 (1), 811 (4), 617 (34), 423 (88), 403 (38), 227 (100), 187 (81), 153 (84) |

[a] For $^{35}$Cl-isotope. [b] Oily isomeric mixture. [c] From pet. ether (60—90 °C).

The crystals which separated from the crown arsane *(6)* fraction (32% of fraction) had a sharp melting point (106.5 °C) and this led us to believe that only one product had been formed.

The structures of the isolated compounds *(1)*, *(3)*, *(5)—(7)* are consistent with the elemental analyses, and mass and $^1$H-NMR spectral data (Table 1).

Received: March 24, 1980 [Z 668b IE]
German version: Angew. Chem. *93*, 117 (1981)

CAS Registry numbers:
*(1)*, 75396-00-8; *(2)*, 76124-37-3; *(3)*, 76124-38-4; *(4)*, 76135-99-4; *(5)*, 76124-39-5; *(6)*, 76124-40-8; *(7)*, 76124-41-9; PhAsLi$_2$, 1073-41-2; PhAsHLi, 40965-94-4; Br(CH$_2$)$_3$Cl, 109-70-6; Cl(CH$_2$)$_3$Cl, 142-28-9

---

[1] *K. Berghus, A. Hamsen, A. Rensing, A. Woltermann, Th. Kauffmann*, Angew. Chem. *93*, 116 (1981); Angew. Chem. Int. Ed. Engl. *20*, 117 (1981).

[2] *Th. Kauffmann, J. Ennen, H. Lhotak, A. Rensing, F. Steinseifer, A. Woltermann*, Angew. Chem. *92*, 321 (1980); Angew. Chem. Int. Ed. Engl. *19*, 328 (1980).

[3] *L. Horner, H. Kunz, P. Walach*, Phosphorus *6*, 63 (1975); *L. Horner, P. Walach, H. Kunz*, Phosphorus Sulfur *5*, 171 (1978); *T. A. DelDonno, W. Rosen*, J. Am. Chem. Soc. *99*, 8051 (1977); Inorg. Chem. *17*, 3714 (1978); *E. P. Kyba, C. W. Hudson, M. J. McPhaul, A. M. John*, J. Am. Chem. Soc. *99*, 8053 (1977).

[4] *A. Tzschach, J. Heinicke*: Arsenheterocyclen. VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1978.

[5] For the preparation of PhAsLiH and PhAsLi$_2$, see *A. Tzschach, G. Pacholke*, Chem. Ber. *97*, 419 (1964).

[6] The yields of *(5)*, *(6)*, and *(7)* are calculated relative to *(1)*, the assumption being made that the formation of *(2)* from *(1)* as well as *(4)* from *(3)* is quantitative.

## Alkyl(dicyclopentadienyl)lutetium Complexes: Monomeric Alkyllanthanoid Derivatives[**]

By *Herbert Schumann, Wolfgang Genthe*, and
*Norbert Bruncks*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

Alkyl derivatives of lanthanoids of low coordination number are very unstable. Hitherto, the isolation of such derivatives at room temperature could be accomplished only with sterically very demanding alkyl groups, with possible association *via* basic ligands or with formation of multinuclear electron-deficient compounds[1]. According to X-ray structure analysis the cyclopentadienyl(methyl)lanthanoid derivatives[2] first described in 1975 are dimeric with CH$_3$ bridges between two lanthanoid atoms[3].

We have now found that dicyclopentadienyllutetium chloride reacts with organolithium compounds in tetrahydrofuran at −78 °C to give monomeric alkyl(dicyclopentadienyl)lutetium derivatives, some of which are remarkably thermostable. Whereas the methyl, ethyl and *n*-butyl derivatives can be detected only NMR spectroscopically in benzene at room temperature as 1:1 complexes with tetrahydrofuran (THF) we have been able to isolate corresponding compounds with larger alkyl or aryl ligands as colorless to pale yellow needles which are stable up to 100 °C (Table 1).

---

[*] Prof. Dr. H. Schumann, Dipl.-Chem. W. Genthe, Dipl.-Chem. N. Bruncks
Institut für Anorganische und Analytische Chemie der technischen Universität Berlin
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] Organometallic Compounds of the Lanthanoids, Part 8. This work was supported by the Fonds der Chemischen Industrie and by the Senator für Wirtschaft des Landes Berlin (ERP grant, Project 2327).—Part 7: *H. Schumann, G. M. Frisch*, Z. Naturforsch. *B 34*, 748 (1979).

Table 1. NMR spectroscopic data of the complexes *(1)*; δ values, in $C_6D_6$, measured relative to benzene and converted with reference to TMS external, $\delta(^1H_{benzene}) = 7.27$, $\delta(^{13}C_{benzene}) = 129$ [a].

| Cpd. | R | Dec. pt. [°C] | $^1$H-NMR $H_\alpha$ | $H_\beta$ | $H_\gamma$ | $H_\delta$ | $H_\varepsilon$ | $^{13}$C-NMR $C_\alpha$ | $C_\beta$ | $C_\gamma$ | $C_\delta$ | $C_\varepsilon$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *(1a)* | $CH_3$ | — | −0.62 s | | | | | | | | | |
| *(1b)* | $C_2H_5$ | — | 0.16 q | 1.77 t | | | | | | | | |
| *(1c)* | $C_4H_9$ | — | 0.15 m | ← 1.27 m → | | | | | | | | |
| *(1d)* | $C(CH_3)_3$ | 70—80 | — | 1.39 s | | | | 38.6 | 36.8 | | | |
| *(1e)* | $CH_2C(CH_3)_3$ | 90—100 | 0.27 s | — | 1.51 s | | | 37.6 | 62.6 | 38.3 | | |
| *(1f)* | $CH_2Si(CH_3)_3$ | 100—110 | −0.63 s | — | 0.55 s | | | 28.3 | — | 5.9 | | |
| *(1g)* | $CH_2C_6H_5$ | 100—110 | 1.97 s | — | ← 7.45 m, 7.37 m, 7.17 m → | | | 48.6 | 128.9 | 125.7 | 118.4 | |
| *(1h)* | $C_6H_4—CH_3$-*p* | 110—120 | — | 7.93 d, ($J = 7$ Hz) | 7.39 d | — | 2.49 s | 184.2 | 142.2 | 129.7 | 134.3 | 22.6 |

[a] Additional $^1$H-NMR signals: 6.15—6.25 (s, $C_5H_5$), 3.3, 1.3 (m, THF); additional $^{13}$C-NMR signals: 111.82—110.79 (5, $C_5H_5$), 73, 26 (m, THF).

$$(C_5H_5)_2LuCl + LiR \xrightarrow[-78\,^\circ C]{THF} (C_5H_5)_2LuR \cdot THF + LiCl$$

*(1a)—(1h)*

The X-ray structure analysis of the trimethylsilylmethyl derivative *(1f)* (Fig. 1) shows that the lutetium is surrounded by a distorted tetrahedral array of the methylene carbon C1, the oxygen of the THF, and the centers of the two cyclopentadienyl ligands. The distance between lutetium and C1 is only about 11 pm shorter than the Yb—C distance in dimeric dicyclopentadienyl(methyl)ytterbium, in which the methyl group bridges two ytterbium atoms[3]. The surprisingly large bond angle of 131 °C at C1 is determined by the spatial requirement of the trimethylsilyl group bound to the same C-atom, and the cyclopentadienyl and THF ligands around the lutetium.

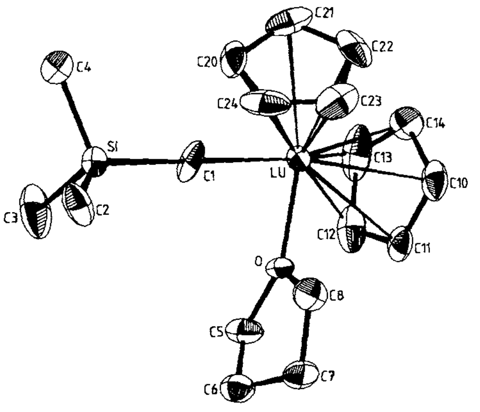


Fig. 1. Structure of $(C_5H_5)_2LuCH_2Si(CH_3)_3 \cdot THF$ *(1f)*; orthorhombic, space group $P2_12_12_1$, $Z = 4$, $a = 1738.1(8)$, $b = 1226.8(3)$, $c = 917.0(3)$ pm, $V = 1.955 \times 10^9$ pm$^3$, $\rho_c = 1.58$ g/cm$^3$; 2735 independent reflections; Syntex $P2_1$ four-circle diffractometer $R = 0.058$. Important bond lengths and angles: Lu—C1 238, Lu—O 229, Lu—RingI 235, Lu—RingII 234, Si—C1 183 pm; Lu—C1—Si 131, C1—Lu—O 96, O—Lu—RingI 106, RingI—Lu—RingII 130, RingII—Lu—C1 111, O—Lu—RingII 104, RingI—Lu—C1 105°.

The new compounds *(1a)—(1h)* are extremely sensitive towards moisture and oxygen. On hydrolysis all the ligands are removed from the lutetium with formation of $Lu(OH)_3$. *(1f)* forms stoichiometric amounts of cyclopentadiene, tetramethylsilane and THF. With $I_2$, on the other hand, only the alkyl moiety is removed; reaction of *(1f)* and $I_2$ leads to $(C_5H_5)_2LuI \cdot THF$ and $(CH_3)_3SiCH_2I$. In the thermolysis of *(1e)* and *(1f)*, which commences at 100 °C, THF is first removed and then at 130 °C [*(1e)*] or 180 °C [*(1f)*] the alkyl residue; *(1e)* yields, *via* β-elimination, isobutane and isobutylene in equimolar amounts, whereas tetramethylsilane is formed from *(1f)*. Above 300 °C the remaining $(C_5H_5)_2Lu$ fragments comproportionate with formation of $(C_5H_5)_3Lu$ which sublimes at this temperature.

### *Procedure*

A solution of $LuCl_3$ (3.3 g, 11.8 mmol) in THF (50 cm$^3$) is treated at room temperature with 9.5 cm$^3$ of a 2.58 M solution of $NaC_5H_5$ in THF and the mixture stirred for 1 h. After cooling to −78 °C, 16 cm$^3$ of a 0.756 M solution of $LiCH_2Si(CH_3)_3$ in pentane is added dropwise and the reaction mixture stirred for 2 h at −78 °C and 6 h at 25 °C. The solvent is removed and the residue dried at room temperature and extracted with toluene (3 × 200 cm$^3$). The residue is dissolved in pentane/diethyl ether (20:1) and cooled within 2 days to −30 °C; yield 4.4 g (81%) yellow needles.

Received: August 5, 1980 [Z 682a IE]
German version: Angew. Chem. *93*, 126 (1981)

CAS Registry numbers:
*(1a)*, 76207-05-1; *(1b)*, 76207-06-2; *(1c)*, 76207-07-3; *(1d)*, 76207-08-4; *(1e)*, 76207-09-5; *(1f)*, 76207-10-8; *(1g)*, 76207-11-9; *(1h)*, 76207-12-0; $Cp_2LuCl$, 76207-13-1; $LiCH_3$, 917-54-4; $LiC_2H_5$, 811-49-4; $LiC_4H_9$, 109-72-8; $LiC(CH_3)_3$, 594-19-4; $LiCH_2C(CH_3)_3$, 7412-67-1; $LiCH_2Si(CH_3)_3$, 1822-00-0; $LiCH_2C_6H_5$, 766-04-1; $LiC_6H_4$-$CH_3$*p*, 2417-95-0

[1] *H. Schumann* in *T. J. Marks, R. D. Fischer:* Organometallics of the f-Elements. Reidel, Dordrecht 1979, p. 81 ff.
[2] *N. M. Ely, M. Tsutsui,* Inorg. Chem. *14*, 2680 (1975).
[3] *J. Holten, M. F. Lappert, D. G. H. Bullard, R. Pearce, J. L. Atwood, W. E. Hunter,* J. Chem. Soc. Chem. Commun. *1976*, 480.

---

## Crystal and Molecular Structure of $[Li(tmen)]_3[Er(CH_3)_6]$[**]

By *Herbert Schumann, Joachim Pickardt,* and *Norbert Bruncks*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

By using *N,N,N′,N′*-tetramethylethylenediamine (tmen) as a stabilizing base we have succeeded for the first time in syn-

---

[*] Prof. Dr. H. Schumann, Doz. Dr. J. Pickardt, Dipl.-Chem. N. Bruncks
Institut für Anorganische und Analytische Chemie der Technischen Universität Berlin
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] Organometallic Compounds of the Lanthanoids, Part 9. This work was supported by the Fonds der Chemischen Industrie and by the Senator für Wirtschaft des Landes Berlin (ERP grant, Project 2327).—Part 8: [5].

thesizing peralkylated lanthanoid complexes[1]. However, the extreme sensitivity of the isolated permethylated erbium and lutetium complexes *(1)* and *(2)*, and the fact that interpretable $^1$H-NMR spectra could only be obtained for the diamagnetic lutetium compound, have so far precluded concrete data on the structure being obtained.

We report here on the X-ray structure analysis of the title compound *(1)*. Single crystals were obtained by slowly cooling a solution of *(1)* in diethyl ether to −30 °C under argon.

The structure analysis shows that lanthanoids can form organometallic compounds in which all coordination sites on the metal are occupied by carbon atoms of *monohapto*-bonded alkyl groups. In the crystal the erbium is surrounded by the 6 methyl groups in a slightly distorted octahedral arrangement. All the Er—C bonds are of equal length, and the methyl groups are bridged pairwise by lithium atoms, resulting in a slight widening of the corresponding Me—Er—Me angles to 93°. The lithium atoms are each located at the centers of tetrahedra made up of two methyl groups and the two nitrogen atoms of a tmen ligand. Thus, an octahedron results that is coupled *via* three corners, which are not linked with each other, to three tetrahedra (Fig. 1). Since both N atoms of a tmen group are coordinated to a lithium atom, *(1)* is monomeric in the crystal. By way of contrast the bidentate dioxane ligands in $[Li(dioxane)]_3[Cr(CH_3)_6]$ function as bridges between two hexamethylchromium units[2].

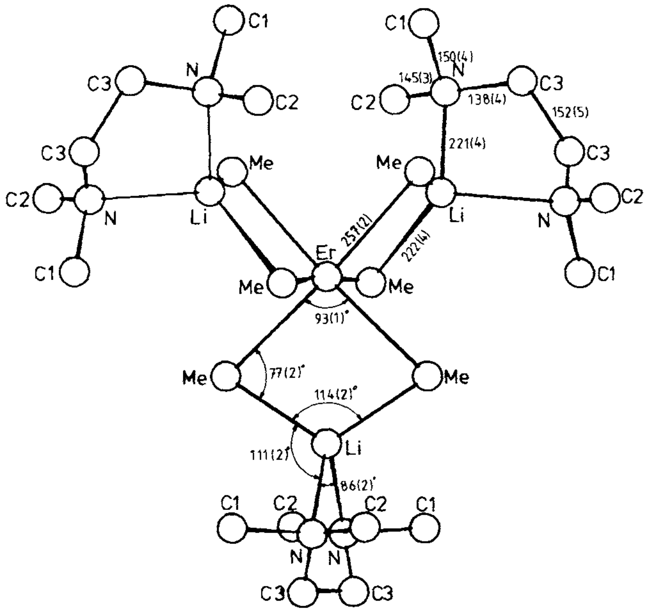


Fig. 1. Structure of $[Li(CH_3)_2NCH_2CH_2N(CH_3)_2]_3[Er(CH_3)_6]$ *(1)*; rhombohedral, space group $R\bar{3}c$, $Z=2$, $a=1309(2)$ pm, $\alpha=79.39(10)°$, $V=2.139\times10^9$ pm$^3$, $\rho_c=0.97$ g/cm$^3$, $l_{pykn}=0.91$ g/cm$^3$; $R=0.085$. Syntex-P2$_1$ four-circle diffractometer; bond lengths in pm.

The bond angles at the lanthanoid as well as the Er—C bond lengths in *(1)*, the first electron-deficient compound with methyl bridges between lithium and a lanthanoid, are comparable with those in electron-deficient compounds with other metal atoms. Thus, the dimeric $[(\eta^5\text{-}C_5H_5)_2YbCH_3]_2$, which contains a $Yb_2(CH_3)_2$ four-membered ring, also possesses an angle of 93° at the ytterbium atom[3]. The bond lengths $d(Yb—C)=254$ pm in $[(\eta^5\text{-}C_5H_5)_2YbCH_3]_2$[3] and $d(Yb—C)=253$ pm in $(\eta^5\text{-}C_5H_5)_2Yb(CH_3)_2Al(CH_3)_2$[4], two further lanthanoid derivatives with electron deficient bonds, correspond to the Er—C bond length of 257 pm. In contrast, the lanthanoid-C distance is shortened if the alkyl group has no bridging function: in $(\eta^5\text{-}C_5H_5)_2LuCH_2Si(CH_3)_3\cdot THF$[5], $d(Lu—C)=238$ pm.

In order to test the validity of this structural principle in the series of the hexamethyl complexes of the lanthanoids, we prepared the complexes *(3)*—*(7)* in the same way as *(1)* and *(2)*.

$$MCl_3 + 6\,LiCH_3 + 3\,tmen \xrightarrow[-78\,°C]{Et_2O} \underset{(1)—(7)}{[Li(tmen)]_3[M(CH_3)_6]} + 3\,LiCl$$

$tmen = (CH_3)_2NCH_2CH_2N(CH_3)_2$

| Cpd. | M | Color | Thermal behavior | |
|---|---|---|---|---|
| *(3)* | Pr | green | dec. pt. | 59—62 °C |
| *(4)* | Nd | blue | dec. pt. | 78—83 °C |
| *(5)* | Sm | yellow | dec. pt. | 85—88 °C |
| *(1)* [1] | Er | pink | m.p. | 138—139 °C |
| *(6)* | Tm | white | m.p. | 109—114 °C |
| *(7)* | Yb | white | m.p. | 141—142 °C |
| *(2)* [1] | Lu | white | m.p. | 141—142 °C |

The compounds *(1)*—*(7)*, which have been completely characterized by elemental analyses, are extremely sensitive towards moisture and atmospheric oxygen; some of them even ignite spontaneously. A notable feature is the enhanced thermal stability of the complexes with increasing atomic weight of the lanthanoid.

Received: August 11, 1980 [Z 682b IE]
German version: Angew. Chem. 93, 127 (1981)

CAS Registry numbers:
*(1)*, 66862-11-1; *(3)*, 76206-86-5; *(4)*, 76206-88-7; *(5)*, 76206-90-1; *(6)*, 76206-92-3; *(7)*, 76206-94-5

---

[1] *H. Schumann, J. Müller*, Angew. Chem. *90*, 307 (1978); Angew. Chem. Int. Ed. Engl. *17*, 276 (1978).

[2] *J. Krausse, G. Marx*, J. Organomet. Chem. *65*, 215 (1974).

[3] *J. Holten, M. F. Lappert, D. G. H. Bullard, R. Pearce, J. L. Atwood, W. E. Hunter*, J. Chem. Soc. Chem. Commun. *1976*, 480.

[4] *J. Holten, M. F. Lappert, G. R. Scollary, D. G. H. Ballard, R. Pearce, J. L. Atwood, W. E. Hunter*, J. Chem. Soc. Chem. Commun. *1976*, 425.

[5] *H. Schumann, W. Genthe, N. Bruncks*, Angew. Chem. *93*, 126 (1981); Angew. Chem. Int. Ed. Engl. *20*, 119 (1981).

## Structure of the Antibiotic Moenomycin A[**]

By *Peter Welzel, Franz-Josef Witteler, Dietrich Müller*, and *Werner Riemer*[*]

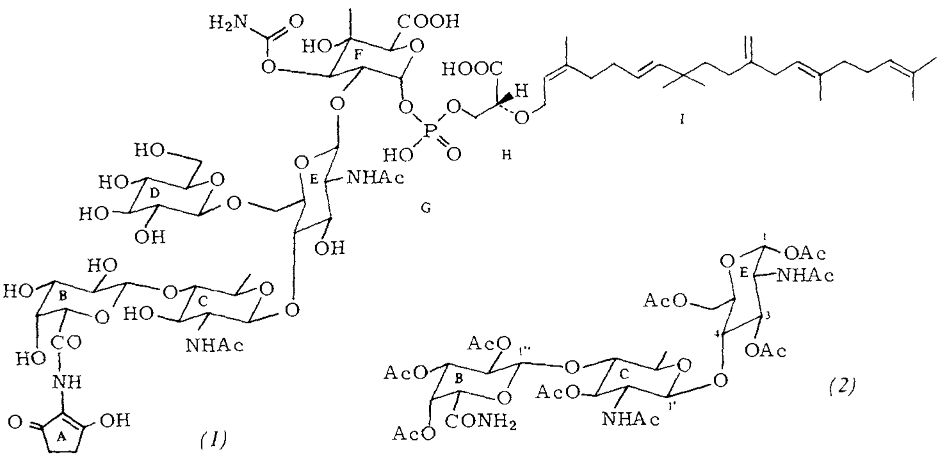
Moenomycin A is a major component of flavomycin®, which is employed in animal nutrition[1]. It inhibits the transglycosylation step[2] in the biosynthesis of murein, the rigid component of the bacterial cell wall. For moenomycin A we propose structure *(1)*.

It was known from degradation studies that moenomycin A is built up of parts A-B-C and D-E-F-G-H-I[3]. Thus, the sugar chain in *(1)* could be cleaved quite selectively at the glycosidic bonds of the two *N*-acetylated amino sugars with

---

[*] Prof. Dr. P. Welzel, Dr. F.-J. Witteler, Dr. D. Müller
Abteilung für Chemie der Universität
Postfach 102148, D-4630 Bochum (Germany)
W. Riemer
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
Stiftstr. 34—36, D-4330 Mülheim/Ruhr (Germany)

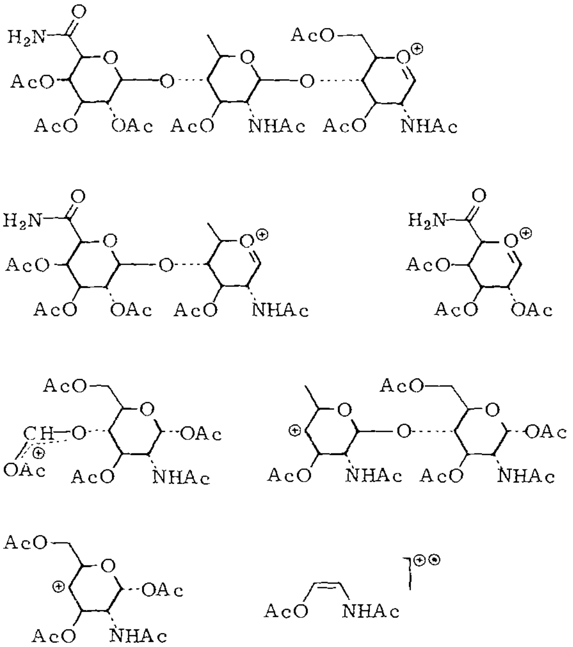
[**] This work was supported by the Fonds der Chemischen Industrie and Hoechst AG. We thank Dr. *H.-W. Fehlhaber*, Hoechst AG, for recording the mass spectra, and Herr *K. Hobert* and Fräulein *A. Ponty* for their valuable assistance.



(1)

(2)

trifluoroacetic acid[4]. In order to determine how the two partial structures are connected to each other we have exploited the observation that glycosides of *free* amino sugars are particularly stable towards hydrolysis[5]. It was to be expected that, after cleavage of the *N*-acetyl groups, the glycosidic bond of the quinovosamine unit (C) could be preserved on acid hydrolysis, not, however, the linkage between the glucosamine (E) and the moenuronic acid unit (F), since moenuronic acid is known to decompose with loss of $CO_2$ and water on acid treatment[3,6]. After cleavage of the amide bonds in *(1)* (1 N NaOH), acid hydrolysis (2 N HCl), reaction of the cleavage products with methanolic HCl and methanolic $NH_3$ (to convert the galacturonic unit into the uronamide), acetylation and chromatographic separations, the trisaccharide derivative *(2)* was obtained with the glycosidic linkage of the quinovosamine unit (C) intact. Total hydrolysis of *(2)* with 2 N HCl or 1.5 N methanolic HCl yielded quinovosamine, glucosamine, and galacturonic acid[7].



Scheme 1. Fragments in the mass spectrum of *(2)* that are important for the structure elucidation.

The sequence of the monosaccharide units in *(2)* follows quite clearly from the fragments of the high resolution mass spectrum shown in Scheme 1. Whether the quinovosamine unit is (1→3) or (1→4) linked to the glucosamine could be elucidated only on the basis of the 250-MHz $^1H$-NMR spectrum, which was completely analyzed by double resonance experiments (Table 1). From the large coupling constants $J_{2',3'}$, $J_{3',4'}$, $J_{4',5'}$ it can be deduced that the quinovosamine unit is present in the $^4C_1$ conformation; $J_{1',2'} = 8.6$ Hz then proves the β-glycosidic linkage of the quinovosamine and glucosamine units. The (1→4) link of the two sugars follows from the chemical shifts of 4-H (ether proton) and 3-H (proton next to an ester group).

Table 1. $^1H$-NMR data of *(2)* (270 MHz, $CDCl_3$).

δ = 6.08 (d, 1-H), 4.40 (m, 2-H), 5.19 (dd, 3-H), 3.70 (dd, 4-H), 3.90 (m, 5-H), 4.14 (dd, 6a-H), 4.50 (dd, 6b-H), 5.80 (d, NH), 4.31 (d, 1′-H), 3.99 (m, 2′-H), 5.04 (dd, 3′-H), 3.51 (dd, 4′-H), 3.4 (m, 5′-H), 1.31 (d, $CH_3$-6′), 4.70 (d, 1″-H), 5.10 (m, 2″-H, 3″-H), 5.78 (narrow, not resolved m ($W_{1/2}$ *ca.* 4 Hz), 4″-H), 4.25 (br. s ($W_{1/2}$ *ca.* 3.4 Hz) 5″-H), 5.88 and 6.59 ($N''H_2$), 1.94, 1.98, 1.98, 2.06, 2.07, 2.07, 2.08, 2.15, 2.19 (Ac), $J_{1,2} = 3.7$, $J_{2,3} = 11.0$, $J_{3,4} = 8.8$, $J_{4,5} = 10.0$, $J_{5,6a} = 1.4$, $J_{5,6b} = 3.5$, $J_{6a,6b} = 12.9$, $J_{2,NH} = 10.0$, $J_{1',2'} = 8.6$, $J_{2',3'} = 10.4$, $J_{3',4'} = 9.2$, $J_{4',5'} = 9.2$, $J_{2',N'H} = 9.6$, $J_{1'',2''} = 7.7$ Hz

In the region F-G-H-I, compound *(1)* exhibits structural analogies with the intermediate consisting of a substituted disaccharide and a polyprenol diphosphate found in the murein biosynthesis, whose use for the synthesis of the polysaccharide chains is inhibited by *(1)* (see [1]).

## *Procedure*

A solution of *(1)* (2.0 g) in 1 N NaOH (16 $cm^3$) is heated under reflux in an argon atmosphere for 24 h; subsequently, the solution is neutralized and lyophilized. The residue dissolved in 10 $cm^3$ of 2 N HCl is heated under reflux for 1 h. After neutralization, the solution is diluted with water and extracted several times with chloroform. The aqueous layer is lyophilized and freed from inorganic salts by chromatography on 50 g of silica gel (2-propanol/conc. $NH_3$ 65:35). The eluate is lyophilized, the residue stirred in 100 $cm^3$ of 1.5% methanolic HCl for 22 h at room temperature, evaporated to dryness, taken up in 80 $cm^3$ of methanol, treated with 30 $cm^3$ of saturated methanolic $NH_3$-solution, stirred for 15 h at 0 °C, and evaporated. The residue is dried in a high vacuum and then acetylated for 3 d at room temperature in 28 $cm^3$ of pyridine and 14 $cm^3$ of acetic acid anhydride in the presence of catalytic amounts of 4-(dimethylamino)pyridine. After dilution with dichloromethane, washing with water, drying, and evaporating, the residue is chromatographed, firstly on 250 g of silica gel (petroleum ether/chloroform/ethanol 4:2:1) and then on a Lobar column (60 g silica gel; toluene/

0570-0833/81/0101-0122 $ 02.50/0

chloroform/ethanol 2:1:1); yield 36 mg *(2)*, m.p. 309—310 °C (from ethanol/petroleum ether).

Received: July 8, 1980 [Z 666 IE]
German version: Angew. Chem. *93*, 130 (1981)

CAS Registry numbers:
*(1)*, 76095-39-1; *(2)*, 76095-40-4

---

[1] Review: *G. Huber* in *F. E. Hahn:* Antibiotics. Vol. V/1. Springer, Berlin 1979, p. 135.

[2] *Y. van Heijenoort, M. Derrien, J. van Heijenoort,* FEBS Lett. *89*, 141 (1978); cf. *H. Suzuki, Y. van Heijenoort, T. Tamura, J. Mizoguchi, Y. Hirota, J. van Heijenoort, ibid. 110*, 245 (1980).

[3] *F.-J. Witteler, P. Welzel, H. Duddeck, G. Höfle, W. Riemer, H. Budzikiewicz,* Tetrahedron Lett. *1979*, 3493, and references cited therein.

[4] *P. Welzel,* Proceedings of the 11th International Symposium on Chemistry of Natural Products, Vol. 4/2, p. 394; Chem. Abstr. *91*, 211687w (1979); *P. Welzel, G. Knupp, F.-J. Witteler, Th. Schubert, H. Duddeck, D. Müller, G. Höfle,* Tetrahedron, in press.

[5] Review: *G. O. Aspinall,* Pure Appl. Chem. *49*, 1105 (1977).

[6] *N. Langenfeld, P. Welzel,* Tetrahedron Lett. *1978*, 1833.

[7] For methods cf. *P. Welzel, F.-J. Witteler, L. Hermsdorf, R. Tschesche, H. Buhlke, P. Michalke, J. Simons, H.-W. Fehlhaber, J. Blumbach, G. Huber,* Tetrahedron, in press.

---

## Tri-*tert*-butylcyclotriarsane[**]

By *Marianne Baudler* and *Paul Bachmann*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

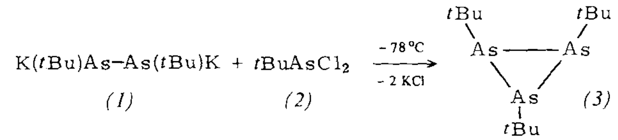
Numerous homo- and heterocyclic phosphorus three-membered ring compounds have become preparatively accessible in recent years[1]. Following the synthesis of the diphosphaarsirane $(t\mathrm{BuP})_2(t\mathrm{BuAs})$[1,2] and the phosphadiarsirane $(i\mathrm{PrP})(t\mathrm{BuAs})_2$[3] the question arose whether also monocyclic triarsanes $(\mathrm{RAs})_3$ are capable of existence and can be isolated. Hitherto, only compounds were known in which the arsenic three-membered ring is stabilized by bracketing in a polycycle [$\mathrm{As_4}$[4a], $\mathrm{As_4S_3}$[4b], $\mathrm{CH_3C(CH_2As)_3}$[4c], $\mathrm{As_7^{3-}}$[4d]] or by complexation [$\mathrm{As_3Co(CO)_3}$[5a], $[(\mathrm{triphos})\mathrm{M}(\mathrm{As_3})\mathrm{M}(\mathrm{triphos})]^{2+}$ (M = Co, Ni)[5b]]. A previously reported triphenylcyclotriarsane[6a] has so far not been confirmed[6b].

We report here on the synthesis of the tri-*tert*-butylcyclotriarsane *(3)*, the first monocyclic homonuclear three-membered ring compound of an element of the 4th period.

Problems were to be expected through oligomerization to higher-membered cycloarsanes $(\mathrm{RAs})_n$ $(n>3)$; owing to the lower bonding energy of the As—As bond compared to that of the P—P bond, such reactions should proceed even more rapidly than in the case of the cyclotriphosphanes[7]. A certain kinetic stabilization of the three-membered ring moiety could, however, be expected by steric shielding with *tert*-butyl substituents.

The simplest method for the synthesis of tri-*tert*-butylcyclotriphosphane[8] cannot be employed for the synthesis of the arsenic compound *(3)*: on dehalogenation of dichloro(*tert*-butyl)arsane with metals we obtained always the cyclotetraarsane $(t\mathrm{BuAs})_4$[9a] as main product; in addition $(t\mathrm{BuAs})_5$ and polycyclic arsanes could be detected by $^1$H-NMR spectroscopy. The thermal stability and tendency of formation of *(3)* are obviously less than in the case of the corresponding cyclotriphosphane.

*(3)* can, however, be obtained as main product by directed [2+1]-cyclocondensation of 1,2-dipotassium 1,2-di-*tert*-butyldiarsenide *(1)* with dichloro(*tert*-butyl)arsane *(2)* in apolar solvents at low temperature.



$(t\mathrm{BuAs})_4$ and small amounts of unidentified compounds are also formed. The product pattern depends on the molar ratio of the reactants, on the concentration of the $t\mathrm{BuAsCl_2}$ solution, the reaction time and the quantities used; the yield of *(3)* which can be isolated pure by low-temperature crystallization and sublimation was optimized by $^1$H-NMR spectroscopy.

The cyclotriarsane *(3)* forms colorless, tabloid shaped crystals (m.p. 41 °C (dec.), sealed tube), which are stable in the dark and in the absence of air at −30 °C. They are readily soluble in benzene or *n*-pentane. On exposure to air they spontaneously ignite, on exposure to light they turn yellow within a few hours, and at room temperature oligomerization gradually takes place to $(t\mathrm{BuAs})_4$. The composition of *(3)* is confirmed by elemental analysis (As, C, H), cryoscopic molecular weight determination (in cyclohexane), and the mass spectrum (field ionization, $M^+$: $m/e = 396$, 100%). The $^1$H-NMR spectrum (benzene) shows two singlets at $\delta = 1.16$ and 1.41 in the ratio 1:2. It follows then that the *tert*-butyl substituents are arranged on both sides of the ring plane; the *all-cis* isomer was not detectable. In agreement with these findings the $^{13}$C{$^1$H}-NMR spectrum (benzene) shows two singlets each for the primary and tertiary C-atoms at 34.48, 32.41 and 35.88, 29.55, respectively of which each high-field signal corresponds to the *trans* substituents. The IR and Raman spectra of *(3)* exhibit characteristic differences from the spectra of $(t\mathrm{BuAs})_4$ in the lower wave number region (cf. Table 1).

Table 1. IR- and Raman frequencies ($<700$ cm$^{-1}$) of $(t\mathrm{BuAs})_3$ *(3)* and $(t\mathrm{BuAs})_4$.

| Cpd. | IR (KI disk) [cm$^{-1}$] | Raman (krypton) [cm$^{-1}$] |
|---|---|---|
| $(t\mathrm{BuAs})_3$ *(3)* | 685 (m), 558 (m), 535 (vw, sh), 515 (vw, sh), 490 (vw, sh), 395 (m), 388 (w, sh), 348 (w), 293 (w), 278 (w) | 540 (w, sh), 513 (m), 398 (vw), 328 (m), 298 (w), 284 (w), 250 (vw), 221 (m), 197 (m), 182 (s), 139 (m), 116 (m), 107 (m, sh) |
| $(t\mathrm{BuAs})_4$ | 699 (w), 565 (vw), 519 (w), 386 (w), 288 (m) | 522 (s), 391 (vw), 308 (m), 294 (m), 292 (m, sh), 217 (s), 158 (s), 123 (m), 112 (s) |

### *Procedure*

A solution of *(2)* (8.4 g, 41.4 mmol, substoichiometric amount) in *n*-pentane (40 cm$^3$) is added dropwise within 30 min at −78 °C to a vigorously stirred suspension of *(1)*[9b] (15.5 g, 45.3 mmol) in pentane (100 cm$^3$). The mixture is stirred for a further 30 min; thereafter the proportion of *(3)* amounts to about 60 mol-% ($^1$H-NMR). The precipitate is rapidly filtered off in the cold and the filtrate which is collected in a precooled vessel is concentrated to about 60 cm$^3$ at −78 °C. After 5 days storage in the cold the solution is siphoned off from any precipitate which has settled out (mainly $(t\mathrm{BuAs})_4$) and concentrated to *ca.* 50 cm$^3$; removal of precipitate is repeated again after 3 days. The workup is monitored by $^1$H-NMR inspection of all fractions. The solution is then concentrated to *ca.* 30 cm$^3$ at −78 °C and the yellowish

---

[*] Prof. Dr. M. Baudler, Dipl.-Chem. P. Bachmann
Institut für Anorganische Chemie der Universität
Greinstrasse 6, D-5000 Köln 41 (Germany)

[**] Contributions to the Chemistry of Arsenic, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 2: *M. Baudler, H.-J. Stassen,* Z. Anorg. Allg. Chem. *345*, 182 (1966).

crude product which has precipitated out after 3 d is separated off. Dissolution in a little pentane at room temperature and cooling to −78 °C yields 3.4 g (21%) of pale yellow *(3)*, purity 90—95% (rest $(t\mathrm{BuAs})_4$, $^1$H-NMR). Molecular sublimation (2 cm) at room temperature and $10^{-4}$ torr, during which partial rearrangement to $(t\mathrm{BuAs})_4$ already takes place, however, affords 1.2 g (7.3%) of colorless, finely crystalline *(3)* as middle fraction; purity 100%.

Received: May 30, 1980 [Z 669 IE]
German version: Angew. Chem. 93, 112 (1981)

CAS Registry numbers:
*(1)*, 37791-66-5; *(2)*, 50307-34-1; *(3)*, 76173-66-5; $(t\text{-BuAs})_4$, 37755-92-3

---

[1] *M. Baudler*, J. Pure Appl. Chem. *52*, 755 (1980); see also *H. Quast*, Nachr. Chem. Tech. Lab. *27*, 120 (1979).
[2] *M. Baudler, S. Klautke*, Z. Naturforsch., in press.
[3] *M. Baudler, D. Habermann*, Angew. Chem. *91*, 939 (1979); Angew. Chem. Int. Ed. Engl. *18*, 877 (1979).
[4] a) *L. R. Maxwell, S. B. Hendricks, V. M. Mosley*, J. Chem. Phys. *3*, 699 (1935); b) *H. J. Whitfield*, J. Chem. Soc. *A 1970*, 1800; J. Chem. Soc. Dalton Trans. *1973*, 1737; c) *J. Ellermann, H. Schössner*, Angew. Chem. *86*, 646 (1974); Angew. Chem. Int. Ed. Engl. *13*, 601 (1974); *G. Thiele, G. Zoubek, H. A. Lindner, J. Ellermann, ibid. 90*, 133 (1978) and *17*, 135 (1978); d) *W. Schmettow, H. G. von Schnering, ibid. 89*, 895 (1977) and *16*, 857 (1977).
[5] a) *A. S. Foust, M. S. Foster, L. F. Dahl*, J. Am. Chem. Soc. *91*, 5631 (1969); b) *M. Di Vaira, S. Midollini, L. Sacconi, F. Zanobini*, Angew. Chem. *90*, 720 (1978); Angew. Chem. Int. Ed. Engl. *17*, 676 (1978).
[6] a) *W. Steinkopf, P. Smie*, Ber. Dtsch. Chem. Ges. *59*, 1453 (1926); b) *F. F. Blicke, L. D. Powers*, J. Am. Chem. Soc. *55*, 315 (1933).
[7] *M. Baudler, B. Carlsohn, B. Kloth, D. Koch*, Z. Anorg. Allg. Chem. *432*, 67 (1977).
[8] *M. Baudler, J. Hahn, H. Dietsch, G. Fürstenberg*, Z. Naturforsch. *B 31*, 1305 (1976); *M. Baudler, Ch. Gruner, ibid. B 31*, 1311 (1976).
[9] a) *A. Tzschach, V. Kiesel*, J. Prakt. Chem. *313*, 259 (1971); b) Prepared according to [9a], but in benzene/hexane (1 : 1), when the salt is obtainable free of solvent.

---

## *cyclo*-Leu$^5$-Enkephalin[1]

By *Horst Kessler* and *Günter Hölzemann*[*]

The discovery, isolation and elucidation of the composition and structure of the enkephalins

H-Tyr$^1$-Gly$^2$-Gly$^3$-Phe$^4$-Xxx$^5$-OH
*(1)*, Xxx = Leu, Leu$^5$-enkephalin;
*(2)*, Xxx-Met, Met$^5$-enkephalin

as endogenous ligands for the opiate receptor aroused considerable attention. Although detailed studies on the conformation of these pentapeptides have indicated a preferred conformation with a β-loop between the amino acids 5→2[2], the backbone and the side chains are very flexible and permit the participation of many conformations at equilibrium in solution[2,3]. Therefore, conclusions on the receptor geometry and comparisons with the steric structure of rigid morphine are problematical. Our findings on cyclic pentapeptides[1,4,5] would lead one to expect considerably restricted mobility in the case of *cyclo*-enkephalins. We report here the synthesis of, and first conformational studies on, cyclo-Leu$^5$-enkephalin *(c1)*[6].

For the synthesis of *(c1)* we did not cyclize a peptide having a natural sequence, but the linear peptide H-Gly-Phe-Leu-Tyr-Gly-X using the azide method. The region Gly$^2$-Gly$^3$ was chosen to ensure minimal steric hindrance during the cyclization, to avoid racemization and to circumvent problems in the hydrazinolysis[7] of the Boc-pentapeptide methyl ester. The ester was obtained from the fragments Boc-Gly-Phe-Leu-OCH$_3$ and H-Tyr-Gly-OCH$_3$, which had been prepared by usual methods of peptide synthesis.

Table 1. 270-MHz $^1$H-NMR data of *cyclo*-Leu$^5$-enkephalin *(c1)* in [D$_6$]-DMSO at 25 °C. δ values, *J* [Hz].

| *(c1)* | Tyr$^1$ [a] | Gly$^2$ | Gly$^3$ | Phe$^4$ [b] | Leu$^5$ |
|---|---|---|---|---|---|
| NH | 8.29 | 8.62 | 7.75 | 8.09 | 7.96 |
| $C_\alpha H$ | 4.23 | A 3.86 | A 3.74 | 4.32 | 4.06 |
| | | B 3.43 | B 3.59 | | |
| $C_\beta H$ | A 2.85 | | | A 2.95 | 1.32 |
| | B 2.84 | | | B 2.94 | |
| $C_\gamma H$ | | | | | 1.52 |
| $C_\delta H$ | | | | | A 0.83 |
| | | | | | B 0.77 |
| $\Delta\delta^{NH}/K$ [c] | 4.49 | 5.09 | 1.14 | 5.13 | 1.50 |
| $^3J_{NHC_\alpha H}$ | 7.8 | A 5.7 | A 4.4 | 8.0 | 8.7 |
| | | B 6.1 | B 6.8 | | |
| $^2J_{HC_\alpha H}$ | | 15.5 | 14.9 | | |
| $^3J_{C_\alpha HC_\beta H}$ | A 7.7 | | | A 8.2 | |
| | B 5.9 | | | B 6.1 | |
| $^2J_{HC_\beta H}$ | 13.6 | | | 14.0 | |

[a] Aromatic protons A 6.94, B 6.64; OH 9.22. [b] Aromatic protons around 7.2. [c] Temperature-dependence of the NH-proton signals between 20 and 100 °C (ppb).

The 270-MHz $^1$H-NMR spectrum of *(c1)* in [D$_6$]-dimethyl sulfoxide ([D$_6$]-DMSO) (see Table 1) is very similar to that of

*cyclo*(Phe$^3$-Gly$^4$-Gly$^5$-Phe$^1$-Phe$^2$)[4,8] *(3)*

The assignment of the Gly$^2$- and Gly$^3$-signals, which suggests itself by way of analogy with *(c1)* and *(3)*, and the differentiation of the Tyr$^1$- and Phe$^4$-signals was confirmed by NOE measurements. Irradiation of the NH frequency produced a more or less significant effect on the α-H atom of the amino acid preceding the peptide sequence[9]. The temperature gradients of the NH signals in *(c1)* and *(3)* and the spectra obtained on titration of the DMSO solution with CDCl$_3$ are also very similar. Such a spectral similarity can only be expected if the conformations of the two peptides resemble each other. Hence, exchange of the amino acids Phe$^3$→Tyr$^1$ and Phe$^2$→Leu$^5$ in the transition from *(3)* to *(c1)* has no effect on the conformation. Arguments regarding the dominating conformation of *(c1)* in solution correspond to those in the case of *(3)*[4]: the internal orientation of the leucine-NH

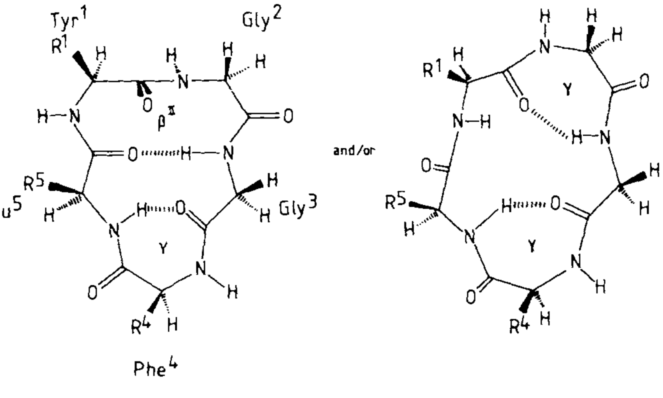


Fig. 1 Conformation of *cyclo*-Leu$^5$-enkephalin *(c1)* in DMSO. R$^1$ = *p*-CH$_2$C$_6$H$_4$OH; R$^4$ = CH$_2$C$_6$H$_5$; R$^5$ = CH$_2$CH(CH$_3$)$_2$. Left: βγ-, right: γγ-conformation.

---

[*] Prof. Dr. H. Kessler, Dipl.-Chem. G. Hölzemann
Institut für Organische Chemie der Universität
Chemiegebäude, Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

(small temperature coefficient, see Table 1) can only be brought about by a γ-loop of the amino acids 5→3, while the NH proton of $Gly^3$ can form a β-loop to the $Leu^5$-CO or a γ-loop to the $Tyr^1$-CO (Fig.1). We do not as yet wish to stipulate a particular conformation, though the sizes of the NH—$C_\alpha$H coupling constants would appear best explained in terms of a γγ-conformation. The poor solubility of *(c1)* in water thwarts a check on the biological activity.

Received: July 21, 1980 [Z 648 IE]
German version: Angew. Chem. *93*, 90 (1981)

CAS Registry number:
*(c1)*, 75975-40-5

---

[1] Peptide Conformations, Part 11. This work was supported by the Fonds der Chemischen Industrie and der Deutschen Forschungsgemeinschaft.—Part 10: *P. Kondor, H. Kessler* in *E. Gross, J. Meienhofer:* Peptides, Pierce Chemical Comp., Rockford, Illinois 1979, p. 181.

[2] *M. Anteunis, A. K. Lala, C. Garbay-Jaureguiberry, B. P. Roques,* Biochemistry *16*, 1462 (1977); *C. R. Jones, V. Garsky, W. A. Gibbons,* Biochem. Biophys. Res. Commun. *76*, 619 (1977), and references cited therein.

[3] *J. Kobayashi, U. Nagai, T. Higashijima, T. Miyazawa,* Biochim. Biophys. Acta *577*, 195 (1979).

[4] *Y. A. Bara, A. Friedrich, H. Kessler, M. Molter,* Chem. Ber. *111*, 1045 (1978).

[5] *H. Kessler, P. Kondor,* Chem. Ber. *112*, 3538 (1979).

[6] *cyclo*-$Met^5$-enkephalin *(c2)* could previously not be obtained free of *S*-oxide [10].

[7] *Y. A. Bara, A. Friedrich, W. Hehlein, H. Kessler, P. Kondor, M. Molter, H. J. Veith,* Chem. Ber. *111*, 1029 (1978).

[8] The amino acids have been numbered in analogy to *(c1)*.

[9] A quantitative evaluation of the effects for the determination of conformation is in progress.

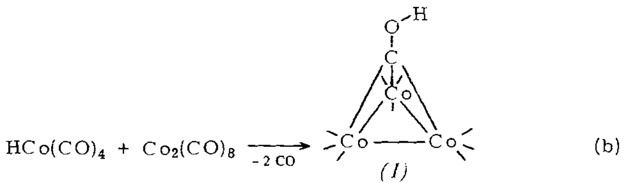
[10] *Note added in proof* (January 1981): Meanwhile we have been able to prepare *(c2)* and found the same conformation as in *(c1)* and *(3)*.

## Crystal and Molecular Structure of $Co_3(CO)_9COH$, A Possible Intermediate in the Reduction of CO by Molecular Hydrogen[**]

By *Hans-Norbert Adams, Giuseppe Fachinetti,* and *Joachim Strähle*[*]

$Co_3(CO)_9C$—OH *(1)* can be obtained in solution by acidification of the $[Co_3(CO)_{10}]^-$ anion[1a]. *(1)* has the property of being quantitatively converted into $HCo(CO)_4$ and $Co_4(CO)_{12}$ (or $Co_2(CO)_8$, depending on the CO partial pressure), thus demonstrating the first conversion of an O-bonded hydrogen to a metal-bonded hydrogen[1a]. Moreover, $HCo(CO)_4$ was converted into the trinuclear cluster $Co_3(CO)_9C$—OH *(1)* on reaction with $Co_2(CO)_8$ in the presence of $NEt_3$, thus showing for the first time that the previously mentioned hydrogen migration can be reverted[1b]. In view of the already established[2] reaction (a) these findings were believed to represent an unprecedented example of a cluster-formation assisted four-electron one-step reduction of CO by molecular hydrogen.

$$H_2 + Co_2(CO)_8 \rightleftharpoons 2\ HCo(CO)_4 \qquad \text{(a)}$$



$$HCo(CO)_4 + Co_2(CO)_8 \xrightarrow[-2\,CO]{} \qquad \text{(b)}$$

*(1)*

The IR and $^1$H-NMR spectra (in solution)[1a] suggested the basic structure shown in equation (b) for *(1)*. However, it was important to verify whether the molecular parameters of *(1)* were in agreement with a substantial reduction of the apical CO group. For the X-ray structure analysis solvent-free *(1)* was prepared by acidification of $LiCo_3(CO)_{10}$.[3] with anhydrous HCl in a hydrocarbon solvent at low temperature (see Procedure).

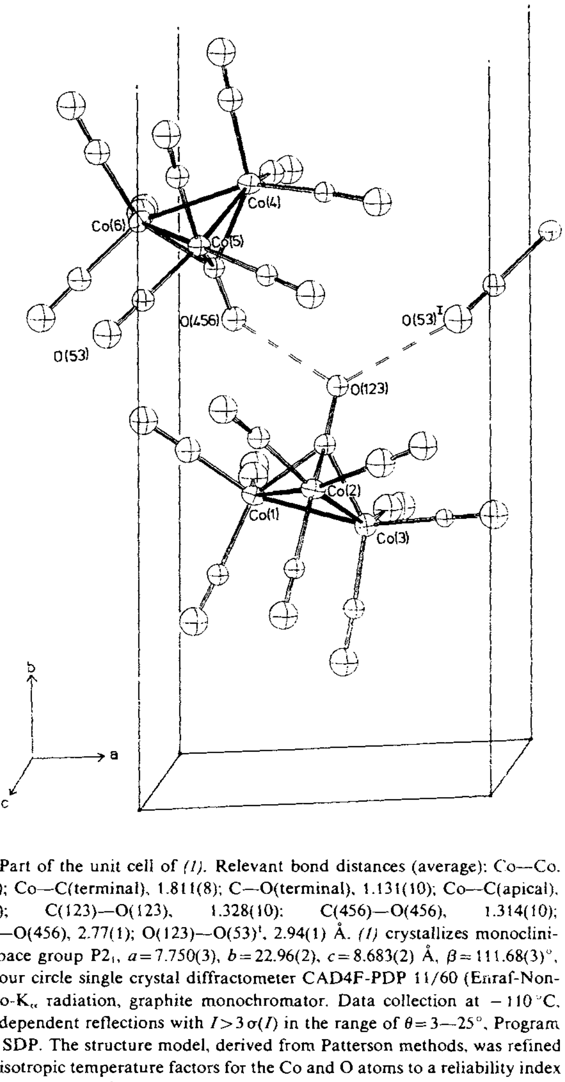


Fig. 1. Part of the unit cell of *(1)*. Relevant bond distances (average): Co—Co, 2.478(5); Co—C(terminal), 1.811(8); C—O(terminal), 1.131(10); Co—C(apical), 1.928(8); C(123)—O(123), 1.328(10); C(456)—O(456), 1.314(10); O(123)—O(456), 2.77(1); O(123)—O(53)$^I$, 2.94(1) Å. *(1)* crystallizes monoclinically, space group $P2_1$, $a$=7.750(3), $b$=22.96(2), $c$=8.683(2) Å, $\beta$=111.68(3)°, $Z$=4, four circle single crystal diffractometer CAD4F-PDP 11/60 (Enraf-Nonius), Mo-$K_\alpha$ radiation, graphite monochromator. Data collection at −110 °C, 1632 independent reflections with $I > 3\sigma(I)$ in the range of $\theta$=3—25°, Program System SDP. The structure model, derived from Patterson methods, was refined with anisotropic temperature factors for the Co and O atoms to a reliability index $R$=0.051. A final difference Fourier map did not show any significant electron density for the H atoms.

In the $Co_3(CO)_{10}$ clusters (Fig. 1) each Co atom is bonded to three terminal CO groups. The three Co atoms form a regular triangle which is completed to a tetrahedron by an apical CO group. The Co—C and C—O distances in the terminal CO groups as well as the Co—Co distances are of the same magnitude as observed in $LiCo_3(CO)_{10} \cdot i Pr_2O$[4]. The position of the hydrogen atom could not be determined with certainty. However, the C—O bond length of the apical CO group was found to be 1.33(1) Å, which clearly indicates that

---

[*] Dr. G. Fachinetti [+]
Istituto di Chimica Generale, Università di Pisa
Via Risorgimento 35, I-56100 Pisa (Italy)
Prof. Dr. J. Strähle, Dr. H.-N. Adams
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

[**] This work was supported by the C.N.R. (Rome) and by the Deutsche Forschungsgemeinschaft. The Authors wish to thank Prof. *F. Calderazzo* for helpful discussions.

[+] Author to whom correspondence should be addressed.

the H atom is bonded to the oxygen atom of the apical CO group. In addition, short intermolecular O—O distances are found between the apical O atoms of two neighboring clusters as well as between O(123) and O(53)$^1$ of a third cluster, thus supporting the assumption of intermolecular hydrogen bridges.

1.33 Å is the longest CO distance found for metal-coordinated CO, thus showing a considerable reduction of CO bond order (the average terminal C—O distance is 1.15 Å; the C—O distance in methanol is 1.43 Å). For comparison: in $[HFe_4(CO)_{13}]^-$[5], which is presented as a model[6a,b] of CO scission to hydrocarbons, the CO distance is 1.26(3) Å.

We suggest *(1)* as a model for hydrogenation of CO to methanol in homogeneous phase. We believe that *(1)* behaves in solution as a discrete molecule with no important intermolecular contacts, as evidenced by its high solubility in hydrocarbons. On the other hand, the multisite interactions in the solid state, similar to those already found[4] in the lithium derivative $LiCo_3(CO)_{10}\cdot i Pr_2O$ qualify *(1)* as a possible model also for the hydrogenation of CO in the heterogeneous phase.

*(1)* could possibly be a real intermediate in the homogeneous phase hydrogenation of CO to methanol[7]; high $H_2$—CO-partial pressures and high temperature are necessary for $HCo(CO)_4$-assisted low-nuclearity endothermic[8] cluster formation. The thermal[6c] and photochemical[9] hydrogenation of $Co_3(CO)_9C$—R to hydrocarbons provides further experimental evidence for this claim.

### *Procedure*

Ether-free $LiCo_3(CO)_{10}$: A suspension of $LiCo_3(CO)_{10}\cdot Et_2O$ (10 g) in diphenyl ether (50 cm$^3$) stirred at 28.5 °C/*ca.* $5\times10^{-2}$ torr for 12 h under argon. The resulting green pyrophoric solid is filtered after addition of toluene (50 cm$^3$), washed with toluene and dried *in vacuo*. The yield is almost quantitative. The IR spectrum of the product in dibutyl ether is superimposable on that of $LiCo_3(CO)_{10}\cdot i Pr_2O$[4] and $LiCo_3(CO)_{10}\cdot Et_2O$[3] in the same solvent.

Solvent-free *(1)*: A suspension of $LiCo_3(CO)_{10}$ (2.8 g) in toluene (10 cm$^3$) and hexane (30 cm$^3$) is acidified, under an Ar atmosphere, at −80 °C with the stoichiometric amount of anhydrous HCl; after 5 minutes' stirring at about −17 °C the mixture is filtered at this temperature. The solution is cooled to −65 °C under a CO atmosphere and allowed to stand overnight; the crystals which separate are finally filtered off and dried *in vacuo* (25% yield). During all of these operations the temperature should not exceed −10 °C. The brick-red compound *(1)* is unstable thermally and must be kept under a CO or an Ar atmosphere at liquid nitrogen temperature.

Received: July 23, 1980 [Z 651 IE]
German version: Angew. Chem. 93, 94 (1981)

---

[1] a) *G. Fachinetti*, J. Chem. Soc. Chem. Commun. *1979*, 397; b) *G. Fachinetti, L. Balocchi, F. Secco, M. Venturini*, Angew. Chem., in press.

[2] *W. Hieber, H. Schulten, R. Martin*, Z. Anorg. Allg. Chem. *240*, 261 (1938).

[3] *G. Fachinetti*, J. Chem. Soc. Chem. Commun. *1979*, 396.

[4] *H.-N. Adams, G. Fachinetti, J. Strähle*, Angew. Chem. *92*, 411 (1980); Angew. Chem. Int. Ed. Engl. *19*, 404 (1980).

[5] *M. Manassero, M. Sansoni, G. Longoni*, J. Chem. Soc. Chem. Commun. *1976*, 919.

[6] a) *E. L. Muetterties, T. N. Rhodin, E. Band, C. F. Brucker, W. R. Pretzer*, Chem. Rev. *79*, 91 (1979); b) *E. L. Muetterties, J. Stein, ibid. 79*, 479 (1979); c) *R. Bergman, L. S. Stuhl*, personal communication to *E. L. Muetterties*, cited in [6b].

[7] *J. W. Rathke, H. M. Feder*, J. Am. Chem. Soc. *100*, 3623 (1978).

[8] *P. Chini, B. T. Heaton*, Top. Curr. Chem. *71*, 1 (1977); *J. A. Connor, ibid. 71*, 71 (1977).

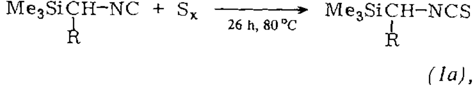
[9] *G. L. Geoffroy, R. A. Epstein*, Inorg. Chem. *16*, 2795 (1977).

## Trimethylsilylmethyl Isothiocyanate, An Isothiocyanatomethanide Equivalent[**]

By *Toshikazu Hirao, Atsushi Yamada, Yoshiki Ohshiro,*
and *Toshio Agawa*[*]

Functionalized isothiocyanates[1a] are useful reagents for heterocycle synthesis[1b], particularly when a carbanion center can be generated in the α-position relative to nitrogen. The metalation of activated isothiocyanate was reported by *Hoppe*[2], but this method is unsatisfactory in the case of methyl isothiocyanate. The well known fluoride ion-induced liberation of carbanions from silyl compounds[3] would indicate that trimethylsilylmethyl isothiocyanate *(1a)* is a suitable precursor for isothiocyanatomethanide *(2)*.

*(1)* was prepared by the addition of sulfur[4] to trimethylsilylmethyl isocyanide[5] in 76% yield. It is a stable liquid at room temperature and can be stored for some time under nitrogen ($\nu_{NCS}=2180$ and 2080 cm$^{-1}$). Compound *(1b)* was prepared analogously (80% yield).



$$Me_3Si\underset{R}{\underset{|}{C}}H{-}NC + S_x \xrightarrow[26\ h,\ 80\,°C]{C_6H_6} Me_3Si\underset{R}{\underset{|}{C}}H{-}NCS$$

*(1a)*, R = H
*(1b)*, R = $SiMe_3$

The isothiocyanate *(1a)* was allowed to react with carbonyl compounds in the presence of a catalytic amount of tetra-*n*-butylammonium fluoride[3a] to produce the oxazolidine-2-thiones *(3)* (Table 1). The reaction proceeds smoothly at room temperature. Potassium fluoride with triethylbenzylammonium chloride (TEBA·Cl) or [18]crown-6 is also effective as a catalyst (Table 1).

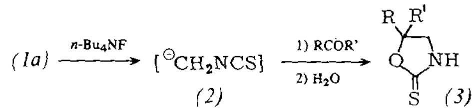


Table 1. Synthesis of oxazolidine-2-thiones *(3)*. Catalyst: $n$-$Bu_4NF$ (0.1 equivalent).

| | | RCOR′ | | *t* | Yield [%] | M.p. [°C] |
|---|---|---|---|---|---|---|
| | | R | R′ | [h] | [a] | [b] |
| *(a)* | | Ph | H | 8 | 74 | 130—131 |
| | [c] | Ph | H | 2 | 74 | |
| | [d] | Ph | H | 5 | 65 | |
| *(b)* | | Et | H | 5 | 63 | 87—89 |
| *(c)* | | *i*Pr | H | 10 | 67 | 101—102 |
| *(d)* | | Ph | Ph | 40 | 25 | 186—188 |
| *(e)* | | Ph | Me | 23 | 35 | 201—203 |

[a] Isolated yield. [b] Uncorrected. [c] Catalyst: KF(1.0) + TEBA·Cl (0.1 equiv.). [d] Catalyst: KF(1.0) + [18]crown-6 (0.1 equiv.). [e] Together with 17% 5-methyl-3-(*N*-methylthiocarbamoyl)-5-phenyloxazolidine-2-thione as a by product.

When bis(trimethylsilyl)methyl isothiocyanate *(1b)* was used in the reaction with benzaldehyde under similar conditions, β-styryl isothiocyanate *(7)*[6] was obtained as a major product along with 5-phenyl-4-(trimethylsilyl)oxazolidine-2-

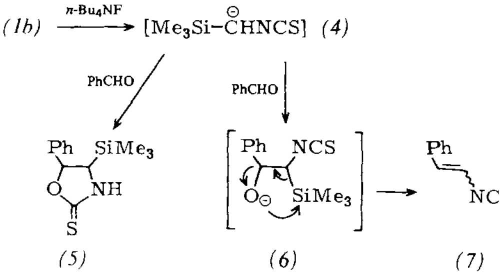
---

[*] Dr. T. Hirao, A. Yamada, Prof. Dr. Ohshiro [+], Prof. Dr. T. Agawa
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Yamadakami, Suita, Osaka 565 (Japan)

[**] This work was supported by a Grant-in-aid for Scientific Research No 475669 from the Ministry of Education and with financial support from Watanabe Memorial Foundation.

[+] Author to whom correspondence should be addressed.

thione *(5)*[6] in 31 and 6% yields, respectively. Nucleophilic attack of the carbanion *(4)* on benzaldehyde leads to the β-trimethylsilyl alkoxide intermediate *(6)*, which fragments *(7)*. The formation of *(5)* can be explained in terms of a ring closure of a rotamer of *(6)*.



It could also be shown that the fluoride-catalyzed reactions of *(1a)* and *(1b)* offer a facile and mild generation of the carbanions *(2)* and *(4)*, respectively.

*Experimental*

*(3a):* A solution of 0.430 g (3.0 mmol) of trimethylsilylmethyl isothiocyanate *(1a)* in THF (2 cm$^3$) was added dropwise at 20 °C to a solution of 78 mg (0.3 mmol) of tetra-*n*-butylammonium fluoride and 0.640 g (6.0 mmol) of benzaldehyde in THF (3 cm$^3$). The resultant mixture was stirred at 20 °C for 8 h, poured into 60 cm$^3$ of water, and extracted with chloroform. The combined organic layer was dried over $Na_2SO_4$ and concentrated *in vacuo*. The residue was chromatographed on silica gel; yield 0.40 g (74%) *(3a)*.

Received: June 2, 1980 [Z 653 IE]
German version: Angew. Chem. *93*, 95 (1981)

---

[1] a) *J. Goerdeler*, Q. Rep. Sulfur Chem. *5*, 169 (1970); *E. Van Loock*, Ind. Chim. Belge *39*, 661 (1974); *R. Esmail, F. Kurzer*, Synthesis *1975*, 301; b) *H. Ulrich:* Cycloaddition Reactions of Heterocumulene. Academic Press, New York 1967.

[2] *D. Hoppe*, Angew. Chem. *84*, 956 (1972); Angew. Chem. Int. Ed. Engl. *11*, 933 (1972); *D. Hoppe, R. Follmann*, Chem. Ber. *109*, 3047 (1976).

[3] a) *E. Nakamura, T. Murofushi, M. Shimizu, I. Kuwazima*, J. Am. Chem. Soc. *98*, 2346 (1976); b) *T. H. Chan, B. S. Ong, W. Mychajlowskij*, Tetrahedron Lett. *1976*, 3253.

[4] *J. V. Nef*, Justus Liebigs Ann. Chem. *280*, 291 (1894); *W. Weith*, Ber. Dtsch. Chem. Ges. *6*, 210 (1873).

[5] *R. West, G. A. Gornowicz*, J. Organomet. Chem. *25*, 385 (1970).

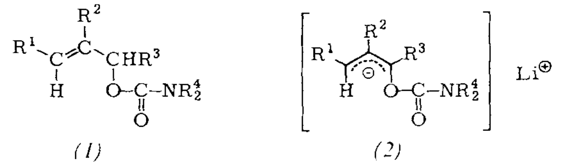
[6] Spectroscopic data of some of the compounds synthesized; *(3a):* IR (Nujol): $\nu = 3160$ (NH), 1520 cm$^{-1}$ (C=S); $^1$H-NMR ($CDCl_3$): $\delta = 3.68$ (dd, 1 H, $J_{gem} = 10.0$ Hz, $J_{vic} = 8.4$ Hz), 4.13 (dd, 1 H, $J_{gem} = 10.0$ Hz, $J_{vic} = 9.2$ Hz), 587 (dd, 1 H, $J_{vic} = 8.4$ and 9.2 Hz), 7.35 (s, 5 H), 8.20 (br. s, 1 H). *(5):* IR (Nujol): $\nu = 3180$ (NH), 1500 (C=S), 1250 cm$^{-1}$ (Si—Me); $^1$H-NMR ($CDCl_3$): $\delta = -0.18$ (s, 9 H), 3.89 (d, 1 H, $J = 9.4$ Hz), 6.06 (d, 1 H, $J = 9.4$ Hz), 7.26—7.47 (m, 5 H), 8.20 (br., 1 H). *(7):* IR: $\nu = 2100$, 2040 (N=C=S), 1620 cm$^{-1}$ (C=C); $^1$H-NMR ($CDCl_3$): $\delta = 6.10$ (2d, 0.88 H, $J = 8.6$ Hz), 6.60 (2d, 1.12 H, $J = 12.2$ Hz), 7.20—7.90 (m, 5 H).

---

# Dilithiated Allyl *N*-Alkyl- or *N*-Phenylcarbamates, Readily Accessible Propionaldehyde-d$^3$ Equivalents[**]

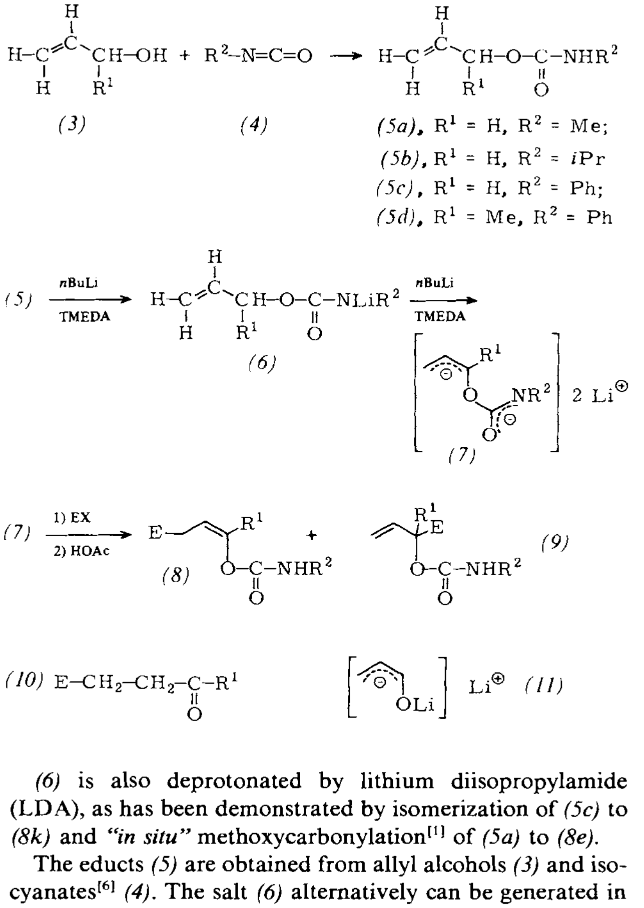
By *Rudolf Hanko* and *Dieter Hoppe*[*]

We recently reported[1] on the deprotonation of allyl *N,N*-dialkylcarbamates *(1)* to (carbamoyloxy)allyllithium compounds *(2)* and their use as "carbonyl-d$^3$ reagents"[2]. On comparing these lithium compounds with other homoenolate equivalents[3] a remarkable feature is their substituent compatibility; even lithium compounds of 1,2,3-trialkyl-substituted 1-oxyallyl anions *(2)* have been obtained[4].



For generation of persistent solutions of *(2)*, their carbonyl function must be protected against nucleophilic attack. This can be achieved by shielding the carbonyl group with sterically demanding *N*-alkyl moieties[5] or—as reported here—by reducing the electrophilicity of the carbonyl group ("electronic protection"). Deprotonation of the allyl *N*-alkyl- or *N*-phenylcarbamates *(5)* provides lithium salts *(6)*, hence even strongly nucleophilic alkyllithium compounds can be used for the metalation.

Double deprotonation of the carbamates *(5)* with 2.1 equivalents of a hexane solution of *n*-butyllithium (*n*BuLi) in tetrahydrofuran (THF)/*N,N,N',N'*-tetramethylethylenediamine (TMEDA) at −78 °C to −50 °C yields stable solutions of dilithiated esters *(7)*. In their reaction with electrophiles (EX) predominantly *Z*-configurated γ-adducts *(8)* are formed, along with small amounts of the allyl esters *(9)* (cf. Table 1). The enol esters *(8)* are hydrolyzable under acidic conditions to yield β-substituted carbonyl compounds *(10)*[4].



*(5a)*, R$^1$ = H, R$^2$ = Me;
*(5b)*, R$^1$ = H, R$^2$ = *i*Pr
*(5c)*, R$^1$ = H, R$^2$ = Ph;
*(5d)*, R$^1$ = Me, R$^2$ = Ph

*(6)* is also deprotonated by lithium diisopropylamide (LDA), as has been demonstrated by isomerization of *(5c)* to *(8k)* and *"in situ"* methoxycarbonylation[1] of *(5a)* to *(8e)*.

The educts *(5)* are obtained from allyl alcohols *(3)* and isocyanates[6] *(4)*. The salt *(6)* alternatively can be generated in a one-pot process by reaction of *(4)* with metalated *(3)*

---

[*] Priv.-Doz. Dr. D. Hoppe, R. Hanko
Organisch-Chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] Metalated Nitrogen Derivatives of Carbonic Acid in Organic Synthesis, Part 19.—Part 18: [1].

(*n*BuLi; cf. *(8j)* and *(9j)* in Table 1). *(7)* thus replaces the unknown[2] "dilithiated allyl alcohol"*(11)*[7]. The ready cleavability of the *Z*-enol esters *(8)* should promote their use as enolate precursors in regio- and diastereoselective C—C coupling.

Table 1. Yields and product ratios in the synthesis of the carbamates *(8)* and *(9)* *via* the dilithiated ester *(7)* [a]. *(5a)*, $R^1=H$, $R^2=Me$; *(5b)*, $R^1=H$, $R^2=i$Pr; *(5c)*, $R^1=H$, $R^2=Ph$; *(5d)*, $R^1=Me$, $R^2=Ph$.

| Educt | EX | Products *(8)* + *(9)* | Yield [%] [e] | *(8)* : *(9)* |
|---|---|---|---|---|
| *(5a)* | MeI | *(8a)* + *(9a)* | 74 [f] | 89 : 11 [i] |
| *(5a)* | *i*PrI | *(8b)* + *(9b)* | 75 [f] | 60 : 40 [i] |
| *(5a)* | $Me_3SiCl$ | *(8c)* + *(9c)* | 55 [g] | 92 : 8 [i] |
| *(5a)* | MeSSMe | *(8d)* | 69 [f] | >97 : 3 [j] |
| *(5a)* [b] | $MeOCO_2Me$ | *(8e)* | 53 [f] | >97 : 3 [j] |
| *(5b)* | DOMe | *(8f)* + *(9f)* | 79 [g] | >90 : 10 [i, j] |
| *(5b)* | *i*PrI | *(8g)* + *(9g)* | 58 [g] | 70 : 30 [i] |
| *(5b)* | $nC_8H_{17}I$ | *(8h)* + *(9h)* | 65 [g] | 66 : 34 [i] |
| *(5c)* | MeI | *(8i)* + *(9i)* | 58 [f] | 85 : 15 [j] |
| *(5c)* [c] | *i*PrI | *(8j)* + *(9j)* | 61 [f, h] | 72 : 28 [k] |
| *(5c)* [d] | HN(*i*$Pr_2$) | *(8k)* | 81 [f] | >97 : 3 [j] |
| *(5d)* [c] | MeI | *(8l)* + *(9l)* | 40 [f] | 90 : 10 [j] |

[a] For conditions see *Procedure*. [b] With 3.3 equivalents LDA and dimethyl carbonate [1] in THF/hexane (2:1) at −78 °C. [c] Solvent: dimethoxyethane. [d] With 2.1 equivalents LDA. [e] Yields of pure *(8)* or *(8)* + *(9)* isolated. [f] After liquid chromatography. [g] After distillation. [h] One-pot process, yields referred to phenyl isocyanate. [i] Determined by gas-chromatography. [j] Determined ¹H-NMR spectroscopically. [k] Determined liquid-chromatographically.

### *Procedure*

A 1.6 N solution of *n*BuLi in *n*-hexane (13.2 cm³, 21 mmol) is added dropwise under $N_2$ at −78 to −60 °C to a solution of *(5)* (10.0 mmol) and TMEDA (1.16 g, 10.0 mmol) in THF (20 cm³) and the mixture finally stirred for 2 h at −50 °C. A solution of EX (see Table 1) (11.0 mmol) in THF (5 cm³) is added to the yellow solution of *(7)* at −78 to −70 °C and the mixture stirred for 1 h, neutralized below −70 °C with glacial acetic acid (1.80 g, 30 mmol), and worked up in the usual way. The crude product of *(8)*[8] and *(9)*[8] is purified by distillation, separation on silica gel (<63 μm) with ether/pentane (1:5), or gas-chromatography (polypropylene glycol 2025 on Chromosorb W, 90 to 180 °C).

Received: August 4, 1980 [Z 672 IE]
German version: Angew. Chem. *93*, 115 (1981)

---

[1] *D. Hoppe, R. Hanko, A. Brönneke*, Angew. Chem. *92*, 637 (1980); Angew. Chem. Int. Ed. Engl. *19*, 625 (1980).

[2] Review: *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979).

[3] a) 1-Oxyallyl anions: *D. A. Evans, G. C. Andrews, B. Buckwalter*, J. Am. Chem. Soc. *96*, 5560 (1974); *W. C. Still, T. L. Macdonald, ibid. 96*, 5561 (1974); *W. Oppolzer, P. H. Briner, R. L. Snowden*, Helv. Chim. Acta *63*, 967 (1980), and references cited therein; *A. Hosomi, H. Hashimoto, H. Sakurai*, J. Org. Chem. *43*, 2551 (1978); *H. J. Reich, R. E. Olson, M. C. Clark*, J. Am. Chem. Soc. *102*, 1423 (1980); *A. P. Kozikowski, K. Isobe*, Tetrahedron Lett. *1979*, 833; *T. Mukaiyama, M. Yamaguchi*, Chem. Lett. *1979*, 457, 1279; b) 1-thioallyl anions: *P. M. Atlani, J. F. Biellmann, S. Dube, J. J. Vicens*, Tetrahedron Lett. *1974*, 2665; *K.-H. Geiss, D. Seebach, B. Seuring*, Chem. Ber. *110*, 1833 (1977); *T. Hayashi, N. Fujitaka, T. Oishi, T. Takeshima*, Tetrahedron Lett. *1980*, 303; c) 1-Aminoallyl anions: *M. Julia, A. Schouteeten, M. Baillarge, ibid. 1974*, 3433; *H. Ahlbrecht, J. Eichler*, Synthesis *1974*, 672; *S. F. Martin, M. T. DuPriest*, Tetrahedron Lett. *1977*, 3925; *A. N. Tischler, M. H. Tischler, ibid. 1978*, 3407; *T. Hassel, D. Seebach*, Angew. Chem. *91*, 427 (1979); Angew. Chem. Int. Ed. Engl. *18*, 399 (1979).

[4] *D. Hoppe, A. Brönneke, R. Hanko*, unpublished results.

[5] Sterically protected lithium compounds *(2)*, $R^4=i$Pr or Et were generated with *n*BuLi in ether/TMEDA; they can be kept in solution at −78 °C [1, 4].

[6] Review: *S. Petersen* in Houben-Weyl-Müller: Methoden der Organischen Chemie. 4th Edn., Vol. VIII. Thieme, Stuttgart 1957, p. 137.

[7] Lithium alkyl oxide adds *n*BuLi; cf. *J. K. Crandall, A. C. Clark*, J. Org. Chem. *37*, 4236 (1972).

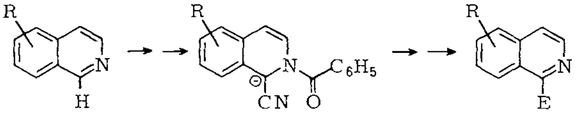
[8] Characteristic spectroscopic data of the products: IR (film): *(8)*: $\nu=1700$ (C=O), 1660 cm⁻¹ (C=C); *(9)*: $\nu=1720$ cm⁻¹ (C=O); ¹H-NMR ($CDCl_3$): *(8a)*—*(8k)*: $\delta=7.0$ (dt, $^3J=6$ Hz, $^4J=1.5$ Hz, H-1), 4.6—5.0 (dt, $^3J=6$ and 7 Hz, H-2); *(9a)*—*(9j)*: $\delta=5.5$—6.0 and 5.0—5.3 (m, H-2 and H-3); 4.6—5.2 (H-1).

---

# Lithiated *N*-pivaloyl-tetrahydroisoquinoline—a Supernucleophile

By *Jean-Jacques Lohmann, Dieter Seebach, Max A. Syfrig*, and *Masaaki Yoshifuji*[*]

The Reissert reaction[1] [equation (a)], an umpolung of the $a^1$ reactivity[2] of isoquinolines, leads to electrophilic substitution at C-1 of the heterocycle; this approach is considered as the method of choice for this transformation. Its limitations, amongst others, are the poor nucleophilicity of the intermediate benzyl-, cyano-, and amide-stabilized carbanions; to our knowledge no alkylation reactions with secondary alkyl halides are known. Furthermore, no 1,1-dialkylated isoquinoline derivatives can be prepared.



(a)

Investigations of the acidity of secondary amines such as *(1)* indicated that as expected, the benzyl site of the corresponding nitrosamines (X = NO) and triphenylacetamides ($X=COC(C_6H_5)_3$) as well as the urea derivative *(4)*, could be readily deprotonated[3]. The nucleophilicity of the lithium compounds obtained however left much to be desired. It is therefore all the more surprising that the pivalylamide *(6)*[4a,b] reacts quantitatively within 5 min with *tert*-butyllithium/tetramethylethylenediamine (*t*BuLi/TMEDA) to produce an orange red solution of the lithium derivative, which at low temperature can be "titrated" against most electrophiles. Products of type *(6)* (Table 1) are produced even when the electrophile is a primary alkyl *chloride*, a *secondary* alkyl iodide[5] or an easily deprotonated ketone. The adducts formed from propionaldehyde and benzaldehyde are separable mixtures of the corresponding hydroxypivalamides *(6h)* or *(6i)*, and the aminoalkyl pivalates *(8)* or *(9)*, each compound being diastereoisomerically pure according to NMR spectroscopy. Dimerization with iodine produced only one isolable product *(10)*, of unknown configuration[6]. The abstraction of the tertiary benzylic proton from *(6a)* ($E=CH_3$) using the conditions described above was also facile, as shown by the formation of the dimethyl derivative *(11)*.

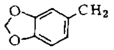
The conversion of the amide *(6)* into the amine *(5)* could best be performed[7] by reaction with exactly one equivalent of the aluminate *(12)*[8] in benzene at 20—80 °C (see example in Table 1). The hydroxyalkylated compounds *(6)* $E=C(OH)R^1R^2$, rapidly rearrange in trifluoroacetic acid to pivalates of type *(8)* or *(9)*[9].

As seen in Table 1, the α-hydroxy-isobutyramide *(3)*[4c] is also a candidate for the alkylation of the tetrahydroisoquinoline system. It may be lithiated by two equivalents *t*BuLi/HMPT and the products cleaved in boiling methanolic potassium hydroxide. We have however been unable to find

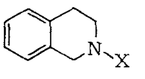
---

[*] Prof. Dr. D. Seebach, Dr. J.-J. Lohmann, Dipl.-Chem. M. A. Syfrig, Dr. M. Yoshifuji
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

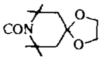
Table 1. Yields (from chromatography and/or recrystallization) and melting or boiling point of the products *(5)*—*(11)*. The reaction of the lithium derivatives *(2)* and *(3)* to give *(6)* and *(7)* respectively E = D, produced in both cases ≧95% monodeuterated compounds ($^1$H-NMR, MS analysis). All spectroscopic data and elemental analyses are consistent with the structures given. For the preparation and data of the aducts *(2)* and *(3)*, see ref. [4b, c].

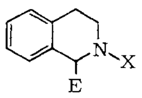
| Educt (Li derivative) | Reagent | Product | E | Yield [%] | M.p. [°C] or B.p. [°C/Torr] |
|---|---|---|---|---|---|
| *(2)* | Methyl iodide | *(6a)* | $CH_3$ | 94 | 66 |
| *(2)* | 1-Chloro-, 1-Bromo-, 1-Iodoctane | *(6b)* | $C_8H_{17}$ | 85, 85, 86 | 40 |
| *(2)* | 2-Iodopropane | *(6c)* | $(CH_3)_2CH$ | 90 | 71 |
| *(2)* | Iodocyclohexane | *(6d)* | $c$-$C_6H_{11}$ | 89 | 125 |
| *(2)* | 3.4-Methylenedioxybenzyl bromide | *(6e)* |  | 77 | 101 |
| *(2)* | Trimethylchlorosilane | *(6f)* | $(CH_3)_3Si$ | 88 | 111 |
| *(2)* | Tributyltin chloride | *(6g)* | $(C_4H_9)_3Sn$ | 84 | 210/0.01 |
| *(2)* | Propanal | *(6h)* and *(8)* | $C_2H_5CH(OH)$ [3:1] | 69 | 129<br>105/0.02 |
| *(2)* | Benzaldehyde | *(6i)* and *(9)* | $C_6H_5CH(OH)$ [3.5:1] | 78 | 160<br>76—78 |
| *(2)* | Cyclopentanone | *(6j)* | $(CH_2)_4C(OH)$ | 75 | 132 |
| *(2)* | Benzophenone | *(6k)* | $(C_6H_5)_2C(OH)$ | 83 | 182 |
| *(2)* | Iodine | *(10)* |  | 45 | 243 |
| *(6a)* | Methyl iodide | *(11)* |  | 59 | 80 |
| *(3)* | Methyl iodide | *(7a)* | $CH_3$ | 56 | 97—98 |
| *(2)* | *(12)* | *(1)* |  | 90 | 115/14 [a] |
| *(6a)* | *(12)* | *(5a)* | $CH_3$ | 77 | 125/14 [a] |
| *(6j)* | *(12)* [c] | *(5j)* | $(CH_2)_4C(OH)$ | 88 | 106 |
| *(3)* | KOH | *(1)* |  | 85 | 150/70 [a] |
| *(7a)* | KOH | *(5a)* | $CH_3$ | 71 | 187 [b] |

[a] Boiling point on Kugelrohr distillation. [b] Picrate; m.p. 187 °C (*Beilstein*: Handbuch der Organischen Chemie, Vol. 20, EII 185). [c] 1.5 equivalents.

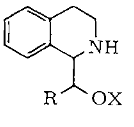


*(1)*, X = H
*(2)*, X = $COC(CH_3)_3$
*(3)*, X = $COC(OH)(CH_3)_2$
*(4)*, X =

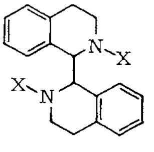




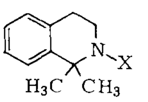
*(5)*, X = H
*(6)*, X = $COC(CH_3)_3$
*(7)*, X = $COC(OH)(CH_3)_2$



*(8)*, R = $C_2H_5$, X = $COC(CH_3)_3$
*(9)*, R = $C_6H_5$, X = $COC(CH_3)_3$



*(10)*, X = $COC(CH_3)_3$



*(11)*, X = $COC(CH_3)_3$

$Na[AlH_2(OCH_2CH_2OCH_3)_2]$

*(12)*

suitable reaction conditions for deprotonation of the corresponding benzamides.

Received: September 29, 1980 [Z 667 IE]
German version: Angew. Chem. *93*, 125 (1981)

CAS Registry numbers:
*(1)*, 91-21-4; *(2)*, 76068-81-0; *(3)*, 76068-82-1; *(5a)*, 4965-09-7; *(5a)*, 76068-83-2; *(5j)*, 76068-84-3; *(6a)*, 76068-85-4; *(6b)*, 76068-86-5; *(6c)*, 76068-87-6; *(6d)*, 76068-88-7; *(6e)*, 76068-89-8; *(6f)*, 76068-90-1; *(6g)*, 76068-91-2; *(6h)*, 76068-92-3; *(6i)*, 76068-93-4; *(6j)*, 76068-94-5; *(6k)*, 76068-95-6; *(7a)*, 76068-96-7; *(9)*, 76068-97-8; *(10)*, 76068-98-9; *(11)*, 76068-99-0; *(12)*, 75339-25-2; *(8)*, 76069-00-6; methyl iodide, 74-88-4; 1-chlorooctane, 111-85-3; 1-bromooctane, 111-83-1; 1-iodooctane, 629-27-6; 2-iodopropane, 75-30-9; iodocyclohexane 626-62-0; 3,4-methylendioxybenzyl bromide, 2635-13-4; trimethylchlorosilane, 75-77-4; tributylin chloride, 995-45-9; propanal, 123-38-6; benzaldehyde, 100-52-7; cyclopentanone, 120-92-3; benzophenone, 119-61-9

---

[1] *A. Reissert*, Ber. Dtsch. Chem. Ges. *38*, 1603, 3415 (1905); Review: *F. D. Popp*, Adv. Heterocycl. Chem. *24*, 187 (1979), and cited literature; see also *G. Stork, R. M. Jacobson, R. Levitz*, Tetrahedron Lett. *1979*, 771.

[2] *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979).

[3] *D. Seebach, D. Enders*, Angew. Chem. *87*, 1 (1975); Angew. Chem. Int. Ed. Engl. *14*, 15 (1975); *B. Renger, D. Seebach*, Chem. Ber. *110*, 2334 (1977); *T. Hassel, D. Seebach*, Angew. Chem. *91*, 427 (1979); Angew. Chem. Int. Ed. Engl. *18*, 399 (1979); *W. Lubosch, D. Seebach*, Helv. Chim. Acta *63*, 102 (1980); *W. Wykypiel, D. Seebach*, Tetrahedron Lett. *1980*, 1927.

[4] a) *N,N*-Dimethylpivalamide could not be metalated without self-condensation [3]. b) From *(1)* and pivaloyl chloride/$Et_3N$ ether at R. T., 90% yield, m.p. = 65 °C. c) From (1-chlorocarbonyl-1-methyl)ethyl acetate/*(1)*/$Et_3N$ in ether, *(1)* X = $COC(OAC)(CH_3)_2$ (m.p. = 61—62 °C) is first produced, whose alkaline hydrolysis gives *(3)* (m.p. = 78 °C). Total yield 74% relative to *(1)*.

[5] With *tert*-butyl iodide no alkylated product is formed, which instead of a radical mechanism [cf. *K. Deuchert, U. Hertenstein, S. Hünig, G. Wehner*, Chem. Ber. *112*, 2045 (1979)] or a *captodative* radical stabilization (*H. G. Viehe, R. Merényi, L. Stella, Z. Tanousek*, Angew. Chem. *91*, 982 (1980); Angew. Chem. Int. Ed. Engl. *18*, 917 (1979)), suggests an $S_N^2$-mechanism.

[6] Cf. *M.-A. Siegfried, H. Hilpert, M. Rey, A. S. Dreiding*, Helv. Chim. Acta *63*, 938 (1980).

[7] The amides *(6)* are just as stable towards hydrolysis by aqueous acid and alkali solutions as they are towards reaction with boiling ethylendiamine or diisobutylaluminum hydride (DIBAH). With $LiAlH_4$ or $LiBHEt_3$ a mixture of *(5)* and the *N*-neopentyl derivative were isolated.

[8] *A. Hajós:* Complex Hydrides. Elsevier, Amsterdam 1979; *J. Vit*, Eastman Org. Chem. Bull. *43* (3), 1 (1970); *J. Málek, M. Černý*, Synthesis *1972*, 217.

[9] The diastereomerically pure amides *(6)*, E = CH(OH)R are unfortunately converted into mixtures of diastereoismers *(8)* or *(9)*. This type of rearrangement has also been observed in peptides having hydroxyalkyl side chains, see e.g. *A. Rüegger, M. Kuhn, H. Lichti, H.-R. Loosly, R. Huguenin, Ch. Quiquerez, A. von Wartburg*, Helv. Chem. Acta *59*, 1075 (1976).

## Radical Complexes of Molybdenum as Reactive Intermediates

By *Dieter Fenske* and *Anestis Christidis*[*]

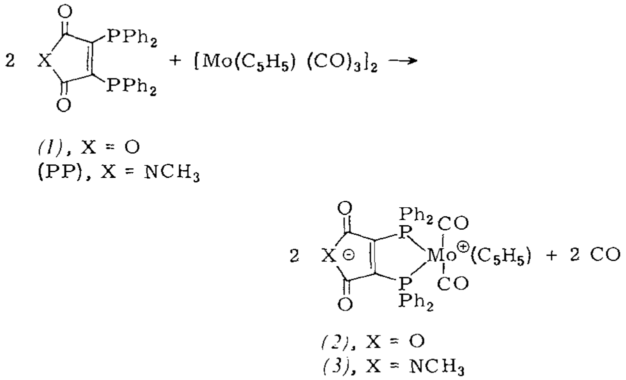
*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

In ligand exchange reactions of metal(0) complexes such as $Co_2(CO)_8$ or $Pd(PPh_3)_4$ with ditertiary phosphanes such as

---

[*] Priv.-Doz. Dr. D. Fenske, A. Christidis
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

bis(diphenylphosphino)maleic anhydride *(1)* and -*N*-methylimide (PP) we observed the formation of paramagnetic complexes in which the coordination of the bidentate ligand to the metal is accompanied by an electron transfer from the metal into a $\pi^*$ orbital of the ligand[1,2]. The ligand is converted into a complex bonded radical anion ($PP^-$), as illustrated by the formulas $Co^+(CO)_3(PP^-)$ and $Pd^{2+}(PP^-)_2$. Such complexes are in part extremely reactive, so they only occur as non-isolable intermediates, *e.g.* in the reaction of $Ni(C_5H_5)_2$ with *(1)*[1]. We have now observed a further secondary reaction to the deep-brown radical complexes *(2)* and *(3)* which are obtainable from $[Mo(C_5H_5)(CO)_3]_2$ and *(1)* or (PP), respectively.



*(1)*, X = O
(PP), X = NCH$_3$

*(2)*, X = O
*(3)*, X = NCH$_3$

The reaction of $[Fe(C_5H_5(CO)_2]_2$ with (PP) or *(1)* analogously leads to paramagnetic complexes of the type $Fe^+(PP^-)(C_5H_5)(CO)$. However, we restricted our studies to *(3)* and its secondary reactions.

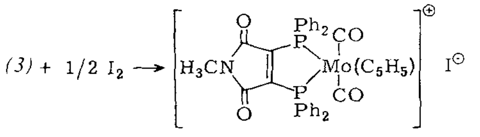
The following findings show that in the formation of *(3)* an unpaired electron is transferred from molybdenum into a $\pi^*$ orbital of the complex bonded ligand.

1. The magnetic moment of *(3)* is obtained from the susceptibility $\mu_{eff}$, which follows the Curie law, $\mu_{eff}=1.72\ \mu_B$ (at 295 K). Accordingly, an unpaired electron is present.

2. The ESR spectrum of *(3)* in tetrahydrofuran consists of a triplet of three groups of signals in the intensity ratio 1:2:1. The triplet structure is due to coupling between unpaired electron and P nucleus, the fine structure of each triplet component to corresponding coupling with the N and H nuclei of the NCH$_3$ group ($a_P=9.28$, $a_N=1.84$, $a_H=0.68$ gauss)[3].

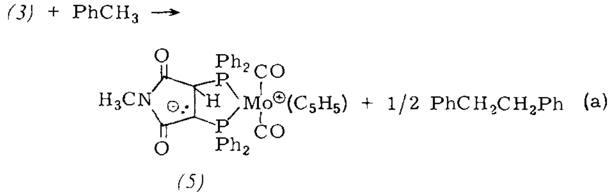
3. In the IR spectrum the $\nu$CO bonds of the ligand PP on complexation to *(3)* are lowered by about 80—100 cm$^{-1}$, as we have previously always observed when such ligands are transformed into radical anions[1,2].

4. Oxidation of *(3)* with $I_2$ in $CH_2Cl_2$ leads to the iodide *(4)* of the cation formed by withdrawal of electrons from *(3)*. *(4)* is diamagnetic and the $\nu$CO bands of the ligand PP occur in the same region as the free ligand. A crystal structure analysis confirms the presence of the complex cation and the anionic nature of the iodine outside of the coordination shell.



*(4)*

The yield of *(3)* is satisfactory only when the synthesis is carried out in a relatively short reaction time; a secondary reaction occurs on prolonged reaction in boiling toluene. On heating a solution of *(3)* in toluene for several days we obtained yellow crystalline *(5)*, which, in contrast to *(3)*, is diamagnetic. According to the IR spectrum, *(5)* contains CO ligands; the ligand PP has somewhat modified IR bands. The phosphorus atoms are no longer symmetry equivalent ($^{31}$P-NMR: $\delta=-26.5$ and $-72.9$, referred to 85% $H_3PO_4$; $J_{P,P}=10$ Hz[4]. A crystal structure determination[5] enabled *(5)* to be characterized and, at the same time, provided an explanation of the secondary reaction that takes place on prolonged heating in boiling toluene [eq. (a)]. The formation of 1,2-diphenylethane could be demonstrated.



*(5)*

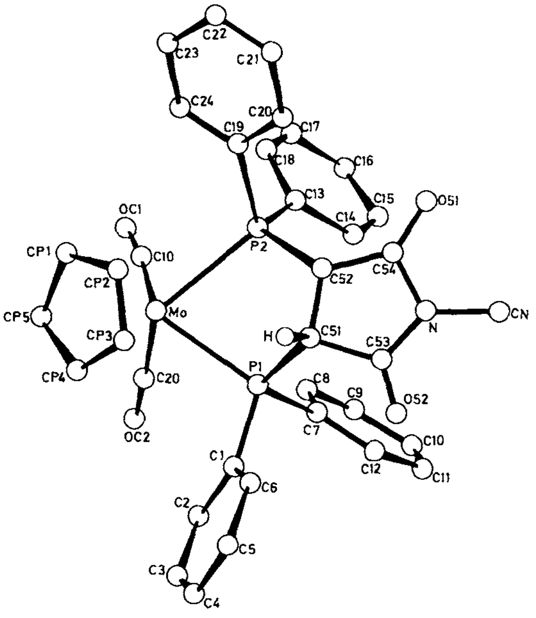


Fig. 1. Molecular structure of the molybdenum complex *(5)* in the crystal [5].

*(5)* crystallizes from toluene as a 1:1 solvate with the solvent. Figure 1 shows the molecular structure, in which the H atoms except that on C51 added during the formation of *(5)* from *(3)* have been omitted; it was unequivocally located in a difference Fourier synthesis. The formation of a CH bond at C51, which previously belonged to the C=C bond in the maleimide system of *(3)*, follows from the sum of the angles of the bonds from C51 to P1, C52 and C53 (332°). The atoms C52, C53, C54 and N in the five-membered ring, on the other hand are planar coordinated.

By addition of the H-atom, C51 becomes a center of chirality, and is probably formed by participation of the previously unpaired electron in the PP radical of *(3)*. The electrons of the original C=C bond are shifted to C52. The strong influence of the new bond system on the bond lengths in the Mo(H—PP$^-$) part of the molecule of *(5)* follows from the following data (in pm):

| | | |
|---|---|---|
| Mo—P1 = 250(0.1) | Mo—P2 = 256(0.1) | |
| P1—C51 = 184(1) | P2—C52 = 175(1) | |
| C51—C52 = 151(1) | C51—C53 = 153(1) | C52—C54 = 140(1) |
| N—C53 = 134(1) | N—C54 = 145(1) | |
| O52—C53 = 123(1) | O51—C54 = 123(1) | |

These distances indicate considerable mesomeric interaction of the free electron pair on C52 with the $>C{=}O$ groups, with the free electron pair on the imide nitrogen, and with the phosphorus atoms.

The cyclopentadiene ring in *(5)* is *pentahapto* bonded to molybdenum. The bond lengths in the $Mo(CO)_2(C_5H_5)$ part of the molecule are normal (in pm):

Mo—CP = 230—236    CP—CP = 139—142
Mo—C10 = 199(1)    Mo—C20 = 196(1)
C10—OC1 = 114(1)    C20—OC2 = 115(1)

A further proof for the constitution of *(5)* is its smooth oxidation to *(4)* [eq. (b)]:

$$(5) + I_2 \rightarrow (4) + HI \qquad \text{(b)}$$

*Procedure*

A solution of $[Mo(C_5H_5)(CO)_3]_2$ (1.2 g, 2.45 mmol) and (PP) (2.36 g, 4.91 mmol) in boiling toluene is stirred until evolution of CO is complete. Brown *(3)* crystallizes from the dark-brown solution; yield 95%.—The iodide *(4)* is prepared by oxidation of *(3)* (2.38 g, 3.41 mmol) with iodine (0.435 g, 3.42 mmol) in ether/1,2-dichloroethane (1:1) at °C; dark-red crystals, yield 80%.—When *(3)* is heated for several days at 80 °C in toluene, *(5)* is obtained as large, yellow crystals; yield 40—60%.

Received: April 30, 1980 [Z 675 IE]
German version: Angew. Chem. *93*, 113 (1981)

---

[1] *D. Fenske*, Angew. Chem. *88*, 415 (1976); Angew. Chem. Int. Ed. Engl. *15*, 381 (1976); Chem. Ber. *112*, 363 (1979); *W. Bensmann, D. Fenske*, Angew. Chem. *90*, 488 (1978); Angew. Chem. Int. Ed. Engl. *17*, 462 (1978).

[2] *W. Bensmann, D. Fenske*, Angew. Chem. *91*, 754 (1979); Angew. Chem. Int. Ed. Engl. *18*, 677 (1979).

[3] We thank Dr. *Korth*, Universität Essen, for recording and discussing the ESR spectrum.

[4] We thank Dr. *Heckmann*, Institut für Anorganische Chemie der Universität Stuttgart for measuring the $^{31}P$-NMR spectra.

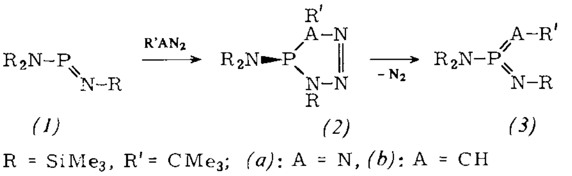
[5] *(5)*·1 toluene, space group $P2_1/n$; $a=964.2(4)$, $b=1457.0(6)$, $c=2602.5$ (9) pm, $\beta=97.45(3)°$, $Z=4$, $\rho_{calc}=1.41$, $\rho_{obs}=1.43$ g/cm$^3$, $\mu(MoK_\alpha)=4.8$ cm$^{-1}$. Low-temperature measurement (−130 °C), Syntex-P2$_1$ diffractometer, up to $2\theta=50°$; 6542 reflections, 5002 with $I>1.96\sigma(I)$. Solution of structure: heavy atom method, anisotropic refinement of all site parameters and temperature factors, $R_1=0.048$, $R_2=0.046$. All H-positions could be found in a final difference Fourier analysis.

---

## $N_2$-Elimination from a [3+2]-Cycloadduct of Diazoalkane and Amino(methylene)phosphane to give a $\lambda^3$-Phosphirane[**]

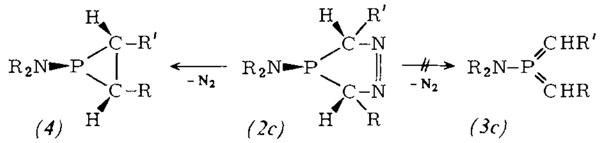
By *Edgar Niecke, Wolfgang W. Schoeller,* and *Dirk-Andreas Wildbredt*[*]

Kinetically stable phosphorus ylides such as *(3a)* and *(3b)* can be obtained by $N_2$-elimination from the thermolabile[1] [3+2]-cycloadducts *(2a)* and *(2b)*, respectively, of the iminophosphane *(1)* and the heteroallenes $R'AN_2$[2].

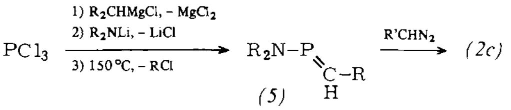


R = SiMe$_3$, R' = CMe$_3$; *(a)*: A = N, *(b)*: A = CH

In an attempt to generate the still unknown bis(methylene)phosphorane *(3c)* in a similar way from the analogue 1,2,4$\lambda^3$-diazaphospholine *(2c)* of *(2b)*, we obtained the $\lambda^3$-phosphirane *(4)* isomeric to the phosphorus ylide *(3c)*.



The highly electrophilic [bis(trimethylsilyl)amino](trimethylsilylmethylene)phosphane *(5)*, which is isoelectronic to *(1)*, proved to be a suitable precursor for the synthesis of *(2c)*. *(5)* can be readily obtained in a one-pot reaction and can be smoothly converted into the desired [3+2]-cycloadduct *(2c)* by reaction with 1-diazo-2,2-dimethylpropane.



The composition and constitution of *(5)*, *(2c)* and *(4)* are confirmed by elemental analysis, mass spectra, NMR data (Table 1) and, in the case of *(5)*, also by the IR spectrum. A noticeable feature on comparison of *(5)* with the known methylene phosphanes[3] is the downfield shift of the $^{31}P$-NMR signal ($\delta=308.7$) and the upfield shift of the $^{13}C$-NMR signal ($\delta=147.9$); this would indicate considerable changes in the polarity of the P=C bond and explain the high reactivity of *(5)* towards dipolar and oxidative addition[4]. The high value for $^2J_{SiCP}$ (40.5 Hz) would suggest existence of the sterically favorable Z-form, which has been demonstrated for the corresponding imine derivative *(1)*[5]. The P=C valence vibrations ($\nu_{P\ CH}=1120$, $\nu_{P\ CD}=1085$ cm$^{-1}$) can be identified by comparison of the very similar IR spectra of *(5)* and *(1)*[6] and of the derivative of *(5)* deuterated at the methylene carbon.

In the [3+2]-cycloaddition product *(2c)* the $^{31}P$-nucleus is drastically shielded ($\Delta\delta=300$ ppm), as is also observed in the transition from *(1)* to *(2a)*. The symmetry of *(2c)*—and thus

Table 1. $^{31}P$-, $^1H$-, $^{13}C$- and $^{29}Si$-NMR data of the compounds *(5)*, *(2c)* and *(4)* [a].

| | *(5)* | *(2c)* | *(4)* |
|---|---|---|---|
| $\delta(^{31}P)$ | 308.7 | 3.6 | −110.5 |
| $\delta(^1H)$ ($J_{HP}$ [Hz]) | | | |
| PNSiMe$_3$ | 0.27 (1.3) | 0.08 (1.3) | 0.20 (1.0) |
| PCSiMe$_3$ | 0.11 (1.3) | 0.14 (0.7) | 0.16 (0.2) |
| PCH(Si) | 7.13 (18.2) | 4.65 (2.5) | 0.59 (4.9)[b] |
| PCH(C) | — | 4.81 (0.5) | 2.19 (1.8)[b] |
| PCCMe$_3$ | — | 1.10 (0.2) | 0.93 (0.7) |
| $\delta(^{13}C)$ ($J_{CP}$ [Hz]) | | | |
| PNSiC$_3$ | 3.5 (6.7) | 4.2 (7.4) | 4.7 (5.7) |
| PCSiC$_3$ | 0.8 (9.0) | −1.4 (5.0) | 2.9 (4.5) |
| PC(Si) | 147.9 (70.3) | 90.4 (54.1) | 21.8 (59.1) |
| PC(C) | — | 110.0 (46.1) | 46.7 (56.4) |
| PCC | — | 35.6 (29.9) | 33.1 (11.2) |
| PCCC$_3$ | — | 24.0 (8.9) | 30.9 (6.0) |
| $\delta(^{29}Si)$ ($J_{SiP}$ [Hz]) | | | |
| PNSi | 6.5 (4.4) | | |
| PCSi | −6.5 (40.5) | | |

[a] 30% solution in CDCl$_3$; H$_3$PO$_4$ as external ($^{31}P$) and TMS ($^1H$, $^{13}C$, $^{29}Si$) as internal standard, 25 °C.

[b] $^{cis}J_{HH}=13.7$ Hz

---

[*] Prof. Dr. E. Niecke, Priv.-Doz. Dr. W. W. Schoeller, Dipl.-Chem. D.-A. Wildbredt
Fakultät für Chemie der Universität
Universitätsstr., D-4800 Bielefeld (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

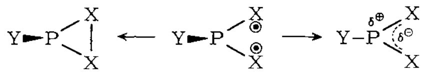
the *trans*-position of the methylene protons to the lone pair at the phosphorus atom—follows from the low absolute contribution of the P—C—H coupling constants.

The geometry in the HC—P—CH fragment of the $\lambda^3$-phosphirane *(4)* is the same; the *cis* relationship of the methylene protons is additionally indicated by the large value of the H—C—C—H coupling constant. A further indication of the special bonding in the phosphirane *(4)* is the marked upfield shift of the $^{31}$P-NMR signal.

An explanation of the findings described in the first paragraph is possible in terms of the Bell-Evans-Polanyi principle[7]. If the diradical *(A)* occurs as hypothetical intermediate in the $N_2$-elimination from the cyclic azo compounds *(2)* then it essentially depends upon two factors as to whether the ylide *(B)* or the three-membered ring *(B')* is formed:

a) on the magnitude of the resonance stabilization, which leads to a preference of the singlet *(B)* over the triplet state *(A)*;

b) on the stability of the X—X bond, whose contribution favors a ring closure to *(B')*.



(B')  (A)  (B)

The formation of the three-membered ring *(4)* in the reaction of *(2c)* would indicate that the gain in energy by cyclization already overcompensates that gained by resonance stabilization. Consistent with this conclusion are the MINDO/3 calculations[8] on this system, which show the ylide form to be the energetically less favorable and give a relatively high energy barrier for a valence isomerization *(B')*$\rightleftharpoons$*(B)* (Fig. 1).

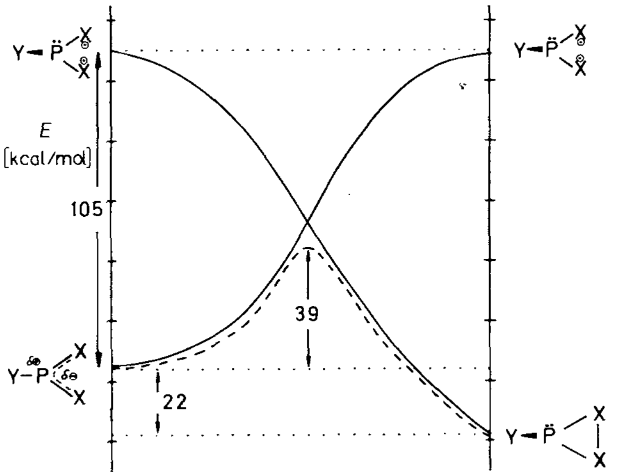


Fig. 1. The Bell-Evans-Polanyi principle for the equilibrium *(B)*$\rightleftharpoons$*(B')*. Dotted line: energy surface for the valence isomerization with $X = CH_2$, $Y = NH_2$ calculated according to the MINDO/3 method [8].

*Procedure*

*(5)*: Bis(trimethylsilyl)chloromethane (18 g, 92 mmol) is allowed to react with Mg (92 mmol) in tetrahydrofuran (THF) (50 cm$^3$) to give the Grignard compound, which is added dropwise into a solution of $PCl_3$ (12.6 g, 92 mmol) in THF (20 cm$^3$) cooled with an ice/salt mixture at such a rate that the temperature does not exceed 10 °C. The mixture is then heated to boiling and treated dropwise with a solution of lithium bis(trimethylsilyl)amide (15.3 g, 92 mmol) in THF (50 cm$^3$). After 1 hours' heating under reflux the solvent is removed and the residue pyrolized in a vacuum at 150 °C. *(5)* distils over as a bright yellow liquid; b.p. 57—59 °C/0.1 torr, yield 13.7 g (54%).

*(2c)*: A stirred solution of *(5)* (5.5 g, 20 mmol) in ether (20 cm$^3$) is treated at 0 °C with an excess of 1-diazo-2,2-dimethylpropane in THF. After 1 hours' stirring at room temperature the solvent is removed and the residue recrystallized from *n*-pentane; yield 4.1 g (55%) *(2c)*, white needles of m.p. 94-96 °C (dec.).

*(4)*: *(2c)* (2.0 g, 5 mmol) is pyrolyzed in a vacuum by heating from 80 to 120 °C. *(4)* distils over as a colorless liquid; b.p. 93—95 °C/0.1 torr; yield 1.4 g (76%).

Received: August 21, 1980 [Z 678 IE]
Supplemented: October 2, 1980
German version: Angew. Chem. *93*, 119 (1981)

---

[1] $\lambda^3$-Tetraazaphospholines that are stable at room temperature are known: *S. Pohl, E. Niecke, H.-G. Schäfer*, Angew. Chem. *90*, 135 (1978); Angew. Chem. Int. Ed. Engl. *17*, 136 (1978).

[2] Review: *E. Niecke* in Spec. Publ.: 30 Jahre Fonds der Chemischen Industrie, Verband der Chemischen Industrie, Frankfurt, October 1980; *E. Niecke, D. A. Wildbredt*, Chem. Ber. *113*, 1549 (1980) *E. Niecke, H. G. Schäfer*, unpublished.

[3] *G. Becker, O. Mundt*, Z. Anorg. Allg. Chem. *462*, 130 (1980); *R. Appel, A. Westerhaus*, Angew. Chem. *92*, 578 (1980); Angew. Chem. Int. Ed. Engl. *19*, 556 (1980); *H. Oehme, E. Leissring, H. Meyer*, Tetrahedron Lett. *1980*, 1141; *Th. C. Klebach, R. Lourens, F. Bickelhaupt*, J. Am. Chem. Soc. *100*, 4886 (1978); *K. Issleib, H. Schmidt, H. Meyer*, J. Organomet. Chem. *160*, 47 (1978).

[4] *E. Niecke, D.-A. Wildbredt*, J. Chem. Soc. Chem. Commun., in press.

[5] *S. Pohl*, Z. Naturforsch. *B 32*, 1344 (1977).

[6] *E. Niecke, W. Flick*, Angew. Chem. *85*, 586 (1973); Angew. Chem. Int. Ed. Engl. *12*, 585 (1973).

[7] *R. P. Bell*, Proc. R. Soc. London *A 154*, 414 (1936); *M. G. Evans, M. Polanyi*, J. Chem. Soc. Faraday Trans. *32*, 1340 (1936).

[8] For the energy of the triplet state *(A)* a vertical excitation from the equilibrium geometry of *(B)* was presumed.

---

## Preparative Separation of Lanthanoids by High-Pressure Liquid Chromatography (HPLC)[**]

By *Werner Weuster* and *Hermann Specker*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

All lanthanoids can be analytically separated in μg amounts by thin layer chromatography and HPLC[1]. It has also proven possible to separate all lanthanoids in ores, industrial products and irradiated fuel elements by HPLC and to determine them with a high degree of accuracy[2].

We have now attempted the isolation of individual lanthanoids in pure form, at first in mg amounts. In a preliminary experiment a mixture containing an overall weight of 4.64 mg of Sm, Gd, Eu and Tb was chromatographed, the technique adopted being based on analytical experience (Fig. 1). Diisopropyl ether/tetrahydrofuran/nitric acid (100:44:3) was used as eluent. The eluate was collected in separate fractions at 0.3 min intervals and the peak areas determined and printed out at the same intervals *via* an in-built integrator, thus enabling a direct determination of the content of each fraction. It can already be seen from Figure 1 that Sm and Tb are present in pure form, while Gd and Eu overlap in two fractions, as was also demonstrated thin-layer chromatographically. As a check, 1% of the neighboring element Eu was

---

[*] Prof. Dr. H. Specker, Dr. W. Weuster
Lehrstuhl Anorganische Chemie I der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)

[**] We thank Dr. *F. Eisenbeiss*, Merck, for providing us with the HPLC column.

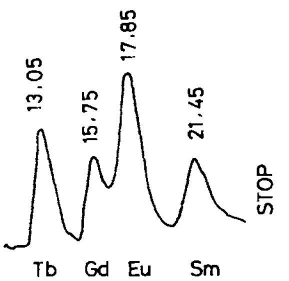


Fig. 1. HPLC separation of the elements Tb, Gd, Eu, and Sm with retention times (min). Column: Merck Si 40 (250 × 7 mm); Apparatus: Hewlett-Packard HPLC 1084B; fluorescence detector, Schoeffel Instruments. Detection: Fluorescence quenching on breakthrough of the lanthanoids without addition of reagent.

added to pure Sm, 1% Gd to the Tb; these additions could be detected very accurately by thin layer chromatography. Thus the purity of Sm and Tb is with certainty >99%. Further investigations with the difficultly separable pair Gd-Eu in different concentration ratios (up to 10:1) give in the case of 17 fractions an overlapping of two fractions, eight fractions of the Gd contained less than 1% Eu; seven fractions of the Eu less than 1% Gd.

As a practical application we have preparatively separated a monazite sand. The quoted amount of lanthanoids in the sample was 5.2 mg. La, Ce, Pr, Nd, Sm, Gd, Y and Er could be detected by HPLC analysis (Fig. 2). Of the total 85 fractions 4 contained pure Er, 2 pure Y, 6 pure Gd, 5 pure Sm, 10 pure Nd, 4 pure Pr, 12 pure Ce and 18 pure La, whereby

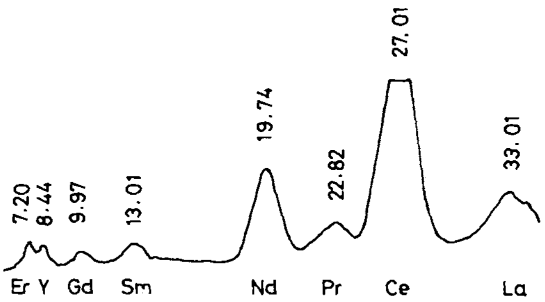


Fig. 2. HPLC separation of a monazite sand with retention times (min). Column, apparatus and detection, see caption to Fig. 1.

the purity is ≧99%, as was confirmed thin layer chromatographically by the addition method. These separations require a total of 35 minutes.

We used columns having a capacity of 5 mg. It is expected that larger columns with the same retention times and considerably higher flow will allow separations on the g scale.

Received: July 30, 1980 [Z 647 IE]
German version: Angew. Chem. 93, 90 (1981)

CAS Registry numbers:
Er, 7440-52-0; Y, 7440-65-5; Gd, 7440-54-2; Sm, 7440-19-9; Nd, 7440-00-8; Pr, 7440-10-0; Ce, 7440-45-1; La, 7439-91-0; Tb, 7440-27-9; Eu, 7440-53-1

---

[1] *K. Jung, H. Specker*, Fresenius Z. Anal. Chem. *288*, 28 (1977); *K. Jung, W. Weuster, H. Specker*, Ber. Bunsenges. Phys. Chem. *83*, 1131 (1979).

[2] *K. Jung, H. Specker*, Fresenius Z. Anal. Chem. *300*, 15 (1980); *R. Starke, W. Weuster, H. Specker, ibid. 300*, 287 (1980).

## BOOK REVIEWS

**Pyrolytic Methods in Organic Chemistry. Application of Flow and Flash Vacuum Pyrolytic Techniques.** By *R. F. C. Brown.* Academic Press, New York 1980. xii, 347 pp., bound $ 38.50.

This is the first book since *Hurd*'s 1929 treatise on "The Pyrolysis of Carbon Compounds" to be devoted to this subject. Written by one of the pioneers of flash vacuum pyrolysis, the book gives a fairly broad account of all pyrolytic methods used in organic chemistry. Although a book of this wide scope cannot possibly be fully comprehensive, all the more important reactions are treated, and a very good selection of references is given. By specifying the scope of each chapter and citing review articles on specialized topics (*e.g.* ester pyrolysis which is not dealt with in detail because an extensive review literature exists) a considerable degree of completeness is achieved, and further study by the interested reader is greatly facilitated. The literature covers the period up till the end of 1977, with a few references from 1978 being included.

After a short introductory chapter, the second chapter deals with apparatus and methods and is very useful for the novice in the field, giving designs and/or photographs of apparatus used by various groups.

The remaining seven chapters review the literature on pyrolysis reactions arranged according to compound type, reaction type, or the nature of the reactive intermediates generated by pyrolysis (free radicals, arynes, and cyclobutadienes; elimination reactions; carbenes and nitrenes; fragmentation of cyclic structures; fragmentation of acyclic structures; cleavage of carbocyclic and heterocyclic systems; rearrangement without fragmentation). Obviously, a uniform arrangement of the material was not intended, and this is largely due to the enormous diversity of reactions covered. It is altogether extremely difficult to classify such extensive material in a consistent manner, and therefore similar reactions are often found in several different chapters (*e.g.* arynes in Chapters 3, 5, and 6; derivatives of *Meldrum*'s acid in Chapters 5, 6, 8, and 9). Such cases are, however, always cross-referenced, so that the reader can easily trace the occurrence of related intermediates in different types of reactions throughout the book.

In some of the chapters detailed mechanistic discussion is limited, and many reaction mechanisms are taken from the original literature without further comment. In keeping with the rather factual presentation of the material, theoretical treatments of important aspects of the chemical reactivity of intermediates otherwise presented in the book are lacking or only briefly mentioned (*e.g.* diradicals, cyclobutadiene, benzynes). Comparisons with photochemical reactions are seldom made, but mass spectrometric analogies are frequently mentioned.

There are several less serious printing mistakes in the formulas, but few in the text, and the references are admirably precise. The layout is excellent and the book is easy to read.

All in all, the book can be strongly recommended to anybody who wishes to use or learn about pyrolysis reactions. Also the active researcher in the field will undoubtedly find it a most welcome reference volume.

*Curt Wentrup* [NB 523 IE]

## Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Das Geschenk der Erde.** Vom Salz zur modernen Chemie. By *H. Seidel* and *R. Wollner.* Econ Verlag, Wien 1980. 160 pp., bound, DM 68.00.—ISBN 3-430-182786

**Annual Reports on NMR Spectroscopy.** Edited by *G. A. Webb.* Academic Press, New York 1980.
Vol. 10A. x, 250 pp., bound, $ 66.00.—ISBN 0-12-505310-X
Vol. 10B. vii, 511 pp., bound, $ 89.00.—ISBN 0-12-505348-7

**Advances in Heterocyclic Chemistry.** Vol. 26. Edited by *A. R. Katritzky* and *A. J. Boulton.* Academic Press, New York 1980. ix, 247 pp., bound, $ 32.00.—ISBN 0-12-020626-9

**Coal Liquefact.** The Chemistry and Technology of Thermal Processes. By *D. Whitehurst, T. O. Mitchell,* and *M. Farcasiu.* Academic Press, New York 1980. xv, 378 pp., bound, $ 19.50.—ISBN 0-12-747080-8

**Annual Reports in Organic Synthesis—1979.** Edited by *L. G. Wade, Jr.* and *J. O'Donell.* Academic Press, New York 1980. xiii, 461 pp., bound, $ 23.50.—ISBN 0-12-040810-4

**Photoelectrochemistry.** By *Yu. Ya. Gurevich, Yu. V. Pleskov,* and *Z. A. Rotenberg.* Consultants Bureau, New York 1980. xiii, 239 pp., bound, $ 39.50.—ISBN 0-306-10953-0

**Electrochemistry.** Vol. 7. By *H. R. Thirsk, W. I. Archer, R. D. Armstrong, J. Grimshaw, N. Lakshminarayanaiah,* and *S. K. Rangarajan.* The Chemical Society, London 1980. xi, 268 pp., bound, DM 132.00.—ISBN 0-85186-870-3. A volume in the series "Specialist Periodical Reports"

**Frontiers of Free Radical Chemistry.** Edited by *W. Pryor.* Academic Press, New York 1980. xiii, 385 pp., bound, $ 27.00.—ISBN 0-12-566550-4

**Advanced Mass Spectrometry.** Applications in Organic and Analytical Chemistry. By *U. P. Schlunegger.* Pergamon Press, Oxford 1980. xii, 143 pp., bound, $ 27.50.—ISBN 0-08-023842-4

**High-Performance Liquid Chromatography.** Advances and Perspectives. Vol. 1. Edited by *Cs. Horváth.* Academic Press, New York 1980. xi, 330 pp., bound, $ 35.00.—ISBN 0-12-312201-5

**Probenahme.** Theorie und Praxis. Vorträge beim 9. Metallurgischen Seminar des Fachausschusses für Metallhüttenmännische Ausbildung der GDMB Gesellschaft Deutscher Metallhütten- und Bergleute. Heft 36. Verlag Chemie, Weinheim 1980. vii, 384 pp., bound, DM 68.00.—ISBN 3-527-25882-5

**Der Weg zum Geprüften Pharmareferenten.** Ein Kompendium in Frage und Antwort. By *R. Murschall.* Verlag Chemie, Weinheim 1980. xvi, 509 pp., bound, DM 64.00.—ISBN 3-527-25877-9

**Neurologie.** Examensfragen Medizin. By *G. Sollberg.* edition medizin im Verlag Chemie, Weinheim 1980. 112 pp., bound, DM 16.00.—ISBN 3-527-15029-3

**Medizinische Psychologie—Medizinische Soziologie.** Examensfragen Medizin. Edited by *W. Rathgeber.* edition medizin im Verlag Chemie, Weinheim 1980. xi, 187 pp., bound, DM 17.00.—ISBN 3-527-15031-5

**Spectroscopic References to Polyatomic Molecules.** By *V. N. Verma.* IFI/Plenum, New York 1980. 126 pp., bound, $ 75.00.—ISBN 0-306-65190-4

**Principles of Applied Clinical Chemistry.** Chemical Backgrounds and Medical Applications. Vol. 3. By *S. Natelson* and *E. A. Natelson.* Plenum Press, New York 1980. vii, 554 pp., bound, $ 42.50.—ISBN 0-306-40276-9

**Handbook of Chemical Microscopy.** Vol. 2. By *E. M. Chamot* and *C. W. Mason.* John Wiley & Sons, New York 1980. ix, 238 pp., bound, $ 14.75.—ISBN 0-471-04122-X

**Herz und Gefäße.** Examensfragen Medizin. By *H.-J. von Mengden.* edition medizin im Verlag Chemie, Weinheim 1980. 256 pp., bound, DM 24.00.—ISBN 3-527-15028-5

**Klinische Chemie.** Lehrbuch zum Gegenstandskatalog. By *G. Peter.* edition medizin im Verlag Chemie, Weinheim 1980. xvii, 561 pp., bound, DM 28.00.—ISBN 3-527-15038-2

**Biologie.** Lehrbuch zum Gegenstandskatalog. By *R. Blaich.* edition medizin im Verlag Chemie, Weinheim 1980. v, 166 pp., bound, DM 17.00.—ISBN 3-527-15027-7

**Pädiatrie.** Lehrbuch zum Gegenstandskatalog. Edited by *F. Küster.* edition medizin im Verlag Chemie, Weinheim 1980. 312 pp., bound, DM 25.00.—ISBN 3-627-15036-6

---

**Editorial office:** Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

**Editor:** *O. Smrekar,* **Translation Editors:** *I. G. Neil and A. Stimson.*

**Publishers:** Verlag Chemie, GmbH. (Managing Directors Dr. *Helmut Grünewald* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE
CHEMIE

Volume 20 · Number 2
February 1981
Pages 135–216

International Edition in English

# Toxication of Foreign Substances by Conjugation Reactions

By Dieter Reichert[*]

Elucidation of the metabolic pathways of foreign compounds in mammalian organisms contributes substantially to the understanding of toxic effects and is therefore a basic component of every risk analysis. The abundance of chemical reactions which take part in metabolic transformations allows one to speculate that we, with our present state of knowledge, are just at the beginning of a development which will help explain the interplay between chemical structure, biochemical transformation and toxic effects. This applies in particular to the conjugation of foreign compounds with structures and molecules endogenous to the body. Until recently it was thought that these conjugation reactions lead to chemically and biologically inert products, which could be easily eliminated by the organism. Using new biological testing procedures and sensitive methods of analysis, this assumption has been refuted. The fact is, that highly toxic, mutagenic and carcinogenic products can result from the chemical interactions of foreign substances with endogenous substrates.

## 1. Introduction

Nowadays we are exposed to a constantly increasing number of xenobiotics, *i.e.* substances foreign to the organism; examples of these are pesticides, solvents, occupationally used compounds, drugs and food additives such as olfactory and taste substances, stabilizers, antioxidants and many others. These xenobiotics have entirely different types of chemical structures. Some are subsequently eliminated unaltered, in urine, feces or exhaled air. These substances often do not cause any effect in the body; they are biologically inactive. Usually, however, foreign compounds are chemically changed in the organism by endogenous, nonspecific enzymes, the so-called "drug-metabolizing enzymes". These metabolic alterations often influence only the toxicological or pharmacological profile of the foreign substance. The products which are formed vary according to the type of metabolic transformation and to the chemical structure of the xenobiotic, and can be either nontoxic and easily eliminated, or be biologically reactive, causing acute toxic damage in organs, as well as mutagenic and carcinogenic effects[1,2].

In the risk assessment of xenobiotics, consideration of chemical reactivity and metabolic studies are the first steps in the investigation. Thereby it is most essential to delineate the reaction pathways and to test the detected metabolites for their potential biological reactivity. The rapid progress in this field is evident from the identification of constantly increasing numbers of metabolic pathways and new types of metabolites[3].

The complexity of the biochemical alterations leading ultimately to toxication or detoxication will be elucidated using the example of conjugation reactions in which endogenous molecules are transferred to functional groups of foreign compounds to form a conjugate.

---

[*] Priv.-Doz. Dr. D. Reichert
Institut für Pharmakologie und Toxikologie der Universität
Versbacher Strasse 9, D-8700 Würzburg (Germany)

*0570-0833/81/0202-0135 $ 02.50/0*

## 2. Metabolic Fate of Xenobiotics in the Organism

Metabolic changes or biotransformations generally take place in two phases (Fig. 1). In Phase I, functional groups are introduced into a lipophilic substance *via* oxidation, reduction or hydrolysis. These reactions are catalyzed by various monooxygenases, reductases or hydrolases. Phase II, which can run either subsequent or parallel to Phase I, is a conjugation reaction. Here an endogenous substance, for example glucuronic acid, is conjugated *via* a transferase to a functional group of a foreign molecule. The result is that the compound becomes more polar, can be more easily eliminated and generally is less toxic. The reaction sequence is illustrated in Figure 2; following the introduction of a functional group into an aromatic or aliphatic molecule *via* oxidation, the endogenous substance is bound to this group[3-5].

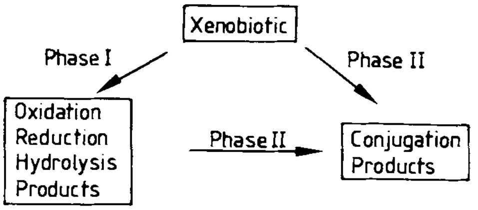


Fig. 1. Scheme of the biotransformation of compounds foreign to the body.

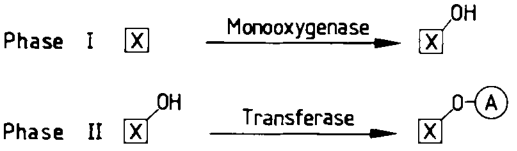


Fig. 2. Scheme of a "functionalization reaction" with subsequent conjugation.

Activation (toxication) of xenobiotics by metabolic conversion was first shown in some oxidation reactions, *i.e.* with benzo[a]pyrene, dimethylnitrosamine or, more recently, with vinyl chloride; only the oxidation products of these compounds are mutagenic and carcinogenic[6]. The oxidation products of the widely used analgesic paracetamol or of the diuretic furosemide are held responsible for liver necrosis[7]. The Phase II reactions known to date, however, often diminish toxic or pharmacologic effects by decreasing the concentration of the biologically active molecule. From this fact the assumption has developed that conjugation reactions are detoxifying reactions, as contrasted with oxidative processes. Nowadays this supposition is no longer valid without qualification, since investigations show that the conjugation products formed are not always as innocuous as had been originally assumed. This fact was recognized essentially after the introduction of biological testing methods which led to new, unexpected findings regarding the significance of conjugation reactions for the detoxication and toxication of compounds foreign to the body.

## 3. Detection of Toxic Metabolites

Metabolic studies can be useful in clarifying the mechanisms of toxicity of xenobiotics. In this respect, one of the greatest difficulties is the unequivocal identification of the respective reactive, and thereby assumedly toxic, metabolites. The proof is often only indirectly attainable on account of the high degree of reactivity and the short half-life of the intermediates. In the meantime, a series of *in vitro* testing methods has been developed; these tests are based principally on the proof of DNA damage in bacterial or mammalian cells. In this review, only the essential tests will be briefly characterized.

### 3.1. Covalent Binding to Macromolecules

The presence of reactive products can be established by the detection of covalent binding to tissue macromolecules such as proteins, DNA or RNA[1,8]. The evidence of covalently bound radiolabel after administration of a radiolabeled xenobiotic in an *in vitro* procedure is a primary testing method for reactive metabolites. By varying the labeling of the molecule it is possible to ascertain which part is covalently bound. The incubation of the assay with the appropriate transferases and cosubstrate provides additional indications of the structural characteristics of the reactive product.

### 3.2. Mutagenicity Tests

In order to determine their mutagenic potential, xenobiotics (or their metabolites) are tested as to whether they induce mutations in genes or chromosomes. Gene mutation tests are carried out on microbial systems; chromosomal damages can be investigated additionally with human cell cultures or with cultured mammalian cells[9-11]

#### 3.2.1. Microbial Tests

The microbial testing system which is currently most often used for the detection of mutagens and/or carcinogens was developed by *Ames et al.*[12]. This procedure employs bacterial strains of *Salmonella typhimurium,* which are incapable due to a point-mutation, of synthesizing the amino acid histidine. The introduction of a mutagen gives rise to back-mutants, which can again produce histidine. They are able to form colonies on nutrient media which do not contain histidine. The colonies are macroscopically visible; their number is an indication of the quantity of back-mutants and allows one to estimate the intensity of a mutagenic effect. One advantage of the Ames-Test is that it enables a differentiation between xenobiotics which cause base-pair substitution mutations and those which induce frame-shift mutations[*]. In the first case, they are generally alkylating compounds of low molecular weight and in the second case they are mostly aromatic substances with two or more rings. An additional attribute of this test is that it enables examination of the mutagenic characteristics of a xenobiotic with enzymes from different species and tissues. Transferases and cosubstrate, along with the foreign compound, are added to the Salmonella strains and incubated. Many reactive, potentially carcinogenic metabolites of xenobiotics have been identified using this effective testing procedure[13].

---

[*] Frame-shift mutations are characterized by deletion or insertion of a nucleotide in the DNA sequence, which results in a shift from the normal in each subsequent group of three nucleotides.

### 3.2.2. Cell Transformation Tests

Cell transformation tests have proven particularly successful—in addition to the Ames Test—for the detection of chemical carcinogens. In this method, mammalian cells (*i. e.* human fibroblasts, liver cells, lymphocytes or hamster embryo cells) are isolated and exposed to the test substance in a culture medium. The cells can then be fixed for cytogenetic studies and microscopic evaluation (chromosome and genome mutations), or they can be added to a culture medium in which only the transformed cells can continue growing[9, 10]. The number of colonies is a measure of a mutagenic effect. As with the Ames Test, microsomal enzymes or transferase activity can also be added with the test substance in order to detect metabolically reactive products as well.

The host-mediated assay, along with a number of additional test systems, is particularly valuable; bacterial or mammalian cells are implanted (generally intraperitoneally) into animals, and the latter treated with the test chemical. The administered cells and their mutants are subsequently recovered and counted. The advantage of this system is primarily that the formation and transformation of the reactive intermediates take place in the host organism itself[14].

## 4. Important Conjugation Reactions

The conjugation reactions which are important in man are listed in Table 1. Quantitatively, the most significant reaction is the glucuronidation of xenobiotics; this is mediated by glucuronyl transferases, which transfer glucuronic acid to numerous substrates. Other transferases transfer sulfate-, acetyl-, glutathione-, glycine- or methyl-residues. The various enzymes are either membrane-bound or dissolved in the cell cytosol (Table 1). Conjugation reactions generally require the expenditure of metabolic energy. One exception is the conjugation with glutathione; when catalyzed by glutathione transferases, glutathione is not only able to bind to substrates but can also react directly with sufficiently electrophilic partners. A decrease in the glutathione content and the appearance of mercapturic acids (*S*-substituted, *N*-acetyl derivatives of cysteine) in urine are proofs of glutathione conjugation and also provide strong evidence for the occurrence of electrophilic, toxic metabolites[15].

Table 1. Important conjugation reactions in humans.

| Conjugation | Enzymes | Subcellular Localization | Functional Groups |
|---|---|---|---|
| Glucuronidation | Glucuronyl transferases | Endoplasmic reticulum | —OH, —COOH, —$NH_2$, NH, —SH |
| Sulfation | Sulfotransferases | Cytosol | —OH, Aryl—$NH_2$ |
| Acetylation | Acetyltransferases | Cytosol | —$NH_2$ |
| Glutathione conjugation | Glutathione transferases | Cytosol | —Halogen, Epoxides, —$NO_2$ |
| Glycine conjugation | Acyltransferases | Mitochondria | —COOH |
| | Glycine transferases | Mitochondria + Cytosol | —COOH |
| Methylation | Methyltransferases | Endoplasmic reticulum + Cytosol | Aryl-OH, —$NH_2$, NH, —N, —SH |

The cyanide-thiocyanate detoxication is not specifically elaborated in Table 1. In this reaction, the toxic cyanide is converted into thiocyanate by the enzyme rhodanese. Thiosulfate serves as the sulfur donor. This reaction has long been employed therapeutically in the administration of thiosulfate in cases of hydrocyanic acid poisoning.

Binding to colamine (2-aminoethanol) is a novel conjugation reaction recently detected in man and animals. Here strongly electrophilic intermediates can react with phosphatidylethanolamine with (enzymic) splitting of phosphatidyl residues. *N*-substituted colamine has been found as a metabolite in the metabolism of halothane (2-bromo-2-chloro-1,1,1-trifluoroethane) and 1,1-dichloroethylene, as well as in blood and urine[16, 17]. In essence, this reaction can be viewed as an inactivation step. The reaction leads, however, to membrane damages, since phosphatidylethanolamine occurs primarily in the organism as a bound component of cell membranes; this is the current explanation for the hepatotoxicity of 1,1-dichloroethylene [17]. The metabolism of this carcinogenic compound is shown in Figure 3.

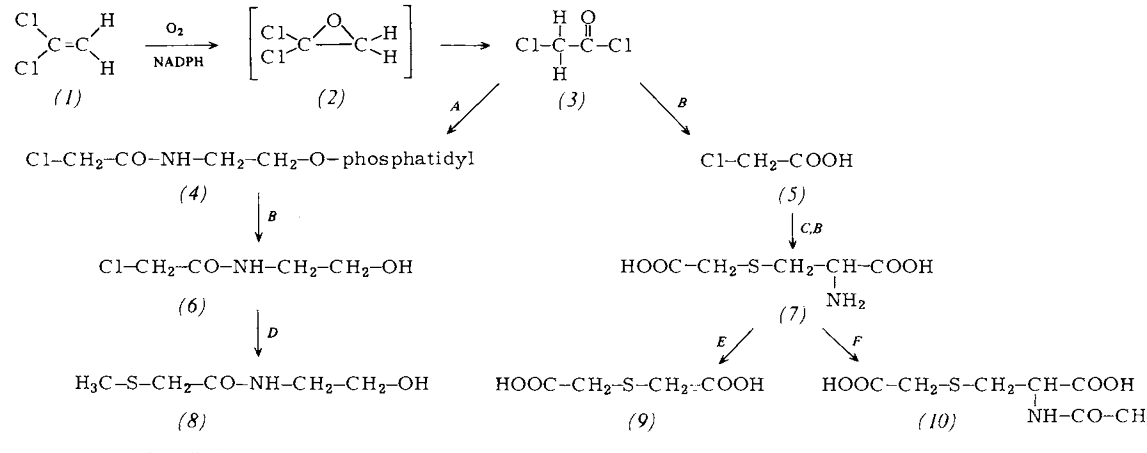


Fig. 3. Metabolism of 1,1-dichloroethylene *(1)*. The metabolites identified were *(5)* as well as *(8)—(10)*. A: reaction with phosphatidylethanolamine, B: hydrolysis, C: reaction with glutathione, D: reaction with methionine, E: deamination and decarboxylation, F: acetylation.

The conjugation reactions cited above also occur in most mammalian organisms. However there are noteworthy qualitative and quantitative differences among some animal species[18,19]. For example, cats have a strongly diminished ability to glucuronidize xenobiotics; guinea pigs do not form mercapturic acids, as the *N*-acetylation of the *S*-substituted cysteines cannot be accomplished: dogs cannot acetylate aromatic amines and hydrazines. Non-human primates resemble man most closely in terms of enzymic makeup.

### 4.1. Activation by Glucuronidation and Sulfation

In the human organism, glucuronidations are carried out on endogenous substances (steroids, thyroxine, bilirubin or serotonin and some amino acids) as well as on xenobiotic substances. In this way the glucuronyl residue can be enzymatically conjugated with a wide spectrum of chemically different compounds (Table 1).

The mechanisms for the formation of glucuronyl- and sulfate compounds are well known[4]. The first step in the biosynthesis of "activated" glucuronic acid is catalyzed by the UDPG-pyrophosphorylase enzyme (UDP = uridine-5′-diphosphate, PP = diphosphate):

$$\text{Glucose-1-phosphate} + \text{UTP} \rightarrow \text{UDP-glucose} + \text{PP}$$

UDP-glucuronic acid is formed by dehydrogenation of UDP-glucose:

$$\text{UDP-glucose} + 2\,\text{NAD}^{\oplus} \rightarrow \text{UDP-glucuronic acid} + 2\,\text{NADH} + 2\,\text{H}^{\oplus}$$

The transfer of UDP-glucuronic acid to the different functional groups (XH) is accomplished by UDP-glucuronyl transferases

$$\text{UDP-glucuronic acid} + \text{R—XH} \rightarrow \text{R—X—}\beta\text{-glucuronide} + \text{UDP}$$

Sulfotransferases transfer the sulfate residue to the hydroxyl and amino groups (Table 1). The sulfation of xenobiotics requires considerable energy. The following reactions make this clear; the sulfate donor is 3′-phosphoadenosine-5′-phosphosulfate (PAPS), which is formed from adenosine-5′-phosphosulfate (APS).

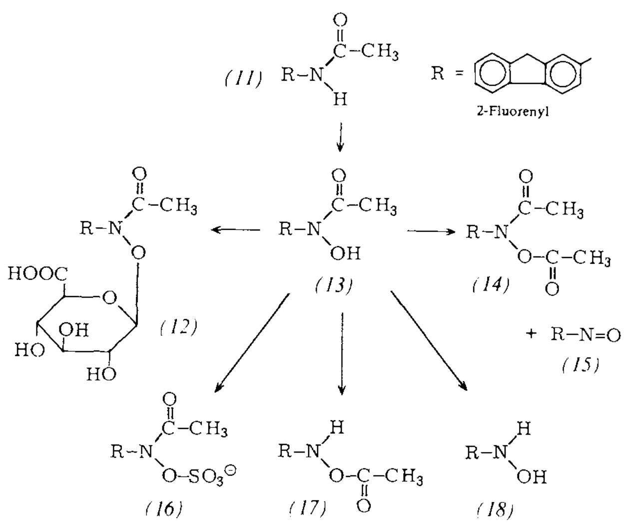
$$\text{APS} + \text{ATP} \rightarrow \text{PAPS} + \text{ADP}$$

APS in turn is formed from sulfate ions and ATP:

$$\text{SO}_4^{2\ominus} + \text{ATP} \rightleftharpoons \text{APS} + \text{PP}$$

Finally, the sulfotransferases transfer the high energy sulfate residue to a functional group (usually —OH) of a xenobiotic:

$$\text{R—OH} + \text{PAPS} \rightarrow \text{R—O—SO}_3^{\ominus} + \text{PAP} + \text{H}^{\oplus}$$



The fact that conjugation reactions can also lead to the toxication of absorbed substances was first established in the case of glucuronidation and sulfation[6,20,21]. *N*-(2-Fluorenyl)acetamide, (2-(*N*-acetylamino-fluorene)) (AAF) *(11)* served as the model compound. This substance is carcinogenic for some animal species and noncarcinogenic for others. There were indications that neither AAF *(11)* nor the oxidation product *N*-hydroxy-AAF *(13)* could be the ultimate cancer causing compound. Both, for example, do not bind to DNA in appropriate test systems. However if one incubates this system with sulfotransferase and glucuronyl transferase, reactive products which can bind to DNA are formed[23]. An intermediate product of these reactions, the *N*-bound sulfate *(16)*, is currently regarded as the ultimate carcinogen in this reaction sequence. This assumption is supported by the highly electrophilic nature of this ester, by a direct correlation of sulfotransferase activity with the formation of hepatic tumors in various rat strains and by a lowered rate of tumor formation if the sulfate concentration in the rat is experimentally reduced[24]. This compound's high biological activity is also demonstrated by a high mutagenic potential[25].

In spite of the apparent key role of the ester of sulfuric acid *(16)* in the origin of hepatic tumors, it was possible to prove that further reaction pathways of *N*-hydroxy-AAF *(13)* to electrophilic products exist. A major metabolite of *N*-hydroxy-AAF *(13)* arises through conjugation with glucuronic acid. This metabolite, AAF-*O*-glucuronide *(12)*, is formed in the liver and can easily reach other tissues *via* the bloodstream. As the ultimate carcinogen, it is held responsible for the formation of extrahepatic tumors, *i.e.* of the mammary glands and of the auditory canal. Similarly, *N*-acetoxy-AF *(17)* and *N*-acetoxy-AAF *(14)* are discussed as ultimate carcinogens, in particular for the extrahepatic tissues named above, for which no measurable sulfotransferase activities have been detected. It is assumed that the cited esters *(14)*, *(16)*, and *(17)* are precursors of the reactive nitrenium ion, which is ultimately responsible for the covalent binding to proteins, RNA or DNA.

This example from experimental cancer research shows how difficult it can be to discover the ultimate carcinogen or the actual toxic agent, particularly if several possible reactive products are identified by metabolic studies.

Other compounds having a hydroxylamine-group exhibit similar properties, in that they form reactive *N*-glucuronides or *N*-sulfates *in vivo* and *in vitro*. Further examples are the glucuronides of *N*-(*p*-biphenyl)hydroxylamine, benzidine, 2-naphthylamine and 1-naphthylamine. Their conjugation products are held responsible for urinary bladder carcinomas[20,22]. Here the glucuronic acid can be bound either as a 1-desoxy derivative or as *N*-glucuronide (Fig. 4).

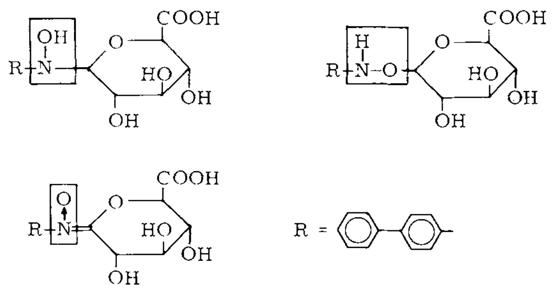
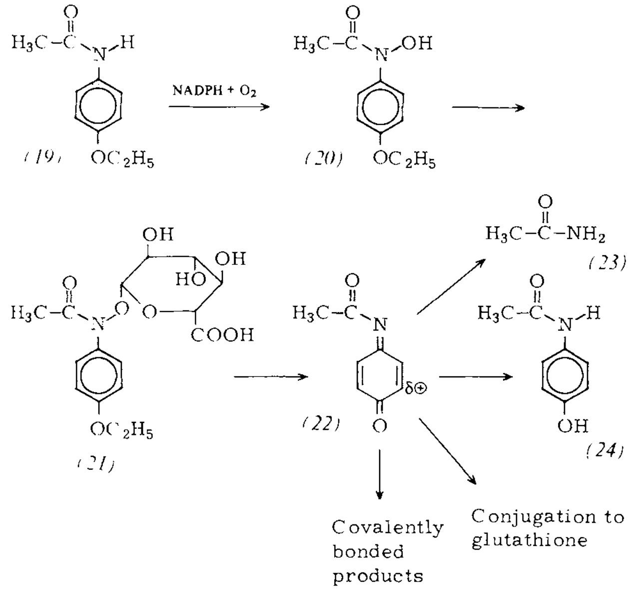


Fig. 4. Carcinogenic glucuronic acid conjugation products of *N*-(*p*-biphenyl)hydroxylamine.

A further example of a *N*-hydroxylation with subsequent glucuronidation is provided by phenacetin, which is widely known as an analgesic. Phenacetin *(19)* is first *N*-hydroxylated to *(20)* and then glucuronidized to *(21)*[26]. In the metabolism of this compound, the formation of a reactive intermediate (*N*-acetyl-imidoquinone) *(22)*, which can bind covalently to proteins, is achieved only *via* the glucuronide or the sulfate. The formation of paracetamol *(24)* *via* a glucuronide is regarded as certain, even if other alternative pathways to that shown are conceivable. The glucuronide is formed in the liver, but it can be transported to other organs, *i. e.* to the kidneys where it can be concentrated in the collecting tubules. It is conceivable that a reactive intermediate could also be formed there, possibly additionally accelerated by the low pH. This could explain the papillary necroses observed with phenacetin abuse[26]; another consequence of such abuse is a high incidence of renal pelvis tumors[27,28]. In this case, the conjugation with glutathione is regarded as an inactivation step, *i. e.* detoxication.



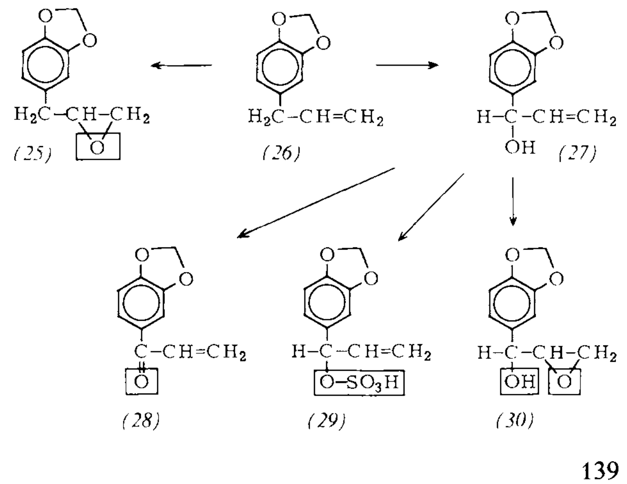
These examples show that *N*-hydroxy compounds such as the hydroxylamines tend to form reactive *N*-bonded sulfates or *O*-glucuronides[29]. Both conjugation products are better suited to bind to nucleic acids than the respective hydroxylamines. The reason for this is that the sulfate- and glucuronide-residues are better leaving groups than the hydroxyl groups and therefore more readily form the electrophilic arylnitrenium ions.

Many aromatic amines are not only used as drugs, as cited above, but are widely dispersed in general in the environment and are, to some extent, known carcinogens. Therefore the incidence of these compounds, as well as the formation of such conjugation products are judged to be toxicologically critical for man. For animal species which are not capable of *N*-hydroxylating amines, these compounds are not carcinogenic, as has been shown by the example of AAF *(11)* (Table 2).

Table 2. *N*-hydroxylation of *N*-(2-fluorenyl)acetamide (AAF) *(11)* in different animal species correlated with carcinogenic activity [30].

| Species | *N*-hydroxylation [% of dose] | Carcinogenic Effect |
|---|---|---|
| Rabbit | 13—20 | + |
| Rat | 0.3—15 | + |
| Man | 4—14 | ? |
| Dog | 5.2 | + |
| Hamster | 5.0 | + |
| Mouse | 1.8—2.3 | + |
| Cat | 1.5 | + |
| Steppe lemming | Traces | − |
| Guinea pig | 0 | − |
| Rainbow trout | 0 | − |

There are a number of other compounds and structures, besides the *N*-hydroxy compounds, which are activated by glucuronidation or sulfation. Safrole *(26)* (4-allyl-1,2-methylenedioxybenzene) is a naturally occurring component of oil of sassafras, certain spices and essential oils. It has also been used as a flavoring component in soft drinks. This substance is hepatotoxic for man and animal[31,32] and produces adenomas and carcinomas of the liver in mice and rats[31,33]. This substance therefore has been prohibited as a food constituent in the USA since 1960. Safrole *(26)* is activated *via* two different metabolic steps in the mammalian organism. The first step in the metabolism of this substance is the oxidation to the proximate carcinogen 1′-hydroxysafrole *(27)*[34]. By means of this "functionalization reaction", the transmittance of endogenous substrates by transferases is made possible. The sulfate *(29)* and the glucuronide can be identified as electrophilic esters; both are regarded as candidate ultimate carcinogenic metabolites and therefore are held responsible



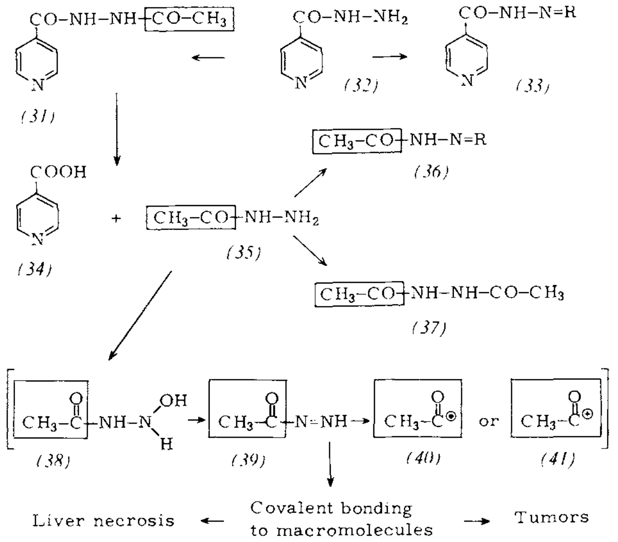
for the formation of liver carcinomas[35]. In addition to these conjugation reactions, the double bond is oxidized to an epoxide [see *(25)* and *(30)*]. Epoxides themselves can often bind covalently to macromolecules. Obviously, not all of the covalently binding structures occurring in the metabolism of safrole *(26)* have yet been clarified.

Numerous other allylic and propenylic allenes, which closely resemble safrole *(26)* in structure, are components of natural foodstuffs or can be used as food additives. One of these representative compounds is estragole (1-allyl-4-methoxybenzene), which is an additive to vinegar and a component of many essential oils and spices, *i. e.* anise, star anise, fennel and tarragon. Even low doses of this substance induce hepatocellular carcinomas in mice[36]. In this case as well, there is first an oxidation to a hydroxy-compound; the formation of an ester of 1′-hydroxyestragole leads to an electrophilic derivative, which is held responsible for the carcinogenic effect of estragole.

### 4.2. Activation by Acetylation

Acetylations take place preferably on substances which have an amino group. The high energy molecule in this case is acetyl coenzyme A, which is formed by numerous intermediary metabolic reactions. *N*-acetylation is a primary inactivation route for numerous drugs of medical interest such as procainamide, hydrazine, sulfamethazine and various other compounds with sulfonamide structures Furthermore, *N*-acetylation is a main pathway in the metabolism of carcinogenic arylamines such as 2-fluorenylamine and 2-naphthylamine[4,37].

An example of a toxication through acetylation is provided by the compound isonicotinic acid hydrazide or isoniazid (INH) *(32)*, which is the most potent tuberculostat currently at our disposal. Following the acetylation on the free amino group of the hydrazide moiety producing *(31)*, hydrolytic cleavage to isonicotinic acid *(34)* and acetylhydrazine *(35)* occurs. Acetylhydrazine *(35)* is regarded as causing liver damage. The molecular basis for this damage is postulated to be the oxidation of acetylhydrazine, which occurs on the endoplasmic reticulum, to a highly reactive acylating and alkylating intermediate. Covalent binding on macromolecules goes along with cell necrosis and possible formation of tumors[38]. These findings explain the high incidence of liver damages by isoniazid *(32)* and the chemically related iproniazid [*(32)*, —NH-*i*Pr instead of —$NH_2$], and at the same time remind one of restraint in the use or in the therapeutic administration of monosubstituted hydrazines. Products *(33)* and *(36)* arise by oxidation with α-oxocarbonic acids.



Inter-individual differences, together with the cited species variations play an important role in conjugation reactions. This is especially true for acetylations, with the genetically determined varying activities of *N*-acetyltransferases. The metabolism of INH *(32)* serves here as an example. Individuals, who are capable of acetylating rapidly, form more acetylhydrazine *(35)*. This genetic polymorphism has important pharmacological and toxicological consequences; the use of normal dosages can cause a rapid decrease in the therapeutically effective serum level of INH *(32)*. The assumption that such rapid acetylators tend more towards liver damage, due to increased formation of acetylhydrazine, has however not been experimentally proven. Persons having a slow acetylator phenotype seem more likely to be threatened by parenchymatous damage, since INH *(32)* can impede the formation—which may be regarded as an inactivation reaction—of diacetylhydrazine *(37)*. In these cases the formation of a hydroxylamine derivative, by oxidation of the amino group, is favored and this leads to further reactive intermediates *(39)* and *(40)* or *(41)*[39].

The polymorphism of acetylation is observed with other substances as well. The individually different enzyme content is possibly also responsible for differing susceptibility to carcinogenic arylamines and their metabolites. Only a few examples are known, such as *p*-aminobenzoic acid, whereby apparently equal rates of acetylation were measured[40].

In some cases, acetylated compounds are less water soluble than their precursors. Examples of such are the pharmacologically employed sulfonamides; sulfapyrazine, sulfathiazole, sulfadiazine or sulfamethazine. In using these drugs, one must expect renal damage, as they can precipitate as crystals due to the acid pH of the urine and the favorable concentrating conditions in the renal tubuli. They then lead to obstruction of the renal tubuli and renal pelvis. Therefore, it is always necessary to assure sufficient fluid intake when sulfonamides are administered[4,5].

### 4.3. Activation by Conjugation with Glutathione

Glutathione (L-γ-glutamyl-L-cysteinylglycine) is dissolved in the cytosol of animal and plant cells. Particularly high concentrations are measured in the liver, in erythrocytes and in the crystalline lens (of the eye) of mammals. Glutathione is synthesized in the cell *via* six enzyme catalyzed reactions in the so-called γ-glutamyl cycle, and then again decomposed into individual amino acids[41].

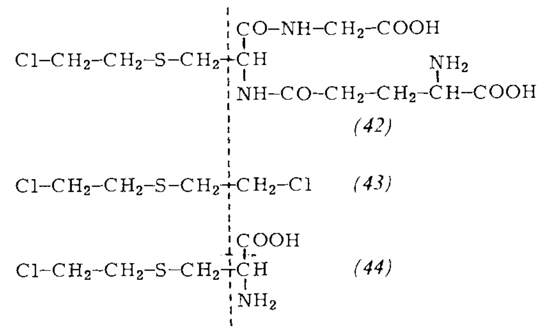
Glutathione has an integral role for a great number of biological functions[41] such as, a) protection of the cell membrane by preservation of essential thiol groups of proteins and other molecules, b) decomposition of hydrogen peroxide or free radicals, c) transport of amino acids, amines or small peptides through cell membranes, and d) detoxication of electrophilic xenobiotics and/or their metabolites *via* conjugation and subsequent elimination of the product as mercapturic acid, whereby glutamate and glycine first split off and then the amino group is acetylated. The reaction sequence is presented in Figure 3, using the metabolism of 1,1-dichloroethylene *(1)* as an example. Numerous mercapturic acids have been isolated[42].

In its reduced form, glutathione is a strong nucleophile. Therefore conjugations can occur either by a direct $S_N2$ reaction of the thiol group with sufficiently electrophilic substrates, or by an enzymic reaction catalyzed by glutathione-*S*-transferases. Up to now, seven of these enzymes from the cytosol of human and animal liver cells have been isolated and purified[43,44]. Glutathione transferases are highly specific in their requirement for glutathione, but multifunctional when involved in the catalysis of reactions with glutathione[45].

Formerly only detoxifying functions were ascribed to conjugations with glutathione. Numerous examples, such as those of paracetamol *(24)* or halogenated aliphatic and aromatic hydrocarbons confirm the protecting action of glutathione against the toxic effects of these foreign substances. It was first shown for paracetamol that a direct correlation exists between the glutathione concentration in the cell and the incidence of covalent bonds with essential nucleophilic cell components[7]. If the glutathione concentration decreases to less than about 30% of the normal value, the protecting capacity is no longer sufficient and the number of covalent bonds increases exponentially, ultimately leading to cell necrosis and parenchymal destruction.

These biochemical correlations are used therapeutically to treat poisonings with mercapturic acid precursors, whereby one attempts to raise the cellular concentration of reactive thiol groups. This is successful with compounds having better bioavailability than glutathione (*i.e.* *N*-acetylcysteine or cysteamine). Severe paracetamol poisonings have been successfully treated using this specific therapy[46,47].

Recently, however, participation of glutathione has also been proven in the activation of xenobiotics to mutagenic and potentially carcinogenic electrophiles. 1,2-Dichloroethane—having an annual worldwide production of almost two million tons[48] and being by far the most highly produced chlorinated aliphatic hydrocarbon—is mutagenic in the Ames Test[49,50]. The activation to a mutagen is observed if a postmitochondrial liver cell fraction[*] is added to the bacteria. The addition of a pure microsomal fraction on the other hand does not lead to an activation. Therefore an activation pathway other than that of oxidation by microsomal mixed-function oxygenases must be involved. Further investigations with pure enzyme preparations and the system of the isolated perfused liver preparation confirmed that the mutagenic effects of 1,2-dichloroethane only increase in the presence of glutathione and the glutathione transferases[50,51]. The prerequisite therefore is enzymic conjugation with glutathione. This reaction leads *via* the substitution of a chlorine atom with glutathione to a β-halogen thioether *(42)*, which is responsible for the mutagenic[50] and carcinogenic[52] effect of 1,2-dichloroethane. Such compounds are highly reactive and have been recognized for a long time for their mutagenic and carcinogenic effects, as is shown for example by the chemical warfare agent mustard gas *(43)*, which carries the same leaving group (Fig. 5). The analogous nitrogen-mustard gas type derivatives are used in chemotherapy for carcinomas. These compounds (for example *N*-oxide-mustard gas or cyclophosphamide) are also carcinogenic in animal experiments.



$$Cl{-}CH_2{-}CH_2{-}S{-}CH_2{-}\overset{CO-NH-CH_2-COOH}{\underset{NH-CO-CH_2-CH_2-\overset{NH_2}{C}H-COOH}{CH}}\quad (42)$$

$$Cl{-}CH_2{-}CH_2{-}S{-}CH_2{-}CH_2{-}Cl\quad (43)$$

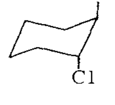
$$Cl{-}CH_2{-}CH_2{-}S{-}CH_2{-}\overset{COOH}{\underset{NH_2}{CH}}\quad (44)$$

Fig. 5. Mutagenic and carcinogenic β-halogen thioethers with the same leaving group; conjugation products of 1,2-dichloroethane with glutathione *(42)*; mustard gas *(43)*; *S*-(2-chloroethyl)-L-cysteine *(44)*.

1,2-Dibromoethane, which is frequently employed as a pesticide and as a gasoline additive, is activated by conjugation with glutathione in the same manner as with 1,2-dichloroethane. The conjugation product, here as well, has strong alkylating properties and can account on a molecular basis for the pronounced mutagenic and carcinogenic effects[52,53] of 1,2-dibromoethane. The above-mentioned β-halogen thioethers *(42)* and *(44)* are subject to further metabolic changes *in vivo* and *in vitro:* 1) oxidative dehalogenation to *S*-(2-hydroxyethyl)-L-cysteine (or *S*-(2-hydroxyethyl)-L-glutathione); 2) conjugation with a further glutathione molecule to form a dithioether. Both metabolic products are biologically inactive. Thus, in metabolism, glutathione conjugation leads initially to a toxication and then later assists in a detoxication of one and the same substance.

Compounds having good leaving groups substituted on vicinal carbon atoms are generally transformed through glutathione conjugation into potential mutagens[54]. The strength of the mutagenic effect is dependent on both the nature and arrangement of the substituents. The more electrophilic the substituent is, the stronger the mutagenic effect. Furthermore, stereochemical factors influence the biological efficacy[50]. Thus, the conjugation product of *cis*-1,2-dichlorocyclohexane *(45)* and glutathione is mutagenic while that of the *trans*-isomer *(46)* is nonmutagenic.

*(45)*



*(46)*

It was surprising to note that these types of structure-effect relationships were ascertained as early as 20 years ago. *S*-(2-chloroethyl)-L-cysteine *(44)* (Fig. 5) was already recognized in 1960 as a highly reactive alkylating compound and was investigated thoroughly as a model substance for a powerful mutagen[55]. This fact should lead to re-examination of the risk analysis process used for exogenous substances. The first

---

[*] *i.e.*, the 9000 g supernatant (S-9) of a liver homogenate.

step in a risk analysis must be the elucidation of the chemical reactivity of the foreign compound which is then correlated to model substances whose toxic potential and pattern of metabolites are known; only then should the microbial tests and metabolic studies be carried out. Had this procedure been used earlier, xenobiotics which were produced for decades in great quantities (as 1,2-dichloroethane or vinyl chloride) would have been recognized sooner as posing a carcinogenic risk.

## 5. Outlook

The examples of toxication by conjugation of compounds foreign to the body with endogenous substances set forth here, make clear the dual function of transferases. In most cases, the pharmacological efficacy is raised by conjugation, and the conjugation products are also usually less toxic. Nevertheless, it could be shown by means of some examples that the transfer of endogenous substrates can also be tied to an activation, *i.e.* toxication of the foreign compound. Risk analysis of compounds foreign to the body is thereby made substantially more difficult. On the one hand, a multitude of metabolic intermediate and end products can be regarded as the ultimate damaging agents; on the other, conjugation reactions are subject to enormous qualitative and quantitative differences among species. Since conditions which are the same as those in man with regard to the metabolism of xenobiotics are not found in any other animal species, each case must be treated separately and the animal species which most closely resembles the circumstances in man, with respect to a specific substance, selected.

Before a total concept of the biological activity of a compound foreign to the body can be developed, all structural changes to which such exogenous compounds in the organism are subject must be examined. Each new metabolite of the foreign compound or biotransformation pathway which is detected could be toxicologically relevant. The examination of even some reactions which had been known for some time and which had been regarded as toxicologically harmless, has indeed demonstrated the complexity of metabolic transformation with the appearance of unexpected, highly toxic products. The great number of endogenous molecules with which foreign compounds can react, allows one to anticipate a multitude of new reaction products and makes the conjugation reaction particularly interesting.

With the introduction of new *in vitro* test systems and sensitive analytical procedures in the risk assessment of xenobiotics, we are at the beginning of a development which acknowledges the full significance of the conjugation reaction for the toxication and detoxication of compounds foreign to the body. The classical assignment of the conjugation reactions to the category of detoxication reactions must finally be abandoned.

Received: October 28, 1980 [A 349 IE]
German version: Angew. Chem. *93*, 135 (1981)

---

[1] *J. R. Gillette*, Biochem. Pharmacol. *23*, 2785 (1974).
[2] *S. Heidelberger*, Annu. Rev. Biochem. *44*, 79 (1975).
[3] *P. Jenner, B. Testa*, Xenobiotica *8*, 1 (1978).
[4] *W. H. Fishman:* Metabolic Conjugation and Metabolic Hydrolysis. Vol. 2. Academic Press, New York 1970.
[5] *J. W. Gorrod, A. H. Beckett*, Drug Metabolism in Man. Taylor & Francis, London 1978.
[6] *J. A. Miller, E. C. Miller* in *H. H. Hiatt, J. D. Watson, J. A. Winston:* Origins in Human Cancer. Cold Spring Harbor Laboratory 1977, p. 605.
[7] *J. R. Mitchell, D. J. Jollow*, Gastroenterology *68*, 392 (1975).
[8] *R. R. Hewitt, J. Harless, R. S. Lloyd, J. Love, D. L. Robberson* in *A. C. Griffin, C. R. Shaw:* Carcinogens: Identification and Mechanisms of Action. Raven Press, New York 1979, p. 107.
[9] *I. F. H. Purchase, E. Longstaff, J. Ashby, J. A. Styles, D. Anderson, P. A. Lefevre, F. R. Westwood*, Nature *264*, 624 (1976).
[10] *B. A. Bridges*, Nature *261*, 195 (1976).
[11] *E. Gebhart:* Chemische Mutagenese. Gustav Fischer, Stuttgart 1977.
[12] *B. N. Ames, J. McCann, E. Yamasaki*, Mutat. Res. *31*, 347 (1975).
[13] *J. McCann, E. Choi, E. Yamasaki, B. N. Ames*, Proc. Natl. Acad. Sci. U.S.A. *72*, 5135 (1975).
[14] *V. F. Simmon, H. S. Rosenkranz, E. Zeiger, L. A. Poirier*, J. Natl. Cancer Inst. *62*, 911 (1979).
[15] *I. M. Arias, W. B. Jakoby*, Glutathione: Metabolism and Function. Raven Press, New York 1976.
[16] *E. N. Cohen, J. R. Trudell, H. N. Edmunds, E. Watson*, Anesthesiology *43*, 392 (1975).
[17] *D. Reichert, H. W. Werner, M. Metzler, D. Henschler*, Arch. Toxicol. *42*, 159 (1979).
[18] a) *A. Aitio:* Conjugation Reactions in Drug Biotransformation. Elsevier/North-Holland, Amsterdam 1978; b) *J. Caldwell* in [18a], p. 477.
[19] *R. T. Williams*, Biochem. Soc. Trans. *2*, 359 (1974).
[20] *E. C. Miller, J. A. Miller*, Pharmacol. Rev. *18*, 805 (1966).
[21] *J. L. Radomski, W. L. Hearn, T. Radomski, H. Moreno, W. E. Scott*, Cancer Res. *37*, 1757 (1977).
[22] *F. Kadlubar, T. Flammang, L. Unruh* in [18a], p. 443.
[23] *J. R. De Baun, E. C. Miller, J. A. Miller*, Cancer Res. *30*, 577 (1970).
[24] *J. R. De Baun, R. Smith, E. C. Miller, J. A. Miller*, Science *167*, 184 (1970).
[25] *V. M. Maher, E. C. Miller, W. Szybalski*, Mol. Pharmacol. *4*, 411 (1968).
[26] *G. J. Mulder, J. A. Hinson, J. R. Gillette*, Biochem. Pharmacol. *27*, 1641 (1978).
[27] *T. Liu, G. W. Smith, J. T. Rankin*, Can. Med. Assoc. J. *107*, 768 (1972).
[28] *T. Murray, M. Goldberg*, Annu. Rev. Med. *26*, 537 (1975).
[29] *C. C. Irving*, Xenobiotica *1*, 387 (1971).
[30] *J. H. Weisburger, E. K. Weisburger*, Pharmacol. Rev. *25*, 1 (1973).
[31] *D. D. Abbott, E. W. Packman, B. M. Wagner, J. W. E. Harrisson*, Pharmacologist *3*, 62 (1961).
[32] *S. S. Epstein, K. Fujii, J. Andrea, N. Mantel*, Toxicol. Appl. Pharmacol. *16*, 321 (1970).
[33] *E. L. Long, A. A. Nelson, O. M. Fitzhugh, W. H. Liver*, Arch. Pathol. *75*, 595 (1963).
[34] *P. Borchert, P. G. Wislocki, J. A. Miller, E. C. Miller*, Cancer Res. *33*, 575 (1973).
[35] *P. G. Wislocki, P. Borchert, J. A. Miller, E. C. Miller*, Cancer Res. *36*, 1686 (1976).
[36] *N. R. Drinkwater, E. C. Miller, J. A. Miller, H. C. Pitot*, J. Natl. Cancer Inst. *57*, 1323 (1976).
[37] *I. B. Glowinski, H. E. Radtke, W. W. Weber*, Mol. Pharmacol. *14*, 940 (1978).
[38] *S. D. Nelson, J. R. Mitchell, J. A. Timbrell, W. R. Snodgrass, G. B. Corcoran III*, Science *193*, 901 (1976).
[39] *J. A. Timbrell, J. M. Wright*, Drug Metab. Dispos. *7*, 237 (1979).
[40] *W. W. Weber, D. W. Hein, M. Hirata, E. Patterson* in [18a], p. 145.
[41] *A. Meister, S. S. Tate*, Annu. Rev. Biochem. *45*, 559 (1976).
[42] *L. F. Chasseaud* in [15], p. 77.
[43] *W. B. Jakoby, W. H. Habig, J. H. Keen, J. N. Ketley, M. J. Pabst* in [15], p. 189.
[44] *K. Kamisaka, W. H. Habig, J. N. Ketley, I. M. Arias, W. B. Jakoby*, Eur. J. Biochem. *60*, 153 (1975).
[45] *W. B. Jakoby*, Adv. Enzymol. Relat. Areas Mol. Biol. *46*, 381 (1977).
[46] *R. G. Peterson, B. H. Rumack*, J. Am. Med. Assoc. *237*, 2406 (1977).
[47] *L. F. Prescott, R. N. Illingworth, J. A. J. H. Critchley, A. T. M. J. Stewart, R. D. Adam*, Br. Med. J. *2*, 1097 (1979).
[48] *G. McConnell, D. M. Ferguson, C. R. Pearson*, Endeavour *34*, 13 (1975).
[49] *H. Brem, A. B. Stein, H. S. Rosenkranz*, Cancer Res. *34*, 2576 (1974).
[50] *U. Rannug, A. Sundvall, C. Ramel*, Chem. Biol. Interact. *20*, 1 (1978).
[51] *U. Rannug, B. Beije*, Chem. Biol. Interact. *24*, 265 (1979).
[52] *W. A. Olson, R. T. Habermann, E. K. Weisburger, J. M. Ward, J. H. Weisburger*, J. Natl. Cancer Inst. *51*, 1993 (1973).
[53] *E. K. Weisburger*, Environ. Health Perspect. *21*, 7 (1977).
[54] *P. J. van Bladeren, A. van der Gen, D. D. Breimer, G. R. Mohn*, Biochem. Pharmacol. *28*, 2521 (1979).
[55] *O. G. Fahmy, M. J. Fahmy*, Genetics *45*, 1191 (1960).

# Protein Differentiation: Emergence of Novel Proteins during Evolution

By Georg E. Schulz[*]

The almost limitless number of proteins can be reduced to approximately 200 basic structures, *i. e.* geometries of polypeptide chains; these form the set from which the tracable protein differentiation started. Protein differentiation begins with a gene duplication. One of the gene products is conserved since it must continue to fulfill the original function. The other gene product is conserved as soon as it has taken over a new function. Comparing amino acid sequences of equivalent proteins in two species yields the evolutionary distance between these species, which allows dating of their common ancestor ("molecular palaeontology"). These comparisons are now applied to the geometries of nonequivalent proteins, elucidating the pathways of protein differentiation.

## 1. Introduction

In today's terrestrial world there exist approximately $10^{11}$ distinct proteins. When all differences between proteins performing corresponding functions in non-identical species are neglected, this number is reduced to about $10^5$. Since such an array is still very large, further reduction is profitable. This is achieved by neglecting all differences in protein functions and concentrating on basic protein structure, *i. e.* the geometries of polypeptide chains. At this level of geometrical comparison, the number of different proteins is merely of the order of $10^2$; such a number corresponds approximately to the number of paintings one would view in an art exhibition. By virtue of this suggested simplification, the protein world becomes as comprehensible as an art gallery.

Both reductions of complexity, from $10^{11}$ to $10^5$, and from $10^5$ to $10^2$, correspond to historical biological processes which ran in the opposite direction; from limited to vast diversity. The first reduction step corresponds to the well-known process of evolution of species whereas the second step reflects the evolution of proteins, or "protein differentiation". The term "differentiation" was chosen[1] because the evolution of proteins resembles the differentiation process of tissue cells; the individual proteins are duplicated like cells (but on a secular time scale). Subsequently, the two copies evolve separately and serve different functions in the organism.

Proteins have to be well characterized if they are to be distinguished from one another. For this purpose, global characteristics such as molecular weight, sedimentation velocity, amino acid composition, *etc.*, do not suffice. The following discussion requires an exact structural description; either knowledge of the total sequence of all amino acid residues along the polypeptide chain (the "protein sequence"), or knowledge of the path of the polypeptide chain in three dimensions (the "protein geometry"). Knowing both sequence and geometry, and therefore the spatial arrangement of all atoms (the "protein structure") is an even better starting point for further investigations[2]. About $10^3$ sequences and $10^2$ geometries and structures are known today[3,4]; this data base is large enough not only to reveal the pathways of protein variations accompanying the evolution of species but also to elucidate the evolutionary pathways of protein differentiation.

## 2. Variations Accompanying Species Evolution

Soon after the first successful sequence analysis it became clear that homologous proteins in different species are not identical in all amino acid residue positions. The copies of the antibacterial protein lysozyme present in man and baboon for example, are not identical in 14 of the 131 positions. Accordingly, one has to accept that 14 amino acid changes occurred during the separate evolution of baboon and man; presumably 7 in each branch. As a general rule, the earlier the branching point the more exchanges have to be expected. Comparing the lysozymes of man and duck, for example, one detects as many as 53 nonidentical amino acid residues.

In order to comprehend these species-specific changes, it is worthwhile to assess the role of macromolecules in the biological system (Fig. 1). The genetic information laid down as a sequence of nucleotides in the DNA, primarily defines the amino acid sequence; given a sequence, the corresponding protein structure is assumed automatically by the sponta-

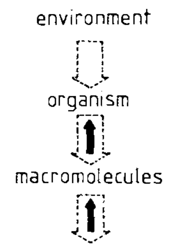


Fig. 1. Position of macromolecules in the biological system. The genetic information laid down in DNA exactly defines the structure of macromolecules; these are for the most part proteins but also include some RNA molecules. The macromolecules in turn exactly define the organism to which they belong. In the time scale of evolution however, the causality is reversed by the effects of mutation and selection. Eventually, the ecological conditions determine the genetic information of an organism.

---

[*] Prof. Dr. G. E. Schulz
Max-Planck-Institut für Medizinische Forschung
Jahnstrasse 29, D-6900 Heidelberg (Germany)

*0570-0833/81/0202-0143 $ 02.50/0*

neous folding process. The structures of RNA molecules, for example ribosomal RNA, are determined in a similar manner. At the next level, each organism is defined by its set of macromolecules. Every variation starts at the DNA level as a mutation of the genetic information, which subsequently is expressed at the macromolecular level and therefore at the level of organisms.

Screening experiments, in which haemoglobins were analyzed, showed that the frequency of spontaneous mutations in man amounts to $10^{-3}$ *per* protein *per* person[5]. If all these mutations were accepted and passed on to the descendants, the $10^5$ generations separating man from the gorilla should have given rise to completely different macromolecules. The α- and β-chains of the haemoglobins of gorilla and man, however, differ by only one amino acid each. Such a limited acceptance of the vast number of spontaneous mutations offered, demonstrates that at the macromolecular level the organisms and environment can select from a virtually unlimited number of mutations in the DNA. As a consequence, in the evolutionary time scale, the information flows in the opposite direction (from top to bottom in Fig. 1).

An example for the acceptance of a mutation, which is understood in detail, is the sickle cell gene of the β-chain of haemoglobin, which in areas subject to malaria is observed with frequencies up to 40%[6]. As shown in Figure 2, the sickle cell gene differs from the normal one by exchange of a glutamic acid for a valine at the protein surface. Through this exchange a linear aggregation of the haemoglobin molecules becomes energetically favored. The arising fibers, stretch the erythrocytes to a sickle-like shape. Since sickle cells tend to break up when passing through the capillaries, the mutation eventually causing anaemic conditions and possibly early death. In spite of the unfavorable consequences for the organism, this mutation has been accepted, because fiber formation impedes the invasion of plasmodia in erythrocytes and thus protects the person carrying the sickle cell-gene to a certain extend against malaria. In this example evolution follows a passage between Scylla and Charybdis; on one side death by malaria, on the other death by anaemia.

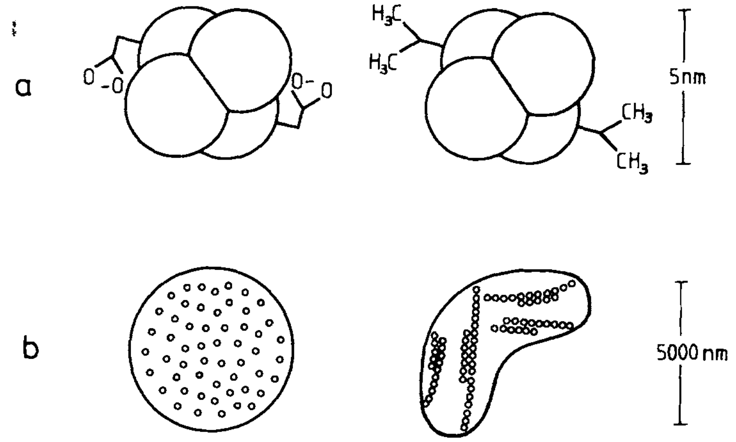


Fig. 2. Sickle cell gene of haemoglobin. a) The difference between sickle cell and normal haemoglobin is the change from glutamic acid to valine in position 6 of the β-chain. b) In erythrocytes, normal haemoglobin occurs monodisperse, in spite of the high concentration of 300 mg/ml, whereas sickle cell haemoglobin aggregates to fibers.

In the case of sickle cell haemoglobin, the environment represented by malaria parasites has forced the acceptance of a mutation that is otherwise deleterious to the organism (Fig. 1). At the macromolecular level the exchange is neutral, because it does not hinder the individual molecule in performing its function; namely transporting $O_2$. This example demonstrates how much a sequence difference observed today depends on details of the environment in the past. Consequently, it seems very unlikely that we can ever completely understand the presently observed protein differences completely. Nevertheless, these differences may still be analyzed statistically in order to elucidate general rules governing protein variations.

If all amino acid exchanges are considered equivalent, a very simple measure of the difference between two sequences arises; the number of residue changes, or in normalized form, the number of residue changes per residue position. In addition, if the frequency of exchange in a given protein can be taken as constant during evolution, this provides a time scale allowing the conversion of a sequence difference into an evolutionary distance, or, into a measure of the time of the branching from a common ancestor. On this basis a "molecular palaeontology" becomes feasible. Let us consider a protein with a given function, for instance lysozyme. If lysozyme sequences of N species are known, one may derive $N\cdot(N-1)/2$ evolutionary distances between these species. These data suffice for arranging the respective species into a phylogenetic tree[3].

As a rule, the molecular palaeontology extends into appreciably earlier times than its conventional counterpart. Using the sequences of cytochrome c-like proteins, for example, allows one to relate bacteria to each other which presumably separated as long ago as about $3\cdot10^9$ years[7]. From the existing $10^5$ proteins which perform a particular function it should be eventually possible to establish $10^5$ phylogenetic trees and to combine them. Drawing from such an extensive data base should render molecular palaeontology a highly accurate method.

Comparative sequence analyses showed that the frequency of change in a given protein depends critically on its interactions with the surrounding material. Histones, for example, are deeply buried in chromatin and form numerous contacts with neighboring molecules. Moreover, as a constituent part of chromatin, histones are required for functions as central to an organism as mitosis and meiosis. Accordingly, they only vary with a rate of 0.1 changes *per* position *per* $10^{10}$ years. Compared to histones the "easy-going" fibrinopeptides, which cover the surface of fibrin preventing spontaneous blood coagulation, change their amino acids a thousand times faster. Fibrinopeptides of species which separated only ten million years ago contain about 20% sequence differences today.

This rule not only applies for structural proteins like histones and fibrinopeptides but also for enzymes. In enzymes, however, the contacts to the surrounding material are of minor importance in relation to their catalytic reactions. Here, one expects that the amino acid residues in the catalytic center would change reluctantly. Exactly this situation has been observed in all known enzymic structures; the catalytic center is strongly conserved. Conversely, the catalytic center of several enzymes was recognized by means of the amino acids conserved. Both rules; conservation of contacts and conservation of chemical reactions, reflect the selectioning influence of organisms (Fig. 1) on the variation of macromolecules.

Amino acid exchanges may destroy proteins if they decrease protein stability. Such exchanges are, however, already discriminated against at the macromolecular level (Fig. 1). This process can be traced in the observed sequences. If the mutation rates in the chain positions at the protein surface are compared with those in the protein interior, it becomes clear that the surface is altered appreciably faster than the interior. This gradient can be explained, because proteins are packed together as tightly as crystals of small molecules, *i. e.* the contacts between different parts of the polypeptide chain are optimised[4]. In contrast to exchanges at the surface, those in the interior invariably disrupt this packing and decrease protein stability; internal changes are therefore rarely accepted.

Up to this point only changes of amino acid residues have been discussed, *i. e.* variations of side chains which conserve the main chain. No reason exists, however, for leaving the main chain untouched during evolution. Main chain modifications, *i. e.* insertions and deletions of amino acid residues, are considerably rarer. In general they appear only after about half the side chains have been altered; at 30% and 15% of remaining sequence identity, the fraction of insertions and deletions increases to 10% and 30%, respectively. After correction for multiple changes at each position, these values indicate that main chain links vary about ten times slower than side chains.

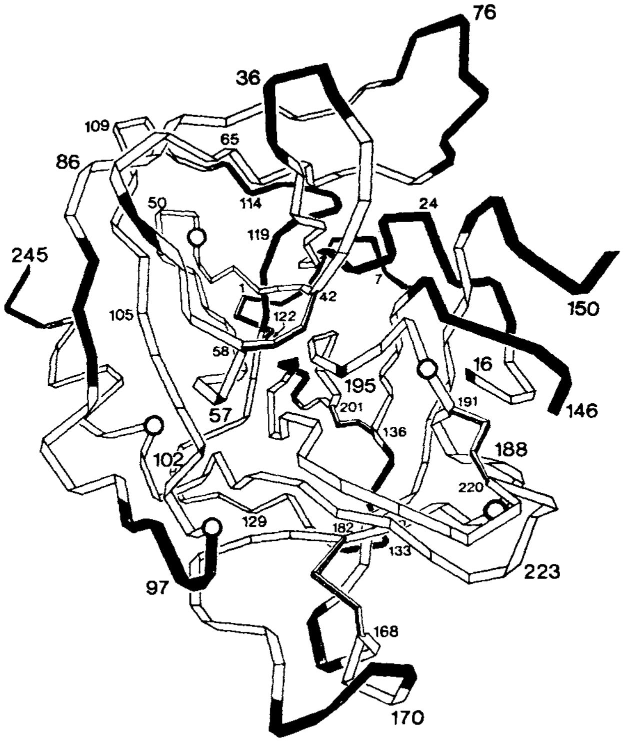


Fig. 3. Overlay of the polypeptide chains of chymotrypsin and protease-B of *Streptomyces griseus*. The chain fold and the numbering scheme of chymotrypsin is used [8]. The dark stretches of the chain are missing in protease-B (cf. chymotrypsin); circles denote the insertions in protease-B. Since both sequences agree in merely 12% of the positions, they could only be aligned after overlaying the chain folds [9]. The topology of the chain between residues 25 and 115 is identical to that between residues 135 and 225.

The two proteins depicted in Figure 3 exhibit 38% insertions and deletions; a sequence alignment becomes virtually impossible with so many main chain modifications. Alignment of such sequences can only be achieved if both protein structures are known. Overlaying the structures than reveals all insertions and deletions and permits the determination of the number of amino acid exchanges. Figure 3 shows in addition that main chain modifications occur exclusively at the protein surface. In the protein interior such modifications would undermine stability even more strongly than amino acid changes, and reduce their chance of being accepted.

Since main chain modifications usually enlarge or shorten chain loops at the surface, they do not affect the general path of the polypeptide chain in three dimensions; the so-called "chain topology". As a consequence, the chain topology is the best conserved property of proteins. It is retained even after all sequence identities have vanished. To date, no example of a protein change occurring during species evolution which altered the chain topology is known.

## 3. Functional Variations

In the course of structural analyses not only similarities between proteins performing identical functions in different species were discovered, but also similarities between proteins performing different functions in the same organism. As an example, the sequences of the digestive enzyme elastase and of the plasma enzyme thrombin have been aligned in Figure 4. The polypeptide chains correspond with each other in as many as 30% of the amino acids, raising the question whether they have a common origin. This question implies that there exists an evolution of proteins, which alters protein function and therefore exceeds the protein variations accompanying the evolution of species.

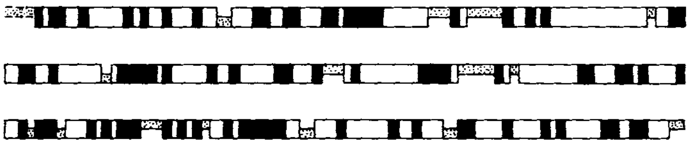


Fig. 4. Comparison of the amino acid sequences of elastase [10] and thrombin [11]. The dark and light regions denote identical and differing amino acid residues, respectively. Dotted regions are insertions in thrombin (upper) and elastase (lower). The compared chain length is 266 residues, 79 of which are identical. Among the $266-79=187$ differences there are 33 insertions and deletions. These numbers amount to $79/266=30\%$ sequence identity and $33/266=12\%$ changes of the main chain.

To answer this question, we estimate the probability of finding the observed sequence identity by chance. Assuming equal probabilities for all 380 possible amino acid exchanges, and that all insertions and deletions have been positively located (Fig. 4), the probability of random coincidence amounts to

$$\left(\frac{1}{20}\right)^{79}\cdot\left(\frac{10}{20}\right)^{187}\cdot\frac{266!}{79!\cdot 187!}\approx 10^{-38}.$$

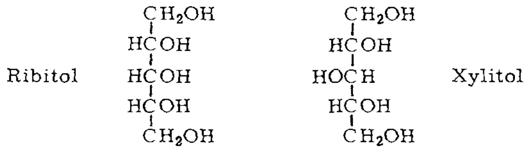
(Numbers stem from the legend to Fig. 4; 20 stands for the 20 standard amino acids)

Without the simplifying assumptions, this value increases by several orders of magnitude. However, the resulting probability remains small enough to exclude, for all practical purposes, coincidence occuring by chance. There must therefore be a reason underlying the discovered sequence identity; either the calculation is completely wrong, because the number of sequences which allow stable proteins is very limited, or, elastase and thrombin are connected by an historical development.

Since numerous stable proteins containing totally different sequences are known, the calculation is approximately correct. As a consequence, an historical connection between these two proteins has to be assumed. Elastase and thrombin originated from a common ancestor, or stated reversely, after separation the proteins have acquired different functions in the organism. At the cellular level such a process is called "differentiation". Transferring this term to the level of macromolecules[1] we refer to "protein differentiation".

An assumption as basic to biology as protein differentiation should be founded on evidence which is more direct than approximately calculated probabilities. Such evidence is available because changes of protein function can be followed directly. It is well known to physicians, that parasites become resistent to an effective drug and that this resistance is hereditary. Most probably, mutations have changed the functions of one or more parasite proteins in such a way that the parasite can resist the drug.

Even more direct evidence was obtained from evolution experiments on *Klebsiella aerogenes*[12]. This organism accepts ribitol as an energy and carbon source, whereas the epimer xylitol can scarcely be used. Both, ribitol and xylitol, are picked up and prepared for further use by the enzyme ribitol dehydrogenase; ribitol is, however, converted 100 times faster than xylitol. This system permits the application of evolutionary pressure to modify the enzyme specificity by offering xylitol exclusively as the carbon and energy source. As a first adjustment to this pressure the bacteria did not alter the specificity of ribitol dehydrogenase, but its concentration by means of gene multiplication; a costly method for balancing low enzymatic activity. However, mutations giving rise to amino acid changes in ribitol dehydrogenase, which improved the conversion of xylitol, emerged at later stages of the experiment. The results show that gene multiplication can occur, and that a change of enzymatic specificity and thus enzyme function is quite possible.



Gene multiplication and functional variation can therefore be observed. As sketched in Figure 5, protein differentiation starts by duplicating or multiplying a gene; during the ensuing development at least one copy of the gene is preserved to fulfill the original function. The additional copies are like children on a playground. Since their gene product is not vital, they experience no pressure from "above" (Fig. 1), and can change freely until they are capable of performing a new function. As soon as the new function becomes vital for the organism however, the gene has come of age and its liberty ends.

Isoenzymes provide examples for early stages of protein differentiation. These groups of enzymes are coded on separate genes, occur in parallel in the same organism, and their functional and structural difference is relatively small. Well-known isoenzymes are the skeletal and heart muscle variants of lactate dehydrogenase, which are in concordance in three quarters of their amino acid residues[13,14]. In comparison, the differences between the three isoenzymes of adenylate kinase are much larger[15]. These isoenzymes are specialized for the cytosol, the intermembrane space of mitochondria, and the matrix of mitochondria, respectively. A clear case of protein differentiation is also observed with the enzyme couple lysozyme and lactalbumin. At the time when mammals appeared, the lysozyme gene was duplicated; one copy retained its antibacterial capability whereas the second copy became an important part of the mammalian milk and thus satisfied newly arising needs. The historical relationship between these two enzymes is beyond doubt, because they show as much as 38% sequence identity. It is worth mentioning that both enzymes operate on saccharides; this aspect of their function has been conserved.

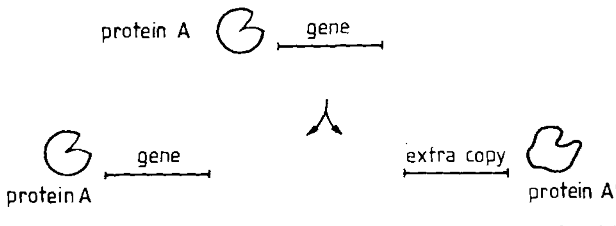


Fig. 5. Schematic representation of gene duplication. After duplicating the original gene, one of the copies produced still fulfills the original function of the protein; it is therefore well conserved. The other product can change quite freely. In cases where gene duplication is only a means for increasing the production, all gene copies are conserved because they are all needed. In the tandem gene duplications listed in Table 1 both products are joined, forming a single chain.

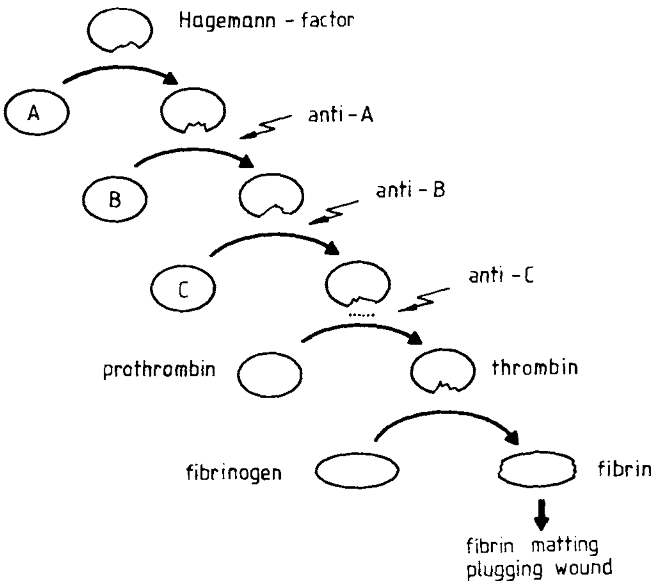


Fig. 6. Simplified scheme of the enzyme cascade for blood coagulation [16]. The Hagemann-factor activates enzyme A, this in turn activates enzyme B, *etc.*, until fibrin matting plugs the wound. At each level, the respective enzyme is specifically inhibited and since several very specific recognition processes are involved, the regulation is extremely exact.

A characteristic example of protein differentiation is found with the blood coagulation cascade sketched in Figure 6. When blood circulation was "invented", a repairing system became necessary to prevent leakage of all fluid after the slightest damage. A feasible method would be to plug the wound by coagulation. However, although this is easy to accomplish, it is most important to plug wounds exclusively and not the circulatory system itself. To achieve this distinction exact control is required. The problem was solved by developing a team of enzymes, ordered strictly hierarchically. On damage, the initial enzyme (Hagemann-factor) is released, and starts activating its subordinates (Fig. 6). At each level, effectors regulate the cascade precisely; each enzyme being extremely specific for its substrate.

Sequence analyses disclosed that the enzymes of this cascade are related to each other. Since thrombin belongs to this group, they are furthermore related to elastase (Fig. 4) and to the digestive enzymes trypsin and chymotrypsin as well as to some structurally known bacterial proteases (Fig. 3). Since blood clotting arose later in evolution than digestion, one can safely assume that the cascade is made up of (highly specialized) descendants of (comparatively primitive) digestive enzymes. Whereas the cascade proteins work in a very well defined manner, on only one substrate, the digestive enzymes "cut" all proteins they encounter to small pieces. Presumably, the cascade proteins did not appear simultaneously but evolved one by one from a single ancestor, proceeding from the bottom to the top of Figure 6. Accordingly, the organism started with an effective but badly regulated repair system which became more and more precisely controlled during evolution. Higher precision and more complexity was attained using proteins created by the differentiation process. A similar cascade is the complement system of the immune response[17] which it is also based on trypsin-like proteins.

The evolution to higher animal forms is also reflected in the differentiation process involving globins. When blood circulation was established, haemoglobin separated from myoglobin; haemoglobin became the far-travelling $O_2$-carrier in the blood, whereas myoglobin stayed in the cell as a local $O_2$-carrier and storage device. With the "invention" of the placenta, an $O_2$-transfer from mother to embryo was needed. For this purpose the $\gamma$-, $\varepsilon$- and $\zeta$-chains of haemoglobin were created, the $O_2$-binding characteristics of which differ from those of $\alpha$- and $\beta$-chains. $\gamma$-, $\varepsilon$- and $\zeta$-chains are produced at early stages of the ontological development; after birth they are superseded by the adult $\alpha$- and $\beta$-forms.

A further relationship was found between the immunoglobulines and HL-A-proteins[18], which label the tissue individually and thus appreciably complicate transplantations from one person to another appreciably. The muscle proteins parvalbumin, troponin-C, the light chains of myosin, and the Ca-dependent regulator protein[19] also have a common ancestor. Furthermore, it is known that historical connections exist between several protease inhibitors and a nerve growth factor[3], as well as connections between the hormones insulin, relaxin, and two tissue growth factors[20].

With a few exceptions, all these differentiated proteins have retained some functional similarity. One has to keep in mind, however, that all examples mentioned above are based on sequence comparisons, which can only reveal initial stages of separate developments. Using structural comparisons, as in Figure 3, or purely geometric comparisons, it should be possible to recognize much more distant relatives.

## 4. Evidence for Distant Relationships

In the course of X-ray structure analyses, pairs of proteins were discovered, which showed no sequence similarity and no functional similarity but resembled one another in their main chain geometries; such a pair is azurin[21] and superoxide dismutase[22]. In both proteins, the chain forms the $\beta$-pleated sheet sketched in Figure 7. The topologies of the $\beta$-sheets are identical. If each of these two proteins consisted of only a single $\alpha$-helix or a simply connected $\beta$-sheet, an explanation for the coincidence would be at hand: such structures are perferred by the chain because they are energetically favored. The observed complexity of the chain geometry, or "chain fold", is a clear indication however, that the coincidence is neither a random nor an energetic phenomenon. Consequently, one has to assume that a relationship between the proteins exists, which is so distant, that in the time course of separate evolution all sequence similarity has been erased, but the strongly conserved chain fold has been retained.

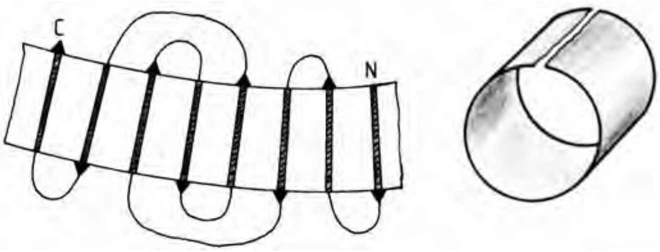


Fig. 7. Concordance of the topologies of the polypeptide chains of azurin [21] and superoxide dismutase [22]. The strands of the antiparallel $\beta$-pleated sheet are drawn as arrows. As indicated, the $\beta$-sheet rolls up forming a barrel.

Table 1. Structural repeats within one chain.

| Protein | Number of repeats |
|---|---|
| Ferredoxin [27] | 2 |
| Parvalbumin [28] | 3 |
| Wheat germ agglutinin [29] | 4 |
| Acid proteases [30, 31] | 4 |
| Hexokinase [32] | 2 |
| Dehydrogenases [33] | 2 |
| Serine proteases [8] | 2 |
| Immunoglobulines [34] | 4 |
| Arabinose-binding protein [35] | 2 |
| Glutathione reductase [36] | 2 |
| Rhodanese [37] | 2 |

In a number of other proteins, similar chain folds showing no sequence similarity are repeated two or more times along a single polypeptide chain. The known examples are listed in Table 1. A very significant similarity is observed in the enzyme rhodanese, in which a complicated chain fold of 140 residues is precisely repeated. Obviously, rhodanese results from a gene duplication with subsequent splicing of the two duplicates, a so called "tandem gene duplication". Since ample evidence for such duplications exists from sequence comparisons in proteins like serum albumin[23,24], haptoglobin[25], and protein-A of *Staphylococcus aureus*[26], they will not be discussed here. In addition to these similarities within one chain, chain fold similarities between parts of different proteins have been found; they will be considered in Section 5.

Although there seems to be no doubt that the observed chain fold similarities indicate historical relationships, the proof is more intuitive and is not as quantitative as for example the probabilities derived above from sequence identities. In order to prove such distant relationships, one has to establish a measure for the similarity of chain folds; furthermore, one has to transpose this measure to a probability. A convenient measure of similarity is the average distance between two chains. This is the distance which remains after both chain folds have been optimally overlayed by computer as sketched in Figure 8a.

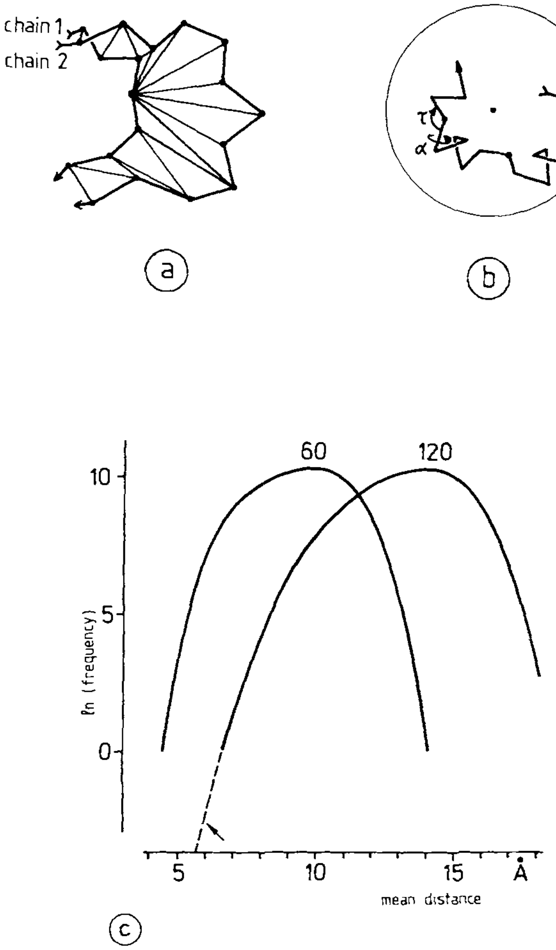


Fig. 8. Distribution of mean distances between two polypeptide chains [38]. a) After optimal relative rotation and translation there remains a residual difference between the two chain geometries. The mean distance between two polypeptide chains is determined by averaging the distances between corresponding $C_\alpha$-atoms. b) The simulation of random geometries is undertaken using conditions as natural as possible. Frequencies of the virtual bond angles τ and dihedral angles α between $C_\alpha$-atoms are adjusted to the observed values. Moreover, the chain simulation accounts for the observed fraction of α-helices, protein globularity, as well as protein density. c) Logarithmic representation of the mean distance distributions for chains with 60 and 120 links, based on about 1 million chain fold comparisons. In order to read the probability for the relationship between the two domains of glutathione reductase (arrow), the respective distribution had to be extrapolated.

This measure of similarity does not solve the problem of relationship *per se*. It only becomes useful if one knows the probability of this similarity occurring by chance. Such a probability can be obtained from the distribution of this measure obtained from comparisons of randomly chosen structures; this distribution has therefore to be calculated. Since, on average, short chains have smaller distances from each other than large chains, not only one but several distributions have to be calculated; one for each given chain length.

In principle one should derive these distributions from comparisons between known protein geometries; the number of known protein geometries is, however, rather small. Moreover, these proteins are distributed over quite a range of different chain lengths. Thus, the number of available comparisons for a given chain length, does not permit a useful distribution curve to be established. Even more seriously, however, the undetected relationships between the structurally known proteins, renders such a distribution meaningless in the most interesting region of small distances: no relationship can be derived from a distribution containing related proteins.

The only solution is to generate chain folds, as naturally as possible, by computer and to compare these simulated chain folds with each other. A chain fold generation method is given in Figure 8b. The resulting folds are globular, their densities correspond to those of proteins, and the dihedral angles between chain links fit the natural distribution. Thousands of such chains were generated and millions of geometric comparisons were carried out, yielding the distributions shown in Figure 8c. Using these, it is now possible to convert any distance between two chain folds (Fig. 8a) into a probability. For this purpose the distribution is integrated from the left side up to the observed distance value, and this integral is then divided by the integral over the total distribution[38].

Applying this method to the similar chain folds of the enzyme glutathione reductase (Table 1), one derives a mean distance of about 6 Å at a (mean) chain length of 120 residues, and therefore a probability for random coincidence of $2\cdot10^{-7}$. A comparison of the two similar chain folds within serine proteases (Table 1) yields a mean distance of about 5 Å at a (mean) chain length of 90 residues, giving rise to a probability for random coincidence of $5\cdot10^{-7}$. These values are so small that a relationship can safely be assumed. In conclusion, the calibration curves of Figure 8c allow one to convert all geometric comparisons between globular proteins into probabilities. On this basis, one can quantify relationships which are too distant to have left any detectable trace in the sequence.

## 5. The Number of Original Protein Structures

As soon as relationships can be quantified, one may ask the question whether all proteins are eventually related to each other, having been descended from a common ancestor with the original protein geometry. With the help of Figure 9 the answer can be easily given. The two protein geometries depicted have absolutely nothing in common; prealbumin consists throughout of an antiparallel β-pleated sheet[39], whereas adenylate kinase[40] contains numerous α-helices and a parallel β-pleated sheet. If these proteins ever had a common ancestor, there is no hope whatsoever of deriving this from the presently existing proteins. Using the similarity analyses described, today's proteins can only be traced back to a rather large group of original structures.

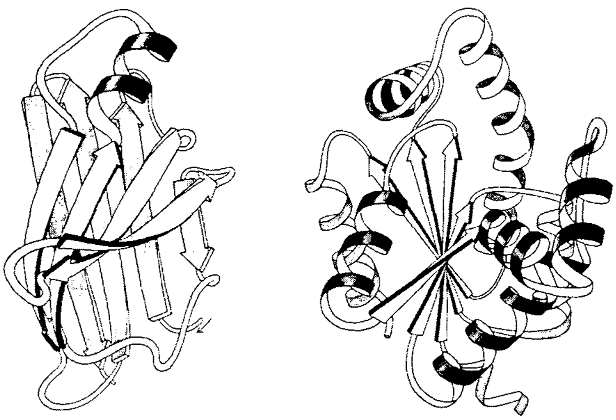


Fig. 9. Topologies of the polypeptide chains of prealbumin (left) and adenylate kinase (right). (Countesy of Dr. *Jane S. Richardson*, Little River Institute, Box 92B, Rt. 1, Bahama, N.C. 27503 (USA).

How large is this group? It has been mentioned above that about $10^5$ proteins with different functions exist. In the course of sequence analyses about $G = 150$ sequences of such proteins have been established, and about $Z = 50$ unexpected relationships have been discovered. According to Poisson statistics the rate of coincidences Z/G, equals the average occupation G/M, where M is the total number of unrelated proteins[41]. Therefore, the number of classes M, into which the $10^5$ functionally different proteins (or the $10^{11}$ distinct proteins) can be arranged, relying on sequence data, is about 500[3]. An analogous estimate can be made for the 70 known chain folds of proteins with different functions. Assuming that a relationship exists as soon as the probability for random coincidence (Fig. 8) drops below 1%, the coincidence rate (between domains, see Section 6) is about 0.3. Using this method it turns out that there are approximately 200 original chain folds, to which all proteins can be traced back.

The chain fold is the most strongly conserved property of a protein and therefore the most useful trait known for distinguishing between original proteins. As a consequence, the chain fold is an efficient criterion for protein classification.

## 6. Domains as Building Blocks

In Section 5, proteins were classified into groups, each of which most probably descended from a single ancestor. This raises the question whether these ancestral proteins were smaller, larger, or equal sized when compared with today's proteins. In cases like cytochromes[7], where evolution can be traced back to very early times, no indication can be detected that early proteins have sizes different from late ones. Proteins do not grow or shrink but merely undergo random fluctuations; the insertions and deletions in the polypeptide chain mentioned above. Presumably, the cytochromes arose with approximately their present size.

This hypothesis is corroborated, in particular, by the frequently encountered domains: these are regions of the chain which form many internal contacts but few contacts with other parts of the chain[4]. All proteins with molecular weights above 20000 are subdivided into at least 2 domains. Very obvious examples are the domains of trypsin-like proteins[8] and of glutathione reductase[36], the geometries of which were compared to each other in Section 4. In the spontaneous folding process after (or during) chain synthesis on the ribosome, the domains most probably assume their final geometries separately and independently from each other.

Domain sizes vary between 50 and 150 amino acids. The lower limit presumably reflects the requirement that proteins—and hence domains—have to be stable and rigid for executing specific functions. Chains with less than 50 links have a rather large surface even if they are globular. Below 50 residues, the fraction of surface residues, and thus the fraction of energetically favorable contacts between water and polar groups of the chain (in particular the peptide bonds), increases to such an extend that these contacts spread the chain. Although no reason for the upper limit is known, it is presumed that the folding of a larger, and therefore more complicated domain becomes geometrically too difficult.

Thus, proteins consist of (one or) several structurally self-supporting parts of defined size, which can be considered as building blocks. Changes of protein size during evolution are for the most part changes in the number of building blocks assembled. In this respect, changes of the sizes of the building blocks themselves play only a minor role. The group classification of Section 5 refers to domains and not to proteins consisting of several domains.

A number of structural analyses showed that identical, or more exactly, similar domains (see Section 4) are encountered in different proteins. This indicates that larger proteins have been assembled using a modular system based on domains as building blocks. The domain module A of Figure 10 is known from Figure 7. It appears singly in superoxide dismutase and azurin, doubly in the light, and four times in the heavy chains of the immunoglobulins. All examples in Table 1 are proteins like the immunoglobulins; they contain

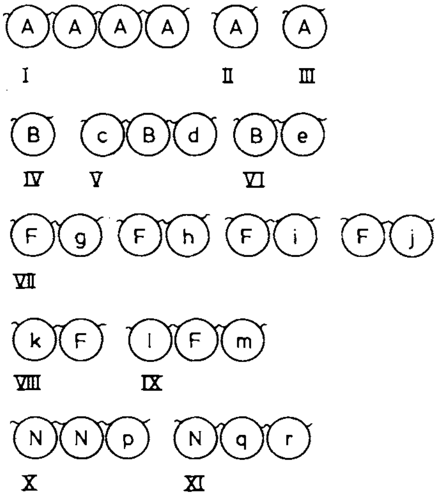


Fig. 10. Domain composition of some proteins. Domains recurring with identical (or more exactly, similar) geometry are labelled with capital letters. I: heavy chains of immunoglobulins [34], II: azurin [21], III: superoxide dismutase [22], IV: triose-phosphate-isomerase [42], V: pyruvate kinase [43], VI: glycolate oxidase [44], VII: lactate-, malate-, glyceraldehyde-3-phosphate dehydrogenases [45], and phosphoglycerate kinase [46, 47], VIII: alcohol dehydrogenase [45], IX: phosphorylase [48], X: glutathione reductase [36], XI: *p*-hydroxy benzoate hydroxylase [49].

structural repeats within one chain, which one can designate as domains.

Domain B of Figure 10 reveals another aspect of the modular system. This domain has been discovered in three different proteins. It not only appears singly in triose-phosphate-isomerase, but is also the central domain along the chain of pyruvate kinase, and finally it is part of glycolate oxidase. In this latter case, the same module is not repeated along a single chain but is combined with different modules to form new composite chains. The same applies for domains F and N of the remaining proteins of Figure 10. As an alternative to the suggested domain combinations, it could be envisaged that the structures result from a separate evolution in which domains B, F, N were particularly strongly conserved. This alternative is rather unlikely, however, because the remaining domains have totally different structures, and furthermore the repeated domains are positioned at completely different parts of the polypeptide chains; domain F appears at the beginning, in the middle, and at the end of the respective polypeptide chains.

Domains F and N indicate another property of the modular system. In all proteins shown, domain F binds the dinucleotide NAD at identical positions of its chain fold. The same applies for domain N, except that it binds two different dinucleotides; FAD at the first domain of glutathione reductase and *p*-hydroxybenzoate-hydroxylase, and NADPH at the second domain of glutathione reductase. With these properties, domains F and N can be considered as carriers of partial functions.

The functional aspect is particularly clear in glutathione reductase, where FAD works as a bridge in the transfer of reduction equivalents from NADPH to oxidized glutathione. Here, three partners join in the catalytic reaction, and each partner binds its specific domain; FAD and NADPH at the first and second domain, respectively, and glutathione at the third[36]. From this observation one may suggest the hypothesis that during evolution, the capability for complicated chemical reactions is acquired by combination of domains carrying the necessary partial functions; the selection of modules is directed by the required reaction. This hypothesis assumes that on the time scale of evolution, genes corresponding to the domains can be freely transferred and fused on the genome. Since gene transfer and fusion processes are known to occur during the differentiation of antibody producing cells in the development of individual organisms[50], this assumption does not pose any serious problem.

## 7. Conclusions

During evolution, the proteins vary as continuously as the species. The observed changes yield important insights into protein structures and above all they permit the distinction between essential and non-essential traits to be made. Newly arising tasks will be accomplished by novel proteins, which are produced by gene duplication of existing proteins and subsequent changes. In this process, the original proteins retain their old functions; the process is called protein differentiation. Quantitative data for the evolutionary distance between two proteins cannot only be derived from sequence comparisons, but also from geometric comparisons. Since geometries are most strongly conserved, such comparisons lead to the recognition of very distant relatives. It is most unlikely that all proteins have descended from a single ancestral structure; rather, one has to assume that there exist about $10^2$ original structures, or more exactly, original domain geometries. Proteins do not grow or shrink unidirectionally during evolution; the encountered changes of size arise from combination of domains. These are gene duplications followed by (gene transfer) and gene fusion. Large proteins are most likely assembled using a modular system, where modules with the required partial functions are selected and assembled. In the light of the gradually emerging order in the protein world, complete comprehension of all protein structures is no longer a utopian dream.

Received: October 3, 1980 [A 350 IE]
German version: Angew. Chem. *93*, 143 (1981)

---

[1] *R. E. Dickerson* in *M. Kimura:* Molecular Evolution and Polymorphism, National Institute of Genetics, Mishima, Japan 1977.

[2] *T. L. Blundell, L. N. Johnson:* Protein Crystallography. Academic Press, London 1976.

[3] *M. O. Dayhoff:* Atlas of Protein Sequence and Structure. Vol. 5, Suppl. 3 and earlier, National Biomedical Research Foundation, Washington, D.C. 1978.

[4] *G. E. Schulz, R. H. Schirmer:* Principles of Protein Structure, Springer, New York 1979.

[5] *K. Sick, D. Beale, D. Irvine, H. Lehmann, P. T. Goodall, S. MacDougall,* Biochim. Biophys. Acta *140*, 231 (1967).

[6] *A. C. Allison,* Sci. Am. *195* (2), 87 (1956).

[7] *R. E. Dickerson, R. Timkovich, R. J. Almassy,* J. Mol. Biol. *100*, 473 (1976).

[8] *J. J. Birktoft, D. M. Blow,* J. Mol. Biol. *68*, 187 (1972).

[9] *L. T. J. Delbaere, W. L. B. Hutcheon, M. N. G. James, W. E. Thiessen,* Nature *257*, 758 (1975).

[10] *D. M. Shotton, B. S. Hartley,* Biochem. J. *131*, 643 (1973).

[11] *S. Magnusson,* Enzymes *3*, 277 (1971).

[12] *B. S. Hartley,* Proc. R. Soc. London *B 205*, 443 (1979).

[13] *S. S. Taylor,* J. Biol. Chem. *252*, 1799 (1977).

[14] *H. H. Kiltz, W. Keil, M. Griesbach, K. Petry, H. Meyer,* Hoppe-Seylers Z. Physiol. Chem. *358*, 123 (1977).

[15] *A. G. Tomasselli, R. H. Schirmer, L. H. Noda,* Eur. J. Biochem. *93*, 257 (1979).

[16] *E. W. Davie, K. Fujikawa,* Annu. Rev. Biochem. *44*, 799 (1975).

[17] *H. J. Müller-Eberhard,* Annu. Rev. Biochem. *44*, 697 (1975).

[18] *P. A. Peterson, L. Rask, K. Sege, L. Klareskog, H. Anundi, L. Ostberg,* Proc. Natl. Acad. Sci. USA *72*, 1612 (1975).

[19] *R. H. Kretsinger,* CRC Crit. Rev. Biochem. *8*, 119 (1980).

[20] *E. Rinderknecht, R. E. Humbel,* FEBS Lett. *89*, 283 (1978).

[21] *E. T. Adman, R. E. Stenkamp, L. C. Sieker, L. H. Jensen,* J. Mol. Biol. *123*, 35 (1978).

[22] *J. S. Richardson, K. A. Thomas, B. H. Rubin, D. C. Richardson,* Proc. Natl. Acad. Sci. USA *72*, 1349 (1975).

[23] *J. R. Brown,* Fed. Proc. Fed. Am. Soc. Exp. Biol. *35*, 2141 (1976).

[24] *A. D. McLachlan, J. E. Walker,* J. Mol. Biol. *112*, 543 (1977).

[25] *J. A. Black, G. H. Dixon,* Nature *218*, 736 (1968).

[26] *J. Sjödahl,* Eur. J. Biochem. *78*, 471 (1977).

[27] *E. T. Adman, L. C. Sieker, L. H. Jensen,* J. Biol. Chem. *248*, 3987 (1973).

[28] *R. H. Kretsinger,* Nature New Biol. *240*, 85 (1972).

[29] *C. S. Wright,* J. Mol. Biol. *141*, 267 (1980).

[30] *J. Tang, M. N. G. James, I. N. Hsu, J. A. Jenkins, T. L. Blundell,* Nature *271*, 618 (1978).

[31] *N. S. Andreeva, A. E. Gustchina,* Biochem. Biophys. Res. Commun. *87*, 32 (1979).

[32] *A. D. McLachlan,* Eur. J. Biochem. *100*, 181 (1979).

[33] *M. G. Rossmann, D. Moras, K. W. Olsen,* Nature *250*, 194 (1974).

[34] *R. Huber,* Trends Biochem. Sci. *1*, 174 (1976).

[35] *F. A. Quiocho, G. L. Gilliland, G. N. Phillips Jr.,* J. Biol. Chem. *252*, 5142 (1977).

[36] *G. E. Schulz, R. H. Schirmer, W. Sachsenheimer, E. F. Pai, Nature 273*, 120 (1978).

[37] *J. H. Ploegman, G. Drenth, K. H. Kalk, W. G. J. Hol, R. L. Heinrikson, P. Keim, L. Weng, J. Russell,* Nature *273*, 124 (1978).

[38] *G. E. Schulz,* J. Mol. Biol. *138*, 335 (1980).

[39] *C. C. F. Blake, M. J. Geisow, I. D. Swan, C. Rerat, B. Rerat,* J. Mol. Biol. *88*, 1 (1974).

[40] *G. E. Schulz, M. Elzinga, F. Marx, R. H. Schirmer,* Nature *250,* 120 (1974).
[41] *G. E. Schulz,* J. Mol. Evol. 9, 339 (1977).
[42] *D. W. Banner, A. C. Bloomer, G. A. Petsko, D. C. Phillips, C. I. Pogson, I. A. Wilson, P. H. Corran, A. J. Furth, J. D. Milman, R. E. Offord, J. D. Priddle, S. G. Waley,* Nature *255,* 609 (1975).
[43] *M. Levine, H. Muirhead, D. K. Stammers, D. I. Stuart,* Nature *271,* 626 (1978).
[44] *Y. Lindquist, C.-I. Brändén,* J. Mol. Biol. *143,* 201 (1980).
[45] *M. G. Rossmann, A. Liljas, C.-I. Brändén, L. J. Banaszak,* Enzymes *11,* 61 (1975).
[46] *C. C. F. Blake, P. R. Evans,* J. Mol. Biol. *84,* 585 (1974).
[47] *T. N. Bryant, H. C. Watson, P. L. Wendell,* Nature *247,* 14 (1974).
[48] *S. Sprang, R. J. Fletterick,* J. Mol. Biol. *131,* 523 (1979).
[49] *R. K. Wierenga, R. J. DeJong, K. H. Kalk, W. G. J. Hol, J. Drenth,* J. Mol. Biol. *131,* 55 (1979).
[50] *N. Hilschmann, H. U. Barnikol, H. Kratzin, P. Altevogt, M. Engelhard, S. Barnikol-Watanabe,* Naturwissenschaften *65,* 616 (1978).

# Alkylsulfamoyl Chlorides as Key Units in the Synthesis of Novel Biologically Active Compounds for Crop Protection

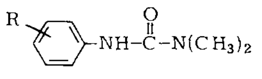
## By Gerhard Hamprecht, Karl-Heinz König, and Gerd Stubenrauch[*]

*Dedicated to Professor Dr. Matthias Seefelder on the occasion of his 60th birthday*

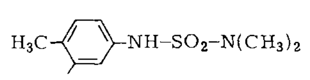
Due to their bifunctional character, alkylsulfamoyl chlorides are versatile units for the synthesis of heterocycles, polar sulfamates, and sulfonamides. In the last decade, synthetic methods of general preparative use have been developed, by means of which amine hydrochlorides, isocyanates, aziridines or tertiary alcohols can be reacted with suitable sulfuric acid derivatives to give novel, variously substituted alkylsulfamoyl chlorides. These compounds can subsequently be converted either to previously unobtainable *N*-alkoxyalkyl-*N*-alkylsulfamoyl chlorides or to novel heterocycles of the type 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxide, 2*H*-1,2,6-thiadiazin-3-one-1,1-dioxide and 2*H*-1,2,4,6-thiatriazin-5-one-1,1-dioxide; these compounds are examples of interesting models which illustrate the relation between the structure and the action of the compound, and in some cases lead to highly selective, ecologically unobjectionable herbicides. On the other hand, the alkylsulfamoyl chlorides themselves can be *N*-acylated to give further 3- to 5-atom bifunctional synthesis units, with which novel heterocyclic syntheses can be carried out. Further uses of the alkylsulfamoyl chlorides include the preparation of biologically active sulfamates, and cycloaddition reactions of *N*-sulfonylamines prepared *in situ.*

## 1. Introduction

In present-day chemical crop protection, carbonic acid derivatives occupy an important place; products derived for example, from isocyanates, such as the *N*-alkyl-*N'*-phenylureas *(1)* are selective herbicidal compounds[2a], which are used today on a worldwide scale in bulk crops such as sugar cane and cotton, to ensure that the increasing demand for foodstuffs and raw fibers will be met.



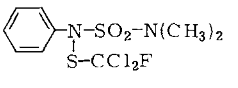
*(1a)*, R = 3-Cl, 4-CH$_3$: Dicuran®
*(1b)*, R = 3-CF$_3$: Cotoran®



*(2)*

In contrast, sulfonic acid derivatives have hitherto found little use. First, the use of monoalkylsulfamoyl chlorides as starting materials, was unknown, and secondly the first investigations of the relation between structure and action, including for example, the replacement of the dimethylcarbamoyl group in *(1)* by the dimethylsulfamoyl group, gave sulfamides *(2)* having only a slight herbicidal action.

Only in the fungicide sector was a sulfonic acid derivative Euparen® *(3)*, prepared from dimethylamidosulfonyl chloride (see Section 2.7) able to acquire practical importance, namely in the control of Botrytis in strawberries[2b].



*(3)*

In contrast, as recently as the 1960's, monoalkylsulfamoyl chlorides were considered to be a class of compounds incapable of existence[3]. Evidently by analogy with carbamyl chlorides, which on heating undergo a reversible cleavage reaction to give isocyanates and hydrogen chloride, it was as-

$$\mathrm{RNH{-}COCl} \rightleftharpoons \mathrm{RN{=}C{=}O} + \mathrm{HCl}$$

$$\underset{(4)}{\mathrm{RNH{-}SO_2Cl}} \xrightarrow{?} [\mathrm{RN{=}SO_2}] + \mathrm{HCl}$$

---

[*] Dr. G. Hamprecht, Dr. K.-H. König, Dr. G. Stubenrauch
BASF AG, Hauptlabor
D-6700 Ludwigshafen (Germany)

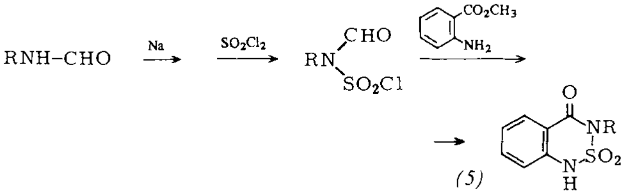
*0570-0833/81/0202-0151 $ 02.50/0*

sumed that the corresponding sulfamyl compounds would show irreversible formation of sulfenes; such compounds were in fact only detected later, by *Burgess et al.*[4], at low temperatures in the presence of bases.

## 2. Syntheses of alkylsulphamoyl chlorides and related intermediates

### 2.1. Synthesis of alkylsulfamoyl chlorides from amine derivatives

*Teufel* succeeded in preparing the first *N*-alkyl-*N*-formylsulfamoyl chlorides with unbranched alkyl groups, by reacting the sodium salts of *N*-alkylformamides with sulfonyl chloride. These were then converted to 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides *(5)* and collected in this form.



*(5)*

However the low yields resulting from the drastic reaction conditions proved an obstacle to a broader use of the reaction.

Free alkylsulfamoyl chlorides *(4)* were first obtained by *Weiss* and *Schulze* by cleavage of sulfamides with sulfonyl

$$\text{RNH-SO}_2\text{-NHR} \xrightarrow{\text{SO}_2\text{Cl}_2} 2\ \text{RNH-SO}_2\text{Cl}\quad \textit{(4)}$$

chloride in an autoclave[6a] and later by heating amine hydrochlorides with sulfonyl chloride in acetonitrile[6b].

$$\text{RNH}_2\cdot\text{HCl} \xrightarrow{\text{SO}_2\text{Cl}_2} \text{RNH-SO}_2\text{Cl}\quad \textit{(4)}$$

The limiting factors were respectively the use of difficultly obtainable sulfamides in a pressure reaction, and solvent losses as a result of partial chlorination to trichloroacetonitrile. The latter compound can for example trimerize exothermally[7] to 2,4,6-tris(trichloromethyl)-1,3,5-triazine in the distillation residue, so that the reaction can only be recommended for use on a laboratory scale.

The direct sulfochlorination of amines required very long reaction times, of the order of 24 hours, and its investigation in other solvents proved unsuccessful. In spite of certain limitations, the above reaction nevertheless dispelled a long held prejudice and opened the way to the use of sulfamyl chlorides in some initial laboratory syntheses of biologically active compounds; in particular, the bifunctional character of the novel two-atom units provided a stimulus to carry out novel heterocyclic syntheses.

### 2.2. Synthesis of alkylsulfamoyl chlorides from isocyanates

In the period which followed, the *N*-alkylsulfamic acids *(6)* (*N*-alkylamido sulfuric acids)[8], prepared from the corresponding isocyanates and sulfuric acid in chlorohydrocarbon solvents, proved to have very diverse uses for the synthesis of α-branched and higher homologues; the acids can be converted to their halides *(4)* in a one-pot process, using a variety of halogenating agents[9].

$$\text{RN=C=O} \xrightarrow[-\text{CO}_2]{\text{H}_2\text{SO}_4} \underset{\textit{(6)}}{\text{RNH-SO}_3\text{H}} \longrightarrow \underset{\textit{(4)}}{\text{RNH-SO}_2\text{Cl}}$$

A selection of these recently prepared intermediates is shown in Table 1.

Table 1. *N*-Alkylsulfamic acids of type *(6)*.

RNH—$SO_3H$ *(6)*

| | R— | M.p. [°C] | Yield [%] |
|---|---|---|---|
| *(6a)* | $(CH_3)_2CH—CH(CH_3)—$ | 152—154 | 93 |
| *(6b)* | $(CH_3)_2CH—CH(C_2H_5)—$ | 102—108 | 90 |
| *(6c)* | $(CH_3)_2CH—CH_2—CH(CH_3)—$ | viscous | 94 |
| *(6d)* | $(CH_3)_2—CH(CH_3)—$ | 184—188 (decomp.) | 93 |
| *(6e)* | Cyclohexyl-$CH(CH_3)—$ | 75—80 | 98 |
| *(6f)* | 1-Norbornyl-$CH(CH_3)—$ | 98—100 | 91 |

Suitable halogenating agents include sulfinyl chloride and phosphorus halides[10], the latter especially in the case of the sparingly soluble *N*-alkylsulfamic acids *(6)*; depending on the chain length of the sulfamic acid moiety, and hence on the ease with which the halides *(4)* may be distilled, yields of 40—85% are achieved. In contrast, phosgenation, in the presence of conventional catalysts, such as tertiary bases or dimethylformamide, proved to give unsatisfactory results, since in some cases the very reactive sulfamoyl chlorides react fur-

$$\underset{\textit{(4)}}{\text{RNH-SO}_2\text{Cl}} \xrightarrow{\text{OHC-N(CH}_3)_2} \text{RNH-SO}_3^{\ominus}\ (\text{CH}_3)_2\overset{\oplus}{\text{N}}\text{=CH-N(CH}_3)_2$$

Table 2. Alkylsulfamoyl chlorides of type *(4)*.

RNH—$SO_2Cl$ *(4)*

| | R— | B.p. [°C/mbar] | $^1$H-NMR ($CDCl_3$, TMS as internal standard, 60 MHz), δ-values |
|---|---|---|---|
| *(4a)* | $C_2H_5—CH(CH_3)—$ | 89—97/2.7 | 0.75—1.05 (t; C—C—$CH_3$), 1.17—1.28 (d; N—C—$CH_3$), 1.3—1.7 (m; $CH_2$), 3.35—3.82 (m; CH), 6.1—6.42 (d; NH) |
| *(4b)* | Cyclopentyl | 107—117/0.13 | 1.3—2.1 (m; $(CH_2)_4$), 3.5—3.7 (m; CH), 6.2—6.55 (s; NH) |
| *(4c)* | $(nC_3H_7)_2CH—$ | 160/0.1 [a] | 0.78—0.96 (t; $CH_3$), 1.1—1.8 (m; $CH_2$), 3.2—3.8 (m; CH), 6.03—6.14 (d; NH) |
| *(4d)* | $nC_6H_{13}—$ | 130/0.13 [a] | 0.79—0.96 (t; $CH_3$), 1.1—1.8 (m; $(CH_2)_4$), 3.14—3.37 (t; $CH_2$—N), 6.59 (s; NH) |
| *(4e)* | $(CH_3)_2CH—CH_2—CH(CH_3)—$ | 140/0.3 [a] | 0.87—0.95 (d; $(CH_3)_2$), 1.26—1.35 (d; $CH_3$), 3.5—4.0 (m; CH), 5.82—5.93 (d; NH) |
| *(4f)* [b] | $Cl—CH_2—CH(C_2H_5)—$ | 104—114/0.5 | 0.96—1.11 (t; $CH_3$), 1.6—1.94 (m; C—$CH_2$C), 3.6—3.95 (m; CH, Cl—$CH_2$), 6.2—6.3 (d; NH) [c] |
| *(4g)* | $CH_3O—CH_2—CH(CH_3)—$ | 125/0.01 [a] | 1.31—1.39 (d; $CH_3$—C), 3.4 (s; $CH_3$—O), 3.45—3.55 (m; CH), 6.6—6.7 (d; NH) [c] |

[a] Oil bath of a rotary evaporator, [b] *(4f)* ≡ *(8c)*, Table 3. [c] 100 MHz.

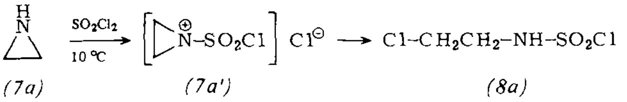
ther, for example with dimethylformamide (DMF), to give amidinium sulfamates, a type of reaction which is known in the case of arylsulfonyl chlorides[11].

"Stable" catalysts for this reaction have proved to be dichloromethyleneammonium compounds[12], which give better phosgenation yields. Table 2 shows a selection of recently prepared alkylsulfamoyl chlorides *(4)*.

These compounds are very reactive and, for example, undergo vigorous exothermic hydrolysis with water. Where the compounds *(4)* distil at temperatures above 125 °C, it is advantageous to employ a thin layer evaporator, since slow decomposition occurs at higher temperatures, evidently with sulfene formation.

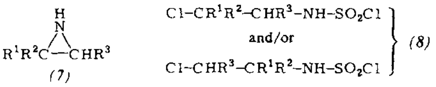
## 2.3. Synthesis of β-(haloalkyl)sulfamoyl halides from substituted aziridines

Specific β-(haloalkyl)sulfamoyl halides *(8)* were synthesized since their potentially cleavable groups permitted unsaturated derivatives, or derivatives with a variety of nucleophilic substituents to be prepared. The ring opening of aziridines *(7)* with sulfonyl halides[13] proved to be a useful method of synthesis; the reaction takes place under extremely mild conditions.



The yield of the reaction depends largely on the solvent employed; we first used carbon tetrachloride, but only obtained about 5% *(8a)*, while with the polar solvent acetonitrile the yield was 65% *(8b)*, so that the actual ring opening step appears to proceed *via* a strongly polar ionic complex intermediate *(7a')*. Whether ring opening occurs in the 2- or 3-position depends on the particular substituents on the ring. Table 3 gives a survey of branched (β-chloroalkyl)sulfamoyl chlorides *(8)*.

Table 3. (β-Chloroalkyl)sulfamoyl chlorides of type *(8)*, from aziridines *(7)*.

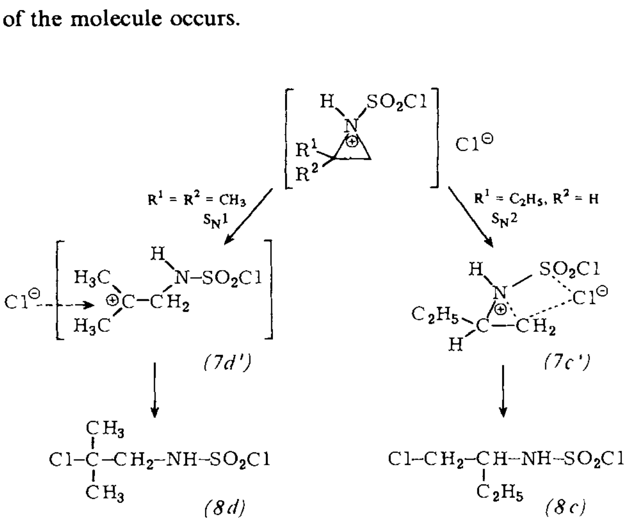


| | Part structure in *(7)* | in *(8)* | | | $n_D^{25}$ | Yield [%] | ¹H-NMR (CDCl₃), TMS as internal standard, 60 MHz), δ-values [a]. |
|---|---|---|---|---|---|---|---|
| *(7b)* | $CH(CH_3)—CH_2$ | *(8b)* | (22%) | $Cl—CH(CH_3)—CH_2—$ | 1.4959 | 55 | 1.53—1.63 (d; $CH_3$) |
| | | *(8b')* | (78%) | $Cl—CH_2—CH(CH_3)—$ | | | 1.41—1.51 (d; $CH_3$), 3.62—3.82 (m; $Cl—CH_2$), 6.0—6.45 (d; NH), |
| *(7c)* | $CH(C_2H_5)—CH_2$ | *(8c)* | [b] | $Cl—CH_2—CH(C_2H_5)—$ | 1.4860 | 52 | *cf.* Table 2m *(4f)* |
| *(7d)* | $C(CH_3)_2—CH_2$ | *(8d)* | | $Cl—C(CH_3)_2—CH_2—$ | 1.4852 | 43 | 1.68 (s; $CH_3$), 3.4—3.55 (d; $CH_2$), 6.2—6.7 (t; NH) |
| *(7e)* | $CH(CH_3)—CH(CH_3)$ | *(8e)* | | $Cl—CH(CH_3)—CH(CH_3)$ | 1.4878 | 44 | 1.38—1.45 (d; $N—C—CH_3$), 1.52—1.59 (d; $Cl—C—CH_3$), 3.7—4.1 (m; N—CH), 4.28—4.55 (m; Cl—CH) |

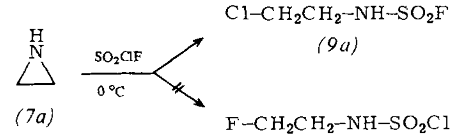
[a] 3.6—3.82 (m; $CH_2$), 6.2—6.6 (NH). [b] *(8c)* ≡ *(4f)*, Table 2.

While *(7b)* gives a mixture of *(8b)* and *(8b')*, ring opening of *(7c)* only gives the α-branched product *(8c)*. The geminally substituted *(7d)*, on the other hand, only gives the β-branched product *(8d)*.

The results described, indicate a competition between two mechanisms. If ring cleavage occurs *via* a carbenium ion ($S_N1$ reaction), then it would be expected, as in *(7d')*, to preferentially occur at the more highly substituted carbon atom rather than formation of a primary carbenium ion. Conversely, the sterically less bulky *(7c')* *a priori* offers less of an obstacle to a bimolecular mechanism, so that here a $S_N2$ reaction, with ring opening and substitution on the same side of the molecule occurs.



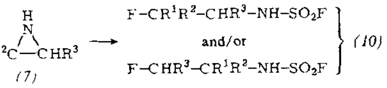
In the reaction of aziridines with sulfonyl chloride fluoride, the more reactive chloride always migrates, so that (β-chloroalkyl)sulfamoyl fluorides such as *(9a)* ($n_D^{25}=1.4363$) are obtained.



Fluorine-substituted alkylsulfamoyl halides—whose synthesis appeared particularly desirable because of the "bioisosteric properties" of fluorine and hydrogen—were obtained by reaction with sulfonyl fluoride. Because of the low boiling point of the halogenating agent (−50 °C), the reaction had to be carried out at lower temperatures, required longer reaction times (6—8 h) and gave yields of only up to 40% (Table 4).

In the reaction with sulfonyl fluoride, the $S_N1$ mechanism is again more important, as substantiated by the higher pro-

Table 4. (β-Fluoroalkyl)sulfamoyl fluorides of type *(10)* from azidiridenes *(7)*.



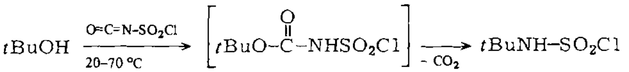
| | Part structure in *(7)* | | | in *(10)* | B.p. [°C/mbar] | $n_D^{25}$ | ¹H-NMR (CDCl₃, TMS as internal standard, 220 MHz), δ-values |
|---|---|---|---|---|---|---|---|
| *(7a)* | $CH_2—CH_2$ | *(10a)* | | $F—CH_2—CH_2—$ | 73—75/13 | 1.3879 | 3.3 and 3.72 (m; N—$CH_2$), 4.03—4.25 and 4.82—5.05 (t; F—$CH_2$), 7.2—7.8 (NH) [a] |
| *(7b)* | $CH(CH_3)—CH_2$ | *(10b)* | (55%) | $F—CH(CH_3)—CH_2—$ | 53—75/0.13 | | 1.30—1.31 and 1.43—1.44 (d; F—C—$CH_3$), 3.2—4.8 (m; $CH_2$) |
| | | *(10b')* | (45%) | $F—CH_2—CH(CH_3)—$ | | 1.3929 | 1.32—1.34 (d; N—C—$CH_3$), 5.7—5.85 (d; NH) |
| *(7c)* | $CH(C_2H_5)—CH_2$ | *(10c)* | (60%) | $F—CH(C_2H_5)—CH_2—$ | 62—79/0.26 | | 1.1—1.6 (t; $CH_3$), 3.26—3.75 (m; N—$CH_2$), 5.58—5.7 (d; NH) |
| | | *(10c')* | (40%) | $F—CH_2—CH(C_2H_5)—$ | | 1.4020 | 1.1—1.6 (t; $CH_3$), 4.32—4.76 (m; F—$CH_2$), 5.58—5.7 (d; NH) |
| *(7d)* | $C(CH_3)_2—CH_2$ | *(10d)* | | $F—C(CH_3)_2—CH_2—$ | 65—72/0.01 | 1.4040 | 1.23 and 1.59 (s; $CH_3$), 3.2 and 3.53 (s; $CH_2$), 5.7—6.1 (NH) [a] |
| *(7e)* | $CH(CH_3)—CH(CH_3)$ | *(10e)* | | $F—CH(CH_3)—CH(CH_3)—$ | 60—72/0.2 | 1.4002 | 1.35—1.37 (d; N—C—$CH_3$), 1.38—1.40 and 1.47—1.49 (d; F—C—$CH_3$, 3.5—3.8 (m; N—CH), 4.55 and 4.77 (s; F—CH), 6.07 (s; NH) |

[a] 60 MHz.

portion of *(10b)* and *(10c)* formed. The reasons may be the lower reaction temperature, the use of catalytic amounts of Lewis acids, and the smaller size of the fluoride ion.

## 2.4. Synthesis of *tert*-alkylsulfamoyl chlorides

The preparation of *tert*-butylsulfamoyl chloride *via* the sulfamic acid[9] or sulfonyl chloride[14] gives only moderate space-time yields. The reaction of *tert*-butanol with chlorosulfonyl isocyanate in nonpolar solvents proceeds more rapidly, *via* decarboxylation of an intermediate chlorosulfonylurethane *(11a)*, to give a high yield of *tert*-butylsulfamoyl chloride *(12a)*[15].



$$t\text{BuOH} \xrightarrow[20\text{–}70\,^\circ\text{C}]{\text{O=C=N–SO}_2\text{Cl}} \left[t\text{BuO–}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{–NHSO}_2\text{Cl}\right] \xrightarrow[-\,\text{CO}_2]{} t\text{BuNH–SO}_2\text{Cl}$$

*(11a)* *(12a)*

The transformation resembles the reaction of carboxylic acids with chlorosulfonyl isocyanate to give acylaminosulfonyl chlorides[16], and is particularly suitable for use with tertiary alcohols (Table 5).

Table 5. *tert*-Alkylsulfamoyl chlorides of type *(12)*.

$RNH—SO_2Cl$ *(12)*

| | R— | B.p. [°C/mbar] | $n_D^{25}$ | ¹H-NMR (CDCl₃, TMS as internal standard, 60 MHz), δ-values |
|---|---|---|---|---|
| *(12a)* | $(CH_3)_3C—$ | 85/0.06 | 1.4579 | 1.4 (s; $CH_3$), 5.9—6.1 (NH) |
| *(12b)* | $C_2H_5C(CH_3)_2—$ | 120/0.13 [a] | 1.4661 | 0.85—1.09 (t; $CH_3$), 1.4—1.9 (m; $CH_2$), 1.45 (s; 2 $CH_3$) |

[a] Thin layer evaporator.

Compounds of type *(12)* can be directly further converted in solution; for distillative purification of sizable batches, it is advisable to use a thin layer evaporator, since for example, compound *(12a)* starts to dealkylate above 140 °C [cf. also the heterocyclic compound *(5e)* derived therefrom].

$$\underset{(12a)}{(CH_3)_3CNH\text{–}SO_2Cl} \xrightarrow[-\,(CH_3)_2C=CH_2]{>140\,^\circ C} \underset{(13)}{NH_2SO_2Cl}$$

## 2.5. Synthesis of *N*-(alkoxy)sulfamoyl chlorides

Because of the sensitivity of the N—O bond, for example of *N*-(triphenylmethyl)-*O*-methylhydroxylamine, in acid medium[17], it initially seemed doubtful whether *N*-(alkoxy)sulfamoyl chlorides *(15)* could be prepared. However, under certain special conditions, namely reaction of the salts *(14)* with phosphorus pentachloride, 60—70% yields proved obtainable (Table 6)[18].

$$(14)\quad RONH—SO_3Na \xrightarrow{PCl_5} RONH—SO_2Cl \quad (15)$$

Table 6. *N*-(Alkoxy)sulfamoyl chlorides of type *(15)*.

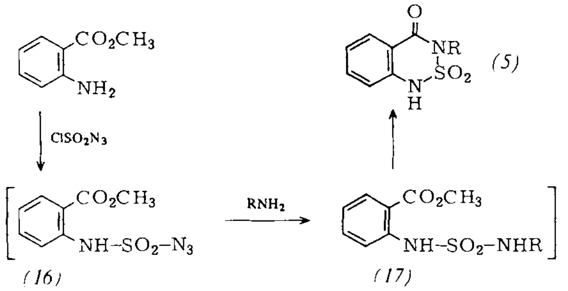
$RONH—SO_2Cl$ *(15)*

| | R | B.p. [°C/mbar] | $n_D^{25}$ | ¹H-NMR (CDCl₃, TMS as internal standard), δ-values |
|---|---|---|---|---|
| *(15a)* | $CH_3$ | 46—48/ 0.2 | 1.4527 | 3.9 (s; $CH_3$), 8.2—8.4 (m; NH) [100 MHz] |
| *(15b)* | $C_2H_5$ | 58—62/ 0.2 | 1.4495 | 1.1—1.3 (t; $CH_3$), 3.9—4.3 (m; $CH_2$) [60 MHz] |
| *(15c)* | $i C_3H_7$ | 138—140/ 0.5 [a] | 1.4516 | 1.2—1.3 (d; $CH_3$), 4.3—4.4 (m; CH) [270 MHz] |

[a] Oil bath of a thin layer evaporator.

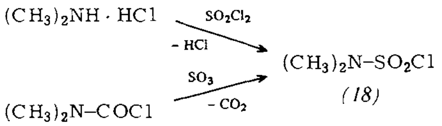
## 2.6. Synthesis of sulfamoyl pseudohalides to circumvent the synthesis of sulfamoyl acid chlorides containing sensitive substituents

To prepare specifically substituted, 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides *(5)*, whose sulfamoyl chloride intermediates were difficult to obtain, the method of *Matier* and *Comer*[14] was modified so that the sulfamoyl azide intermediate *(16)* was only handled in solution and the product *(17)* was purified, before alkaline cyclization, by washing with dilute acid. "Sensitive" substituents, R, in this context are *e.g.* cyclopropyl, phenyl and allyl (see Table 13, Section 3.1).

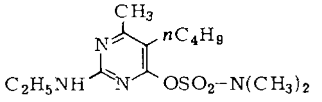


## 2.7. Conversion of monoalkylsulfamoyl chlorides to novel substituted dialkylsulfamoyl chlorides

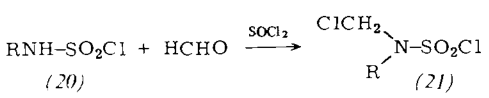
In contrast to the monoalkylsulfamoyl chlorides the corresponding dialkyl derivatives *(18)* were obtained no less than a century ago by *Behrend,* who heated dimethylamine hydrochloride with sulfonyl chloride[19]. This has remained the method of preparation ever since (although polar solvents have been substituted), apart for the method involving sulfonation of carbamyl chlorides[20].



However, the drastic reaction conditions involved in sulfochlorination and sulfonation prevent the controlled introduction of heterosubstituents, such as halogen atoms or alkoxy groups, so that until now only commercial products derived from *N,N*-dialkylsulfamoyl chlorides were known; *e.g.* Euparen *(3)*[2b], mentioned at the outset, or the fungicide Bupirimate *(19)*[21].



(19)



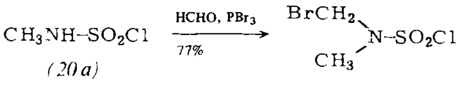
$$\mathrm{RNH{-}SO_2Cl + HCHO \xrightarrow{SOCl_2} (ClCH_2)(R)N{-}SO_2Cl}$$

(20) (21)

The starting point for an alkylating synthesis appeared to be the *N*-monosubstituted sulfamoyl chloride. On addition of sulfinyl chloride to a mixture of *(20)* and formaldehyde, rapid evolution of gas commenced and after brief heating, high yields of novel *N*-alkyl-*N*-(chloromethyl)sulfamoyl chlorides *(21)* were obtained in high yield (Table 7)[22].

The use of phosphorus tribromide, instead of sulfinyl chloride, gives the corresponding *N*-(bromomethyl) compounds, *e.g.* the analogue of *(21a)* (b.p. = 84—92 °C/0.2 mbar).

With paraldehyde and sulfinyl chloride, a mixture of *(22)* and its dehydrohalogenation product *(23)* was obtained[23].



$$\mathrm{CH_3NH{-}SO_2Cl \xrightarrow[77\%]{HCHO,\ PBr_3} (BrCH_2)(CH_3)N{-}SO_2Cl}$$

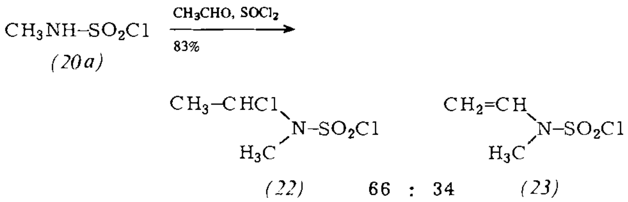
(20a)

Table 7. *N*-Alkyl-*N*-(chloromethyl)sulfamoyl chlorides of type *(21)*.

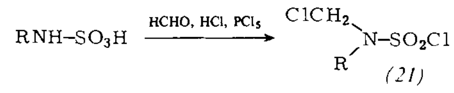
$ClCH_2NR{-}SO_2Cl$ *(21)*

| | R | B.p. [°C/mbar] | $^1$H-NMR ($CDCl_3$, TMS as internal standard, 60 MHz), δ-values |
|---|---|---|---|
| *(21a)* | $CH_3$ | 54—60/0.1 | 3.12 (s; $CH_3$), 5.3 (s; $CH_2$) |
| *(21b)* | $C_2H_5$ | 61—65/0.01 | 1.24—1.49 (t; $CH_3$), 3.38—3.73 (m; C—$CH_2$—N), 5.38 (s; Cl—$CH_2$—N) |
| *(21c)* | $iC_3H_7$ | 75—83/0.2 | 1.35—1.45 (d; $CH_3$), 3.95—4.5 (m; CH), 5.26 (s; $CH_2$) |
| *(21d)* | $nC_6H_{13}$ | 130/0.01 | 0.86—0.97 (t; $CH_3$), 1.2—1.85 (m; $(CH_2)_4$), 3.42—3.6 (t; C—$CH_2$—N), 5.42 (s; Cl—$CH_2$—N) [100 MHz] |

Treating the reaction mixture with hydrogen chloride gas, and concentrating it below 50 °C, gave the pure α-(chloroethyl) compound *(22)*. [*(22)*, b.p. 73-79 °C/0.6 mbar; $^1$H-NMR ($CDCl_3$, TMS int., 60 MHz); δ = 1.71-1.83 (d; $CH_3$—C), 3.03 (s; $CH_3$—N), 6.02-6.32 (m; CH)].



In addition to the sulfamoyl chlorides, the sulfamic acids from which they were derived could also be converted into *(21)*, using somewhat more drastic reaction conditions, *i.e.* prior treatment with hydrogen chloride gas, and use of phosphorus pentachloride; the yield being 50—70% depending on the chain length[22].

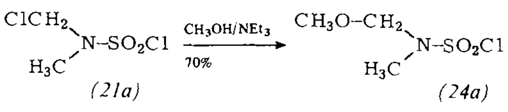


$$\mathrm{RNH{-}SO_3H \xrightarrow{HCHO,\ HCl,\ PCl_5} (ClCH_2)(R)N{-}SO_2Cl}$$

(21)

However, because of the formation of traces of toxic α-haloethers, the batches have to be distilled carefully, and the volatile fractions hydrolyzed with water. The acute oral toxicity of *(21)* in rats[24] is of the same order of magnitude of that found with conventional corrosive acid halides: *(21a)*, 1000 mg/kg; *(21)*, R = $nC_3H_7$, 2210 mg/kg.

The bifunctional character of the novel derivatives *(21)* makes additional reactions possible. Surprisingly, the α-halogen atom in *(21a)* could be replaced by reaction with sodium methoxide, or better still with excess alcohol in the presence of stoichiometric amounts of base, without a reaction occurring at the acid chloride group:



$$\mathrm{(ClCH_2)(H_3C)N{-}SO_2Cl \xrightarrow[70\%]{CH_3OH/NEt_3} (CH_3O{-}CH_2)(H_3C)N{-}SO_2Cl}$$

(21a) (24a)

Higher and unsaturated alcohols reacted similarly (see Table 8)[25].

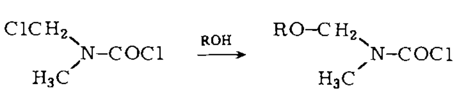
*König* had described a similar selective alkoxylation of *N*-(chloromethyl)-*N*-methylcarbamoyl chloride; there, in spite of the aminal structure of the compound, *N*-(alkoxymethyl)-

Table 8. *N*-(Alkoxymethyl)-*N*-alkylsulfamoyl chlorides of type *(24)*.

$R^1O—CH_2N(R^2)—SO_2Cl$ *(24)*

| | $R^1$ | $R^2$ | B.p. [°C/mbar] | $^1$H-NMR ($CDCl_3$, TMS as internal standard, 60 MHz), δ-values |
|---|---|---|---|---|
| *(24a)* | $CH_3$ | $CH_3$ | 93/11 | 3.02 (s; N—$CH_3$), 3.37 (s; O—$CH_3$), 4.63 (s; O—$CH_2$) |
| *(24b)* | $CH_3$ | $C_2H_5$ | 102—106/ 0.01 | 1.23—1.44 (t; C—$CH_3$), 3.34—3.69 (m; C—$CH_2$), 3.39 (s; O—$CH_3$), 4.72 (s; O—$CH_2$) |
| *(24c)* | $CH_3$ | cyclo-hexyl | 102—106/ 0.01 | 1.1—2.2 (m; Cyclohexyl), 3.35 (s; O—$CH_3$), 4.79 (s; O—$CH_2$) |
| *(24d)* | $CH_2$=CH—$CH_2$ | $CH_3$ | 60—63/ 0.01 | 3.01 (s; $CH_3$), 4.0—4.09 (d; C—$CH_2$—O), 4.7 (s; O—$CH_2$—N), 5.02—6.1 (m; $CH_2$=CH) |

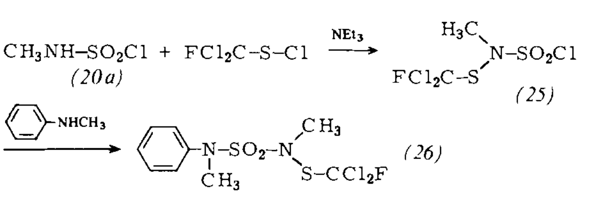
*N*-methylcarbamoyl chlorides were obtained in good yields[26].



From the point of view of their reactivity, the sulfamoyl chlorides *(24)* are comparable with the dialkylsulfamoyl chlorides without additional functional groups; biologically active sulfamate esters derived from them also showed a comparable alkylating action[27].

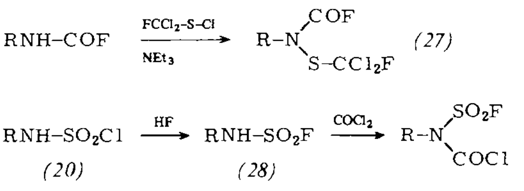
## 2.8. Acylation of monoalkylsulfamoyl chlorides, to novel polyatomic synthetic units

As early as the 1960's, *Schulze* and *Weiss* had prepared fungicidal sulfamides of type *(26)*[28] derived from an *N*-(alkylsulfenyl)-*N*-methylsulfamoyl chloride, the acyl derivative having been prepared *in situ* from sulfamoyl chloride and sulfenyl chloride.

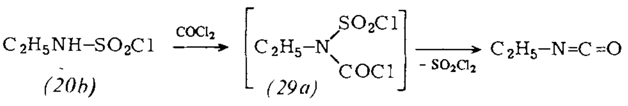


Similar intermediates *(25)* were subsequently isolated (by analogy with carbamoyl halides, which only react in the form of their fluorides)[29], by first synthesizing the corresponding *N*-alkylsulfamoyl fluorides *(27)* and then reacting these with an acyl halide[30].

*Bartholomew* and *Kay* subsequently applied the reaction with phosgene directly to two sulfamoyl chlorides *(20)* [or *(4)* or *(8)*], but found that a special kieselguhr filter aid was necessary if substantial amounts were to be isolated[31].

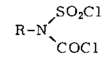


We have found that *N*-alkyl-*N*-(chlorocarbonyl)sulfamoyl chlorides *(29)* are very sensitive to impurities, which catalyze their decomposition; for example, when *(20b)* was reacted with phosgene without a filtration aid, we isolated ethyl isocyanate as a volatile decomposition product, instead of *(29a)*.



We subsequently found that preparative synthesis by this reaction benefited from a two-phase washing process with water (the products being surprisingly stable to water), and in this way it proved possible to isolate good yields of the compounds *(29)*, which constitute triatomic bifunctional units for synthesis (Table 9)[32].

Table 9. *N*-Alkyl-*N*-chlorocarbonylsulfamoyl acid chlorides of type *(29)*.

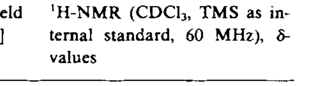

$R{-}N(SO_2Cl)(COCl)$

*(29)*

| | R | B.p. [°C/mbar] | Yield [%] | $^1$H-NMR ($CDCl_3$, TMS as internal standard), δ-values |
|---|---|---|---|---|
| *(29a)* | $C_2H_5$ | 57/0.12 | 85 | 1.46—1.49 (t; $CH_3$), 4.19—4.28 (m; $CH_2$) [270 MHz] |
| *(29b)* | $nC_3H_7$ | 67—72/ 0.12 | 78 | 0.81—1.1 (t; $CH_3$), 1.5—2.1 (m; C—$CH_2$), 3.8—4.08 (t; N—$CH_2$) [60 MHz] |
| *(29c)* | $nC_4H_9$ | 70—76/ 0.12 | 68 | 0.85—1.03 (t; $CH_3$), 1.28—1.81 (m; $CH_2$—$CH_2$—C), 3.45—3.59 (t; N—$CH_2$) [100 MHz] |
| *(29d)* | Cyclo-hexyl | 100—105/ 0.12 | 68 | IR: νC=O 1755 cm$^{-1}$ |

In the same way, reaction of sulfamoyl chlorides *(20)* [or *(4)* or *(8)*] with chloroformic acid esters gave yields of up to 91% of *N*-(alkoxycarbonyl)-*N*-alkylsulfamoyl chlorides *(30)*, which serve as triatomic synthesis units of graded reactivity (Table 10)[32].

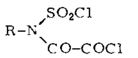
Table 10. *N*-(Methoxycarbonyl)-*N*-alkylsulfamoyl chlorides of type *(30)*.

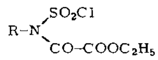


| | R | B.p. [°C/mbar] | Yield [%] | $^1$H-NMR ($CDCl_3$, TMS as internal standard, 60 MHz), δ-values |
|---|---|---|---|---|
| *(30a)* | $CH_3$ | 49—51/ 0.13 | 91 | 3.32 (s; N—$CH_3$), 3.85 (s; O—$CH_3$) |
| *(30b)* | $C_2H_5$ | 50—60/ 0.1 | 90 | 1.25—1.49 (t; C—$CH_3$), 3.75—4.15 (m; N—$CH_2$), 3.9 (s; O—$CH_3$) |
| *(30c)* | Cl—$CH_2CH_2$ | 84—88/ 0.11 | 86 | 3.55—3.8 (t; Cl—$CH_2$), 4.05—4.28 (t; N—$CH_2$), 3.91 (s; O—$CH_3$) |
| *(30d)* | $nC_3H_7$ | 70—72/ 0.13 | 82 | 0.96—1.0 (t; $CH_3$), 1.73—1.88 (m; C—$CH_2$), 3.86—3.92 (t; N—$CH_2$), 3.98 (s; O—$CH_3$) |
| *(30e)* | $iC_3H_7$ | 60—64/ 0.12 | 79 | 1.47—1.58 (d; C—$CH_3$), 3.9 (s; O—$CH_3$), 4.45—4.92 (m; CH) |
| *(30f)* | Cyclo-hexyl | 91/0.12 | 50 | 1.1—2.05 (m; $(CH_2)_5$), 3.82 (s; O—$CH_3$), 4.05—4.4 (m; CH) |

The tetra-atomic bifunctional synthesis units *(31)* and *(32)* can be obtained by reaction of *(20)* [or *(4)* or *(8)*] with oxalyl dichloride or oxalate ester chlorides respectively (Table 11)[32].

Table 11. *N*-(Chlorooxalyl)- and *N*-(ethoxyoxalyl)-*N*-alkylsulfamoyl chlorides of type *(31)* and *(32)* respectively.

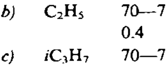
*(31)*

$R{-}N(SO_2Cl){-}CO{-}COCl$

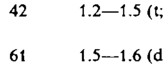

$R{-}N(SO_2Cl){-}CO{-}COOC_2H_5$
*(32)*

| | R | B.p. [°C/mbar] | Yield [%] | $^1$H-NMR ($CDCl_3$, TMS as internal standard, 60 MHz), δ-values |
|---|---|---|---|---|
| *(31a)* | $CH_3$ | 60—65/2 | 58 | 3.3 (s; $CH_3$) |
| *(31b)* | $C_2H_5$ | 70—72/ 0.4 | 42 | 1.2—1.5 (t; $CH_3$), 3.7—4.1 (m; $CH_2$) |
| *(31c)* | $iC_3H_7$ | 70—72/ 0.4 | 61 | 1.5—1.6 (d; $CH_3$), 4.3—4.8 (m; CH) |
| *(31d)* | $nC_4H_9$ | 75—84/ 0.65 | 54 | 0.9—1.1 (t; $CH_3$), 1.2—1.5 (m; $CH_2$), 1.6—1.9 (m; $CH_2$), 3.8—4.1 (m; N—$CH_2$) [220 MHz] |
| *(32a)* | $CH_3$ | 80—82/ 0.65 | 61 | 3.4 (s; N—$CH_3$), 1.3—1.5 (t; C—$CH_3$), 4.2—4.6 (m; $CH_2$) |
| *(32b)* | $C_2H_5$ | 75—83/ 0.52 | 70 | 1.3—1.5 (t; $CH_3$), 3.8—4.1 (m; $CH_2$) [100 MHz] |
| *(32c)* | $iC_3H_7$ | 78—82/ 0.52 | 75 | 1.4—1.6 (d; $CH_3$), 4.4—4.7 (m; CH) |

Finally, the novel sulfamoyl chlorides *(33)* and *(34)* shown below, which are penta-atomic synthesis units, were obtained by reaction of *(20)* [or *(4)* or *(8)*] with chlorocarbonyl isocyanate or chlorocarbonyl isocyanide dichloride respectively, (Table 12)[33].

Table 12. *N*-(Isocyanatocarbonyl)- and *N*-(dichloromethylenecarbamoyl)-*N*-alkylsulfamoyl chlorides of type *(33)* and *(34)* respectively.

*(33)*

$R{-}N(SO_2Cl){-}CO{-}N{=}C{=}O$


$R{-}N(SO_2Cl){-}CO{-}N{=}CCl_2$
*(34)*

| | R | B.p. [°C/mbar] | Yield [%] | $^1$H-NMR ($CDCl_3$, TMS as internal standard, 220 MHz), δ-values |
|---|---|---|---|---|
| *(33a)* | $CH_3$ | 55—60/ 0.2 | 71 | 3.6 (s; $CH_3$) |
| *(33b)* | $C_2H_5$ | 68—70/ 0.3 | 66 | 1.3—1.5 (t; $CH_3$), 3.8—4.2 (m; $CH_2$) [60 MHz] |
| *(33c)* | $iC_3H_7$ | 70—72/ 0.3 | 71 | 1.5—1.6 (d; $CH_3$), 4.6—5.0 (m; CH) [80 MHz] |
| *(33d)* | $nC_4H_9$ | 70—75/ 0.3 | 67 | 0.8—0.9 (t; $CH_3$), 1.1—1.2 (m; $CH_2$), 1.4—1.6 (m; $CH_2$), 3.9 (m; —N—$CH_2$) |
| *(34a)* | $CH_3$ | 75—82/ 0.2 | 71 | 3.51 (s; $CH_3$) |
| *(34b)* | $C_2H_5$ | 68—75/ 0.2 | 70 | 1.3—1.38 (t; $CH_3$), 3.98—4.08 (m; $CH_2$) |
| *(34c)* | $iC_3H_7$ | 66/0.02 | 70 | 1.52—1.58 (d; $CH_3$), 4.76—4.92 (m; CH) |
| *(34d)* | $nC_4H_9$ | 88—95/ 0.02 | 67 | 0.94—1.0 (t; $CH_3$), 1.38—1.5 (m; $CH_2$), 1.75—1.88 (m; $CH_2$), 3.99—4.09 (m; N—$CH_2$) |

The acylated bifunctional *N*-alkylsulfamoyl chlorides *(29)*—*(34)* are attractive intermediates for the preparation of five- and six-membered heterocycles. Their use in synthesizing biologically active compounds will be dealt with in Section 3.8.

## 3. The route from the intermediate to novel reference structures of biologically active compounds

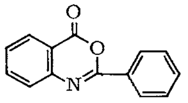
Whilst in the early 1960's world-wide chemical crop protection research still resulted in the annual appearance of about 25 biologically active compounds on the market, this number has dropped in the interim to about 15[34]. The lower rate of innovation is less a reflection of a decline in intensive research than of the high degree of development achieved in technology. The enormous rise in development costs as a result of toxicological and metabolic investigations, and extensive clearance procedures, which may vary from country to country, makes the market launch of a novel biologically active compound a high-risk decision nowadays, in view of already existing solutions to various problems and intensive competition.

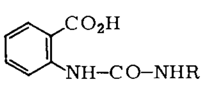
This makes it all the more important, not least for economic reasons, to investigate novel intermediates by broad and systematic variation, involving a number of reference structures, and to achieve new insight into the relationship between structure and activity.

### 3.1. 3-Substituted 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides

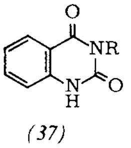
An example of the use of intermediate products to be found in BASF research, is provided by the quinazolinediones, which have been known for some time.

In conjunction with the observation that 3,1-benzoxazin-4-ones *(35)*, derived from anthranilic acid, exhibited selectivity in Indian corn and grain[35], anthranilic acid was first combined with the known urea structure. While the resulting open-chain compounds *(36)* proved to have only a low herbicidal activity, their cyclization gave active quinazoline-2,4-diones *(37)*[36] which, especially on subsequent hydrogenation and *N*-acylation, to give compound *(38)* R = $iC_3H_7$, exhibited selectivity in potatoes and Indian corn[37]. At the same time, they are structurally related to the herbicidal uracils *(39)* and *(40)* developed by Du Pont[38,39], with which they ultimately share a common prototype in nature, uracil *(41)*.

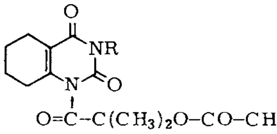

*(35)*, Benthranil



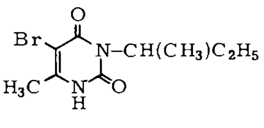
*(36)*, R = Alkyl



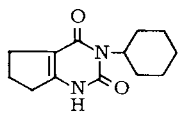
*(37)*



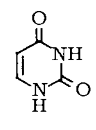
*(38)*, BAS 3490 H



*(39)*, Bromacil

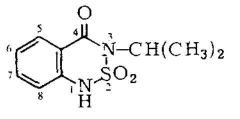


*(40)*, Lenacil



*(41)*, Uracil

To broaden the selectivity of *(37)*, the next modification of the molecule was to replace a carbonyl by a sulfonyl group, using alkylsulfamoyl chlorides; in this way, *Zeidler* and *Fischer* discovered the highly active herbicides, 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides, such as Basagran® *(5a)*[40] (biologically active compound: bentazone).



*(5a)*, Basagran®

Basagran® *(5a)* is nowadays employed extensively as a selective, postemergence herbicide in numerous crops such as soybean, rice, Indian corn, grain and groundnuts, and is distinguished by a high degree of tolerance by crop plants, and low toxicity ($LD_{50}$ for oral administration to rats; 2063 mg/kg). In view of its favorable—viewed also on the long term—ecotoxicology, it is nowadays one of the modern, crop treatment agents.

*(5a)* is at the same time an example of the "bioisosteric" replacement of the carbonyl group by a sulfur dioxide group, which has similar electronic properties; in both cases, the acid amide proton is acidic. According to X-ray structural analysis (Fig. 1)[41], the two nitrogen atoms lie in the plane of the benzene ring; the sulfur atom, on the other hand, is splayed out sufficiently far that one of the associated oxygen atoms lies in the plane of the benzene ring, whilst the other is almost at right angles to this. A striking feature is the difference between the two N—S bonds; the shorter bond length, 1.60 Å, in the case of the aryl-(N—S) bond is intermediate between that of a single bond (1.74 Å) and double bond (1.54 Å)[42] and indicates a considerable (d-p)π overlap and conjugation with the aromatic structure. This is largely absent in the isopropyl nitrogen (N—S = 1.67 Å), so that here the single-bond character predominates.

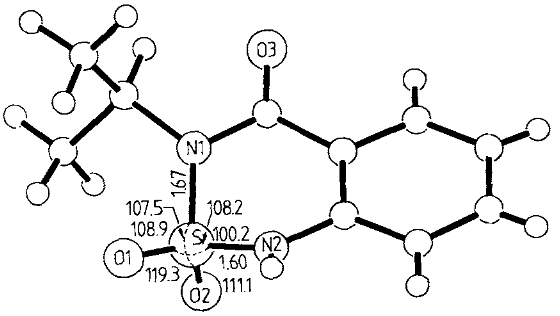


Abb. 1. Bond lengths [Å] and bond angles [°] of *(5a)* in the crystal [41].

Bentazone *(5a)*, acts by inhibiting photosynthesis; this inhibition can be measured in a Hill reaction on isolated chloroplasts[43] (see Section 3.2). Tolerant plants overcome the observed reduction in $CO_2$ assimilation relatively rapidly, after application of the biologically active compound, while with controllable weeds any such assimilation is checked.

The biologically active compound[44] is metabolized *via* a hydroxylation of the arene in positions 6 and 8, followed—depending on the species of plant—by conjugation to monosaccharides and oligosaccharides (in soybean) or ultimately by further degradation, to natural aminoacids (rice). Neither residues of the intact biologically active compound, nor residues of its hydroxy-metabolites, are detectable in the seeds of the plants.

In the soil, the half-life is 2—5 weeks; analogous hydroxy-metabolites are incorporated, in insoluble form, into humic acids in the soil.

In parallel to the biological development, the process chemistry had to be advanced. The difficulties observed in the preparation of the biologically active compound directed our interest first of all to known heterocyclic reactions. *Inter alia*, we carried out alkylation experiments on the 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxide described by *Cohen et al.*[45], but these always led only to the isomeric 1-alkyl-1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides instead of the desired 3-alkyl derivatives[46].

A breakthrough, both with respect to the preparation of the compounds and in the fine selection of biological properties, was only achieved through the systematic development of novel sulfamoyl chloride syntheses (see Sections 2.2—2.6). Thus variously substituted 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides *(5)* became obtainable in high yields *via* methyl anthranilate and alkaline cyclization[47] or *via* anthranilic acid and cyclization under acid conditions[48]. Table 13 shows a selection of these derivatives, which previously could not be prepared.

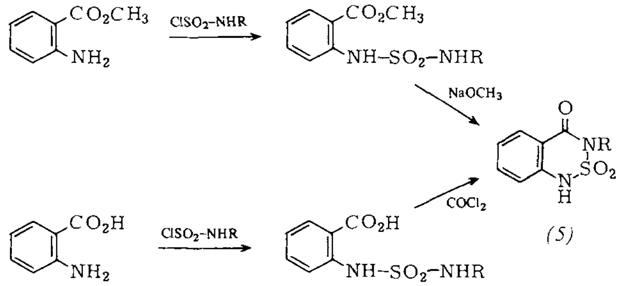
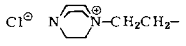
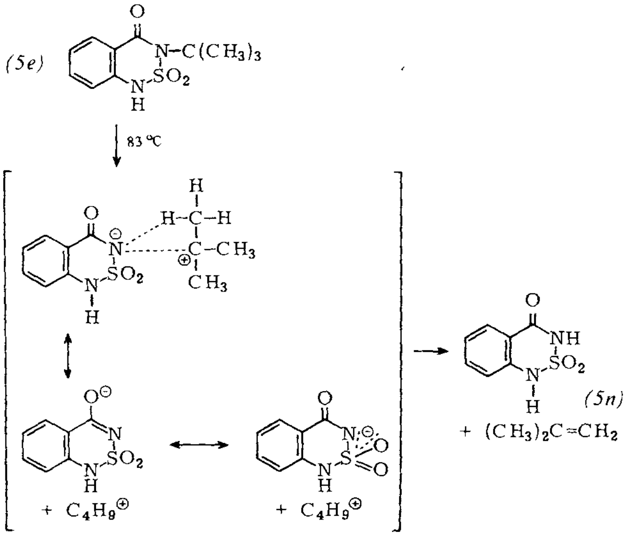


Table 13. Substituted 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides [49] of type *(5)*.

| | R— | M.p. [°C] | | R | M.p. [°C] |
|---|---|---|---|---|---|
| *(5a)* | $(CH_3)_2CH—$ | 135-137 | *(5h)* | $Cl—CH_2CH_2—$ | 165—167 |
| *(5b)* | $C_2H_5—CH(CH_3)$ | 112—114 | *(5i)* | $F—CH_2CH_2—$ | 162—164 |
| *(5c)* | $(C_2H_5)_2CH—$ | 128—132 | *(5j)* | $C_6H_5—$ | 192—195 |
| *(5d)* | $(CH_3)_2CH—CH(CH_3)—$ | 118—122 | *(5k)* | $CH_3O—CH_2—CH(CH_3)—$ | 95—96 |
| *(5e)* | $(CH_3)_3C—$ | 83 (decomp.) | *(5l)* | $Cl^{\ominus}(CH_3)_3N^{\oplus}—CH_2CH_2—$ | 252 |
| *(5f)* | Cyclopropyl | 168—170 | *(5m)* |  | 234 (decomp.) |
| *(5g)* | $CH_2{=}CH—CH_2—$ | 154—158 | | | |

The biologically active compounds *(5)* are freed from the auxiliary base by stirring the mixture in water and acidification, or by alkaline extraction followed by acidification. However to avoid hydrolysis, the alkaline cyclization can also be carried out with aqueous alkali followed by rapid acidification.

Only *(5a)* required special synthetic conditions; because of its screened sulfonamide proton, alkaline cyclization only proved possible with lithium methoxide in DMSO as the solvent. Surprisingly *(5e)* decomposes above 83 °C, with elimination of isobutene, giving compound *(5n)*.



The ease with which *(5e)* thermolyzes, indicates the intermediate formation of the 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxide anion, stabilized by the carbonyl and the sulfur dioxide group, as "leaving group". The reaction has a parallel in the dealkylation of tertiary *N,N'*-dialkylsulfamides, which, in the presence of trifluoroacetic acid, decompose into monoalkylsulfamides and *tert*-butyl trifluoroacetate[50].

*(5l)* and *(5m)* are derived from *(5h)* by a substitution reaction with tertiary base, effected by heating for 8 hours at 80 °C in dioxane; however, in contrast to Cycocel® (2-chloroethyl-(trimethyl)ammonium chloride), which is a growth regulator, compound *(5l)* shows only slight activity.

With respect to their herbicidal action, the α-branched derivatives (Table 13) are distinctly superior to the non-branched derivatives. For example, compounds *(5b)* to *(5d)*, show very good toleration in rice, Indian corn, soybean and wheat, even at 4 kg/ha, while having the same action on weeds as the isopropyl compound *(5a)*; furthermore, they show slight activity against barnyard grass and annual bluegrass.

### 3.2. Application of the Hill reaction to the systematic design of biologically active compounds

In spite of the high selectivity and activity of whatever structure of biologically active compound has proved best in screening tests, the chemist can ultimately not be sure whether any additional substituents might not lead to an improvement in these properties. Thus, the simple α-branching in the 3-position, and the non-substitution of positions 1 and 5—8 were in the first place suggested by the prototype compounds *(37)* and *(40)*, but were also chosen for economic reasons. Simple considerations however show that even monosubstitution by 10 different substituents in the aromatic ring, and in positions 1 and 3 of an alkyl residue having up to four atoms, would require the synthesis of 1.76 million different compounds to cover each permutation.

To permit sensible use of available capacity for synthesizing compounds, it is advantageous to employ biological testing models which permit a deeper insight into plant-physiological phenomena, for example through measurements of the Hill reaction[51]. For such measurements, plant leaves—mustard leaves are commonly used—are homogenized in a high frequency disperser, and the material then separated in an ultracentrifuge. *Hill* was the first to discover that isolated chloroplasts in the presence of Fe(III)-salts, develop oxygen continuously when exposed to light. This so-called "Hill reaction", entails cleavage of a water molecule in a primary photochemical reaction, into oxygen, protons and electrons. Instead of the natural electron acceptor NADP, synthetic acceptors, for example potassium hexacyanoferrate, which on reduction undergo an easily measureable change in absorption, are generally added. The quantitative determination of the amount of $Fe^{2+}$ formed per unit time is carried out photometrically at 510 nm, after addition of phenanthroline. For herbicides, which inhibit the Hill reaction, the concentration of the inhibitor (in %) is plotted against the logarithm of the herbicide concentration. The $pI_{50}$ (the negative logarithm of the concentration required for 50% inhibition) can then easily be read off the graph. In experiments with series of chemical compounds, a semiquantitative method is in most cases considered adequate; in this, the inhibition is measured first at a biologically active compound concentration of $10^{-5}$ mol/dm$^3$ and additionally at a lower concentration ($10^{-6}$ or $10^{-7}$ mol/dm$^3$). The determination of the absolute $pI_{50}$ is relatively involved, since the value also depends on the manner in which the chloroplasts have been prepared, their concentration and the membrane integrity[52].

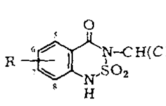
To the synthetic chemist, the value of the $pI_{50}$ measurement is that the actual herbicidal action is separated from other factors (albeit these are vital in practical use) such as stability, metabolism, and uptake and transportation of the biologically active compound by the leaves or roots, and thus provides him with guidance for optimization to achieve maximum activity (for examples of $pI_{50}$ values, see Table 14).

### 3.3. Synthesis of aryl-substituted 3-alkyl-1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides

Using the methods of synthesis described in this article, and employing substituted 2-aminobenzoic acid, we prepared a range of very diverse aryl-substituted 3-alkyl-1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides, of which a selection is shown in Table 14, alongside their corresponding $pI_{50}$ values.

It also proved possible to prepare certain derivatives directly, by halogenating or nitrating compound *(5a)* under mild conditions, without ring cleavage; in such reactions, it is the 6-position which is predominantly attacked first, after

Table 14. Aryl-substituted 3-alkyl-1$H$-2,1,3-benzothiadiazin-4-one-2,2-dioxides of type *(42)*.



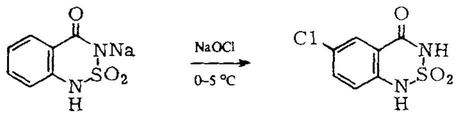
*(42)*

| | R | M.p. [°C] | $pI_{50}$ [a] |
|---|---|---|---|
| *(42a)* | 5-Cl | 175—177 | 3.38 |
| *(42b)* | 6-Cl | 190—194 | 4.06 |
| *(42c)* | 7-Cl | 155—159 | 4.36 |
| *(42d)* | 8-Cl [53] | 84—88 | 4.92 |
| *(42e)* | 6,8-$Cl_2$ | 158—161 | 4.92 |
| *(42f)* | 8-$CH_3$ [54] | 125—126 | 4.17 |
| *(42g)* | 6-$NO_2$ | 205—208 | 3.91 |
| *(42h)* | 6,8-$(NO_2)_2$ | 202—205 (decomp.) | — |
| *(42i)* | 8-Br | 105—109 | — |
| *(42j)* | 6-SCN | 170—173 | 3.93 |

[a] See Section 3.2. High $pI_{50}$ values indicate good herbicidal properties.

which excess electrophilic agent attacks the 8-position. As an example *(5a)* reacts with $SO_2Cl_2$ at 70 °C to give *(42b)* and *(42d)* in a 4:1 ratio when treated with $HNO_3$ at 30 °C, compound *(5a)* only gives the 6-nitro derivative *(42g)*.

*(43)*

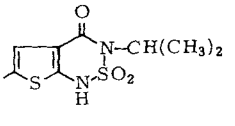


*(44)*

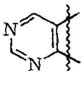
Even under the very mild reaction conditions which were actually investigated for the synthesis of specific $N$-substituted derivatives, for example the reaction of the sodium salt of *(5a)* with chlorine thiocyanate at 15—20 °C to *(42j)* or of *(43)* with sodium hypohalite, substitution took place exclusively in the 6-position possibly *via* a rearrangement, to *(44)* (m.p. = 228—230 °C, decomp.).

As shown by the photosynthesis inhibition values ($pI_{50}$) in Table 14, the herbicidal activity increases, in the case of chlorine-substitution, from the 5-position to the 8-position; a similar relation was also found for methyl-substitution. In fact, both *(42d)* and *(42f)* proved to have strong herbicidal properties, the latter furthermore being selective in cotton cultures. Additional 1-substitution as in *e.g.* *(53c)* however makes the use of these compounds even more interesting to the biologist, because of the *safety of the effect*, and accordingly this pattern of substitution has been developed further (see Table 16). It must however be stated that combining the synthetic work with $pI_{50}$ measurements allowed the number of laboratory experiments to be effectively reduced, and at the same time allowed identification of that part of the molecule responsible for biological activity.

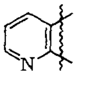
Among the numerous derivatives with heterocyclic substituents which we prepared, only the pyridine derivative[55] *(47)* and its salts exhibit powerful herbicidal action. In particular, the excellent postemergence action against dead nettle and dog's mercury, when using 1 kg/ha, deserves mention. The compound exhibits good selectivity towards rice, Indian corn and barley cultures.



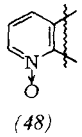
*(45)*



*(46)*



*(47)*



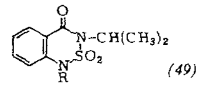
*(48)*

The $N$-oxidation of *(47)* to *(48)* is accompanied by a complete loss of activity.

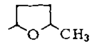
### 3.4. Synthesis of 1,3- and 1,3,8-substituted 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides

The free NH-group in the 1-position of *(5a)* has acidic character and may therefore be expected to undergo a range of alkylation reactions[45]. For example, alkylation using lower dialkyl sulfates in an aqueous alkaline medium, and the reaction of previously formed salts with alkyl halides or arylsulfonates under anhydrous conditions both proceed smoothly; Table 15 shows a small selection of the compounds prepared.

Table 15. 1-Substituted 3-isopropyl-1$H$-2,1,3-benzothiadiazin-4-one-2,2-dioxides of type *(49)* [56], *(50)* and *(51)*.



*(49)*-*(51)*

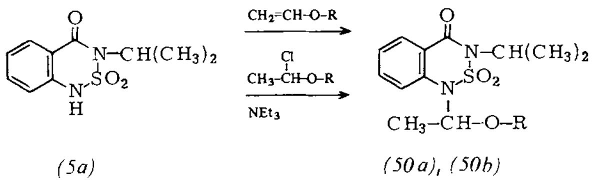
| | R | M.p. [°C] |
|---|---|---|
| *(49a)* | $CH_3$ | 54—55 |
| *(49b)* | $C_2H_5$ | 56—58 |
| *(49c)* | $CH_2$—C—CH | 108—112 |
| *(49d)* | $CH_2$—CN | 119—121 |
| *(49e)* | $CH_2$—SCN | 124—126 |
| *(49f)* | $CH_2$—$N_3$ | 83 |
| *(50a)* | $CH(CH_3)$—$OCH_3$ | [a] |
| *(50b)* | $CH(CH_3)$—$OC_2H_5$ | [b] |
| *(50c)* | $CH(CH_2Cl)$—$OCH_3$ | 109—111 |
| *(50d)* |  | 116—118 |
| *(51a)* | $CH_2OH$ | 95 (decomp.) |
| *(51b)* | $CH_2Cl$ | 116—122 |
| *(51c)* | $CH_2O$—2,4,6-$Cl_3C_6H_2$ | 198—203 |
| *(51d)* | $CH_2SCH_3$ | 84—87 |
| *(51e)* | $CH_2OCHO$ | 99—104 |
| *(51f)* | $CH_2NH$—1-Br—4,6-$(NO_2)_2C_6H_2$ | 131—137 |
| *(51g)* | $CH_2OCH_3$ | [c] |

[a] $n_D^{25} = 1.5240$. [b] $n_D^{25} = 1.5235$. [c] $n_D^{25} = 1.5420$.

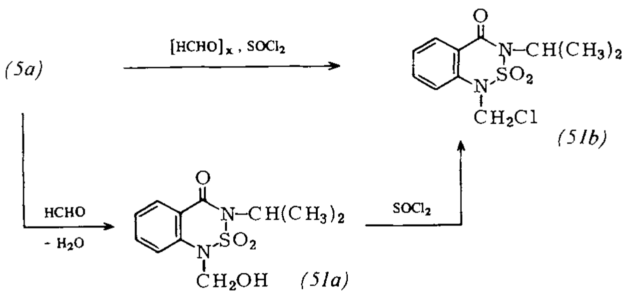
It also proved possible to carry out acylations using a range of organic and inorganic acid halides and anhydrides, again under anhydrous conditions, with or without the aid of an organic base[57]. Similar experiments on the synthesis of arylsubstituted derivatives have also been carried out by others[58].

While amines do not react with vinyl ethers, *(5a)* and other 3-alkyl-1$H$-2,1,3-benzothiadiazin-4-one-2,2-dioxides *(5)* react with vinyl ethers, in the presence of a catalytic amount of an acid, to give a high yield of the corresponding 1-(α-alkoxyalkyl) derivatives *(50)* (Table 15)[59]. As a result of the acidifying influence of the sulfonyl group, the aniline group acquires an activity comparable to that of phenols with respect to adduct formation with the vinyl ether. As may be expected, the resulting group can be removed again in acid media. The formation of the adduct directly, avoids handling α-haloethers, which also react smoothly.

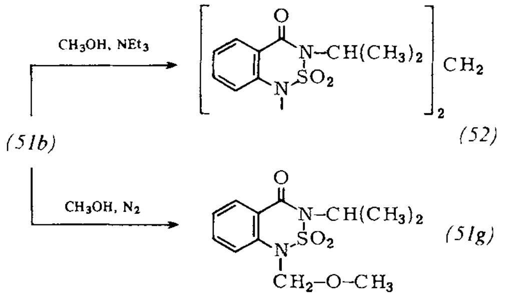
Substituted 1-chloromethyl-1$H$-2,1,3-benzothiadiazin-4-one-2,2-dioxides such as *(51b)* can be obtained in virtually quantitative yield by reacting *(5a)* with paraformaldehyde



and sulfinyl chloride in an inert solvent. If aqueous formaldehyde is used and the water is removed, it is also possible to isolate *(51a)* and react it analogously with a halogenating agent to give *(51b)*. If *(51b)* is to be isolated, the latter procedure is preferred, in order to avoid formation of α-halo-ethers.



In general, *(51b)* can be washed with water, but it is more advantageous to carry out a one-pot reaction with the nucleophilic agent, followed by extraction with alkali to hydrolyze traces of haloether. Compound *(51b)* is very reactive, *i. e.* it reacts with a wide range of nucleophilic agents, such as phenols, thiols, carboxylic acids or amines, in the presence of a base (Table 15)[60]. Under the same reaction conditions, alcohols or alcohoxides gave only the dimer *(52)* (m.p. = 182—186 °C), in addition to starting material.

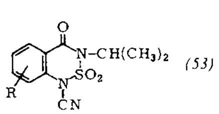


Only if the base was omitted and hydrogen chloride flushed out of the refluxing reaction mixture by means of an inert gas was it possible to isolate high yields of compound *(51g)* and higher analogues[61].

A further group of biologically interesting 3-alkyl-1$H$-2,1,3-benzothiadiazin-4-one-2,2-dioxides are the 1-carbonitriles *(53)*[62]. Compound *(53a)* is formed on reaction of *(5a)* with cyanogen bromide and compounds *(53b)* to *(53e)* are obtained from the corresponding precursors of type *(42)*, (Table 16).

The herbicidal action of 1-substituted 3-alkyl-1$H$-2,1,3-benzothiadiazin-4-one-2,2-dioxides is markedly substituent dependent. Thus, for example, *(49a)* and *(49b)* (Table 15) are substantially less active than their analogues *(49c)* to *(49f)* with larger substituents. The advantage of these relative to the standard compound is due to their high compatibility with crop plants such as potato, onion and sunflower.

Table 16. 3-Isopropyl-4-oxo-3,4-dihydro-1$H$-2,1,3-benzothiadiazin-1-carbonitrile-2,2-dioxides of type *(53)*.



| | R | M.p. [°C] | | R | M.p. [°C] |
|---|---|---|---|---|---|
| *(53a)* | H | 100—101 | *(53c)* | 8-Cl | 123—124 |
| *(53b)* | 8-CH₃ | 103—104 | *(53d)* | 8-Br | 136—140 |
| | | | *(53e)* | 7-Cl | 146—147 |

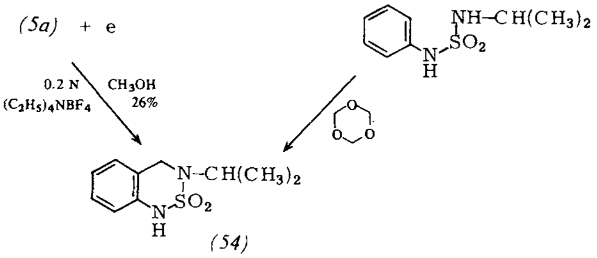
The 1-acyl-substituted derivatives, and the vinyl ether adducts *(50)* (Table 15), on the other hand, more closely resemble the standard *(5a)* with respect to selectivity and action. In some cases, however, they are more effective against charlock, chamomile and goosefoot.

A noteworthy feature of derivatives with substituted 1-methyl groups (Table 15) is the emergence of a new crop plant compatibility, for example in the use of *(51b)* or *(51g)* with cotton, with a certain reduction in the spectrum action.

The same effect was also observed with *(42f)*[54] and *(53b)*; the latter being further characterized by greater activity against chickweed and cleavers. In addition *(53c)* proved useful in controlling deadnettle and dog's mercury.

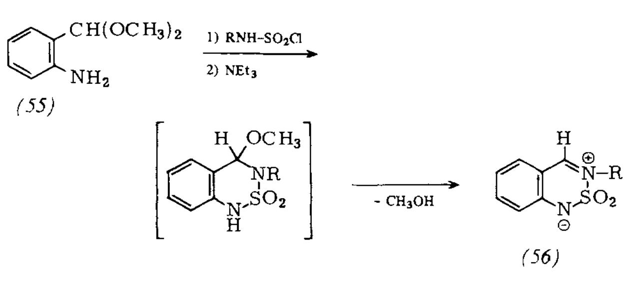
### 3.5. 3-Alkyl-3,4-dihydro-1$H$-2,1,3-benzothiadiazin-2,2-dioxides and Related Compounds

The carbonyl group in compound *(5a)* can be reduced electrolytically, so that 3,4-dihydro-3-isopropyl-1$H$-2,1,3-benzothiadiazin-2,2-dioxide *(54)* is obtained.

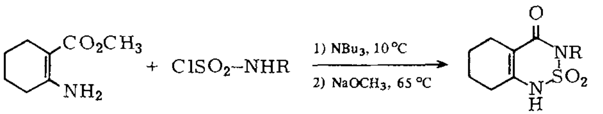


The same heterocyclic compound was later also prepared by *Pews*[63], who cyclized $N$-isopropyl $N'$-phenylsulfamide with trioxane.

Other compounds in which the carbonyl group has been converted to a derivative are meso-ionic 2,1,3-benzothiadiazin-2,2-dioxides of type *(56)* which are obtained directly on reaction of 2-aminobenzyldehyde-acetals such as *(55)* with alkylsulfamoyl chlorides[64].



Aryl-hydrogenated 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides are difficult to obtain by catalytic hydrogenation of the corresponding benzo-heterocyclic compound. A better method employs β-enaminocarboxylic acid esters, for example methyl 2-aminocyclohex-1-ene-1-carboxylate *(57)*, which is converted directly into the 5,6,7,8-tetrahydro-derivative *(58)* (m.p. = 196—198 °C decomp.) in a one-pot process, by reaction with *N*-isopropylsulfonyl chloride *(20c)* followed by heating the mixture with sodium methoxide.

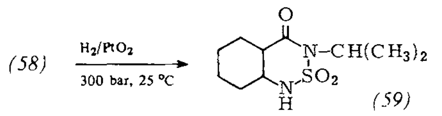


*(57)* *(20c)* *(58)*

R = $CH(CH_3)_2$

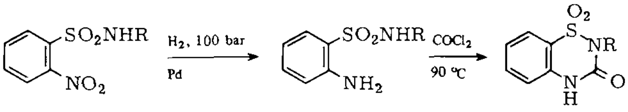
*Kloek* and *Leschinsky* had developed a multi-step synthesis of the same compound[65].

Finally, *(58)* was transformed into *(59)* (*cis*:*trans* mixture, m.p. = 95—110 °C) by catalytic reduction.



Surprisingly, all the hydrogenated analogs described in this Section proved only to have a low herbicidal activity in spite of their structural similarity to the commercial product Basagran® *(5a)* or the uracil derivative lenacil *(40)*.

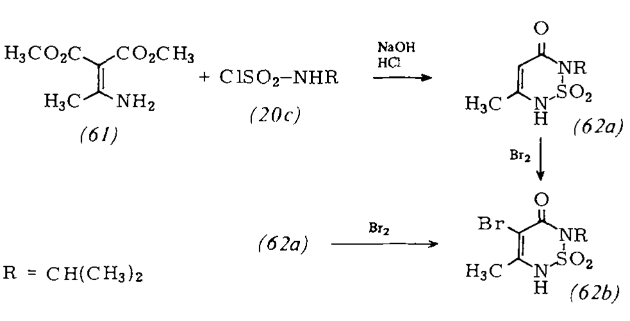
In conclusion, it may be noted that the 2-alkyl-2*H*-1,2,4-thiadiazin-3-one-1,1-dioxides *(60)*, which are inversely isomeric to *(5a)* and are derived from *o*-nitrobenzenesulfonamides by reduction and phosgene cyclization, prove to be weaker herbicides than the corresponding compounds of type (5) *(42)*[66].



*(60)*

### 3.6. 2*H*-1,2,6-Thiadiazin-3-one-1,1-dioxides

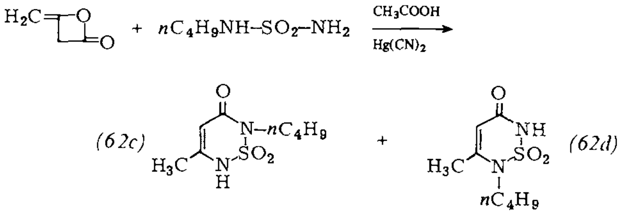
The concept of this class of compounds again arose from a natural substance, namely uracil *(41)*, mentioned at the outset. Reaction of (1-aminoethylidene)malonic acid derivatives such as *(61)* with alkylsulfamoyl chlorides such as *(20c)*, led to cyclization giving *(62a)*; subsequent halogenation gave novel derivatives such as *(62b)*[67].



*(61)* *(20c)* *(62a)*

R = $CH(CH_3)_2$ *(62b)*

Compared to the earlier condensation reaction of diketene with sulfamides, sulfamoyl chlorides are more selective, since sulfamides had always led to an isomeric mixture; here of *(62c)* and *(62d)*[69].

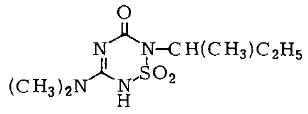


*(62c)* *(62d)*

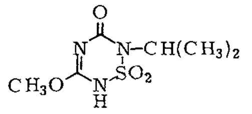
Although compound *(62b)* is isosteric with branched bromacil derivatives *(39)*, it does not have a herbicidal action; the reason appears to be that bromine is more easily eliminated from *(62b)*[69].

### 3.7. 2*H*-1,2,4,6-Thiatriazin-5-one-1,1-dioxides

The synthesis of these compounds has been pursued by two industrial laboratories. Following on its own development work leading to the fungicide Bupirimate® *(19)*[21], ICI produced 3-dimethylamino derivatives *(63)*[70], which can be used to control mildew and rust, and also have a herbicidal action in rice.



*(63)*

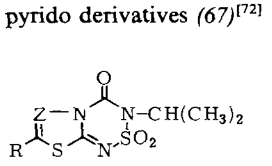


*(64)*

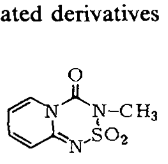
In BASF, it was principally the search for further fields of use of sulfamoyl chlorides as heterocyclic synthesis units, which led to the herbicidal 3-alkoxy derivative of type *(64)*[71]. These compounds are particularly suitable for the selective control of cyperaceae in rice, but, in contrast to *(63)*, have only a slight fungicidal action.

### 3.8. Five- and Six-membered ring heterocycles from acylated alkylsulfamoyl chlorides

With the object of investigating the biological action of 1,2,4,6-thiatriazin-5-one-1,1-dioxides fused to a heterocyclic structure, substituted [1,3,4]thiadiazolo[3,2-*c*][1,2,4,6]thiatriazinone dioxides *(65)* and analogous thiazolo derivatives *(66)*, pyrido derivatives *(67)*[72] and other related derivatives

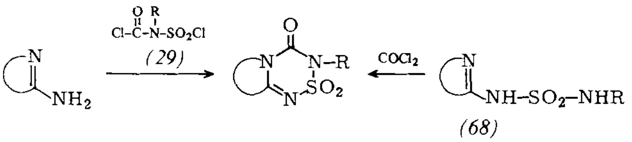


*(65)*, Z = N, R = $(CH_3)_3C$
*(66)*, Z = CH, R = H



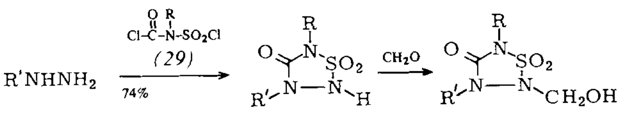
*(67)*

were prepared, but proved only to have a low herbicidal activity[73]. A suitable method of synthesis is direct condensation of a 2-amino-azaheterocyclic compound with the acylated sulfamoyl chloride *(29)*; however, the yields obtained by this method are mostly lower than in the case of stepwise synthesis by phosgenation of the sulfamides *(68)* (*cf.* [72]).



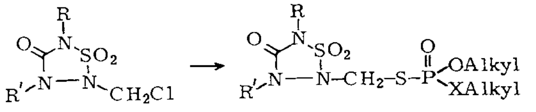
(29) (68)

In contrast, alkylhydrazines react very smoothly with *(29)* to give 3,5-dialkyl-1,2,3,5-thiatriazolidin-4-one-1,1-dioxides *(69a)*[72]. These can next be hydroxymethylated with formaldehyde, similarly to compound *(51b)*, to give *(69b)*.



(29) (69a) (69b)

The latter can then be converted, with sulfinyl chloride, to the very reactive 2-chloromethyl derivatives *(69c)*. Their subsequent reaction with phosphate salts gives novel heterocyclic phosphoric acid derivatives of type *(70)*, which can be used in plant protection, hygiene and storage protection areas[74].

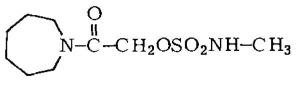


(69c) (70)

## 4. Future Prospects

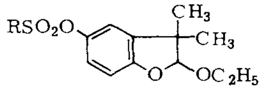
Work on 1*H*-2,1,3-benzothiadiazin-4-one-2,2-dioxides as modern crop protection agents has led, *via* alkylsulfamoyl chlorides which could be produced industrially, to a range of new heterocyclic synthesis reactions which have had repercussions in additional fields of use.

As an example of a sulfamoyl ester, we may mention sulfglycapin *(71)*[75] which, when used in rice crops, selectively controls species of cyperaceae and of barnyardgrass and, in particular, weeds such as *Leptochloa fascicularis* and *Leersia oryzoides*, which hitherto have been difficult to destroy.



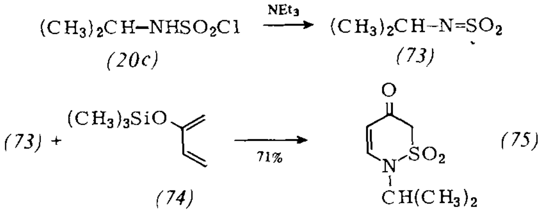
(71)

As regards herbicidal sulfamoyl aryl esters, *Rohr* and *Fischer* showed, in the case of compound *(72b)*, which is analogous to ethofumesate *(72a)*[76] (a selective herbicide in beet), that herbicidal receptors in the plants cannot differentiate biologically between the two types of sulfonic acid derivatives[77].



*(72a)*, R = $CH_3$ : Ethofumesate
*(72b)*, R = $CH_3NH$

The ability to use the sulfamoyl chlorides to synthesize a new category of double bond rich material, the *N*-sulfonylamines[4], has only very recently been employed in adduct formation with activated dienes. Thus, *(73)* smoothly undergoes adduct formation with *(74)*, to form 1,2-thiazin-5(6*H*)-one-1,1-dioxides such as *(75)*[78]; these constitute a novel heterocyclic six-membered ring system, which is evidently formed *via* a two-stage mechanism.



(20c) (73) (74) (75)

A century after the discovery of dimethylsulfamoyl chloride, the chemistry of monoalkylsulfamoyl chlorides has essentially been advanced by industrial laboratories. The fact that these compounds have now become industrially readily available, together with their reactivity and bifunctional character, may be expected to stimulate the broader use of these synthesis units, which show many interesting aspects with respect to preparative possibilities and biological properties.

*The late Dr. A. Fischer deserves great credit in connection with the discovery of the first biologically active 1H-2,1,3-benzothiadiazin-4-one-2,2-dioxides. We particularly want to thank Dr. B. Würzer and co-workers for the broad biological testing, which further stimulated the progress of our research. In addition to those whose names appear in the literature references, we would also like to thank the following colleagues, at this point, for their kind collaboration; Dr. G. Retzlaff for measuring and interpreting photosynthesis inhibition values, Dr. W. Bremser for the spectroscopic aspects of our work and Dr. H. Pütter for electrochemical experiments.*

Received: February 28, 1980,
supplemented: December 22, 1980 [A 351 IE]
German version: Angew. Chem. 93, 151 (1981)

---

[1] *R. Wegler:* Chemie der Pflanzenschutz- und Schädlingsbekämpfungsmittel. Springer, Berlin 1970.
[2] a) see [1], Band 5, p. 126 and 127; b) see [1] *ibid.*, Band 2, p. 95.
[3] *L. Audrieth, A. Vandi, T. Moeller,* J. Org. Chem. *26*, 1136 (1961).
[4] *G. M. Atkins, E. M. Burgess,* J. Am. Chem. Soc. *89*, 2502 (1967).
[5] *H. Teufel,* DBP 1120456 (1959), Geigy.
[6] a) *G. Weiss, G. Schulze,* DBP 1121060 (1960), BASF; b) *G. Schulze, G. Weiss,* DBP 1242627 (1964), BASF; *G. Weiss, G. Schulze,* Justus Liebigs Ann. Chem. *729*, 40 (1969); cf. *N. C. Hansen,* Acta Chem. Scand. *17*, 2141 (1963).
[7] *K. Dachlauer,* DBP 682391 (1937).
[8] *G. Hamprecht, D. Mangold, K. H. König,* DBP 2164197 (1971), BASF.
[9] *G. Hamprecht, D. Mangold, K. H. König,* DBP 2164176 (1971), BASF.
[10] *K. H. König, G. Hamprecht,* DOS 2514937 (1975), BASF.
[11] *H. Schindlbauer,* Monatsh. Chem. *100*, 1590 (1969).
[12] *K. H. König, G. Hamprecht,* DOS 2513997 (1975), BASF.
[13] *G. Hamprecht,* DOS 2301207 (1973), BASF; in part presented at the VIIth Int. Symp. Org. Sulfur Chem., Hamburg, July 1976.
[14] *W. L. Matier, W. T. Comer,* J. Med. Chem. *15*, 538 (1972).
[15] *W. Rohr, G. Hamprecht,* DOS 2401819 (1974), BASF.
[16] *R. Graf,* DBP 931225 (1952), Hoechst.
[17] *E. B. Ayres, C. R. Hauser,* J. Org. Chem. *13*, 116 (1948).
[18] *A. Parg, G. Hamprecht,* DOS 2827871 (1978), BASF.
[19] *R. Behrend,* Chem. Ber. *14*, 1810 (1881).
[20] *E. Stein,* DBP 946710 (1956), Bayer.
[21] *A. M. Cole, A. W. Turner, B. K. Snell,* DAS 2265029 (1972), ICI.
[22] *G. Hamprecht,* DOS 2553460 (1975), BASF.

[23] *S. Kersten, G. Hamprecht,* DOS 2553461 (1975), BASF.
[24] *R. Munk,* BASF, unpublished results.
[25] *G. Hamprecht,* DOS 2634485 (1976), BASF.
[26] *K. H. König,* DBP 1252655 (1964), BASF.
[27] *G. Hamprecht,* IVth Int. Congress Pesticide Chem. (IUPAC), Zürich, July 1978.
[28] *G. Schulze, G. Weiss,* DBP 1188582 (1965), BASF.
[29] *E. Klauke, E. Kühle,* DAS 1297095 (1967), Bayer.
[30] *E. Kühle, E. Klauke,* DOS 1943234 (1969), Bayer. In the case of chlorodifluoromethanesulfenyl chloride, the acylation of a sulfamoyl chloride was subsequently also described; dissoverers *E. Kühnle, E. Klauke,* DOS 1953356 (1969), Bayer.
[31] *D. Bartholomew, I. T. Kay,* J. Chem. Res. *1977,* 2801.
[32] *G. Hamprecht, A. Parg, K. H. König,* DOS 2828969 (1978), BASF.
[33] *A. Parg, G. Hamprecht, K. H. König,* DOS 2911456 (1979), BASF.
[34] *J. R. Corbett,* Chem. Ind. (London) *1979,* 772.
[35] *M. Seefelder, A. Fischer,* DBP 1191171 (1962), BASF.
[36] *G. Scheuerer, A. Zeidler, A. Fischer,* DBP 1210242 (1964), BASF.
[37] *A. Zeidler, A. Fischer, G. Scheuerer,* Z. Naturforsch. *B 24,* 740 (1969).
[38] *H. M. Loux,* US-Pat. 3235357 (1966), Du Pont.
[39] *E. J. Soboczenski,* US-Pat. 3235360 (1966), Du Pont.
[40] *A. Zeidler, A. Fischer, G. Weiss,* DBP 1542838 (1966), BASF.
[41] Carried out by *E. Hädicke,* BASF.
[42] *E. B. Cain, F. A. Kanda,* Z. Kristallogr. *135,* 253 (1972).
[43] *G. Retzlaff, A. Fischer,* Mitt. Biol. Bundesanst. Land- Forstwirtsch., Berlin-Dahlem *151,* 179 (1973).
[44] *S. Otto, P. Beutel, N. Drescher, R. Huber:* Advances in Pesticide Science. Part III. Pergamon Press, Oxford 1979, p. 551.
[45] *E. Cohen, B. Klarberg,* J. Am. Chem. Soc. *84,* 1994 (1962).
[46] *G. Hamprecht, A. Zeidler, K. H. König, D. Mangold,* IIIrd Int. Congress Pesticide Chem. (IUPAC), Helsinki, July 1974; Kem.-Kemi *1974,* 590.
[47] *D. Mangold, K. H. König, G. Hamprecht,* DOS 2357063 (1973), BASF.
[48] *G. Hamprecht, K. H. König, G. Bolz,* DBP 2104682 (1971), BASF; *G. Hamprecht, K. H. König, G. Bolz,* DOS 2105687 (1971), BASF.
[49] *A. Fischer, K. H. König, G. Hamprecht,* DOS 2349114 (1973), BASF.
[50] *J. D. Catt, W. L. Matier,* J. Org. Chem. *39,* 566 (1974).
[51] *A. Trebst, W. Draber:* Advances in Pesticide Science. Part II. Pergamon Press, Oxford 1979, p. 223.
[52] *S. Izawa:* Photosynthesis I. Springer, Berlin 1977, p. 266.
[53] *L. H. McKendry, W. P. Bland,* DOS 2443901 (1974), Dow.
[54] *L. H. McKendry, W. P. Bland,* DOS 2444383 (1974), Dow.
[55] *A. Fischer, W. Rohr, G. Hamprecht,* DOS 2430353 (1974), BASF.
[56] *G. Hamprecht, G. Stubenrauch, H. Urbach, B. Würzer,* DOS 2656290 (1976), BASF.
[57] *A. Zeidler, A. Fischer, G. Hamprecht, P. Schmidt,* DOS 2444822 (1974), BASF.
[58] *L. H. McKendry, W. P. Bland,* US-Pat. 4051130 (1977), Dow.
[59] *A. Fischer, G. Hamprecht, R. Huber,* DOS 2355113 (1973), BASF.
[60] *A. Fischer, G. Hamprecht,* DOS 2458343 (1974), BASF.
[61] *G. Hamprecht, U. Schirmer, B. Würzer, G. Retzlaff,* DOS 2553209 (1975), BASF.
[62] *G. Stubenrauch, G. Hamprecht, B. Würzer, G. Retzlaff,* DOS 2656289 (1976), BASF.
[63] *R. G. Pews,* US-Pat. 4189572 (1980), Dow.
[64] *A. Parg, G. Hamprecht,* Justus Liebigs Ann. Chem. *1979,* 1130.
[65] *J. A. Kloek, K. L. Leschinsky,* J. Org. Chem. *43,* 3824 (1978), give the melting point as 188–192 °C.
[66] *A. Zeidler,* BASF, unpublished experiments.
[67] *H. Hansen, K. H. König, W. Rohr,* Justus Liebigs Ann. Chem. *1979,* 950.
[68] *J. Diez, G. Garcia-Munoz, R. Mondronero, M. Stud,* J. Heterocycl. Chem. *10,* 469 (1973).
[69] *K. Pilgram, R. D. Skiles, ibid., 17,* 977 (1980).
[70] *I. T. Kay,* DOS 2508832 (1975), ICI.
[71] *G. Hamprecht, R. D. Acker, B. Würzer,* DOS 2933889 (1979), BASF.
[72] *D. Bartholomew, I. T. Kay,* J. Chem. Res. *1977,* 2813.
[73] *R. D. Acker, B. Würzer,* BASF, unpublished experiments.
[74] *A. Baumann, K. Kiehs, G. Hamprecht, A. Lange, H. Adolphi,* Dtsch. Pat.-Anm. P 3003977.1 (1980).
[75] *A. Fischer, W. Rohr,* DBP 2219923 (1972), BASF.
[76] *P. S. Gates, J. Gillon, D. T. Saggers,* DAS 1926139 (1969), Fisons.
[77] *A. Fischer, W. Rohr,* DOS 2324592 (1973), BASF.
[78] *J. A. Kloek, K. L. Leschinsky,* J. Org. Chem. *44,* 305 (1979).

# Irritant and Defense Substances of Higher Plants—A Chemical Herbarium[**]

**By Hermann Schildknecht[*]**

*Dedicated to Professor Karl Freudenberg on the occasion of his 95th birthday*

All living organisms respond to stimulation, reacting more or less sensitively and more or less typically to a wide variety of energy forms such as light, heat, gravity, pressure (sound), electricity—and chemicals. A living organism responds to an irritation by releasing irritants which—as potential defense substances—are directed against the attacker or assist the organism endogenously in an intrinsic defence reaction. Often very small energy changes perceived by the plant are enough to induce a series of physiological processes ultimately manifested as a glandular reaction or even movement. The irritants involved in these processes act on membranes as defense substances in the presence of an attacker, or as endogenous factors in their own cellular environment. These chemically very diverse low-molecular active principles have been found in many parts of plants and in many plant families. For this reason alone we could speak of a chemical herbarium, but the case is even stronger because, in this botanical documentation, not only the individual chemicals are considered in context but also whole sets of interacting substances, since it is only in these sets that optimal activity is found (just as one considers not only the parts of a plant but also the whole plant in botany).

## 1. Introduction

A hundred years ago, in 1880, the "Power of Movement in Plants"[1] appeared as one of the later Volumes of the collected works of *Charles Darwin.* In this book, some 500 pages long, *Darwin* described a fascinating behavior pattern according to which all rootlets, shoots, petioles, and leaves perform elliptical to circular motion. Why did *Darwin* begin, at the age of 71 and not in the best of health, 5 years before his death in 1882, a series of painstakingly planned experiments with about a dozen genera from completely different plant families on the circumnutation induced by light and gravity?

---

[*] Prof. Dr. H. Schildknecht
Organisch-Chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg (Germany)

[**] Plant Defense Substances, Part 14.—Part 13: [185].

His own discovery of the principle of evolution compelled him to do so, for according to this it was impossible that the climbing plants should have developed into many groups if all plants did not possess some small capacity for movement of this kind[2]. As he then went on to include plant sleep, the so-called nyctitropic movement, in his considerations, *Darwin* was on the verge of a purely phenomenological contemplation that "it is hardly possible to doubt that plants must derive some great advantage from these remarkable powers of movement"[1].

Likewise a hundred years ago, the physiological foundations of plant defense behavior were discussed by *Wilhelm Pfeffer* in his general considerations "On the Nature of Stimulation Processes"[3]. *Pfeffer*'s approach was that of a man of exact natural science, although it was not particularly substance-oriented; to him stimulation processes were at first only excitation processes and "accordingly, specifically for example, the sudden stimulation reactions (such as the closing of the leaves of the sensitive plant) are not of such general significance as the host of the slow and constantly occurring reactions and regulations"[4]. However, even in Volume II of *Pfeffer*'s Plant Physiology[5] one can read, that "it is presumably precise chemical stimuli that play a prominent role in the autoregulatory guidance of inner activity and thus also of autonomous movement."

Here unequivocal reference is made to chemistry, the material basis of all stimulation processes, which at every turn, including the domain of plant defense mechanisms, confronts the natural-products chemist with ever new perspectives. It is a stimulating but sometimes also a demanding task for analytical chemists to correlate observations with chemical structures, revealing that *Martin Lindauer* had hit the nail right on the head in his book "The Biological Clock"[6] when he said that the basic requirement for all life is having the right substance in the right quantity, at the right place, and at the right time.

To the chemist the right substance means knowing the correct structure of an active principle, which is only optimally effective when, as per *Paracelsus*, the dose is also correct. The right place for a plant defense substance is, for example, the stinging hair or the cuticular tissue, and in the case of a movement factor the cell membrane, where it must be present at the right time when the plant is about to fold its leaves to sleep. The aim of the following considerations is to present the biological phenomenon of plant defense, with these aspects as the guiding motif.

## 2. Irritant and Defense Substances from Glandular Hairs

### 2.1. The Defense Substances of *Urtica dioica*, *Laportea moroides*, and *Jatropha urens*

#### 2.1.1. The Organs of Defense

The chemical interaction between life-forms—their chemical ecology—can be illustrated particularly well with the example of defense substances as used by the stinging nettle. Here a mechanical defense and a chemical defense are combined.

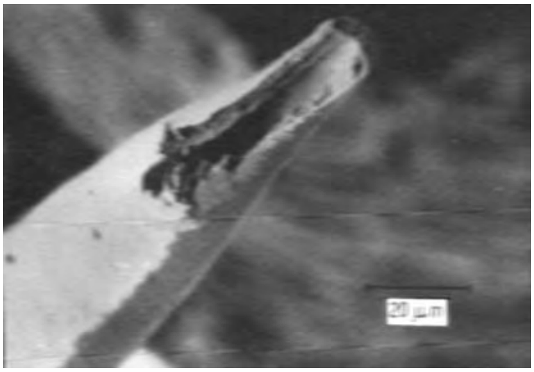


Fig. 1. Stinging nettle *(Urtica dioica)* trichome with a broken-off stinging hair tip, taken with a Kontron scanning electron microscope.

The hairs of the stinging nettle (Fig. 1) are poison reservoirs with siliculated tips at the upper end. The tips break off easily making each hair into a sharp-pointed cannula through which some 0.003 $mm^3$ of the total quantity of 0.008 $mm^3$ of liquid poison flows into the injured skin. This results in the familiar stinging from which the whole plant takes its name. *Laportea moroides*, another member of the *Urticaceae* family, is markedly more toxic; one prick may easily give rise to long-lasting pain, the injured skin area remaining sensitive to pressure, cold, and moisture for days and even weeks (Fig. 2). *Laportea* has yet another form of defense:

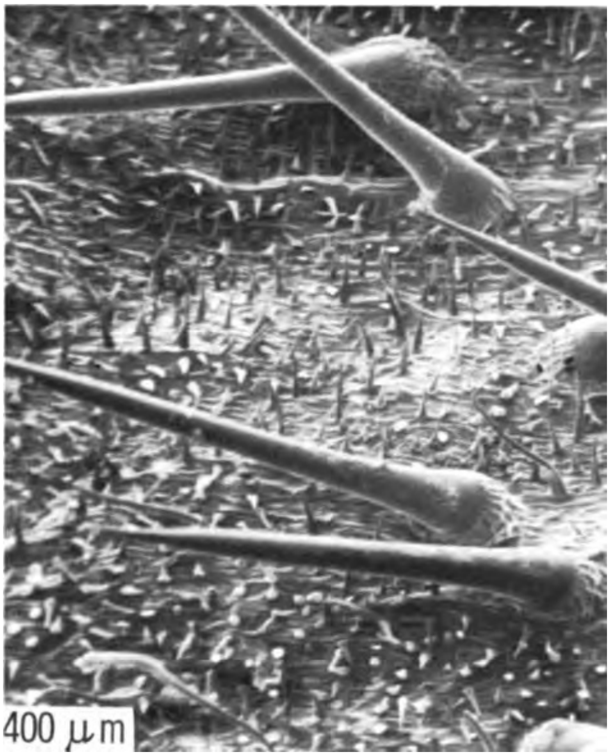


Fig. 2. Stinging hairs of *Laportea moroides*, taken with a Kontron scanning electron microscope.

when its leaves are picked in a greenhouse, a keen sensation of irritation to the mucous membranes of the nose and the eyes is experienced, which can only be prevented by the use of a gas mask. The initial pain is attributed to the same compounds as in the stinging hairs, and the long-term effect to a higher-molecular, nondialyzable substance whose action may possibly be based on the release of endogenous histamine.

The *L. moroides* bush grows in the wild in eastern Australia, but, of course, in Europe it must be kept in a greenhouse. Propagation from seed, which can be gathered at all times of the year, presents no problems.

The up to 1-cm long stinging hairs of *Jatropha urens*, a member of the *Euphorbiaceae*, are particularly distinctive. Like other plants with stinging hairs, in its homeland in Central and South America it is a troublesome weed. When touched, the tip of the *Jatropha urens* stinging hair breaks off and the poison, a strong irritant, drips out (Fig. 3). One can well imagine that the fruits important for continuation of the species, protected with stinging hairs (Fig. 4), are effectively defended in this way.

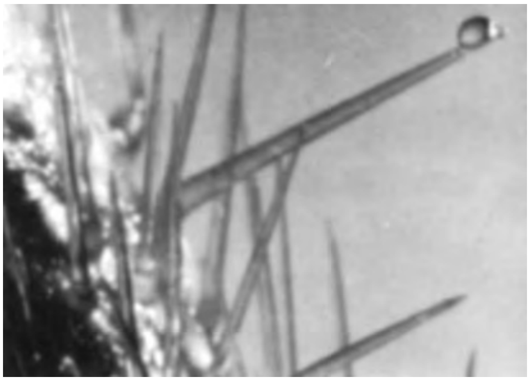


Fig. 3. Stinging hairs (8 mm long) of *Jatropha urens* (macro-photograph), after the poison has emerged from the broken-off tip.

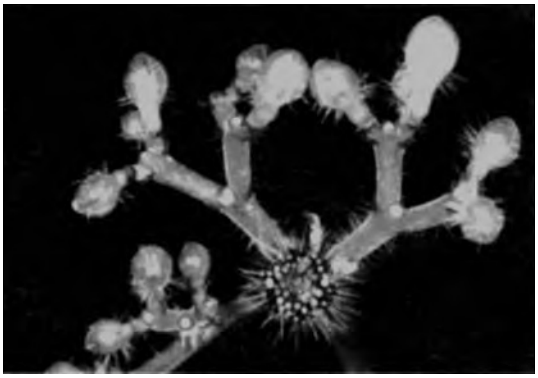


Fig. 4. Fruit of *Jatropha urens* surrounded by many stinging hairs (diameter 15 mm).

While the defense substances of the above plants have often been studied in the past, it is only in the last few years that a satisfactory understanding has been achieved.

### 2.1.2. History of the Active Principles in Stinging Hairs

Since the suggestion put forward by *Gorup Besanez*[7] in 1849 formic acid has time and again been held responsible for the easily demonstrable action of nettles[8], although *Haberlandt*[9] questioned this as early as 1886 and suspected a dissolved, albumin-like substance, or perhaps even an enzyme; on this point see Table 1. *Flury*[10] suggested a nonvolatile, nitrogen-free acid as the toxic principle, while *Nestler*[11] attributed the stinging primarily to the mechanical stimulus, but conceded that an enzyme might also be involved. However, these findings were unable to explain the

Table 1. The history of the constituents of plants' stinging hairs (after [16 and 17]). U = *Urtica*, L = *Laportea*, T = *Tragia*, J = *Jatropha*, O = *Loasa* (chile nettle).

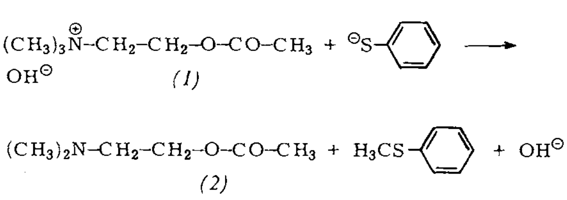
| Authors (chronological) | Formic acid | Acetylcholine *(1)* | Histamine *(3)* | Serotonin *(5)* | Alkaloid | Acetic acid | Enzyme | Glycoside | Protein | Tartaric acid | Resinic acid | Calcium | Salt | Calcium-sensit. factor |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Hooke* (1665) | | | | | | | | | | | | | U | |
| *Gorup Besanez* (1849) | U | | | | | | | | | | | | | |
| *Rauter* (1872) | | | | | | | | U | | | | | | |
| *Bergmann* (1882) | U | | | | | | | | | | | | | |
| *Haberlandt* (1886) | | | | | | | U | | | | | | | |
| *Tassi* (1886) | | | | | | O | | | | | | | | |
| *Gibson, Warham* (1890) | | | | | | | | | | U | | | | |
| *Ritterhausen* (1892) | T | | | | | | | | | | | | | |
| *Giustniani* (1896) | | | | | U | | | | | | | | | |
| *Dragendorf* (1905) | U | | | | | | U | U | | | | | | |
| *Knoll* (1905) | | | | | | | | | T | | | T | | |
| *Petrie* (1906) | L | | | | | L | | | | | | | | |
| *Winternitz* (1907) | U | | | | U | | | | | | | | | |
| *Flury* (1919) | U | | | | | | | | | | | | | |
| *Nestler* (1925) | U | | | | | | U | | | | | | | |
| *Flury* (1927) | | | | | | | | | | U | L | | | |
| *Kroeber* (1928) | | | | | | | | U | | | | | | |
| *Starkenstein, Wasserstrom* (1933) | | | | | U | | | U | | | | | | |
| *Emmelin, Feldberg* (1947) | | U | | | | | | | | | | | | |
| *Collier, Chesher* (1956) | | U | U | U | | | | | | | | | | |
| *Robertson, MacFarlane* (1957) | | L | L | L | | | | | | | | | | |
| *Pilgrim* (1959) | | | | | | | | | | | | | | U |
| *Schildknecht, Bayer* (1960) | | | U | | | | | | | | | | | |
| *Saxena* et al. (1966) | | U | U | U | | | | | | | | | | |
| *Thurston* (1969) | | | | | | | | | | | | | T | |
| *Schildknecht, Edelmann* (1971) | | J | | | | | | | | | | | | |
| *Vialli* et al. (1973) | | | | U | | | | | | | | | | |
| *Villalobos* (1975) | | | | | | | | | | | | | | |

action of the stinging-nettle poison. In 1947, *Emmelin* and *Feldberg*[12] were the first to detect a histamine- and acetylcholine-like action on guinea-pig intestine, a finding supplemented in 1956 by *Collier* and *Chesher* with a muscle-contracting toxic component[13].

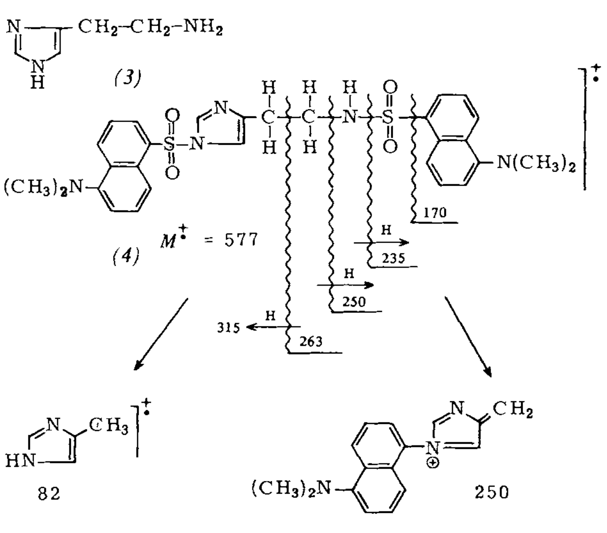
A more detailed chemical identification of the physiologically active constituents of stinging-nettle secretion commenced in 1960[14], when biogenic amines became detectable by paper- and thin-layer chromatography and later fluorimetrically as well[15]. Reliable identification of the stinging-hair poisons began with a clean isolation of the hairs by shaving, with the aid of an electrostatic air separation[14] of the hairs and the leaves, or by separating the hairs from deep-frozen leaves[16]. Even when the pure defense organs have been obtained (2 g of stinging hairs from 2 kg plant), the detection of the biogenic amines still remains problematic, since these biologically very active substances are present only in small quantities and moreover are very unstable.

### 2.1.3. Mass Spectrometry of the Biogenic Amines

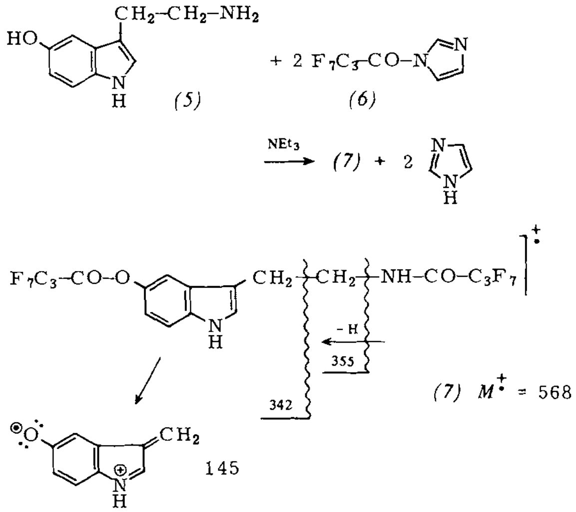
According to *Jenden et al.*[18], for the detection of acetylcholine *(1)*, the latter is demethylated with thiophenolate in butanone at 80 °C to dimethylaminoethyl acetate *(2)*, which can be readily detected by gas chromatography on an 8%-SP-1000 separation column combined with mass-spectrometry through the characteristic base peak with $m/e = 58$.



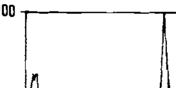
Histamine *(3)* can be reliably identified only after derivatization with dimethylaminonaphthalenesulfonyl chloride (DANS)[19,29]. The dansyl product *(4)* is strongly fluorescent and can be detected even in very small quantities, after preparative TLC, by mass spectrometry on the basis of its clear fragmentation pattern, as shown in the scheme below, the masses $m/e = 577$ and 82 being particularly informative.



Serotonin *(5)* can only be isolated sufficiently for an analysis when the stinging hairs have been extracted with acetone and the biogenic amine *(5)* has been made highly volatile for gas chromatography. A mild but effective method is derivatization with heptafluorobutyrylimidazole (HFBI) *(6)* in the dark at room temperature, with triethylamine as a catalyst, in dry ethyl acetate[21].



On a packed 3% OV 101 separation column the reaction products obtained give a complex gas chromatogram so that the desired serotonin derivative *(7)* from the stinging hairs of *Urtica dioica* and *Laportea moroides* had to be detected by mass-fragmentography with a combination of GC and MS by monitoring the characteristic $m/e$ values 355, 342, and 145 (Fig. 5). The detection of serotonin in the stinging hairs of *Urtica dioica* in this way remains problematic on account of the small quantity present, in contrast to *Laportea moroides*. The same is true of the biogenic amines 2-amino-1-phenylethanol *(8)* and tyramine *(9)*, which can be found



*(8)*

*(9)*

amongst the *Urtica* defense substances only by using mass-spectrometry. The thin-layer chromatogram reveals other amines as well, but these could not be identified.

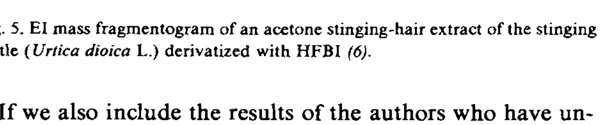


Fig. 5. EI mass fragmentogram of an acetone stinging-hair extract of the stinging nettle (*Urtica dioica* L.) derivatized with HFBI *(6)*.

If we also include the results of the authors who have undertaken comparative physiological experiments[12-14], we arrive at the following synopsis of concentrations of the active principles in the stinging hairs of these *Urtica, Laportea,* and *Jatropha* species; cf. Table 2.

Table 2. Comparison of the concentrations of the three most important stinging-hair amines acetylcholine *(1)*, histamine *(3)* and serotonin *(5)*.

| Stinging hairs of | Stinging hair content [mm³] | *(3)* [μg] | *(5)* [μg] | *(1)* [μg] |
|---|---|---|---|---|
| *Urtica dioica* | 0.008 | 0.01 | 0.004 | 0.04 |
| *Laportea moroides* | 0.07 | 0.025–0.05 | 0.001 | 0.01–0.025 |
| *Jatropha urens* | 1 | 1–2 | 0.5–1 | — |

The histamine and serotonin contents of the stinging hairs of *J. urens* can be determined from the size of the spots in the thin-layer chromatogram[16,23]. The high content of biogenic amines in *J. urens* accords well with the experience on handling this plant, but an unquantifiable toxic action persists even after the use of suitable antagonists[22,12]. In addition, it is difficult to determine how much secretion is active in the skin after one prick, this being a function of the size of the stinging hair.

### 2.1.4. The Function of Biogenic Amines

The three biogenic amines *(5)*, *(3)* and *(1)* which are also the most important ones according to *Guggenheim*[24], have thus been reliably detected in the glandular hairs of the poisonous plants under discussion. Their pharmacological properties and their occurrence in animals' defense organs clearly demonstrate the defensive function of these plant toxins.

Histamine *(3)* and serotonin *(5)* are stored as tissue hormones in mast cells, basophilic leucocytes, and thrombocytes, from which they can be released by certain stimuli. Acetylcholine *(1)* is a neurotransmitter formed in cholinergic nerve cells, and is responsible for the transmission of nerve impulses.

Many animal defense secretions contain histamine and serotonin[25]. These are found in coelenterate venoms and in the venom of ***Phoneutria nigriventer*** from the family of South American comb spiders. Histamine is present in the venom apparatus of bees and histamine and serotonin in that of wasps. This mixture is supplemented in hornet venom by a strikingly large quantity of acetylcholine (5% of dry matter), which is responsible almost exclusively for the action of hornet stings on the heart. *(3)* has an acute effect on the circulation, and all three biogenic amines cause the initial pain after the sting. The round stingray *(Urolophus halleri)* is also actively venomous; its venom contains two highly-toxic protein fractions as well as serotonin.

The simple biogenic amines are found everywhere in the defense secretions of the skin glands of amphibians. Serotonin occurs in practically all tree frogs *(Hylidae)* and in the coral-finger tree-frog *(Hyla caerula)* it is also accompanied by histamine and the decapeptide caerulein. The skin secretion of the orange-speckled toad *(Bombina variëgata variëgata)* has a characteristic smell inducing violent sneezing and catarrh-like symptoms in man, and contains 5-hydroxytryptamine (serotonin) in an amount of 10% of the dry weight; another typical feature is that free amino acids are present, as well as low-molecular peptides.

### 2.1.5. Further Investigations

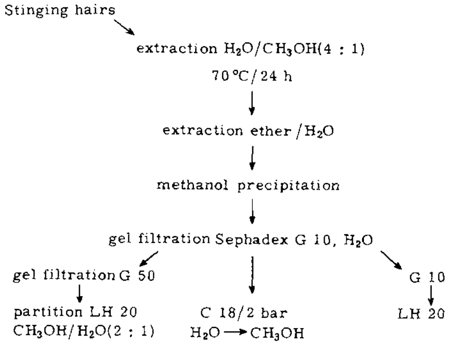
*Hemolysins:* In addition to the large stinging hairs of *Laportea moroides,* Figure 2 shows a large number of smaller gland cells which may be the source of a sneeze-promoting secretion, like the toad secretion just mentioned. The catarrhal symptoms also persist for three hours without abatement after picking *Laportea* stems, before gradually subsiding.

Whereas unfortunately it has proved impossible to detect and isolate the relevant components of the active principle *via* the vapor phase, it was found that the toxic effect is accompanied by a hemolyzing component of the secretion from the pure stinging hairs. Shaved stems of *L. moroides* are inactive (Table 3; for preparation of the extract see Table 4).

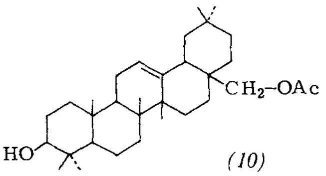
Table 3. Hemolytic indices of extracts from various parts of the *L. moroides* plant; $HU_{50}$ gives the quantity of hemolysin (in grams) necessary to release 5 g of hemoglobin from an erythrocyte suspension with potentially 10 g of hemoglobin.

| Sample | $HU_{50}$ |
|---|---|
| Pure stinging hairs | 1.19 |
| Stems with stinging hairs | 33.45 |
| Stems without stinging hairs | 930.24 |

Table 4. Preparation of an extract of the stinging hairs of *L. moroides*.



In comparison, the hemolytic index of Merck's "Saponin weiss" is 0.156. This comparison is permissible, insofar as after careful chromatographic separation on molecular sieves a *Laportea* hemolysin was isolated from the active-principle mixture, whose aglycone according to high-resolution mass-spectrometry could be a pentacyclic triterpene. *(10)* would be a possible compound from the oleanane series.



*(10)*

The proposed structure may be regarded as a useful working model, since the field of the active principles under discussion is like a jungle, in which any aid to orientation can only lead forward. The main aim here is to correlate ostensibly unconnected findings in such a way that generally valid principles will emerge. The membrane activity of saponins is manifested here in the case of the *Laportea* hemolysin, as it is in the case of leaf movement factor 1 from *Albizzia lophanta* (cf. Section 8.3).

The *Jatropha* hemolysin is not detectable in 3.7 mg of dried secretion from 2000 stinging hairs. However, it has an

$HU_{50}$ of 1.266 when the secretion is dripped directly into an erythrocyte suspension. It is very probable that a protein is present[26, 16].

*Free Sugars and Amino Acids:* Whereas on the basis of dialysis experiments and enzymatic tests *Robertson* and *MacFarlane* 1957[22] only suspected an oligosaccharide with a molecular weight of 1000, glucose, fructose, and sucrose have now been detected in the poison secretion of *L. moroides* by GC-MS after persilylation[16]. The same sugars are found in the sweet-tasting secretion of *J. urens* (cf. Fig. 6).

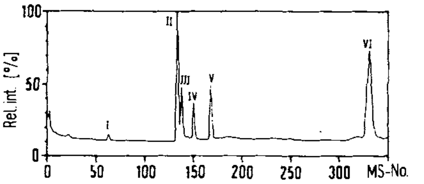


Fig. 6. Reconstructed gas chromatogram of silylated stinging hair fluid of *J. urens* on 3% OV 101, glass column, 2 m, 1/4" temperature conditions: column 140 °C isothermically, from spectrum 21 heated to 240 °C at 4 °C/min; injector 240 °C (III to VI, see Table 5).

A comparison of the retention times of fractions III to VI and of reference substances is given in Table 5. The assignment of the retention times is confirmed by corresponding mass spectra and high-pressure liquid chromatograms. Table 6 shows that sugars are present in the stinging hairs of *J. urens* in quantities comparable to those of the physiologically active amines histamine *(3)* and serotonin *(5)*.

Table 5. Retention times of fractions III to VI (see Fig. 6) and the corresponding reference substances (TMS = trimethylsilyl).

| Fraction/Reference | Retention time [min] |
|---|---|
| III | 14.3 |
| IV | 15.74 |
| V | 17.74 |
| VI | 30.3 |
| TMS-D-Fructofuranose | 14.34 |
| TMS-α-D-Glucopyranose | 15.86 |
| TMS-β-D-Glucopyranose | 17.72 |
| TMS-Sucrose | 30.24 |

Table 6. Sugar and amine content of the stinging hairs of *J. urens*.

| Sugar | μg/hair | Amine | μg/hair |
|---|---|---|---|
| Fructose | 0.8 | Histamine | 1–2 |
| Glucose | 0.68 | Serotonin | 0.5–1 |
| Sucrose | 0.56 | | |

The determination of the free amino acids in the stinging fluid of *J. urens* is sensible if only because this is a pure secretion, free from other cell constituents. In addition, it is suspected that the free amino acids form part of a whole complex of active principles, as is the case with many amphibian poisons and biogenic amines. As can be deduced from the elution diagrams (Fig. 7), the 18 amino acids detected include the most important ones; glutamic acid is particularly well represented (17.5 wt-%), as is aspartic acid (10.3 wt-%). The presence of the sugars and of the free amino acids could raise the activity.

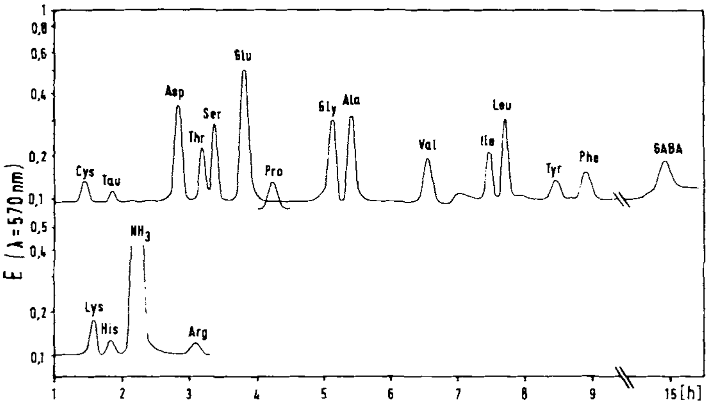


Fig. 7. Elution diagram of the amino acids from the stinging fluid of *J. urens*; taken with the Labotron amino-acid analyzer. GABA = γ-aminobutyramide.

## 2.2. The Primrose Defense Substances

### 2.2.1. The Defense Organ

*Primula obconica,* the Japanese primrose, is a pretty and unassuming but poisonous plant, known also as pot or poison primrose. The poison, contained in glandular hairs growing all over the plant (cf. Fig. 8), is apparently secreted constantly and for allergic people can pollute the atmosphere. However, the glandular hairs differ markedly from the trichomes of the previously mentioned *Urticaceae* and *Euphorbiaceae.*

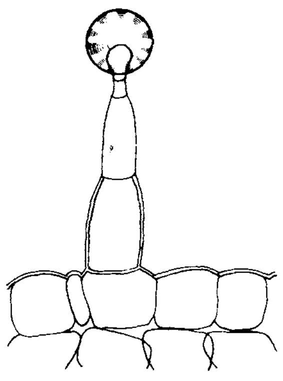
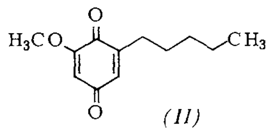


Fig. 8. Glandular hair of poison primroses with droplet of poison, schematic.

Thus, with the aid of the scanning electron microscope the tips of the stinging hairs of *L. moroides* were found to contain silicon and potassium, and in addition calcium was found at the tip break-points, its content increasing toward the base[191]. None of these elements are found in the stinging hairs of *J. urens*, where instead after the tip has been broken off a sharp-pointed cannula forms at the tapered site (see Fig. 1). This too is absent in the primroses covered with glandular hairs, so that the defense substances become active under the skin not mechanically but only on account of their special molecular structure.

### 2.2.2. Chemistry and Toxicology of Primrose Defense Substances

Around the turn of the century, when many varieties of primrose were already grown commercially, alarming articles appeared in leading medical publications describing the irritant action of primroses on the skin and almost resulting in a ban on their cultivation. *Nestler*[27] found that the action is due to yellow crystals appearing in the secretion, and *Bloch* and *Karrer*[28] that the isolated compound (primin) is in fact highly toxic to the skin of people especially sensitive to primroses. The yellow primin can be sublimed, is steam-volatile, forms a dark-colored product with hydroquinone and a precipitate with 2,4-dinitrophenylhydrazine, and quite generally speaking tends to exhibit the reactions of a quinone rather than of a lactone as suspected by *Bloch* and *Karrer*[28]. On the basis of an electron-pyrolysis analysis and of IR and NMR data, primin was finally identified as 2-methoxy-6-*n*-pentyl-*p*-benzoquinone *(11)*[29]. The fact that this quinone is the sought-for allergen could be demonstrated by *Hjorth* and *Fregert*[30] in Lund, Sweden on patients clinically sensitive to the plant. A comparison with synthetic variants of primin (methoxyquinones with longer or shorter side chains) was very informative: only the primin was strongly active even in patients with a low sensitivity (cf. Table 7). Most of the patients reacted to the 6-methyl and the 6-ethyl derivative only when administered in highly concentrated solutions. An allergic effect was sometimes also observed with methoxyquinones substituted at C-5 of the quinone nucleus, but only in very sensitive subjects. The optimal length and position of the side chain can be regarded as an immunological factor, but it can also correspond to increased skin permeability. Apparently the quinone allergens form antigens freely, only when the stereochemistry of the molecule permits a protein to interact with it easily. On the other hand, quinones with short side chains are too soluble in water and those with long side chains are too lipophilic.


*(11)*

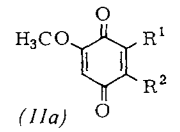
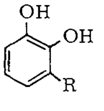

*(11a)*

Table 7. Test reactions of 20 patients to primin *(11)*, as well as some variants and isomers *(11a)*. $c=0.48$ mmol/dm$^3$.

| $R^1$ | $CH_3$ | | $C_2H_5$ | | $C_3H_7$ | | $C_4H_9$ | $C_5H_{11}$ | $C_6H_{13}$ | H | | H | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $R^2$ | H | | H | | H | | H | H | H | $C_5H_{11}$ | | $C_6H_{13}$ | |
| Conc. | $10 \times c$ | $c$ | $10 \times c$ | $c$ | $10 \times x$ | $c$ | $c$ | $c$ | $c$ | $10 \times c$ | $c$ | $10 \times c$ | $c$ |
| 1 | | + | | + | | + + | + + + + | + + + + [a] | | | | | |
| 2 | + | − | | + | | + + | + + + | + + [a] | + + + | | − | | + |
| 3 | + + | − | | + | | + + | + + + [a] | + + + [a] | + + | | + + + | | + |
| 4 | + | − | | + | | + + + | + + | + + + | + + + | | + + | | + + |
| 5 | + | − | | + | | + + | + + | + + | + + | | + | | + |
| 6 | + | − | + | − | | + + | + + + | + + + | + + | | + | | + |
| 7 | + + | − | + + | − | | + + | + [a] | + + [a] | + + [a] | | + + | | + + |
| 8 | − | | − | | | + + | + + | + + [a] | + + [a] | | + + | | − |
| 9 | + | − | + + | − | | + + | + | + + + [a] | + + + | | − | | − |
| 10 | − | − | + | − | | − | + | + | + | + | − | + | − |
| 11 | | − | | − | + | − | + | + | + | | − | | − |
| 12 | + | − | + | − | + | − | + | + | + | | − | | − |
| 13 | − | − | | − | − | − | + | + + + | + + | | − | | − |
| 14 | + + | − | + | − | + + | − | + + | + + | + + | | − | | − |
| 15 | − | − | + | − | + | − | + | + | + | + | − | + | − |
| 16 | − | − | + | − | + | − | + | + | + | − | − | − | − |
| 17 | | − | | − | | − | + + | + + | + + | | − | | − |
| 18 | | − | − | − | − | − | + | + + | + | | − | | − |
| 19 | + | − | − | − | + | − | + + | + + | − | | − | | − |
| 20 | − | − | − | − | − | − | − | + | − | | − | | − |

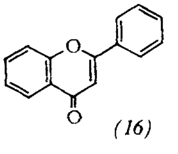
[a] Concentration: $c/4$.

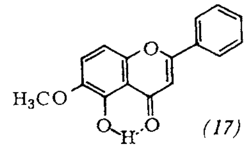
The fact that *p*-benzoquinone and toluquinone provoke no reaction whatever also shows the importance of the methoxy group in the physiologico-chemical action. Here we are dealing with an especially impressive example of a structure-action relationship of a phytotoxin. Similar considerations were borne in mind by *Baer et al.*[31] when they attempted to interpret the extreme contact dermatitis caused by urushiol, the toxic irritant principles of poison ivy *Rhus toxicodendron L.*; in this case a mixture of catechols *(12)*, *(13)*, *(14)*, and *(15)* is present.



*(12)*, R = $(CH_2)_{14}$–$CH_3$
*(13)*, R = $(CH_2)_7$–CH=CH–$(CH_2)_5$–$CH_3$
*(14)*, R = $(CH_2)_7$–CH=CH–$CH_2$–CH=CH–$(CH_2)_2$–$CH_3$
*(15)*, R = $(CH_2)_7$–CH=CH–$CH_2$–CH=CH–$CH_2$–CH=$CH_2$

Thus, it is only necessary to synthesize the appropriate chemical variants to be able to draw conclusions about evolutionary analogies. However, urushiol leads us beyond its own plant family and back to the *Primulaceae*, since here too phenols are found as potential contact allergens. Particularly in the primroses dusted as though with flour we find, as a first line of defense, pure flavone *(16)* and 5-hydroxy-6-methoxyflavone *(17)*[32]. Neither *(16)* nor *(17)* is by nature allergenic[32], but they can become allergenic after repeated contact, as happened to *Nestler* in the course of his work[33].


*(16)*


*(17)*

In the quinones of the *Primulaceae* at least, we find true defense substances, if only because the compounds are produced and stored in special defense organs. This is also indicated by the occurrence of quinones in the defense glands of ground beetles[34], earwigs[35], and diplopods[36], where the defense function of the quinones is undisputed[37]. The pygidial defense glands of the dytiscids, predacious aquatic beetles, contain above all aromatic hydroxycarboxylic acids, with which these insects protect themselves from life-threatening attack by fungi[38].

Quinones and phenols are also the active principles that play an essential part in the competition between different higher plants and between higher plants and microorganisms. In botanical literature references of this nature are found under the term allelopathy[39]. However, before we embark upon this field of defense chemistry, mention should be made of the analysis and the toxicology of the defense substances, directed—as in the case of the *Urticaceae, Euphorbiaceae,* and *Primulaceae*—against our own main defense organs, the mucous membranes; the term "skin-to-skin effect" would be appropriate in this context.

## 3. Irritants and Defense Substances from the Bast and the Berries of the Thymelaeaceae

The bast of a bush (Fig. 9), which in early spring could represent welcome fresh food for famished wild animals such as the deer and the rabbit, is protected from them by a toxin which, by inducing an extremely severe mucosal irritation, would spoil once and for all even the most voracious appetite. The recurring description of the striking efficacy of daphne poison, upon which man as researcher and healer has lavished special attention through the ages, is enough to support this theory[40].

Fig. 9. *Daphne mezereum*, the spurge laurel.

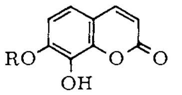
*Johann Friedrich Gmelin,* the father of the author of "Gmelin's Handbook of Inorganic Chemistry", gives a description in his general history of plant toxins[41] which is illuminating for our theme of the defense substances of plants insofar as it clearly portrays the associated physiological effects and gives a list of vivid names by which the plant is known:

"Mezereum, lousewort, spurge laurel, devil-in-the-bush, virgin's bower, mountain pepper, spurge olive, *Daphne Mezereum* Linn. All parts of this plant, the roots, the bark, leaves, and above all the berries have a quite extraordinary pungency and when rubbed on the skin produce reddening and blistering, but if swallowed they result in a fearful and sustained burning in the mouth and the throat often in real inflammation of these parts, in an unslakable thirst, the most violent vomiting, persistent and dreadful diarrhea, stomach pains that endure long after, sleepless nights, a raging fever, indescribable physical weakness, and peeling of skin all over the body. Death is not uncommon. The mere effluvia of the flowers can cause fainting in unventilated rooms. Even the smoke of the wood in which they were smoking their meat proved fatal to some soldiers in Corsica after convulsions and a sensation of being choked. In cattle the berries give rise to bloody stools, and to wolves and dogs they are deadly. The flowers are carefully avoided by bees."

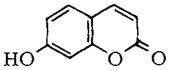
It should be noted that the daphne toxin, mezerein[42], occurs in particularly high concentrations in the fruits, important for preservation of the species[43], just as the strongest nonprotein poison, tetrodotoxin, occurs predominantly in the ovaries and testicles of the globefish[25]. However, the mezerein in the fruits (Fig. 10) could also be there to help in wide dispersal of the seeds for propagation of the species because of its strongly purgative action[44].

Fig. 10. The shiny red berries of *Daphne mezereum.*

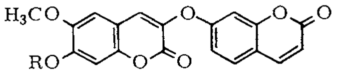
Rather fewer physiologically active compounds now regarded as defense substances had been classified before the actual defense substance of the spurge laurel, *i.e.* the resinous inflammatory principle[45], was isolated in pure form. *Zwenger*[46] established the structure of daphnin *(18)* and found umbelliferone *(19)* by dry distillation of the bark. As early as 1870 *Casselmann*[47] described a volatile "coccognin", which may well have been the sublimable daphnetin *(20)* discovered in 1879 by *Stünkel*[48]. In 1963 *Tschesche et al.*[49] reported a dicoumarin, daphnoretin *(21)*, and its glycoside daphnorin *(22)*. Guided by an inflammation test in experiments on themselves, *Schildknecht* and *Edelmann* (1967)[50] isolated 400 mg of crystalline mezerein from 1 kg of dried seed, whose inflammation threshold was 0.2 μg/mouse ear and whose median inflammatory dose (see Table 8)[51] was 0.023 : 1.27 μg/mouse ear[52]. Mezerein is considerably cocarcinogenic[53]. The inflammatory power and the cocarci-



*(18)*, R = Glucosyl
*(20)*, R = H



*(19)*



*(21)*, R = H
*(22)*, R = Glucosyl

nogenic action, although weaker than those found by *Hecker et al.*[54] for the most active phorbol ester, are nonetheless of comparable magnitude. That was reason enough to determine the structure of mezerein, which has the empirical formula $C_{38}H_{38}O_{10}$ (Table 8). In the absence of equipment for X-ray structural analysis, mainly spectroscopic methods were used[55] leading, surprisingly, to the discovery of an orthobenzoic acid ester and a cinnamalacetic acid residue. However, the basic structure, the hydrocarbon daphnane, can be compared with phorbol ester type structures from the *Euphorbiaceae.* In this way a structure was found for mezerein that resembled the structure established by *Stout et al.* for daphnetoxin *(23)* using X-ray structure analysis[56] and, after slight revision, was confirmed at the same time by *Ronlan* and *Wickberg*[57].

All *Thymelaeae* species are poisonous[58] and are avoided by cattle even in coastal regions where nothing else grows than, for example, the salt-tolerant *Thymelaea hirsuta*[59] (cf. Fig. 11 and 12). In their natural surroundings only two plant families, one of them the *Thymelaeaceae,* are poisonous to camels[60], and we now know that this is due to skin-irritant compounds very closely related to mezerein *(23)* in their chemical composition[61]. The name thymelein *(25)* has been suggested for the skin-irritant defense substance of *T. hirsuta* which was isolated and whose structure was clarified in 1974. The skin-irritant compounds from *Daphne gnidium*, which is probably the most poisonous plant in the Mediterranean region (cf. Fig. 13), is painstakingly avoided by herds of goats in the carique (wild fig) and maquis (scrub) areas in southern France even in times of severe food shortages[62], have a very similar structure.

Fig. 11. Branches of *Thymelaea hirsuta.*

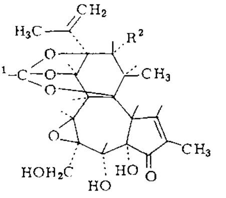
Fig. 12. Leaves and flowers of *Thymelaea hirsuta.*

Fig. 13. A *Daphne gnidium* bush.

The irritants are also present in the bast and the berries, and even in the leaves, and again they are chemically related to the mezerein from *D. mezereum*[63].

The already mentioned daphnetoxin *(23)* was the first of these compounds to be isolated; it was followed by a substantially stronger skin-irritant compound, the cinnamic ester *(27)* of 12-hydroxydaphnetoxin, whose alkaline saponification yields cinnamic acid and mezerenol *(26)*, the hydrolysis alcohol of mezerein. This defense substance was isolated as an antileukemic compound from *Gnidia lamprantha Gilg* and called gnidicin *(27)*[64]. Another active component of the skin-irritant mixture from *D. gnidium* proved to be similar in structure to huratoxin *(28)*, except that it was the ortho-ester of *trans*-2,4-decadienoic acid *(29)* (Table 8).

Table 8. Irritant defense substances from plants of the order *Thymelaeales* [65] (after [55, 61, 63]).



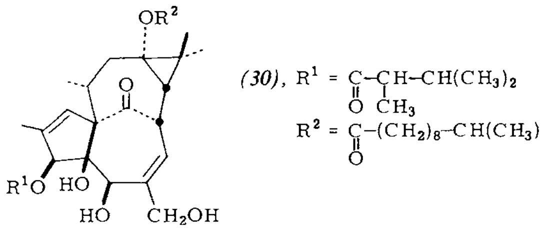
*(23)-(29)*

| No. | Name | $R^1$ | $R^2$ |
|---|---|---|---|
| *(23)* | Daphnetoxin, | $C_6H_5$ | H |
| *(24)* | Mezerein | $C_6H_5$ | $OCO—(CH{=}CH)_2—C_6H_5$ |
| *(25)* | Thymeleine | $(CH{=}CH)_2—(CH_2)_4—CH_3$ | $OCO—C_6H_5$ |
| *(26)* | Mezerenol | $C_6H_5$ | OH |
| *(27)* | Gnidicin | $C_6H_5$ | $OCO—CH{=}CH—C_6H_5$ |
| *(28)* | Huratoxin | $(CH{=}CH)_2—(CH_2)_8—CH_3$ | H |
| *(29)* | | $(CH{=}CH)_2—(CH_2)_4—CH_3$ | H |

Euphorbias protect themselves in a number of ways by the production of a milky latex. This allows wound closure after damage to the plant, but the fluid is also a strong skin irritant and accordingly has the same defensive function as the toxin in bast plants of the Thymelaeales group just described. Alongside the thorny opuntias, the Canary Island euphorbia *(E. canariensis)*, the leafless bush euphorbia *(Euphorbia aphylla)*, and the *Euphorbia regis-ubae* are the most widespread in mountain regions (cf. Fig. 14)[66]. The strongly skin-irritant active principles are esters of phorbol, *e.g.* 12-*O*-tetradecanoylphorbol 13-acetate (TPA)[67] from purging croton *(Croton tiglium)*, a member of the *Euphorbiaceae*.

Fig. 14. Euphorbias growing alongside opuntias, avoided by grazing cattle.

Whether it grows in meadows or pastures, cattle avoid the cypress spurge *(Euphorbia cyparissias)* with the strongly irritant active principles in its sap. From the parts of the plant growing above the soil and from the root *Hecker* and *Ott*[68] extracted *inter alia* 14 more or less irritant diterpene esters of the polyfunctional alcohols 13-hydroxyingenol and 13,19-dihydroxyingenol, *e.g.* 3-*O*-(2,3-dimethylbutyryl)-13-*O*-isododecanoyl-13-hydroxyingenol *(30)*.

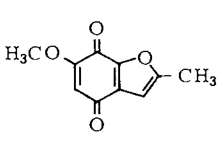


*(30)*, $R^1 = \overset{\displaystyle O}{\overset{\|}{C}}—\underset{\displaystyle CH_3}{CH}—CH(CH_3)_2$ (O below C)

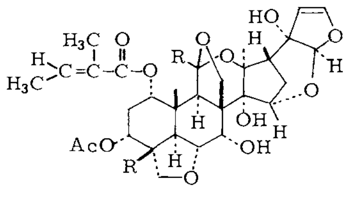
$R^2 = C(=O)—(CH_2)_8—CH(CH_3)_2$

## 4. Defense Against Insects

Many plants are not eaten by insects only because they offer no incitement to them. The ultimate eating signal is a chemical one. The silk worm is lured to the plant on which it feeds by terpenes—sterols induce the creature to bite at it, and only when cellulose and sugar are present is the food swallowed[69]. If one of these chemical reflex-triggers is lacking, the plant will not be damaged. There are, however, a number of substances, *e.g.* alkaloids, that serve as active deterrents and as it were "poison" the plant. The wild potato is "soured" for the larva of the Colorado beetle by an alkaloid; in the *Nicotiana* species, of which tobacco is a member, it is the nicotine, located in the tips of the glandular hairs, that performs this function. It thus becomes an insecticide, since aphids are not only prevented from sucking the plant but are actually paralyzed and destroyed. If we consider the fundamentals of this phenomenon of plant self-defense it soon becomes clear that many so-called secondary plant constituents must be mentioned at this point, *e.g.* acameline *(31)*, which *Schmalle* and *Hausen* isolated from the blackwood *Acacia melanoxylon* of the *Mimosaceae* family and identified as *(31)*[70].



*(31)*

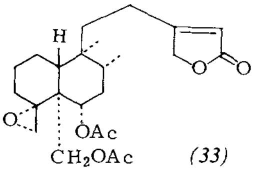


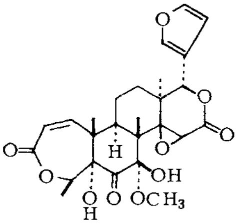
*(32)*, R = $C(=O)—OCH_3$

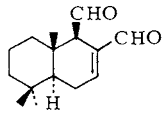
### 4.1. Defense Substances as Protection Against Predators

The deterrent substances described most often are those directed against the African armyworm, *Spodoptera esempta* and *S. littoralis*[71]. The active principle azadirachtin *(32)* has also been isolated from the Indian neem tree *(Azadirachta indica)* and from the closely related species *Melia azedarah*, together with meliantril, the substance that inhibits destruction by locusts.

From the leaves of the bugle *Ajuga remota (Labiatae)*, which are not attacked by the African armyworm, the eating-inhibitor ajugarine *(33)* has been isolated, a subtance also effective on locusts[71]. How complicated the structure of active principles of this kind can be is demonstrated by the formula of harrisonin *(34)* from the African bush *Harrisonia abyssinica* Oliv, a *Simarubaceae.* 650 g of root bark yielded 70 mg of the crystalline harrisonin *(34)*[71]. The structure was determined almost exclusively by $^{13}$C-NMR spectra. Harrisonin acts as an antibiotic against *Bacillus subtilis* and is also cytotoxic. From the bark of an East African *Canellaceae, Warburgia stuhlmannij,* the eating-inhibitor polygodial *(35)* was isolated and its structure was elucidated[72]. This sesquiterpene still acts as a very efficient armyworm deterrent in a concentration of 0.1 ppm.

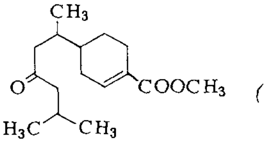

*(33)*


*(34)*

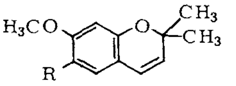

*(35)*

### 4.2. Defense Substances as Development Inhibitors

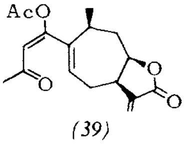
Maturation is a hormone-regulated process even when we are talking about the development of an insect larva into the imago. The fact that the host plants of the phytophages "know" this is a still unsolved puzzle of co-evolution, in the course of which all organisms have adjusted to one another.

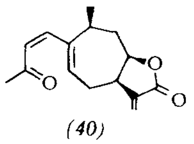

*(36)*

Juvabione *(36)*, a third-generation insecticide, is a juvenile-hormone analogue with a development-inhibiting action, extracted from the wood of the balsam fir. Juvenile-hormone antagonists can also inhibit the development of insects. *Bowers*[73] isolated active principles of this type from the leaves of the familiar ornamental plant *Ageratum houstoneanum* and called the antijuvenile hormones 7-methoxy- *(37)* and 6,7-dimethoxy-2,2-dimethylchromene *(38)* precocenes.


*(37)*, R = H
*(38)*, R = $CH_3O$

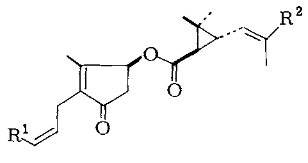
From the leaves of the clover *Xanthium canadense Mill.*, an annual weed, *K. Kawazu et al.*[74] isolated a remarkably effective insect-development inhibitor. The compounds responsible for the larval growth inhibition, santhumin *(39)* and 8-*epi*-xanthine *(40)*, were isolated by means of liquid-liquid extraction and chromatography[74].


*(39)*


*(40)*

### 4.3. Defense Substances as Insecticides

When we refer to the antijuvenile hormones discovered by *Bowers*[73] as 4th generation insecticides we are in fact neglecting the natural insecticidal substances of *Chrysanthemum cinerariaefolium.* The action of this plant was discovered simply by observing that veritable mountains of dead insects of various kinds were often found in places where it grows. The insecticides of pyrethrum, which are obtained from the flower heads, namely pyrethrin I *(41)* and II *(42)*, cinerin I *(43)* and II *(44)*, and jasmolin I *(45)* and II *(46)*, are cyclopentenyl esters of chrysanthemumic acid[75]. Along with nicotine, pyrethrum is the strongest insecticidal plant-defense substance known.



| | $R^1$ | $R^2$ |
|---|---|---|
| *(41)* | $CH_2{=}CH$ | $CH_3$ |
| *(42)* | $CH_2{=}CH$ | $CO_2CH_3$ |
| *(43)* | $CH_3$ | $CH_3$ |
| *(44)* | $CH_3$ | $CO_2CH_3$ |
| *(45)* | $C_2H_5$ | $CH_3$ |
| *(46)* | $C_2H_5$ | $CO_2CH_3$ |

## 5. Phytonicides and Wound Gases

The higher plants live mainly on carbon dioxide and water. Unlike many creatures, they do not go in search of their food but need light to synthesize it, and therefore have large assimilating external surfaces. Because of this they are easy prey, and only by producing solid, liquid, and above all gaseous defense substances can a plant, rooted as it is to the spot, procure living space for itself and protect it. *Tokin*[76] called these bactericidal, protozoacidal, and fungicidal substances "which are related to the protective and healing powers of plant organisms" phytonicides.

*Tokin* discovered the action of the phytonicides in 1928 and 1929, when he vainly attempted to convince himself of the validity of *Gurwitsch*'s theory of mitogenetic rays. What *Gurwitsch et al.*[77] regarded as the action of invisible radiation could in *Tokin*'s opinion be explained much better by the presence of volatile active principles.

### 5.1. The Phytonicide Test and the Isolation of Volatile Microbicidal Defense Substances

Defense substances are mainly emitted by a plant from damaged parts such as leaves. They are primarily protozoacidal and fungicidal, and according to *Tokin*[76] can easily be detected with a protozoa test (cf. Fig. 15). The time needed to destroy ciliates is observed, as is the behavior in the killing of protozoa on the basis of differential phytonicidal action.

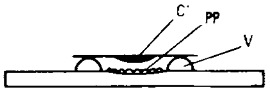


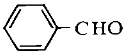
Fig. 15. *Tokin*'s test arrangement for the aerial phytonicides of a plant pulp PP, C = ciliates from a hay infusion in a drop of water, V = vaseline sealing ring.

For their elucidation the volatile active principles are isolated *via* the vapor phase by headspace analysis, *i. e.* by adsorption or by passing the gases and vapors into water or freon 11[78-80]. The active principles are then obtained by ice zone melting[81], normal freezing[82], or by extraction of the aqueous solution with freon 11[83]. The substances isolated by adsorption on a Tenax column of an environmental gas chromatograph are desorbed by heating the column and analyzed by GC-MS.

## 5.2. The Chemical Nature of the "Aerial Phytonicides" of Foliage Plants

The volatile defense substances from the leaves, buds, and bark of the bird-cherry *Prunus padus* are benzaldehyde *(47)* and hydrocyanic acid *(48)*. It is indicative of the defensive function of the aerial phytonicides that they are about ten times as active from the buds as from the leaves. It has likewise been proved that hydrocyanic acid is given off by the leaf pulp of the mountain ash *Sorbus aucuparia*, quickly destroying gnats when they land on the pulp. Although many plants are able to give off enzymatically released hydrocyanic acid, according to *Paris*[84] we cannot conclude from this that cyanogenic glycosides must be the precursors. The defense function of hydrocyanic acid is also indicated by the fact that arthropods use it as a poison gas[85,86].

*(47)*



HCN *(48)*

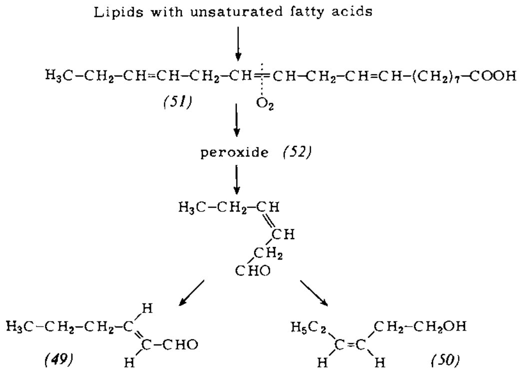
The most widespread aerial phytonicide of foliage plants is *trans*-2-hexenal *(49)*, which was detected as early as 1912 by *Curtius* and *Franzen* as a leaf aldehyde in the steam distillate of hornbeam leaves. However, the intact trees of *Robinia pseudoacacia* also constantly give off small quantities (3 $\mu g/m^3$ air) of *trans*-2-hexenal *(49)* into their surroundings. *(49)* has also been shown to be a leaf phytonicide of the common oak *(Quercus pedunculata)*, alder *(Alnus glutinosa)*, blackcurrant *(Ribes nigrum)*, lupin *(Lupinus angustifolius)*, bilberry *(Vaccinium myrtyllus)*, red whortleberry *(Vaccinium vitis-idaea)*, privet *(Fraxinus ligustrum)*, and grass. *(49)* as well as *cis*-3-hexen-1-ol *(50)* also occurs in the scent of the flowers[79]. It is therefore not surprising that the defense substances of pentatomid bugs *(Pentatomidae)* are in the main *(49)* besides octenal and decenal. Since bedbugs also store *(49)* in addition to *n*-octenal in their defense glands, it may be assumed that the leaf bugs do not take up the *trans*-2-hexenal from the leaves but synthesize it themselves[88,89].

## 5.3. "Phytons" as Wound Gases

*Trans*-2-hexenal *(49)* not only enables the higher plants to surround themselves with a zone of defense but also to protect themselves when damaged against microorganism infestation and in the event of more severe damage even to regenerate. Thus, at low concentrations *(49)* stimulates callus formation, while at higher concentrations it promotes sprouting. In primary suberization and callus formation the action of *(49)* by far surpasses that of the wound hormone traumatic acid[87]. It is therefore understandable that small ground shrubs such as the bilberry and the red whortleberry give off more *trans*-2-hexenal when damaged than *e. g.* locust trees[88].

After mechanical damage, physiological and chemical changes take place in the damaged plant cells and cell compartments[90], which lead to the production of the wound gases *(49)* and *(50)*[91]. It is assumed that the precursor of these hexene derivatives is linolenic acid *(51)*, which on penetration of oxygen into the wound is split into two 6-carbon fragments by an enzyme bound to the thylacoid structure of the plastids, the decomposition proceeding *via* an intermediate peroxide *(52)* (Table 9).

Table 9. Biosynthesis of the leaf aldehyde *(49)* and leaf alcohol *(50)* (after [90]).



This is a general mechanism of biosynthesis, so that the different activities in the leaves of different plants are merely due to different hexenal doses and not, as *Tokin* thought, to structurally different phytonicides.

The above growth-promoting properties of *trans*-2-hexenal are the exact counterpart of what must be understood by the term "phytonicidal". For this reason, the term "phyton"[87] should be adopted instead to denote all substances given off by higher plants for their protection, both when they are protozoacidal, bactericidal and fungicidal and when they act as growth-promoting substances like the wound gases *trans*-2-hexenal *(49)* and ethylene. In this way misunderstandings would be avoided, and since the same root is used we would be reminded of the term "phytonicides". It is incomprehensible how *Tokin*'s work could be forgotten, so that for example *Gross*[92] regarded the fungitoxic plant constituents, which *Stoessl*[93] called preinfectional defense substances, as phytoalexins (cf. Section 7).

We can therefore speak of phytons whenever excretory active principles, and not only those of phytonicidal nature, exert their effect. Substances of this type are given off into their surroundings not only by the assimilating plant organs. The flowers of higher plants are a special source of phytons with an action spectrum whose significance is perhaps still unrecognized.

### 5.4. Flower Phytons as Irritants in Flower Ecology

The flower is almost invariably the most beautiful part of a plant, and its chemistry is also as a rule particularly attractive because of the sweet-smelling substances involved. However, flowers are sometimes protected by ugly, though useful, thorns and poisonous spines (see Fig. 4). Should unpleasant flower scents be included in the same category? Scent may well have several functions to perform, even though one should not, like *Müller*[94,95], under the influence of Darwin's theory of natural selection, ascribe a function to each flower characteristic. We know that flower scents have a short-range rather than a long-range action, but our knowledge of them is still very scant[96], particularly as regards their composition. Only recently has it become possible to formulate a more or less satisfactory picture of a bouquet, as can be seen from the analytical results obtained with extremely delicate instrumental techniques.

The blossoms of the sweet chestnut emit a stink rather than a fragrance—at least for the human nose. Yet they lure many beetles, and in particular ladybugs *(Coccinella septempunctata)*, especially since these blossoms also secrete a little nectar. The scent was analyzed by GC-MS after a special headspace extraction of catkins still on the tree[83]. The gas chromatogram gives a glimpse of "untouched nature", for only a few of the many peaks have been ascribed to known substances. However, these few compounds already indicate how many functions are encoded in a flower's fragrance (Fig. 16).

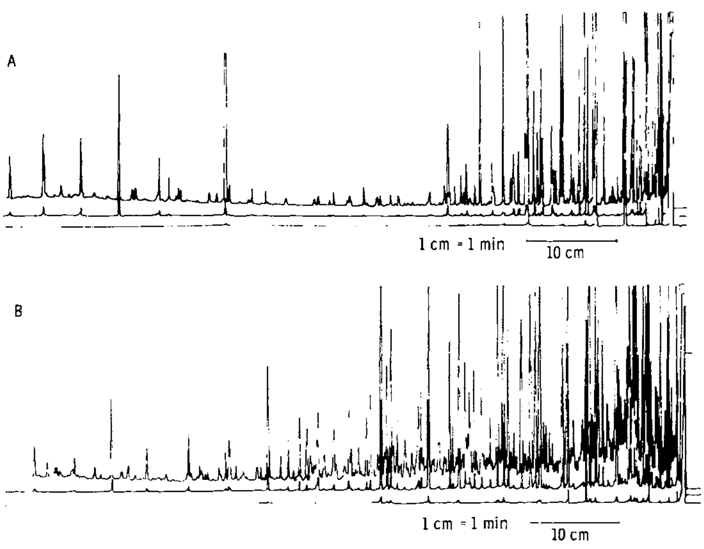
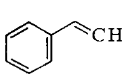
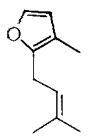


Fig. 16. Gas chromatogram of the fragrance of living chestnut blossoms (A) and chestnut honey (B) (GC-MS system, Finnigan, Model 3200 F-003).

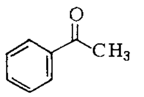
The main peaks appearing after the peaks for the solvents (chloroform, 1,2-dichloroethane, and toluene) correspond to styrene *(53)*, rosefuran *(54)*, acetophenone *(55)*, and 3-phenyl-1-propanol *(56)*. These compounds are also found in honey scent when a headspace analysis is performed on honey that has been collected fresh and undiluted from the honeycombs of beehives in a chestnut wood. The gas chromatogram from the headspace analysis (Fig. 16) shows that the substances determining the fragrance of sweet-chestnut honey are styrene *(53)* and a rosefuran that has not been precisely identified, as has also been shown by a "sniff test"[97]. The flower fragrance also includes ethyl butyrate, diethyl carbonate, isopentanol, limonene, *trans*-2-hexenal *(49)*, ethyl benzene, ethyl carbonate, α-pinene, acetoin, *cis*-hexenyl acetate, 2-methyl-4-octanone, *cis/trans*-3-hexen-1-ol, diacetonyl alcohol, *cis*-linalool oxide, *o,m,p*-tolylaldehyde, 1-phenylpent-en-4-one, naphthalene, ethyldihydronaphthalene, 1-phenylethanol, and benzyl alcohol.



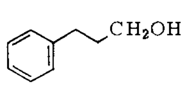
*(53)*



*(54)*



*(55)*



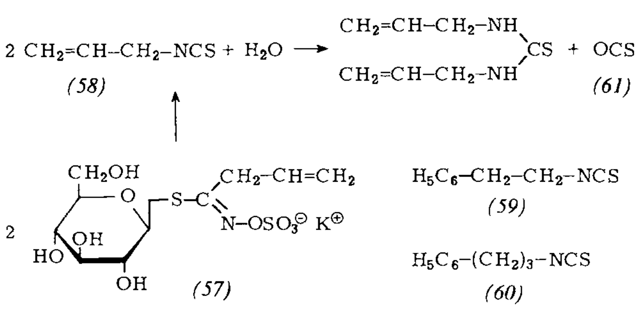
*(56)*

The real purpose behind this still incompletely determined mixture of substances is unknown. It certainly contains defense substances acting as eating-inhibitors or having a microbicidal effect. The significance of this combination of active principles will only be recognized when chemists and biologists join forces to obtain a solution.

### 5.5. Defense Substances in the Roots

*Virtanen*[98] has identified the lacrimatory substances in the onion, which according to *Tokin*[76] have a particularly high phytonicidal activity.

The volatile phytonicides of the horseradish *Cochlearia armoracia* are to be sought primarily among isothiocyanate esters. Thus, on comminution of this root allyl isothiocyanate *(58)* is produced by enzymatic hydrolysis of sinigrin *(57)*, in addition to phenylethyl isothiocyanate *(59)* and phenylpropyl isothiocyanate *(60)*. By an enzymatic process the ester *(58)* gives rise to carbon oxysulfide *(61)*, identified by its melting point, molecular weight, and IR spectrum[99]. On comminution of 5 kg of horseradishes 60 mg of OCS is obtained, which exerts an antibiotic action on gram-positive bacteria and explains why the bactericidal action of finely comminuted horseradish is far greater than that of the corresponding quantity of allyl isothiocyanate[100].

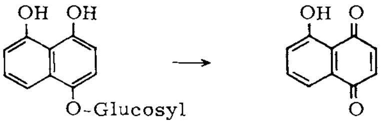


## 6. The Defense Substances of Allelopathy

Many of the hundreds of substances emitted day and night above and below ground by the higher plants into their biotope are defense substances by means of which the individuals of a given natural community protect their living space and strive for dominance, often becoming weeds in this way. Strong chemical interaction between the higher plants is thus set up, a "chemical ecology", or interaction between higher plants and microorganisms. This phenomenon, by which plants assert themselves chemically over other forms of life, has been called allelopathy by *Molisch*[101], and in 1969—1970 *Müller* discussed in detail the biochemical parameters inherent in this concept[102-104].

### 6.1. Allelopathic Defense Substances from the Foliage of Leaf Plants

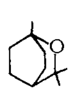
Partly for historical reasons, a discussion of typical allelopathic active principles should start with a naphthoquinone known as juglone *(63)*, which can poison the whole area overshadowed by a walnut tree, a phenomenon already reported by *Pliny the Elder*[105]. The precursor *(62)*[106], which can be found in the leaves, fruits, and roots of all walnut species *(Juglandaceae)*, is carried by rainwater into the soil, where it is quickly oxidized to *(63)* and inhibits, *inter alia*, the growth of grasses *(Gramineae)*, tomato plants, potatoes, and apple trees. The vegetation under a walnut tree is thus severely depopulated. Juglone *(63)* is highly toxic, a 10-ppm aqueous solution inhibiting the growth of tomato seedlings by 50% and a 100-ppm solution destroying them completely[107].



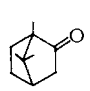
*(62)* *(63)*

Storage of the compound in the form of a hydroquinone which has to be activated by oxidation to the corresponding quinone *(63)*, is reminiscent of the defense chemistry of the bombardier beetle, which stores hydroquinone in its defense bladder until it has been disturbed; the hydroquinone is then oxidized explosively to *p*-benzoquinone in a catalytic process occurring in a kind of combustion chamber[108,109].

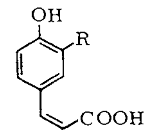
Some particularly volatile terpenes play a significant part in the interspecific interaction of plant communities (allelochemical effect[110]). In the chaparral of southern California on many loamy soils, grasses can only encroach one or two meters upon *Salvia leucophylla*, a sage, and *Artemisia california*, a mugwort. According to *Muller* and *Chou*[111], the cause of this warding-off of competitors is not shade, aridity, nutrients, or any animal influence but the gas-chromatographically detectable monoterpenes 1,8-cineol *(64)* and camphor *(65)*; the main phytotoxins given off, in vapor form, by *S. leucophylla* are *(64)* and *(65)*; these are again washed by rain into the ground, where, bound in a soil colloid, they exert a germination-inhibiting effect on grass seed. Another ubiquitous and dominant shrub of the southern Californian chaparral, adenostoma, excretes some defense substances which are carried by rainwater and dew into the soil, from where they can easily be extracted[111]. Both in the aqueous extract of adenostoma branches and in the alkaline ethanol extract ferulic acid *(66)*, *p*-coumaric acid *(67)*, syringic acid *(68)*, vanillic acid *(69)*, and *p*-hydroxybenzoic acid *(70)* have been identified. All these phenols, and also the phenols detected in adenostoma leaves, namely arbutin *(71)*, hydroquinone *(72)*, and umbelliferone *(73)*, proved in a bioassay on the growth of the seeds of *Lactuca sativa* to be strongly toxic[112].



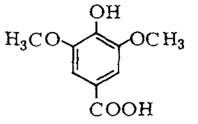
*(64)*



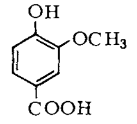
*(65)*



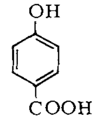
*(66)*, R = OCH$_3$
*(67)*, R = H



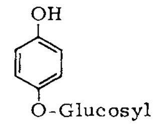
*(68)*



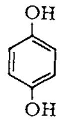
*(69)*



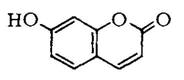
*(70)*



*(71)*



*(72)*



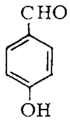
*(73)*

Of the eight compounds named above, the five *(66)—(70)* found in the soil are not necessarily responsible for the growth-inhibiting allelochemical effect, since this is also observed in the absence of phenols. The allelopathic effect traceable back directly to the roots should therefore be given much more consideration in future ecological studies.

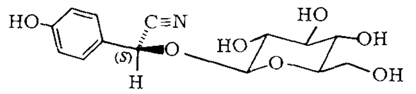
### 6.2. Allelopathic Defense Substances of the Rhizosphere

*Remmert*[39] reports a particularly impressive case of competition between trees and Scotch heather *(Calluna vulgaris)*. The latter asserts itself against its far larger competitors by damaging the mycorrhiza necessary for the trees' sustenance. Once the heather has asserted itself with the aid of these allelopathic defense substances, as *e.g.* in the northwestern Spanish province of Galicia, reforestation with oak, a species basically indigenous to the region, is possible only to a moderate degree. *Ballester et al.*[113] were completely successful in demonstrating, in germination experiments, the allelopathic action of ten phenols, among them again vanillic acid *(69)* from besom heath *(Erica scoparia)*.

The couch grass *(Agropyron repens)*, one of the six most widespread weeds of Central Europe, is suspected of excreting from its creeping rhizomes a phytotoxin having an adverse effect on the germination and growth of cultivated plants. According to *Tauscher et al.*[115], the inhibitor is not the acetylenic hydrocarbon agropyrene mentioned in this connection[114], but a phytotoxin with a molecular weight of less than 1000. The rhizome exudates of Johnson grass *(Sorghum halepense)*, familiar as a troublesome weed on cultivated land almost everywhere in the world, influence especially the germination and growth of all competitor plants. *Rice et al.*[116] have demonstrated that this root-allelopathic effect is due to hydrocyanic acid *(48)* and *p*-hydroxybenzaldehyde *(74)* from the phytotoxin dhurrin *(75)*, whose steric configuration was established by *Towers* on the basis of $^1$H-NMR measurements[117,118].

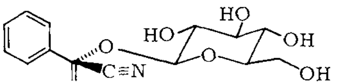


*(74)*

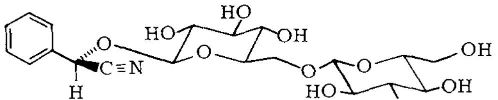


*(75)*

*(75)* is a cyanogenic glycoside, which thus belongs to a class of compounds already named as precursors of the aerial phytonicides of *Rinaceae* mentioned in Section 5.2, namely benzaldehyde *(47)* and hydrocyanic acid *(48)*. Cyanogenesis, the ability of certain plants to liberate hydrogen cyanide, has been known for centuries. More than 800 plant species from up to 80 plant families can produce HCN[119], the general rule being that both these defense substances, *e.g. (47), (48)*, and their precursors prunasin *(76)* and *(77)*, are nontoxic to their producers. On the other hand, HCN also has an inhibiting action on the respiration of the isolated roots of peach trees[120]. This implies autointoxication by the tree's own defense substance, but on balance the substance is beneficial, insofar as the living space is not populated more and more densely with its descendants but rather tends to spread out. The chemical interactions involved in the formation of plant populations, and the mechanisms on which they are based, are still largely virgin territory awaiting the attention of ecologists, biologists, and chemists.



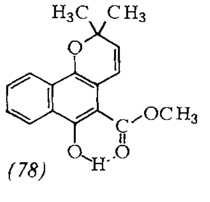
*(76)*



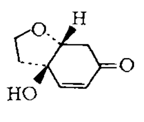
*(77)*

### 6.3. Further Studies

The rhizosphere often contains, in the truest sense of the word, the root upon which the thriving of many higher plants is based in a sometimes inhospitable biotope. The substances acting here have just been discussed. However, we must not forget all the secondary plant constituents for which the correct bioassay has not yet been found, but which on the basis of their organ-specific location in the plant, and also on the basis of the time of their occurrence, should be included in the group of allelopathically active substances. In the roots of the common catchweed *(Galium mollugo)* we find, particularly in the fall, a yellow compound called mollugin with the structure *(78)*[121]. Further work is needed to establish whether the particularly resistant meadow weed *(G. mollugo L.)* establishes itself in a species-rich biotope by means of this methyl 6-hydroxy-2,2-dimethyl-2*H*-naphthol[1,2-*b*]pyran-5-carboxylate *(78)*. The same applies to the (3a*R*,7a*R*)-3a-hydroxy-3,3a-7,7a-tetrahydro-1-benzofuran-6(2*H*)-one *(79)*, described as a constituent of the growing tips of the foxglove *(Digitalis purpurea)* by *Raymakers* and *Compernolle*[122]; the structure assigned has now been corrected[123].



*(78)*



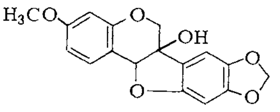
*(79)*

## 7. Phytoalexins, the Defense Substances Responsible for Plant Resistance[124-127]

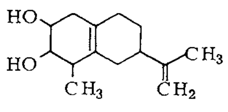
*Ward*[128] in England and *Bernard*[129] in France were the first to observe that pathogenic fungi often grow more slowly in plant tissue because the plant reacts defensively to the attack. It is even possible for resistance to develop. Thirty years later *Müller* and *Börger*, in the Arbeitsberichte der Biologischen Reichsanstalt für Land- und Forstwirtschaft in Berlin-Dahlem, published their phytoalexin theory of the resistance of plants to disease[130], according to which the resistance phenomenon in the plant kingdom is based on a chemical defense mechanism as well as on organ-specific structural barriers and other resistance factors against pathogenic microorganisms. The fungitoxic antibiotics formed endogeneously after an infection in a so-called "defense necrosis" can comprise isoflavanoids, terpenoids, polyacetylenic compounds, and dihydrophenanthrenes, and thus belong to the chemically already known substance classes of secondary constituents. The host plants can be found amongst the *Leguminosae, Solanaceae, Malvaceae, Convolvulaceae, Umbelliferae, Gramineae, Rosaceae,* and *Compositae, i.e.* practically throughout botany. To include here all the phytoalexins known so far would be a case of obscuring the wood by the trees, especially as it is still a subject of controversy whether phytoalexins can really be regarded as the defense substances of higher plants without any reservations[123]. On the other hand, in a consideration of defense substances, no environment may be ignored, be it in the macro or in the micro sphere, outside, or even inside the living plant organism.

### 7.1. Structure and Occurrence of Phytoalexins

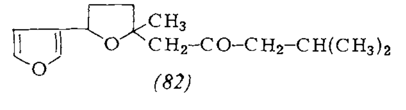
The weakly antibiotically active pisatin *(80)* from garden peas *Pisum sativum* L. *(Leguminosae)*[131], rishitin *(81)* from the potato *Solanum tuberosum* L. *(Solanaceae)*[132], and the ipomeamarone *(82)* from the sweet potato *Ipomoea batatas* Lam. *(Convolvulaceae)*[133] were the first phytoalexins to be isolated from infected plant tissue, characterized, and identified chemically[134].



*(80)*

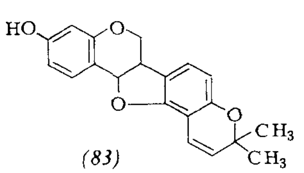


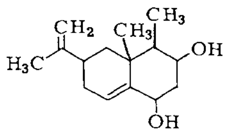
*(81)*



*(82)*

*Leguminosae* in general form isoflavanoids as pterocarpanoid phytoalexins; these have been encountered at all times in the healthy tissue of many plant species. An example is phaseolin *(83)*, which is very probably produced by a combination of the shikimate and acetate-malonate routes of biosynthesis. The *Solanaceae* phytoalexins belong to the group of terpenoids, as do the above-mentioned rishitin *(81)* and the sesquiterpene capsidiol *(84)* isolated from the fruit of the sweet pepper after the latter had been infected with a number of fungi[135-137]. The acetylenic phytoalexins *trans,trans*-3,11-tridecadiene-5,7,9-triyne-1,2-diol *(85)* and *trans*-11-tridecen-3,5,7,9-tetrayne-1,2-diol *(86)*, obtained from the infected hypocotyls of safflower *(Carthamus tinctorius)*, are also not unusual components for the *Compositae*. Dihydrophenanthrenes can be expected in orchids, *e.g.* orchinol *(87)*.

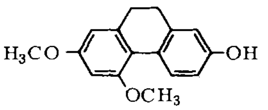

*(83)*


*(84)*

$CH_3CH{=}CH{-}(C{\equiv}C)_3{-}CH{=}CH{-}CHOH{-}CH_2OH$ *(85)*

$CH_3CH{=}CH{-}(C{\equiv}C)_4{-}CHOH{-}CH_2OH$ *(86)*

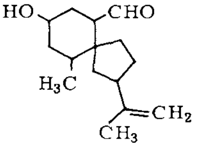
It has been observed that tissue fragments of the military orchis *(Orchis militaris)* form the phytoalexin *(87)* 36 h after infection, the maximum concentration occurring only 8 days later.


*(87)*

### 7.2. Phytoalexins—the Chemical Response to a Stimulus

Early on in phytoalexin research it was discovered that even cell-free extracts of sprouting conidia or of fungal cultures can trigger the formation of phytoalexins in tissue treated with them[138-140], but the isolation and demonstration of the biologically active eliciting substances in pure form presented major problems. To begin with it was only known that macromolecules are involved in the induction of phytoalexins. *Metlitskii et al.*[141] demonstrated that the maximum activity of an extract of sprouting zoospores of potato blight *P. infestans* in the formation of the phytoalexins *(81)* and of lubimin *(88)* in potato tissue is closely connected with a protein fraction.

In the context of the irritant and defense substances of higher plants, forming the subject of this review, it is important that phytoalexins are "stress compounds"[142] formed in response to many stimuli, *e.g.* cold[143] or UV light[144,145]. Even the toxic heavy metals are possible phytoalexin inductors[146-149], above all mercury and copper.


*(88)*

The response to an abiotic elicitor such as $CuCl_2$ is less specific[127], but it may be that we have yet to recognize the prevailing guiding principle, which may not be structural in nature at all but perhaps physiological, for plants react specifically in certain host-parasite combinations[127]. In the following section we shall see that this can also lead to a chemical selectivity of endogenously active defense substances.

## 8. Leaf Movement Factors as Endogenously Active Defense Substances of Sleeping and Sensitive Plants

In the discussion of the phenomenon that even purely physical stimuli induce the formation of phytoalexins we must admit that no corresponding selectively active biochemical mechanism has yet been discovered. It may well be that chemists dare not think heuristically and use a guide to trace back the route taken by nature in the evolution of the defense mechanisms mentioned at the beginning of this article. Thus, as a working hypothesis one could take membrane activity as the principle of endogenously acting "tamed defense poisons". Experimentally, these substances are indicated by a bioassay with the sensitive plant *Mimosa pudica* L., the prime example of plants exhibiting external movements in response to irritation.

### 8.1. Bioassay for Movement Factors

Wherever a movement factor is suspected, its aqueous extract is prepared and tests are performed on it as such or after separation into its components, making use of the rapid reactivity of *Mimosa pudica* L. (Fig. 17). This test is carried out in a climatic chamber with a leaf of *M. pudica* placed in a solution of the supposed active principles. The movement factors are drawn up and cause each pair of pinnules to fold up neatly one behind the other. For the evaluation of the amount of the movement factor it is important to remember that the correlation between the time of response and the concentration of the test solution is not linear but is better described by a hyperbola[151].

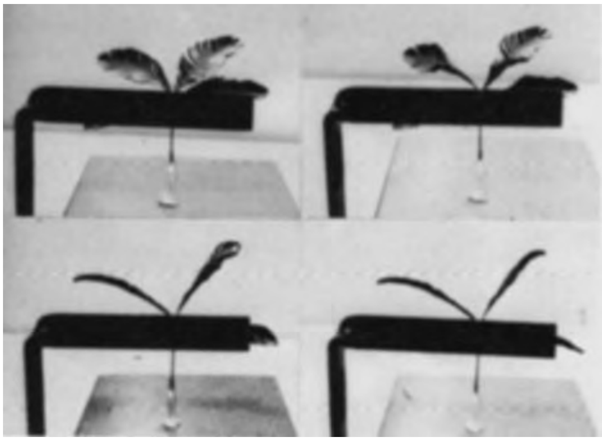


Fig. 17. Bioassay for the detection of leaf movement factors. The supposed active principle is placed in a small glass vase and is drawn up by the rachis of *M. pudica*. After a short time the plant reacts by folding up its pinnules [150].

Some very active and less active substances can be characterized by the Fitting-Hesse-Schildknecht test[150]. According to *Fitting*[152], they are very diverse in nature but always membrane-active; the cause of the visible movement is loss of semipermeability and thus ultimately a) a change in submicroscopic structures in the boundary plasma layers and b) the resulting intercellular escape of tissue sap from the vacuoles of the joints. Membrane processes of this kind are always associated with changes in electric potential, the cell becoming depolarized. An action potential is triggered, which is used in an electrophysiological test for the evaluation of an irritant. The visual test is better suited to the movements discussed here, because it yields detailed information on the nature of the chemonastic compounds[153].

### 8.2. Plants with Chemonastic and Nyctinastic Substances

The term "nastic movement" denotes a movement in plants which is determined anatomically and occurs independently of the direction of stimulation. When the stimulus is chemical, the movement is said to be chemonastic[5]. In certain insectivorous plants the bending movement is induced externally by certain substances, for example by proteins, ammonia, or phosphate, similarly to the case of a tactile stimulus. Stimulants can, however, also be formed and become active within the plant (endogenous chemonasty). An endogenous chemonastic action must be assumed above all for the compounds that give rise to sudden water movements in the vascular bundles in *M. Pudica* L., without the aid of physiological reactions, as the stimulus is conducted[154] even through dead cells and in dead stems and leaf fragments[5,155]. They are found everywhere in plants of the *Leguminosae* family, but especially when the green parts of the plants are extracted, which react seismonastically and nyctinastically, *i.e.* which perform a bending movement as a result of vibration impact, or a pull or periodically, dependent on the time of day[156,157]. The *Leguminosae* listed in Table 10 have been investigated preferentially[158-168], although plants from the *Oxalidaceae* family also exhibit nyctinasty (Fig. 18) and thus contain demonstrable leaf movement factors[169].

Fig. 18. Common yellow oxalis *(Oxalis stricta* L.) [169] in the early morning (left) and "sleeping" at 2 a.m. (right).

Table 10. Plants whose extracts are „active" in the bioassay [170].

| Plant | *t* [s] | Location |
|---|---|---|
| *Mimosa pudica* | 25 | Heidelberg |
| *Robinia pseudacacia* | 60 | Heidelberg |
| *Acacia karroo* | 30 | Heidelberg |
| *Acacia dealbata* | 40 | Southern France |
| *Acacia melanoxylon* | | Heidelberg |
| Phyllodes | 110 | |
| Pinnae | 50 | |
| *Albizzia lophanta* | 50 | Heidelberg |
| *Gleditsia triacanthos* | 60 | Heidelberg |
| *Delonix regia* | 50 | Teneriffe |
| *Glycine max.* | 120 | Heidelberg |

### 8.3. Leaf Movement Factors (LMF) of *Albizzia lophanta*[171]

The periodic leaf movements during the day—called sleep movements by *Linnaeus* and nyctinasty by *Pfeffer*—of *Albizzia lophanta* and *A. Julibrissin* are based on turgidity changes in the pulvini, cushionlike enlargements at the base of the petioles[172]. They are closely related to endogenous factors of the physiological clock[173], whose internal stimulation makes the pinnae fold up and thus screen the plant from external irritation. The challenge to the chemist is to discover the chemical basis of this fascinating physiological process (Fig. 19).

Fig. 19. *Albizzia lophanta* by night. Research plot at Hainsbachweg, Heidelberg (Germany).

Using high-pressure liquid chromatography *Hein*[165] isolated from a chemonastically active extract of *A. lophanta* a chemonastically active fraction having all the known properties of saponins. The fraction was so strongly hemolytic that for this reason alone a membrane-active substance could be suspected. The aglycone of this first LMF from an *Albizzia* species, called A-LMF 1, is according to a mass-spectrometric analysis most similar to the acacic acid lactone found in many African *Albizzias*. At least here the defense substances of the *Leguminosae* can be compared with the phytoalexins, which are after all often found among already known secondary plant constituents.

### 8.4. Leaf Movement Factors (LMF) of *Acacia karroo*

*Acacia karroo* is not sensitive, but it too folds up its pinnae at night, when it looks like a stimulated mimosa (Fig. 20).

Fig. 20. *Acacia karroo (Acacieae)*, photographed by day (left) and by night in the greenhouse of the Institute of Organic Chemistry, University of Heidelberg (Germany) [161].

For 10 years now it has been the object of many investigations on leaf movement factors, K-LMF, responsible for the nyctinasty illustrated in Figure 20[160, 161]. Probably the most important result, and one in many respects guiding further work, was that K-LMF 1 must be very similar to the LMF 1 of *Mimosa pudica*[160]. *Lang*[161] was then able to establish the identity of K-LMF 1 with M-LMF 1 by means of $^{13}$C-NMR spectroscopy (Fig. 21).

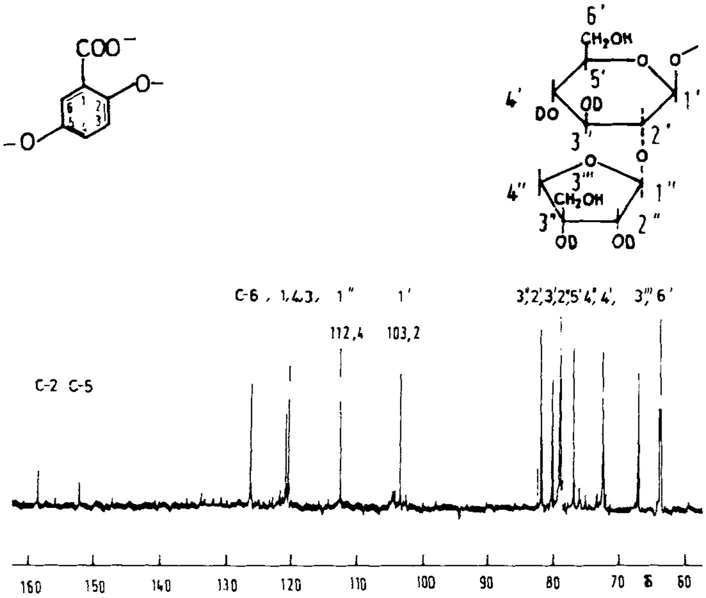
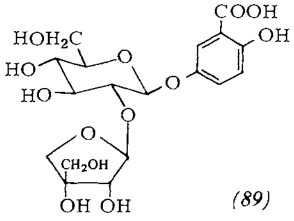


Fig. 21. 75.46 MHz $^{13}$C-NMR spectrum of K-LMF 1 in $D_2O$. Technique: Broadband decoupling. Reference signal: C-3 of gentisic acid maltoside [175] (after [189]).

According to this, the K-LMF 1 and M-LMF 1 from the chemonastically active fraction of *A. karroo* and *M. pudica* is the gentisic acid derivative *(89)*, the first factor to be isolated from the active mixture in pure form. It has already been found that for optimal activity still other glycosides of aromatic hydroxyacids must be present. For example, *Schumacher*[162] suspected a derivative of gallic acid, which may even be present as a sugar sulfate.



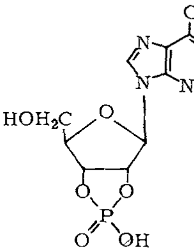
*(89)*

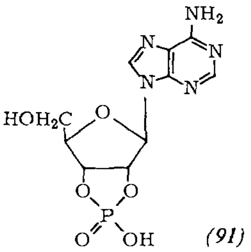
### 8.5. The Leaf Movement Factors of *Mimosa pudica* L. (M-LMF)

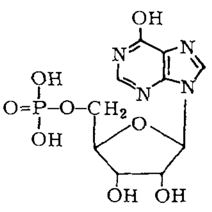
Sensitive plants were much discussed by philosophers even in the pre-Christian era, various theories being advanced to account for the rapid mimosa reaction. However, only recently were investigators courageous enough to see a clear defense reaction in the fact that at the slightest touch the pairs of pinnules fold together, first the pinnae and then the whole leaf pressing close to the stem, and the whole plant pressing itself to the ground like a hen threatened by a hawk (Fig. 22). We agree with *Hassenstein*[190] that this behavior represents a beautiful example of plant mimicry.

Fig. 22. Young plants of *M. pudica* in the greenhouse of the Institute of Organic Chemistry, University of Heidelberg (Germany); top: undisturbed; bottom: blown upon.

In 1916 *Ricca* first postulated that this fascinating behavior pattern, as *Darwin* had called it[1], must be due to a stimulant substance[176], which was subsequently characterized by *Fitting* (1936)[177], *Soltys et al.* (1936)[178, 179], and a little later by *Hesse*[180] as a hydroxycarboxylic acid with a molecular weight of between 350 and 450. This was confirmed by *Banarjee et al.*[181] in 1946. A reductone was still suspected in 1957[182]. The fact that the long sought leaf movement factor from *M. pudica* is the gentisic acid glucoapioside *(89)* was first fully recognized in 1978[185], and the last structure problems were solved by co-analytical investigation[161,162]. Already then there were some indications that M-LMF 1 cannot be the only cause of the movement mechanism. The scatter of the response times was greater than could be explained on statistical grounds. The active principle found is but one factor in a stimulation chain that definitely also comprises amino acids[183] and possibly even an inhibitor, D-pinitol[187]. In any event, it seemed appropriate to look for further members of this chain, and such were found in a highly enriched active principle fraction[184]. Of the maximum of five further components, one was obtained in the pure state by making use of solubility differences and with the aid of UV, IR, and $^1$H-NMR spectroscopy identified as 2′,3′-guanosine cyclomonophosphate *(90)*. Besides this M-LMF 2, an M-LMF 3 has also been identified, 2′,3′-adenosine cyclomonophosphate *(91)*, on the basis of its similar structure. Although *(90)* and *(91)* are inactive in pure form in the above-described bioassay, they are definitely also important components of the whole active principle complex. One could almost suppose that these LMF are stimulus-potentiating factors, just as the 6-hydroxypurine-5′-mononucleotide *(92)* was identified as a long-sought flavor potentiator[186].


*(90)*


*(91)*


*(92)*

This comparison is pertinent, if only because both processes are membrane-bound. However, the search must continue for the missing LMF, which include a gallic acid derivative with an as yet unknown structure, as in the case of *Acacia karroo.*

## 9. Epilogue

Anyone who has succeeded in finding his way through *Darwin*'s ideas will also have the courage to extend *Darwin*'s tendency to generalize[2] to the defense substances of higher plants, arriving ultimately at the concept of plant behavior. For according to the Darwinian principle of evolution, defense movements must also make use of defense chemicals, which were perhaps at first intended only for protection with glandular hairs. Whether indeed the defense substances are considered on their own, for example as gland secretions, or whether they are seen in the context of an endogenous defense mechanism, *e.g.* as phytoalexins or leaf movement factors, their function can be recognized only in terms of a struggle of the higher plants for existence.

Such trains of thought are supported by considerations on the coevolution of plant enemies, which not only have a resistance towards plant defense substances but even use the latter for their own defense. A specialist of this sort is, *e.g.*, the larva of the ichneumonidae *Neodiprion sertifer*, which, in a coevolutionary sense, does not only not respect the terpenoid defense substances of pine trees but even makes use of them as a defense substance for itself.

In explaining the numerous possibilities of the defense of higher plants against actual and potential parasites a natural scientist does not look for a generalizing model but rather attempts to link together the many findings. For a natural products chemist this approach forms a sound basis for the discovery of new active principles.

*I wish to express my sincere thanks to numerous colleagues, both past and present, who have contributed so much to the work cited in this paper and to the development of this area of chemistry. I thank Herr W. Schmitt for his help with the horticultural work, Herr H. Spiess for taking the photographs, and Frau G. Büchler for typing the manuscript. Many of the investigations mentioned here would not have been possible without generous support by BASF AG and especially by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.*

Received: January 7, 1981 [A 352 IE]
German version: Angew. Chem. *93*, 164 (1981)
Translated by AD-EX Translations Ltd., London

---

[1] *Ch. Darwin:* The Power of Movement in Plants. 1st Edit. John Murray, London 1880. Translation: *Ch. Darwins* collected works. Vol. 13: Das Bewegungsvermögen der Pflanzen. E. Schweizerbart'sche Verlagsbuchhandlung (E. Koch), Stuttgart 1881.
[2] *Darwin, Charles,* Autobiographie. Edited by *S. L. Sobol.* Urania-Verlag, Leipzig 1959.
[3] *W. Pfeffer:* Pflanzenphysiologie. 1st Edit. Verlag von Wilhelm Engelmann, Leipzig 1880.
[4] As [3], 2nd Edit., Leipzig 1897, Vol. I, p. 19.
[5] As [3], 2nd Edit., Leipzig 1897, Vol. II, p. 462.
[6] *M. Lindauer:* Die Biologische Uhr. Franz Steiner Verlag, Wiesbaden 1980.
[7] *E. F. Gorup Besanez,* J. Prakt. Chem. *48*, 191 (1849).
[8] *E. Bergmann,* Bot. Z. *39*, 730 (1882).
[9] *G. Haberlandt,* Sitzungsber. Akad. Wien *93*, 122 (1886).
[10] *F. Flury,* Dtsch. Pharm. Ges. *24*, 650 (1919).
[11] *A. Nestler,* Ber. Dtsch. Bot. Ges. *43*, 497 (1925).
[12] *N. Emmelin, W. Feldberg,* J. Physiol. *106*, 440 (1947).
[13] *H. O. Collier, G. G. Chesher,* Brit. J. Pharmacol. *11*, 186 (1956).
[14] *I. Bayer,* Diplomarbeit, Universität Erlangen-Nürnberg 1960.
[15] *M. Vialli,* Acta Histochem. *45*, 270 (1973).
[16] *R. Burk,* Dissertation, Universität Heidelberg 1978.
[17] *E. L. Thurston, N. R. Lersten,* Bot. Rev. *1969*, 393.
[18] *D. J. Jenden, I. Hantin, S. J. Lamb,* Anal. Biochem. *1968*, 125.
[19] *N. Seiler, H. Schneider, K. D. Sonnenberg,* Z. Anal. Chem. *252*, 127 (1970).
[20] *R. Burk,* Diplomarbeit, Universität Heidelberg 1976.
[21] *J. J. Franken, M. M. F. Trijbels,* J. Chromatogr. *91*, 425 (1974).
[22] *P. A. Robertson, W. V. MacFarlane,* Aust. J. Exp. Biol. Med. Sci. *35*, 381 (1957).
[23] *G. Edelmann,* Dissertation, Universität Heidelberg 1968.
[24] *M. Guggenheim:* Die Biogenen Amine. 4th Edit. S. Karger, Basel 1951.
[25] *G. Habermehl:* Gift-Tiere und ihre Waffen. Springer, Berlin 1976.
[26] *B. Klein,* Dissertation, Universität Heidelberg 1981.
[27] *A. Nestler:* Hautreizende Primeln. Gebr. Bornträger, Berlin 1904.
[28] *B. Bloch, P. Karrer,* Vierteljahresschr. Naturforsch. Ges. Zürich *72*, 1. Beibl. (1927).
[29] *H. Schildknecht, I. Bayer, H. Schmidt,* Z. Naturforsch. *B 22*, 36 (1967).
[30] *N. Hjorth, S. Fregert, H. Schildknecht,* Acta Derm. Venereol. *49*, 552 (1969).

[31] *H. Baer, R. Watkins, P. Kurtz, J. Byck, C. Dawson,* J. Immunol. *99,* 370 (1967).

[32] *H. Schmidt,* Dissertation, Universität Heidelberg 1965.

[33] *A. Nestler,* Ber. Dtsch. Bot. Ges. *30,* 330 (1912).

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

[35] *H. Schildknecht, K. H. Weis,* Z. Naturforsch. *B 15,* 755 (1960).

[36] *H. Schildknecht, K. H. Weis,* Z. Naturforsch. *B 16,* 810 (1961).

[37] *M. Barbier:* Introduction à l'écologie chimique. Masson, Paris 1976.

[38] *H. Schildknecht,* Endeavour *30,* 136 (1971).

[39] *H. Remmert:* Ökologie. 2. Aufl. Springer, Berlin 1980.

[40] *P. A. Matthioli:* Kreuterbuch. Gedruckt zu Frankfurt am Mayn, MDC.

[41] *J. F. Gmelin:* Allgemeine Geschichte der Pflanzengifte. 2nd Edit., in der Raspeschen Buchhandlung, Nürnberg 1803.

[42] *O. Gessner:* Die Gift und Arzneipflanzen von Mitteleuropa. Carl Winter, Universitätsverlag, Heidelberg 1953.

[43] *A. Oken:* Allgemeine Naturgeschichte für alle Stände. 3rd Vol. Botanik. Hofmann Verlag, Stuttgart 1842, p. 1496.

[44] *L. Lewin:* Gifte und Vergiftungen. 5th Edit. of Lehrbuch der Toxikologie. Haug, Ulm 1962 (reprint).

[45] *F. Lartigue,* S. Trommsdorffs J. *18* (1811).

[46] *G. Zwenger,* Justus Liebigs Ann. Chem. *115,* 1 (1860).

[47] *W. Casselmann,* Neues Jahrb. Pharm. *23,* 302 (1870).

[48] *E. Stünkel,* Ber. Dtsch. Chem. Ges. *12,* 102 (1879).

[49] *R. Tschesche, U. Schacht, G. Legler,* Justus Liebigs Ann. Chem. *662,* 113 (1963); Naturwissenschaften *50,* 521 (1963).

[50] *G. Edelmann,* Dissertation, Universität Heidelberg 1968.

[51] *E. Hecker, R. Schmidt,* Fortschr. Chem. Org. Naturst. *31,* 377 (1974).

[52] *H. Schildknecht, G. Edelmann, R. Maurer,* Chem.-Ztg. *94,* 347 (1970).

[53] *E. Hecker,* Z. Krebsforsch. *65,* 325 (1963).

[54] *E. Hecker,* Planta Med., Suppl. 1968, 24.

[55] *H. Schildknecht, R. Maurer,* Chem.-Ztg. *94,* 849 (1970).

[56] *G. H. Stout, W. G. Balkenhol, M. Poling, G. L. Hickernell,* J. Am. Chem. Soc. *92,* 1070 (1970).

[57] *A. Ronlan, B. Wickberg,* Tetrahedron Lett. *1970,* 4261.

[58] *P. Fournier:* Le livre des plantes medicinales et veneneuses de France. Vol. III. Verlag Paul Lechevalier, Paris 1948.

[59] *M. R. I. Saleh, D. Y. Haddad, T. M. Warg,* J. Pharm. Sci. UAR *4,* 49 (1963).

[60] *C. R. Metcalfe, L. Chalk:* Anatomy of the Dicotyledons. Vol. I, II. Clarendon Press, Oxford 1957, p. 285, p. 1169.

[61] *V. Reimann-Dubbers,* Dissertation, Universität Heidelberg 1974.

[62] *E. Hegi:* Illustrierte Flora von Mitteleuropa, Vol. V/2. J. F. Lehmanns Verlag, München 1965.

[63] *U. Gehlhaus-Klamant,* Dissertation, Universität Heidelberg 1975.

[64] *S. M. Kupchan, J. G. Sweeny, R. L. Baxter, T. Murae, V. A. Zimmerly, B. R. Sickles,* J. Am. Chem. Soc. *97,* 672 (1975).

[65] Lehrbuch der Botanik, by *E. Strasburger, F. Noll, H. Schenck, A. F. W. Schimper,* 31st Edit. revised by *D. von Denffer, F. Ehrendorfer, K. Mägdefrau, H. Ziegler.* Gustav-Fischer-Verlag, Stuttgart 1978, p. 808.

[66] *H. Moeller:* Kanarische Pflanzenwelt. Fred Kolbe, Puerto de la Cruz, Tenerife. 1978.

[67] *W. Hoppe, F. Brandl, I. Strell, M. Röhrl, I. Gassmann, E. Hecker, H. Bartsch, G. Kreibich, Ch. von Szczepanski,* Angew. Chem. *79,* 824 (1967); Angew. Chem. Int. Ed. Engl. *6,* 809 (1967).

[68] *E. Hecker, H. Ott,* Experientia *37,* 88 (1981).

[69] *K.-H. Scharf:* Pflanzen und Tiere schützen sich vor Feinden. Maier, Ravensburg 1977.

[70] *H. W. Schmale, B. M. Hausen,* Tetrahedron Lett. *21,* 149 (1980).

[71] *K. Nakanishi,* Pontif. Accad. Sci. Scr. Varia *41,* 185 (1976).

[72] *I. Wubo, K. Y. Lee, M. Pettei, F. Pilkiewicz, K. Nakanishi,* J. Chem. Soc. Chem. Commun *1976,* 1013.

[73] *W. S. Bowers,* Pontif. Accad. Sci. Scr. Varia *41,* 129 (1976).

[74] *K. Kawazu, S. Nakjima, M. Aliza,* Experientia *35,* 1294 (1979).

[75] *M. Elliot, N. F. Janes,* Chem. Soc. Rev. *7,* 473 (1978).

[76] *B. P. Tokin:* Phytonzide. VEB Verlag Volk und Gesundheit, Berlin 1956.

[77] *A. Gurwitsch, S. Grabje, S. Salkind,* Arch. Entwicklungsmech., Org. *100,* 11 (1923).

[78] *H. Schildknecht, G. Rauch,* Z. Naturforsch. *B 16,* 301 (1961).

[79] *G. Sann,* Diplomarbeit, Universität Heidelberg 1978.

[80] *B. Kolb:* Applied Headspace Gaschromatography. Heyden, London 1980.

[81] *H. Schildknecht, A. Mannl,* Angew. Chem. *69,* 634 (1957).

[82] *H. Schildknecht, G. Rauch, F. Schlegelmilch,* Chem.-Ztg.-Chem. Appar. *83,* 549 (1959).

[83] *A. Rapp, W. Knipser,* Chromatographia *13,* 698 (1980).

[84] *R. Paris* in *T. Swain:* Chemical Plant Taxonomy. Academic Press, London 1963, p. 337.

[85] *H. Schildknecht, U. Maschwitz, D. Krauss,* Naturwissenschaften *55,* 230 (1968).

[86] *H. E. Eisner, D. Alsop, T. Eisner,* Psyche *74,* 107 (1967).

[87] *H. Schildknecht, G. Rauch,* Z. Naturforsch. *B 16,* 422 (1961).

[88] *H. Schildknecht,* Angew. Chem. *75,* 762 (1963); Angew. Chem. Int. Ed. Engl. *3,* 73 (1964).

[89] *F. Waterhouse, D. A. Forss, R. H. Hackmann,* J. Insect Physiol. *6,* 113 (1961).

[90] *F. Elstner,* Biol. Unserer Zeit *8,* 82 (1978).

[91] *F. Drawert, W. Heimann, R. Emberger, R. Tressl,* Justus Liebigs Ann. Chem. *694,* 200 (1966).

[92] *D. Gross,* Fortschr. Chem. Org. Naturst. *34,* 187 (1977).

[93] *A. Stoessl,* Recent Adv. Phytochem. *3,* 143 (1970).

[94] *H. Müller:* Die Befruchtung der Blumen durch Insekten und die gegenseitige Anpassung beider. Leipzig 1873.

[95] *H. Müller:* Die Alpenblumen, ihre Befruchtung durch Insekten und ihre Anpassung an dieselben. Leipzig 1881.

[96] *H. Kugler:* Blütenökologie. Gustav-Fischer-Verlag, Stuttgart 1970.

[97] *A. Rapp, W. Knipser, L. Engel, H. Ullemeyer, W. Heimann,* Vitis *19,* 13 (1980).

[98] *A. I. Virtanen,* Angew. Chem. *74,* 374 (1962); Angew. Chem. Int. Ed. Engl. *2,* 299 (1962).

[99] *H. Schildknecht, G. Rauch,* Z. Naturforsch. *B 17,* 800 (1962).

[100] *A. G. Winter, M. Hornbostel,* Naturwissenschaften *40,* 489 (1953).

[101] *H. Molisch:* Der Einfluß einer Pflanze auf die andere, Allelopathie. Fischer, Jena 1937.

[102] *C. H. Muller,* Vegetatio *18,* 348 (1969).

[103] *C. H. Muller,* Recent Adv. Phytochem. *3,* 105 (1970).

[104] *C. H. Muller* in *K. L. Chambers:* Biochemical Coevolution. Oregon State University Press, Corvallis, Oregon 1970.

[105] *Ch. J. Soderquist,* J. Chem. Educ. *50,* 782 (1973).

[106] *C. Daglish,* Biochem. J. *47,* 452 (1950).

[107] *K. C. Lee, R. W. Campbell,* Hortscience *4,* 297 (1969).

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

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

[110] *R. H. Whitaker, P. P. Feeny,* Science *17,* 757 (1971).

[111] *C. H. Muller, C. H. Chou* in *J. B. Harborne:* Phytochemical Ecology. Academic Press, London 1972.

[112] *J. K. McPherson, C. H. Chou, C. H. Muller,* Phytochemistry *10,* 2925 (1971).

[113] *A. Ballester, J. M. Albo, E. Vieitez,* Oecologia (Berlin) *30,* 55 (1977).

[114] *W. Treibs,* Chem. Ber. *80,* 97 (1947).

[115] *H. Nikolai,* Diplomarbeit, Universität Heidelberg 1979.

[116] *A. S. Abdul-Wahab, E. L. Rice,* Bull. Torrey Bot. Club *94,* 486 (1967).

[117] *G. H. Towers, A. G. McInnes, A. C. Neish,* Tetrahedron *20,* 71 (1964).

[118] *B. Tauscher, D. Schiller,* unpublished.

[119] *S. D. Seigler,* Phytochemistry *14,* 9 (1975).

[120] *A. E. Gilmore,* Proc. Am. Soc. Hortic. Sci. *73,* 99 (1959).

[121] *H. Schildknecht, F. Straub, V. Scheidel,* Justus Liebigs Ann. Chem. *1976,* 1295.

[122] *A. Raymakers, F. Compernolle,* Phytochemistry *12,* 2287 (1973).

[123] *H. Pfaff,* Diplomarbeit, Universität Heidelberg 1980.

[124] *I. A. M. Cruickshank,* Pontif. Accad. Sci. Scr. Varia *41,* 509 (1977).

[125] *D. Gross,* Fortschr. Chem. Org. Naturst. *34,* 187 (1977).

[126] *J. A. Kuc* in *R. Heitefuss, P. H. Williams:* Encyclopedia of Plant Physiology, New Series, Vol. 4. Springer, Berlin 1976, p. 632.

[127] *H. Grisebach, J. Ebel,* Angew. Chem. *90,* 668 (1978); Angew. Chem. Int. Ed. Engl. *17,* 635 (1978).

[128] *H. M. Ward,* Ann. Bot. (London) *19,* 1 (1905).

[129] *N. Bernard,* Ann. Sci. Nat. Bot. Biol. Veg. *14,* 221 (1911).

[130] *K. O. Müller, H. Börger,* Arb. Biol. Reichsanst. Land- Forstwirtsch. Berlin-Dahlem *23,* 189 (1940).

[131] *I. A. M. Cruickshank,* Aust. J. Biol. Sci. *15,* 147 (1962).

[132] *K. Tomyama, T. Sakuma, N. Ishizaka, N. Sato, N. Katsui, M. Tagasuki, T. Masamune,* Phytopathology *58,* 115 (1960).

[133] *T. Akazawa,* Arch. Biochem. Biophys. *90,* 82 (1960).

[134] *S. Hess, L. Hadwiger, M. Schwochau,* Phytopathology *61,* 79 (1971).

[135] *A. Stoessl, C. Unwin, W. Ward,* Phytopathol. Z. *74,* 141 (1972).

[136] *A. Stoessl, C. Unwin, W. Ward,* Phytopathology *63,* 1225 (1973).

[137] *M. Gordon, A. Stoessl, J. Stothers,* Can. J. Chem. *51,* 748 (1973).

[138] *J. A. Bailey, G. A. Carter, R. A. Skipp,* Physiol. Plant. Pathol. *8,* 189 (1976).

[139] *J. Nüesch,* Symp. Soc. Gen. Microbiol. *13,* 335 (1963).

[140] *K. Uehara,* Nippon Shokubutsu Byori Gakkaiho (Ann. Phytopath. Soc. Jpn.) *24,* 224 (1959).

[141] *L. V. Metlitskii, T. D'Yakov Yu, O. L. Ozeretskovskaya, L. A. Yurganova, L. I. Chalvov, N. I. Vasyukova,* Izv. Akad. Nauk SSSR Ser. Biol. *3,* 399 (1971).

[142] *A. Stoessl, J. B. Stothers, E. W. B. Ward,* Phytochemistry *15,* 855 (1976).

[143] *J. E. Rahe, R. M. Arnold,* Can. J. Bot. *53,* 921 (1975).

[144] *M. A. Bridge, W. L. Klarman,* Phytopathology *63,* 606 (1973).

[145] *L. A. Hadwiger, M. E. Schwochau,* Plant Physiol. *47,* 588 (1971).

[146] *I. A. M. Cruickshank, D. R. Perrin,* Aust. J. Biol. Sci. *16,* 111 (1963).

[147] *W. G. Rathmell, D. S. Bendall,* Physiol. Plant. Pathol. *1,* 351 (1971).

[148] *W. L. Klarman, J. B. Sanford,* Life Sci. *7,* 1095 (1968).

[149] *M. E. Schwochau, L. A. Hadwiger,* Arch. Biochem. Biophys. *126,* 731 (1968).

[150] *H. Schildknecht,* Nachr. Chem. Tech. Lab. *26,* 283 (1978).

[151] *T. Sibaoka,* Sc. Rep. Tohoku Univ. Ser. 4 (Biol.) *20,* 72 (1953).

[152] *H. Fitting,* Jahrb. Wiss. Bot. *39,* 424 (1930).

[153] *H. Schildknecht:* Über die Chemie der Sinnpflanze Mimosa pudica L. Springer, Berlin 1978.
[154] *M. H. Dutrochet:* Mémoir. p. servir à l'histoire d. végétaux. Brüssel 1837.
[155] *G. Haberlandt:* Das reizleitende Gewebesystem der Sinnpflanze. Verlag Wilhelm Engelmann, Leipzig 1890.
[156] *W. Haupt:* Bewegungsphysiologie der Pflanzen. Thieme, Stuttgart 1977.
[157] *F. Jakob:* Bewegungsphysiologie der Pflanzen. Akademie-Verlag, Berlin 1966.
[158] *B. Tauscher,* Dissertation, Universität Heidelberg 1975.
[159] *F. Moeschler,* Dissertation, Universität Heidelberg 1979.
[160] *J. Edelmann,* Dissertation, Universität Heidelberg 1978.
[161] *F. Lang,* Dissertation, Universität Heidelberg 1980.
[162] *K. Schumacher,* Diplomarbeit, Universität Heidelberg 1980.
[163] *G. Koch,* Diplomarbeit, Universität Heidelberg 1980.
[164] *F. Mayer,* Diplomarbeit, Universität Heidelberg 1980.
[165] *M. Hein,* Diplomarbeit, Universität Heidelberg 1980.
[166] *P. Fischer,* Diplomarbeit, Universität Heidelberg 1978.
[167] *G. M. Kresbach,* Diplomarbeit, Universität Heidelberg 1981.
[168] *Th. Markert,* Diplomarbeit, Universität Heidelberg 1981.
[169] *R. Söllner,* Diplomarbeit, Universität Heidelberg 1980.
[170] *M. Weber, I. Püschel, B. Schmich,* unpublished.
[171] We thank Prof. *Mondon* for supplying us with seeds of *A. lophanta.*
[172] *R. L. Satter* in *W. Haupt, M. E. Feinleib:* Physiology of Movements. Springer, Berlin 1979, p. 442.
[173] *E. Bünning:* Die physiologische Uhr. Springer, Berlin 1977.
[174] *E. Bünning, I. Moser,* Proc. Natl. Acad. Sci. USA *62,* 1018 (1969).
[175] *U. Stollenwerk,* Diplomarbeit, Universität Heidelberg 1977.
[176] *U. Ricca,* Nuovo G. Bot. Ital. (Nuova Seria) *23,* 51 (1916).
[177] *H. Fitting,* Jahrb. Wiss. Bot. *83,* 270 (1936).
[178] *A. Soltys, K. Umrath,* Biochem. Z. *284,* 247 (1936).
[179] *A. Soltys, K. Umrath, Ch. Umrath,* Protoplasma *31,* 454 (1938).
[180] *G. Hesse,* Biochem. Z. *303,* 152 (1957).
[181] *B. Banerjee, G. Bhattacharya, D. M. Bose,* Trans. Bose Res. Inst. Calcutta *16,* 155 (1944–1946).
[182] *G. Hesse, B. Banerjee, H. Schildknecht,* Experientia *13,* 13 (1957).
[183] *H. Schildknecht, B. Tauscher, M. Pesh-Imam, W. Beltle, P. Kunzelmann, D. Schneider,* Naturwissenschaften *65,* 125 (1978).
[184] *G. Esswein,* Dissertation, Universität Heidelberg 1981.
[185] *H. Schildknecht, B. Tauscher, H. Moeschler, J. Edelmann* in Symposium Papers, Half-Hour Plenary Lectures, 11. Int. Symp. Chem. Natural Products, Papers. Vol. 4, Part 1. Bulgarian Academy of Science, Sofia 1978, p. 97.
[186] *T. A. Rohan* in *J. B. Harborne:* Phytochemical Ecology. Academic Press, London 1972.
[187] *H. Schildknecht, D. S. P. Iyengar,* Naturwissenschaften *62,* 533 (1975).
[188] *B. Moser,* Dissertation, Universität Heidelberg 1971.
[189] *P. Kunzelmann,* unpublished.
[190] *B. Hassenstein,* private communication 1978.
[191] Investigated using the Cambridge S4/10 Scanning Electron Microscope with an Ortec X-ray spectrometer system *(M. Gaster,* Sedimentforschungsinstitut der Universität Heidelberg).

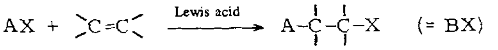
# COMMUNICATIONS

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

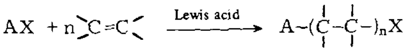
## Lewis Acid Catalyzed Alkylations of CC-Multiple Bonds; Rules for Selective Enlargements of Carbon Skeletons[**]

By *Herbert Mayr*[*]

Lewis acid catalyzed addition reactions of alkyl halides to olefins (eq. I) are usually not considered for CC—bond formations[1a,b], since reactions of this type frequently do not terminate at the 1:1-stage but provide polymeric products (eq. II).



$$\mathrm{AX} + \mathrm{>C{=}C<} \xrightarrow{\text{Lewis acid}} \mathrm{A{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}X} \quad (=\mathrm{BX}) \qquad (\mathrm{I})$$



$$\mathrm{AX} + n\,\mathrm{>C{=}C<} \xrightarrow{\text{Lewis acid}} \mathrm{A{-}(\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-})_nX} \qquad (\mathrm{II})$$

In this communication a simple rule is presented, which demonstrates that with definite pairs of olefins and alkyl halides the selective formation of 1:1-products can be achieved.

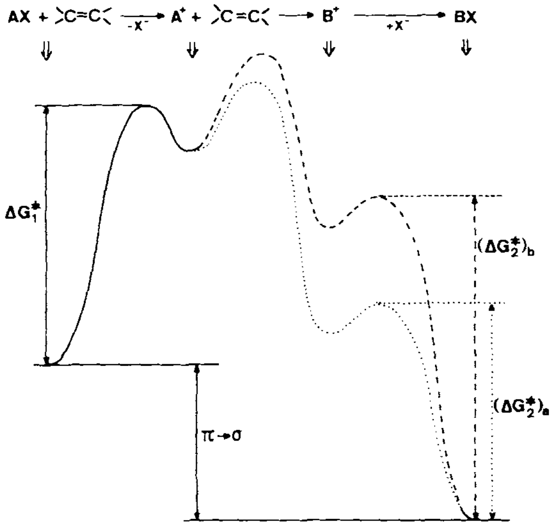


Fig. 1. Energy profile of the addition of an alkyl halide AX to olefins. Case a) (·····): $\Delta G^{\dagger} > \Delta G^{\ddagger}_2$; case (b) (– – – –): $\Delta G^{\dagger} < \Delta G^{\ddagger}_2$ (see text).

In Figure 1 the overall reaction is split into three independent steps: 1) dissociation of AX and formation of carbenium ion $A^+$; 2) addition of $A^+$ to the CC-multiple bond, and formation of the new carbenium ion $B^+$; 3) ion combination. Two cases for different magnitudes of $\Delta G^{\dagger}$ and $\Delta G^{\ddagger}_2$ are treated in Figure 1:

a) A carbenium ion $B^+$, which is more stabilized than $A^+$, forms in the addition step *i.e.* $(\Delta G^{\ddagger}_2)_a < \Delta G^{\dagger}$[2] (dotted line). After a small degree of conversion AX, BX and unreacted olefins are present in the reaction mixture. Since $(\Delta G^{\ddagger}_2)_a < \Delta G^{\dagger}$, BX is ionized more rapidly by the Lewis

---

[*] Dr. H. Mayr
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

acid than AX, and $B^+$ reacts with further olefin. This process is repeated; the olefin polymerizes whereas AX does not react further. b) Now, carbenium ion $B^+$ is less stable than $A^+$, *i.e.* $(\Delta G^{\ddagger}_{2}) > \Delta G^{\ddagger}_{1}$[2]. Figure 1 (broken line) shows that the addition step may also be exothermic in this case, since energy is gained from the conversion of a $\pi$-into a $\sigma$-bond[3]. Now AX dissociates faster than BX and adds to the olefin while the concentration of BX increases.

From these considerations it is concluded that *Lewis acid catalyzed additions of alkyl halides to CC-multiple bonds can only lead to 1:1-products if the educts dissociate more rapidly than the products. In other words, polymerization can only be inhibited if the initial carbenium ion $A^+$ is better stabilized than $B^+$*. Of course formation of BX is also impossible, if $B^+$ is a highly unstable intermediate; the condition $\Delta G^{\ddagger}_{1} < \Delta G^{\ddagger}_{2}$ therefore is a necessary but not a sufficient criterion for formation of 1:1-addition products.

These conclusions are based on the assumption that the rates of addition reactions are roughly proportional to the dissociation rates of the corresponding alkyl halides. This condition is fulfilled in the absence of large steric effects, since $\Delta G^{\ddagger}$ for the addition reactions of carbenium ions $A^+_1, A^+_2, \ldots A^+_n$ to a standard olefin decreases with increasing stability of $A^+_n$ (Leffler-Hammond postulate[4]).

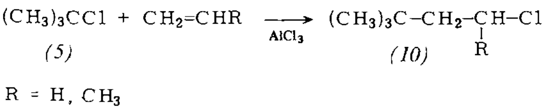
Since most information about carbenium ion stability comes from solvolysis studies, we used the solvolysis constants determined in 80% ethanol (Table 1) for the approximate determination of the relative magnitudes of $\Delta G^{\ddagger}_{1}$ and $\Delta G^{\ddagger}_{2}$. Although this procedure is certainly subject to error, the following examples show that the data are transferable. The formation of 1:1-adducts, as shown in eq. I, is only observed if the structural type of the product BX is located above that of educt AX in Table 1.

Table 1. Solvolysis constants of alkyl chlorides in 80% aqueous ethanol at 25 °C.

| | RX | $10^6 k_1$ [$s^{-1}$] | Lit. |
|---|---|---|---|
| *(1)* | $CH_2{=}CPhCl$ | $\approx 10^{-10}$ | [a] |
| *(2)* | $(CH_3)_2CHCl$ | $2 \times 10^{-3}$ | [5a] |
| *(3)* | $CH_2{=}CH{-}CH(CH_3)Cl$ | $5 \times 10^{-1}$ | [5b] |
| *(4)* | $CH_3{-}CH{=}CH{-}CH_2Cl$ | $\approx$ 1 | [b] |
| *(5)* | $(CH_3)_3CCl$ | 9 | [5b, c] |
| *(6)* | $C_6H_5{-}CH(CH_3)Cl$ | $1 \times 10^{1}$ | [5d] |
| *(7)* | $(CH_3)_2C{=}CH{-}CH_2Cl$ | $\approx 4 \times 10^{2}$ | [b] |
| *(8)* | $(C_6H_5)_2CHCl$ | $2 \times 10^{3}$ | [5b] |
| *(9)* | $CH_3O{-}CH_2Cl$ | $\approx 1.5 \times 10^{7}$ | [5e] |

[a] Estimated from the activation parameters of the solvolysis of α-bromostyrene [5f]. [b] Calculated from $k_1$ [3] and the reaction rate ratio at 44.6 °C in 80% ethanol, which was obtained from the data in [5g] using the Winstein-Grunwald relationship [5b, c].

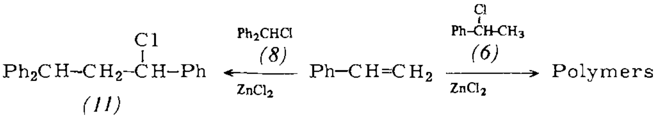
*Examples: Schmerling* reported the predominant formation of the 1:1-product *(10)* in the aluminum chloride catalyzed reaction of *tert*-butyl chloride *(5)* with ethene and propene[6]; in both cases slowly ionizing alkyl halides (primary and secondary respectively) are formed from the more reactive substrate *(5)*. Additions to *iso*-butene were not reported.



$$\underset{(5)}{(CH_3)_3CCl} + CH_2{=}CHR \xrightarrow[AlCl_3]{} \underset{(10)}{(CH_3)_3C{-}CH_2{-}\underset{R}{\underset{|}{C}}H{-}Cl}$$

R = H, $CH_3$

While the zinc chloride catalyzed addition of benzhydryl chloride *(8)* to styrene resulted in a 54% yield of the addition product *(11)*[7], the reaction of 1-phenylethyl chloride *(6)* and styrene only produced polymeric material under the same reaction conditions. In the first case the reaction terminates at the 1:1-product stage since the rapidly dissociating alkyl halide *(8)* yields *(11)*, a product of type *(6)*, which dissociates more slowly than *(8)* (Table 1). In the second case both educt and product are of the same structural type.



$$\underset{(11)}{Ph_2CH{-}CH_2{-}\overset{Cl}{\overset{|}{C}}H{-}Ph} \xleftarrow[ZnCl_2]{\underset{(8)}{Ph_2CHCl}} Ph{-}CH{=}CH_2 \xrightarrow[ZnCl_2]{\underset{(6)}{Ph{-}\overset{Cl}{\overset{|}{C}}H{-}CH_3}} \text{Polymers}$$

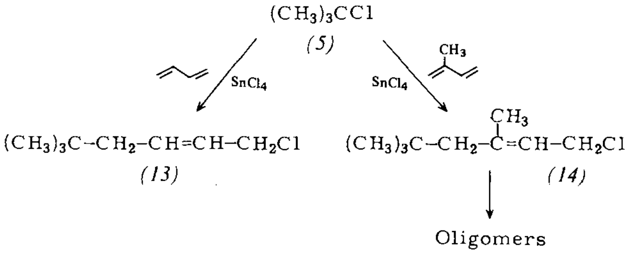
The high yields of 1:1-products observed in the Lewis acid catalyzed additions of RX to alkynes[8] can also be attributed to the slow solvolysis rates of vinyl halides.

$$R^1{-}Cl + R^2{-}C{\equiv}C{-}R^3 \xrightarrow{ZnCl_2} R^1R^2C{=}CR^3Cl$$

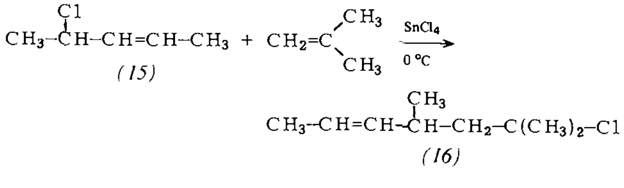
$$(E)\text{-}(12) + (Z)\text{-}(12)$$

$R^1$ = $t$Bu, $PhCH_2$, $Ph_2CH$; $R^2$ = H, Alkyl; $R^3$ = Alkyl, Aryl

The $SnCl_4$ catalyzed reaction of *tert*-butyl chloride with butadiene yields the allyl chloride *(13)*[9]; in contrast only oligomers resulted when *(5)* was reacted with isoprene. *Petrov* and *Leets* accounted for the latter observation, suggesting that isoprene reacted more rapidly with *(14)* than with *(5)*; Table 1 permits a quantitative explanation. Compound *(4)*, the model for *(13)*, dissociates more slowly, whereas *(7)*, the model for *(14)*, dissociates faster than *(5)*.

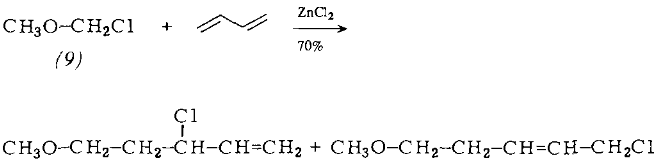


Consequently, the dialkylallyl chloride *(15)*, with a similar solvolysis constant to *(7)*[5g, 10] gives the 1:1-product *(1b)* with *iso*-butene[11].



$$\underset{(15)}{CH_3{-}\overset{Cl}{\overset{|}{C}}H{-}CH{=}CH{-}CH_3} + CH_2{=}C(CH_3)_2 \xrightarrow[0\,^\circ C]{SnCl_4} \underset{(16)}{CH_3{-}CH{=}CH{-}\overset{CH_3}{\overset{|}{C}}H{-}CH_2{-}C(CH_3)_2{-}Cl}$$

In the presence of $ZnCl_2$ or $HgCl_2$, chlorodimethylether *(9)* can be added to a series of olefins *e.g. iso*-butene, 2-methyl-2-butene, 1,3-butadiene and 1,3-cyclohexadiene[12]. Again, the high dissociation rate of the educt *(9)* (Table 1) accounts for the exclusive formation of 1:1-products. According to a qualitative analysis, the synthetically important



Lewis acid catalyzed additions of acetals and ketals to enol ethers[1c], as well as the ionic additions of haloalkanes to haloalkenes. (Prins reaction)[1a] are also in agreement with this rule. The lack of appropriate solvolysis data precludes a quantitative treatment however.

*Scope and limitations.* This rule has been deduced for addition reactions in which low equilibrium concentrations of carbenium ions are involved. Therefore it cannot be applied if educts and products are markedly ionized under reaction conditions, or if generation and trapping of carbenium ions are irreversible processes, a situation which is encountered in cationic additions initiated by silver trifluoroacetate[13]. Furthermore, this rule is not applicable to substitution reactions in which the addition step is followed by rapid elimination; electrophilic aromatic substitutions and the reactions of siloxyalkenes with alkyl- and acyl halides fall into this category[14]. The influence of steric effects is currently being investigated.

Received: May 14, supplemented October 2 1980 [Z 683 IE]
German version: Angew. Chem. *93*, 202 (1981)

CAS Registry numbers:
*(1)*, 618-34-8; *(2)*, 75-29-6; *(3)*, 563-52-0; *(4)*, 591-97-9; *(5)*, 507-20-0; *(6)*, 672-65-1; *(7)*, 503-60-6; *(8)*, 90-99-3; *(9)*, 107-30-2; *(10)*, (R=H) 2855-08-5; *(10)*, (R=CH₃) 33429-72-0; *(11)*, 70550-48-0; *(13)*, 1871-70-1; *(14)*, 76358-37-7; *(15)*, 1458-99-7; *(16)*, 76358-38-8; *(17)*, 35707-80-3; *(18)*, 3577-82-0; ethene 74-85-1; propene 115-07-1; styrene 100-42-5; butadiene 106-99-0; isoprene 78-79-5; isobutene 115-11-7; 2-methyl-2-butene 513-35-9; (1-chloroethyl)benzene, styrene polymers 76358-36-6

---

[1] a) *L. Schmerling* in G. A. Olah: Friedel-Crafts and Related Reactions, Vol. II, Chapt. 26. Interscience, New York 1963; b) *J. Mathieu, J. Weill-Raynal:* Formation of C—C-Bonds. Vol. I—III, Thieme, Stuttgart 1973—1979; c) see [16], Vol. III, p. 196 *et seq.*

[2] We follow *Bethell* and *Gold*'s definition, according to which the dissociation rate of RX is considered to reflect the stability of the carbenium ion R⁺: *D. Bethell, V. Gold,* Carbonium Ions, Academic Press, London 1967, p. 88.

[3] The conversion of stable carbenium ions into less stable carbenium ions, is frequently applied to intramolecular cyclization reactions; cf. for example *W. S. Johnson,* Angew. Chem. *83*, 33 (1976); Angew. Chem. Int. Ed. Engl. *15*, 9 (1976).

[4] *J. E. Leffler, E. Grunwald:* Rates and Equilibria of Organic Reactions. Wiley, New York, 1963, p. 156, 163.

[5] a) *K. A. Cooper, E. D. Hughes,* J. Chem. Soc. *1937*, 1183; b) *E. Grunwald, S. Winstein,* J. Am. Chem. Soc. *70*, 846 (1948); c) *A. H. Fainberg, S. Winstein, ibid. 78*, 2770 (1956); d) *V. J. Shiner, Jr., W. E. Buddenbaum, B. L. Murr, G. Lamaty, ibid. 90*, 418 (1968); e) *T. C. Jones, E. R. Thornton,* ibid. *89*, 4863 (1967); f) *C. A. Grob, G. Cseh,* Helv. Chim. Acta *47*, 194 (1964); g) *A. Streitwieser, Jr.:* Solvolytic Displacement Reactions. McGraw Hill, New York 1962, p. 78.

[6] *L. Schmerling,* J. Am. Chem. Soc. *67*, 1152 (1945); *L. Schmerling, E. E. Meisinger, ibid. 75*, 6217 (1953).

[7] a) *F. Marcuzzi, G. Melloni, G. Modena,* J. Org. Chem. *44*, 3022 (1979); b) In contrast to this *G. A. Olah, S. J. Kuhn,* and *D. G. Barnes* (J. Org. Chem. *29*, 2685 (1964) reported the formation of 1:1-products from *(6)* and styrene; presumably reaction conditions play an important role if dissociation rates of educts and products, are very similar.

[8] See [7a], and earlier work cited therein; cf. also *H. Mayr, I. K. Halberstadt,* Angew. Chem. *92*, 840 (1980); Angew. Chem. Int. Ed. Engl. *19*, 814 (1980).

[9] *A. A. Petrov, K. V. Leets,* J. Gen. Chem. USSR *26*, 1263 (1956); *Z. N. Kolyaskina, A. A. Petrov, ibid. 32*, 1067 (1962).

[10] *H. Mayr, W. Förner, P. von R. Schleyer,* J. Am. Chem. Soc. *101*, 6032 (1979).

[11] *M. L. Genusov, A. A. Petrov,* J. Gen. Chem. USSR *33*, 2787 (1963); *K. V. Leets, V. O. Chernyshev, T. I. Pekhk, K. A. Rang, A. Yu. Erm,* J. Org. Chem. USSR *14*, 852 (1978).

[12] *F. Straus, W. Thiel,* Justus Liebigs Ann. Chem. *525*, 151 (1936); *cf.* also *H. Gross, E. Höft,* Angew. Chem. *79*, 358 (1967); Angew. Chem. Int. Ed. Engl. *6*, 335 (1967).

[13] *H. M. R. Hoffmann, G. F. P. Kernaghan, G. Greenwood,* J. Chem. Soc. *B, 1971*, 2257.

[14] *J. K. Rasmussen,* Synthesis, *1971*, 91.

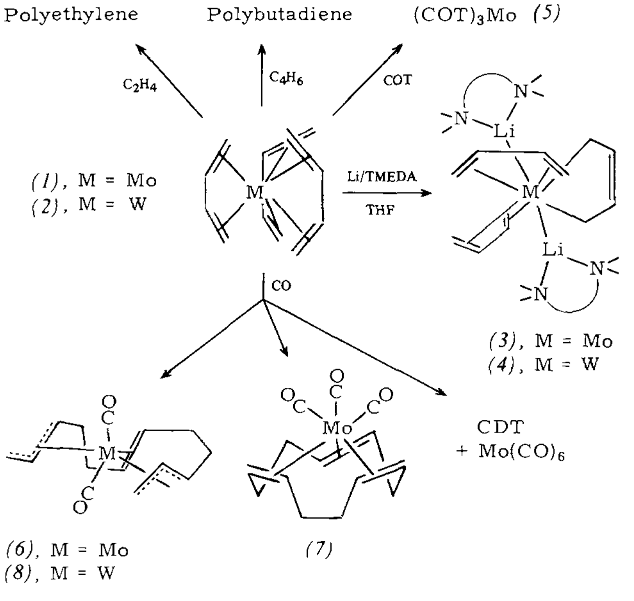
---

## Reductive Synthesis and Reactivity of Tris(butadiene)molybdenum and -tungsten

By *Wolfgang Gausing* and *Günther Wilke*[*]

*Dedicated to Professor Karl Freudenberg on the occasion of his 95th birthday*

Tris(butadiene)-molybdenum *(1)* and -tungsten *(2)* were first obtained in small amounts by *Skell et al.*[1a] by co-condensation of the metals with butadiene. The X-ray structure analysis of *(1)*[1b] shows the $\eta^4$-complexed butadiene molecules to have an *s-cis* conformation and a trigonal-prismatic arrangement. As far as the reactivity of *(1)* and *(2)* is concerned only the stability of the two substances towards air has so far been mentioned. *(1)* and *(2)* would now appear to be interesting starting compounds for studying the chemistry of olefin-molybdenum and -tungsten complexes, all the more so as they are attractive sources for "naked" molybdenum or tungsten[2]. We report here the synthesis of such complexes *via* a conventional route and discuss a few of their reactions.



---

[*] Prof. Dr. G. Wilke, Dr. W. Gausing
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr (Germany)

Molybdenum and tungsten chlorides ($MoCl_5$, $MoCl_4 \cdot 2THF$, $MoCl_3 \cdot 3THF$, $WCl_6$, $WCl_4 \cdot 2THF$) can be converted into *(1)* and *(2)* by reduction with magnesium in a tetrahydrofuran (THF)/butadiene mixture at low temperatures. The NMR and IR spectra of the two complexes are very similar, so that *(2)* probably has the same structure as *(1)*. Detailed $^1H$-NMR investigations reveal that in *(2)* an exchange process for the methylene hydrogen atoms, presumably involving formation of an intermediary metallacyclopentene[3] is occurring. Consistent with this hypothesis, *(1)* and *(2)* react at low temperatures with lithium in the presence of tetramethylethylenediamine (TMEDA) to give the adducts *(3)* and *(4)*, respectively, which have been shown by IR and NMR spectroscopy to contain an $\eta^2$-bonded besides two $\eta^4$-bonded $C_4H_6$ ligands. By analogy to the olefin-$Li_2Ni$ complexes[4], we suggest structures with dilithium-transition metal groupings for *(3)* and *(4)*.

At elevated pressures and temperatures *(1)* and *(2)* induce the polymerization of both butadiene as well as ethylene; in the reaction of *(2)* with ethylene, oligomers are also formed. On reaction with cyclooctatetraene (COT), and with carbon monoxide, it is clear that butadiene is more firmly complexed in *(2)* than in *(1)*. Thus, reaction of *(1)* with COT yields labile $(COT)_3Mo$ *(5)*; compound *(2)*, on the other hand, does not undergo any well defined reaction with COT, even at elevated temperatures. Solutions of *(1)* react with CO under normal pressure at 50–60 °C to give $Mo(CO)_6$ and a mixture of isomeric 1,5,9-cyclododecatrienes (CDT) (*ttt*:*ttc*:*tcc* = 1:13.6:15.7), whereas *(2)* reacts only under drastic conditions to give $W(CO)_6$ without any noticeable amounts of CDT being liberated. The compounds *(6)* and *(7)* have been previously isolated and are possible intermediates of the stoichiometric synthesis of CDT on molybdenum. From the reaction of *(2)* with carbon monoxide, we were able to isolate *(8)*. According to NMR and IR spectra *(7)* contains a *trans,cis,cis*-1,5,9-cyclododecatriene (*tcc*-CDT) complexed to molybdenum, while *(6)* and *(8)* contain $C_{12}H_{18}$ chains with a complexed *trans* double bond and *trans,syn*-substituted $\eta^3$-allyl groups[5]. The reaction sequence $(1) \rightarrow (6) \rightarrow (7) \rightarrow \mathrm{CDT} + Mo(CO)_6$ serves as a model for the catalytic synthesis of CDT on transition metals[2].

The isomerization of an $\eta^4$-bonded butadiene to an $\eta^2$-bonded ligand (*vide supra*) is reminiscent of the exhaustively investigated reactions of the allyl-transition metal compounds[7]. $\eta^3$-$\eta^1$-Isomerizations of allyl complexes are discussed, in particular, as a reaction step preceding C—C coupling in catalytic cyclooligomerizations of 1,3-dienes[6]. By analogy, one can assume that coupling of an $\eta^4$-bonded butadiene ligand with suitable substrates—*e.g.* with further butadiene in the stoichiometric synthesis of CDT on molybdenum—is preceded by isomerization to an $\eta^2$-bonded butadiene. Further evidence of this being the case is furnished by investigations on (COT)Zr- and (COT)Hf-butadiene complexes[8].

### *Procedure*

A suspension of magnesium sand (12 g, 0.494 mol; activated by heating with $I_2$ *in vacuo* and etching with $C_2H_5I$) in *ca.* 1.7 dm$^3$ THF was treated at −20 °C with 180 cm$^3$ liquid butadiene and 74.5 g (197.4 mmol) $MoCl_4 \cdot 2THF$[9]. After 48 hours' stirring at −20 to −15 °C a greenish-brown solution was formed. After concentration by evaporation at −10 °C the resulting residue was dried at room temperature in an oil-pump vacuum and then extracted with toluene. The brown toluene solution after removal of solvent by distillation *in vacuo* gave a tacky residue, which was extracted with *ca.* 3.5 dm$^3$ pentane. The brown crude product obtained after cooling the extract in a vacuum was dissolved in a little warm THF (50 °C) and the solution stored for 24 h at −20 °C. After dilution with *ca.* 150 cm$^3$ cold ether the crystalline precipitate was recovered by filtration at −20 °C, washed with ether, and dried in an oil-pump vacuum. Yield: 14.5 g (56.2 mmol $\hat{=}$ 29%) $(C_4H_6)_3Mo$ *(1)*. The NMR, IR and MS data agree, within the accuracy of measurement, with the data quoted by *Skell et al.*[1].

Received: July 1, 1980 [Z 659 IE]
German version: Angew. Chem. *93*, 201 (1981).
Publication delayed at Authors' request

CAS Registry numbers:
*(1)*, 51733-17-6; *(2)*, 51733-16-5; *(3)*, 76137-05-8; *(4)*, 76137-07-0; *(5)*, 76137-08-1; *(6)*, 76137-09-2; *(7)*, 76156-56-4; *(8)*, 76137-10-5; *ttt*-CDT, 676-22-2; *ttc*-CDT, 706-31-0; *tcc*-CDT, 2765-29-9; $Mo(CO)_6$, 13939-06-5; $MoCl_4 \cdot 2THF$, 16998-75-7; $WCl_4 \cdot 2THF$, 34445-14-2; $MoCl_3 \cdot 3THF$, 31355-55-2; $MoCl_5$, 10241-05-1; $WCl_6$, 13283-01-7; $C_2H_4$, 74-85-1; $C_4H_6$, 106-99-0

---

[1] a) *P. S. Skell, E. M. Van Dam, M. P. Silvon,* J. Am. Chem. Soc. *96*, 626 (1974); b) *P. S. Skell, M. J. McGlinchey,* Angew. Chem. *87*, 215 (1975); Angew. Chem. Int. Ed. Engl. *14*, 195 (1975).

[2] *G. Wilke,* Angew. Chem. *75*, 10 (1963); Angew. Chem. Int. Ed. Engl. *2*, 105 (1963).

[3] *R. Benn, G. Schroth,* J. Organomet. Chem., in press.

[4] *K. Jonas,* Angew. Chem. *87*, 809 (1975); Angew. Chem. Int. Ed. Engl. *14*, 752 (1975); *D. J. Brauer, C. Krüger, J. C. Sekutowski,* J. Organomet. Chem. *178*, 249 (1979).

[5] An almost identical arrangement of the $C_{12}H_{18}$ chain has been demonstrated by an X-ray structure analysis for the $C_{12}H_{18}RuCl_2$ obtainable from butadiene and $RuCl_3$: *J. E. Lydon, J. K. Nicholson, B. L. Shaw, M. R. Truter,* Proc. Soc. Chem. *1964*, 421. As intermediate products of the butadiene trimerization on "naked" nickel[2], two isomers of $C_{12}H_{18}Ni$ can be isolated which contain *cis*-oriented, *anti*-substituted $\eta^3$-allyl groups as well as a complexed *trans*-double bond [6].

[6] *G. Wilke,* Pure Appl. Chem. *50*, 677 (1978).

[7] *G. Wilke et al.,* Angew. Chem. *78*, 157 (1966); Angew. Chem. Int. Ed. Engl. *5*, 151 (1966); *E. G. Hoffmann, R. Kallweit, G. Schroth, K. Seevogel, W. Stempfle, G. Wilke,* J. Organomet. Chem. *97*, 183 (1975).

[8] *L. Stehling, G. Wilke,* J. Organomet. Chem., in press.

[9] *J. Chatt, A. G. Wedd,* J. Organomet. Chem. *27*, C15 (1971).

---

## Synthesis, Isolation, and Identification of Translationally Isomeric [3]Catenanes[**]

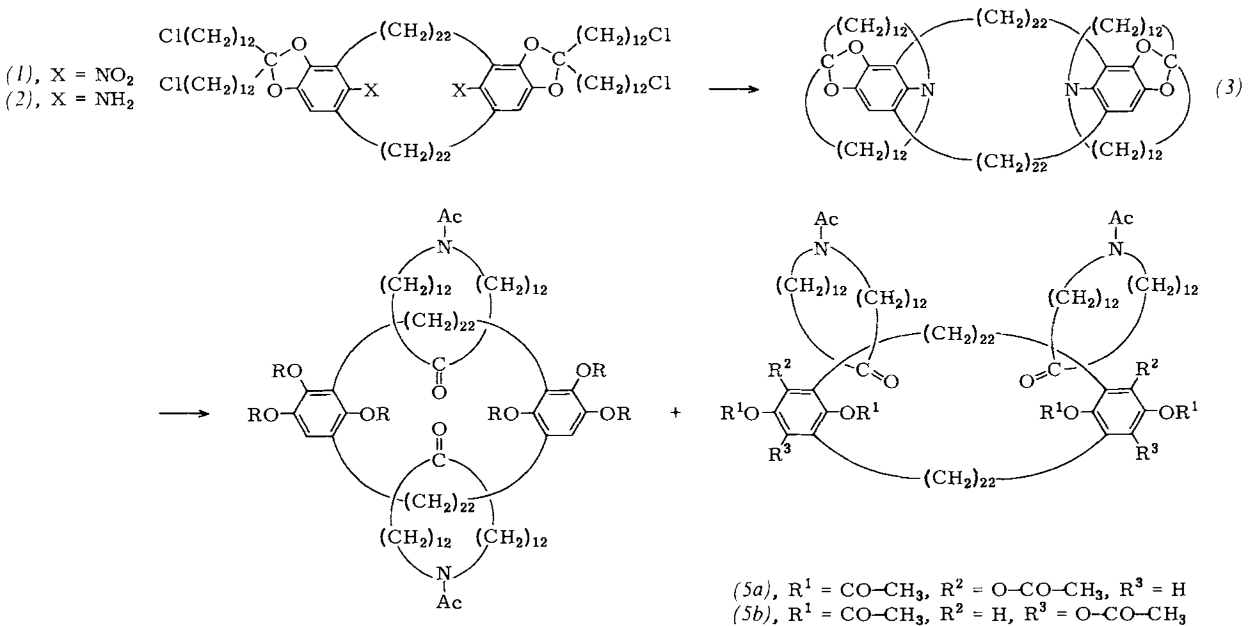
By *Gottfried Schill, Klaus Rissler, Hans Fritz,* and *Walter Vetter*[*]

In connection with our studies on the synthesis and physico-chemical properties of [3]catenanes containing a central macrocarbocycle[1] we have cyclized the diamine *(2)*, obtained from the dinitro compound *(1)*[2] by catalytic reduction with Raney nickel in 2-pentanol[3], in the presence of $Na_2CO_3$ and NaI under high dilution conditions. Three monomeric cyclization products were isolated in yields of 21, 7.7 and 0.9% by chromatography. It follows from spectroscopic data that the main product has the structure *(3)*[4].

---

[*] Prof. Dr. G. Schill [+], Prof. Dr. H. Fritz, Dr. K. Rissler
Chemisches Laboratorium der Universität
Albertstr. 21, D-7800 Freiburg (Germany)
Dr. W. Vetter
Hoffmann-La Roche & Co. AG, Zentrale Forschungseinheit
CH-4002 Basel (Switzerland)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.



(1), X = $NO_2$
(2), X = $NH_2$
(3)

(4), R = CO–$CH_3$
(6), R = $CH_3$

(5a), $R^1$ = CO–$CH_3$, $R^2$ = O–CO–$CH_3$, $R^3$ = H
(5b), $R^1$ = CO–$CH_3$, $R^2$ = H, $R^3$ = O–CO–$CH_3$
(7a), $R^1$ = $CH_3$, $R^2$ = $OCH_3$, $R^3$ = H
(7b), $R^1$ = $CH_3$, $R^2$ = H, $R^3$ = $OCH_3$

The mass spectrum of *(3)* shows the molecular ion as base peak at *m/e* = 1550 and only slight fragmentation, characteristic for doubly bridged compounds of the type *(3)*[5]. Consistent with the $C_{2v}$ symmetry required for *(3)*, the $^{13}$C-NMR spectrum (90.5 MHz) contains one set of signals for each of the C-atoms of the benzene rings, of the four $(CH_2)_{12}$-bridges over the benzene rings, and each of the two diastereotopic $(CH_2)_{22}$-bridges. Also in agreement with the symmetry in *(3)*, the 360-MHz $^1$H-NMR spectrum shows only one signal for each of the aromatic protons and the diastereotopic protons of the four N—$CH_2$ groups, but two signals for the benzylic $CH_2$-groups of the $(CH_2)_{22}$ bridges.

As in earlier procedures[6] the chemical bonds between the benzene rings and the double-bridge systems were cleaved in two steps. The dipyrocatechol obtained by acid-catalyzed hydrolysis of the two acetal groups was dehydrogenated with iron(III) sulfate to the corresponding 4-amino-1,2-benzoquinone. Its hydrolysis in the acidic reaction medium yielded a compound containing 2-hydroxy-1,4-benzoquinone structural units. Reductive acetylation with zinc/acetic anhydride/sodium acetate afforded a mixture of products which could be separated by preparative layer chromatography on silica gel with ethyl acetate into two fractions ($R_f$ = 0.30 and 0.21). The more rapidly eluted compound is assigned the constitution *(4)*, the more slowly eluted fraction consists of a mixture of hitherto inseparable *(5a)* and *(5b)*.

The assignment of the structures *(4)* and *(5a, b)* to the two fractions is based on the assumption that the chromatographic differences between *(5a)* and *(5b)* should be less than that between *(5a)* or *(5b)* and *(4)*. The $^{13}$C-NMR spectrum of *(4)* shows only one set of signals for the C-atoms of the aromatic rings and of the three different *O*-acetyl groups. On the other hand, since the two macrocycles in *(4)* are heterotopic, two signals each are observed at 210.66 and 210.62 and 42.86 and 42.81, respectively, for the C-atoms of the keto-carbonyl groups and the α-$CH_2$ groups. The signals of the other heterotopic C-atoms of the macrocycles overlap.

The $^{13}$C-NMR spectrum of the mixture of *(5a)* and *(5b)* shows signals with very similar chemical shifts to those of *(4)*. Two signals differing by less than 0.5 ppm are observed for each of the C-atoms of the aromatic rings and for the *O*-acetyl groups. Consequently, a maximum of only two signals is observed for the C-atoms of the now enantiotopic macroheterocycles, *e.g.* at δ = 210.28 and 210.19 for the keto-carbonyl C-atoms and at 42.79 and 42.74 for the C-atoms of the α-$CH_2$-group.

The $^1$H-NMR spectrum (360 MHz) of *(4)* shows a singlet at δ = 6.96 for the aromatic proton. Correspondingly, in the case of the mixture of *(5a)* and *(5b)* two signals are observed at δ = 6.96 and 6.95.

In the compounds *(4)*, *(5a)* and *(5b)* a new form of isomerism is present, for which we propose the term *translational isomerism* because such isomers are only interconvertible by translation of the 26-membered macroheterocycles across a high steric barrier. This isomerization is so strongly hindered by bulky aromatic components in these compounds that isolation of the isomers is possible. When heated to 200 °C, *(6)* or *(7a)* and *(7b)* slowly decompose; mutual isomerization is not observed.

In the two phase system benzene/30% aqueous solution of sodium hydroxide both *(4)* as well as *(5a)* and *(5b)* can be hydrolyzed and converted into the hexamethyl ethers *(6)* and *(7a,b)*, respectively, with tetrabutylammonium sulfate as catalyst and dimethyl sulfate, without isolation of intermediate products, and converted into the hexamethyl ethers *(6)* and *(7a, b)*, respectively. Remarkably, the translational isomers do not interconvert, even at the reaction temperature of 80 °C. Signal patterns corresponding to those in the acetyl derivatives are observed in the $^1$H- and $^{13}$C-NMR spectra of *(6)* and the $^1$H-NMR spectrum of the mixture of *(7a)* and *(7b)*.

It cannot be established with certainty whether *(6)* differs from *(7a)* and *(7b)* mass spectrometrically. During the recording of the mass spectra (MS 9, 70 eV) it was not possible to accurately reproduce all peak intensities, even under identical conditions of sample introduction and evaporation (*ca.* 300 °C). Consequently, the following intensity data hold both for *(6)* as well as for *(7a)* and *(7b)*. The molecular ion shows an intense peak at $m/e=1790$ (25%[7] of the base peak at $m/e=55$). The peak of the ionized [2]catenane is observed at $m/e=1369$ (50%). If a thermal decomposition of the catenane structure is excluded then formation of this ion from the doubly charged molecular ion of the [3]catenane must be assumed. The molecular ion of the macrocarbocycle appears at $m/e=948$ (50%). The peaks at $m/e=895$ (30%), 684.5 (3%) and 474 (10%) represent the same structures again, but this time as doubly charged ions. The complete fragmentation patterns of the two macrocyclic components are found in the low mass range in addition to the protonated molecular ion of the macroheterocycle at $m/e=422$ (50%)[8]. Surprisingly, besides this ion yet another ion occurs at $m/e=436$ (25%), presumably formed by transfer of a methyl group from a methoxy group of the macrocarbocycle to the amide group of a macroheterocycle.

Received: July 28, 1980 [Z 674 IE]
German version: Angew. Chem. 93, 197 (1981)

CAS Registry numbers:
*(1)*, 76156-57-5; *(2)*, 76137-19-4; *(3)*, 76137-20-7; *(4)*, 76137-22-9; *(6)*, 76137-24-1

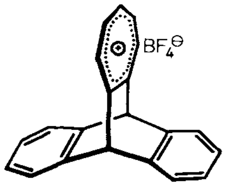
---

[1] *G. Schill, K. Murjahn, W. Beckmann,* Chem. Ber. *105,* 3591 (1972); *G. Schill, C. Zürcher, ibid. 110,* 2046, 3964 (1977).
[2] Part of the Dissertation by *K. Rissler,* Universität Freiburg, 1981.
[3] Use of 2-pentanol in such cyclizations: *G. Schill, H. Fritz et al.,* unpublished.
[4] The structure of the other two cyclization products: *G. Schill, H. Fritz et al.,* unpublished.
[5] *G. Schill, K. Murjahn, W. Vetter,* Justus Liebigs Ann. Chem. *740,* 18 (1970); *G. Schill, W. Vetter,* Chem. Ber. *104,* 3582 (1971).
[6] *G. Schill,* Chem. Ber. *100,* 2021 (1967).
[7] The intensity data are only to be regarded as reference values (± 30%) and are quoted without isotopic contributions.
[8] *W. Vetter, G. Schill,* Tetrahedron *23,* 3079 (1967); *W. Vetter, E. Logemann, G. Schill,* Org. Mass Spectrom. *12,* 351 (1977); *G. Schill, G. Doerjer, E. Logemann, W. Vetter,* Chem. Ber. *113,* 3697 (1980).

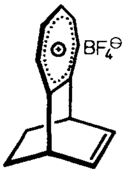
## 1,4-Dihydro-1,4-ethenobenzotropylium Tetrafluoroborate; Synthesis and Intramolecular Charge-Transfer Interaction[**]

By *Tomoo Nakazawa, Keiji Kubo,* and *Ichiro Murata*[*]

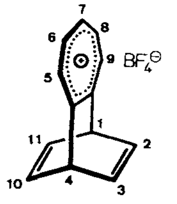
We have already reported the syntheses of the bridged tropylium ions *(1)*[1] and *(2)*[2], the model compounds for intramolecular charge-transfer (CT) interaction between the tropylium ion and remote π-systems which are not in parallel planes. As part of our program to design a simplified molecule capable of retaining intramolecular CT interaction between nonparallel donors and acceptors, we wish to draw attention to some of the novel structural features of compound *(3)*; a molecule constructed of amalgamated tropylium ion and barrelene (bicyclo[2.2.2]octatriene) frameworks. Studies on *(3)* provide useful information not only on the intramolecular CT interaction between donor and acceptor, with rigid spatial arrangement, but also on the π-π interaction between two ethylene π-systems incorporated into a bicyclo[2.2.2]octane framework.



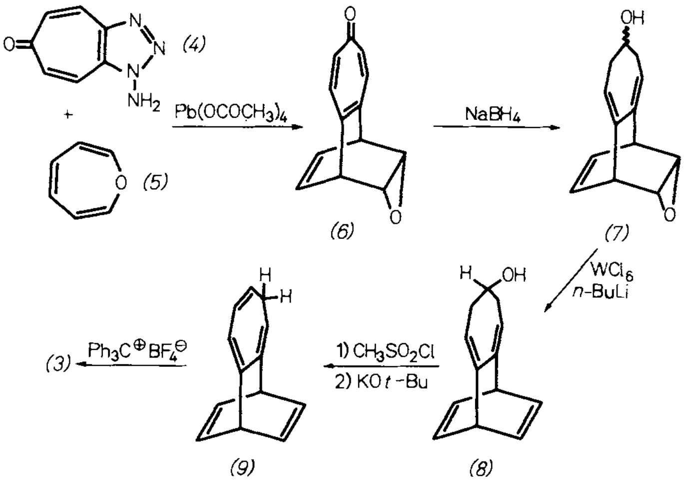
*(1)*



*(2)*



*(3)*



The synthetic route to *(3)* is shown in Scheme 1. The bridged tropone derivative *(6)* [pale yellow needles, m.p. = 166.5 °C, dec. (benzene)][3] was obtained in 95% yield by a procedure developed by us recently[4], which consists of treatment of a mixture of 1-amino-1*H*-cycloheptatriazol-6-one *(4)*[5] and 2 equivalents of oxepin *(5)*[6] with 1 equivalent of lead tetraacetate. Reduction of *(6)* with sodium borohydride (in 98% methanol, room temp., 2 h) gave the epimeric mixture of the alcohols *(7)* [colorless needles, m.p. = 98—104 °C, yield 79%][3]. Transformation of *(7)* into the tetraenol *(8)* [colorless needles, m.p. = 127—129 °C (hexane and benzene), yield 45%][3], which was unsuccessful when attempted with the usual deoxygenating reagents, was effected by using lower valent tungsten chloride prepared *in situ* from tungsten hexachloride and 2 equivalents of *n*-butyllithium in tetrahydrofuran[7]. The tetraenol *(8)* could be converted quantitatively into its mesylate ($CH_3SO_2Cl/Et_3N$ in dichloromethane, 0 °C, 10 min), which, without purification, afforded the cycloheptatriene derivative *(9)* [colorless liq., yield 50% referred to *(8)*][3], on treatment with 2.5 equivalents of potassium *tert*-butoxide (THF, −45 °C, 1.5 h). Conversion of *(9)* into the desired cation *(3)* was accomplished by use of trityl

Table 1. Spectroscopic properties of *(3)*.

| UV/VIS $\lambda_{max}$ [nm] ($\log\varepsilon$) in $CH_2Cl_2$ | UV/VIS $\lambda_{max}$ [nm] ($\log\varepsilon$) in $CH_3CN$ | $^1H$-NMR in $CD_2Cl_2$ δ-value | $^{13}C$-NMR in $CD_3CN$ δ-value |
|---|---|---|---|
| 234 (4.63) | 230.2 (4.69) | 5.73 (m, 1,4-H) | 56.8 (C-1,4) |
| 274.4 (4.02) | 270.7 (4.04) | | 139.7 (C-2,3,10,11) |
| 340 (3.56) | 334 (3.56) | 7.20 (m, 2,3,10,11-H) | 146.7 (C-5,9) |
| 378 sh (3.40) | 374 sh (3.37) | | 148.8 (C-7) |
| | | 8.67—8.98 (m, 5,6,7,8,9-H) | 153.1 (C-6,8) |
| | | | 176.1 (C-4a,9a) |

---

[*] Prof. Dr. I. Murata [+], K. Kubo
Department of Chemistry, Faculty of Science, Osaka University
Toyonaka, Osaka 560 (Japan)
Prof. Dr. T. Nakazawa
Department of Chemistry, Medical University of Yamanashi
Nakakoma-gun, Tamaho-mura, Yamanashi 409-38 (Japan)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by a Grant-in-Aid for Scientific Research (No. 343007) from the Ministry of Education, Japan.

tetrafluoroborate in dichloromethane at −74 °C. The tetrafluoroborate of cation *(3)*, which was obtained in 47% yield as greenish yellow needles, decomposed at 204—207 °C (acetonitrile or ethyl acetate)[3], but is very stable under ambient conditions. Assignment of structure is supported by its $^1$H- and $^{13}$C-NMR spectra shown in Table 1.

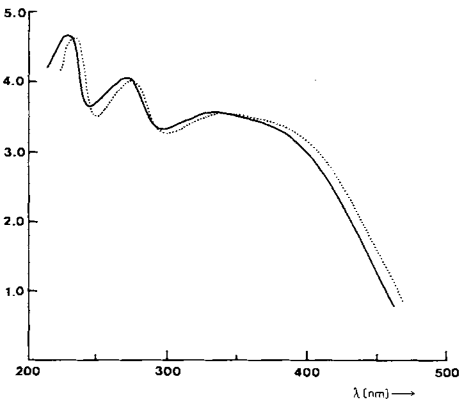


Fig. 1. UV/VIS spectrum of *(3)* in $CH_3CN$ (——) and in $CH_2Cl_2$ (······).

The UV/VIS spectrum of *(3)* (Fig. 1) exhibits a broad and intense CT absorption in the 300 to 450 nm region which is solvent dependent, and shows a bathochromic shift in the less polar dichloromethane. The broad shape of this CT absorption suggests that the band consists of two or more electronic transitions. This is confirmed by the curve resolution (331 and 387 nm) and by the MCD spectrum of *(3)* which shows a positive peak with its maximum at 333 nm and a negative trough at 387 nm in the CT region[8]. Since the interaction between the two non-conjugated ethylene π-orbitals in *(3)* gives rise to two occupied π-orbitals, the two observed CT bands at 387 and 333 nm are assigned to the electronic transitions from the HOMO and the next HOMO of the two interacting ethylene π-orbitals, to the LUMO of the tropylium π-orbital, respectively. In fact, the energy difference of these two CT transitions (0.52 eV) is roughly equal to the orbital energy gap of bicyclo[2.2.2]octadiene, $\varepsilon(b_2(\pi)) - \varepsilon(a_1(\pi)) = 0.58$ eV, measured by PE spectroscopy[9].

The thermodynamic stability of *(3)* was evaluated by means of its $pK_{R^+}$ value, which is found to be $7.0 \pm 0.2$ in 20% aqueous acetonitrile. It is evident that the stability of the tropylium ion is markedly diminished in *(3)* compared with *(2)* ($pK_{R^+} = 8.4_7$)[2] and its dihydro analog ($pK_{R^+} = 8.8_2$)[2]. This trend observed on successive introduction of the double bond in the ethano-bridge system can be attributed to the decrease in the electron-donating inductive effect of the bridged alkyl group[2].

Received: July 28, 1980 [Z 684 IE]
German version: Angew. Chem. 93, 195 (1981)

CAS Registry numbers:
*(3)*, 76466-39-2; *(4)*, 56598-81-3; *(5)*, 291-70-3; *(6)*, 76466-75-6; *(7)*, 76466-76-7; *(8)*, 76466-77-8; *(9)*, 76466-78-9

---

[1] a) *T. Nakazawa, I. Murata*, J. Am. Chem. Soc. 99, 1996 (1977); b) *T. Nakazawa, N. Abe, K. Kubo, I. Murata*, Tetrahedron Lett. *1979*, 4995.

[2] *T. Nakazawa, Y. Niimoto, K. Kubo, I. Murata*, Angew. Chem. 92, 566 (1980); Angew. Chem. Int. Ed. Engl. *19*, 545 (1980).

[3] Satisfactory elemental analyses and spectroscopic data were obtained for all new compounds reported.

[4] *T. Nakazawa, I. Murata*, Angew. Chem. 87, 742 (1975); Angew. Chem. Int. Ed. Engl. *14*, 711 (1975).

[5] Due to practical difficulties in the separation, a 5.2:3.2 mixture of *(4)* and the 2-amino-2*H*-cycloheptatriazol-6-one was used for the preparation of *(6)*. See ref. [4].

[6] *E. Vogel, R. Schubart, W. A. Böll*, Angew. Chem. *76*, 535 (1964); Angew. Chem. Int. Ed. Engl. *3*, 510 (1964); *E. Vogel, H. Günther*, Angew. Chem. *79*, 429 (1967); Angew. Chem. Int. Ed. Engl. *6*, 385 (1967); *E. Vogel, W. A. Böll, H. Günther*, Tetrahedron Lett. *1965*, 609.

[7] *K. B. Sharpless, M. A. Umbreit, M. T. Nieh, T. C. Flood*, J. Am. Chem. Soc. *94*, 6538 (1972).

[8] *M. Hatano, A. Tajiri*, unpublished results. We wish to thank Professor *Hatano* and Dr. *Tajiri*, Chemical Research Institute of Non-aqueous Solutions, Tohoku University, for communicating their results to us prior to publication.

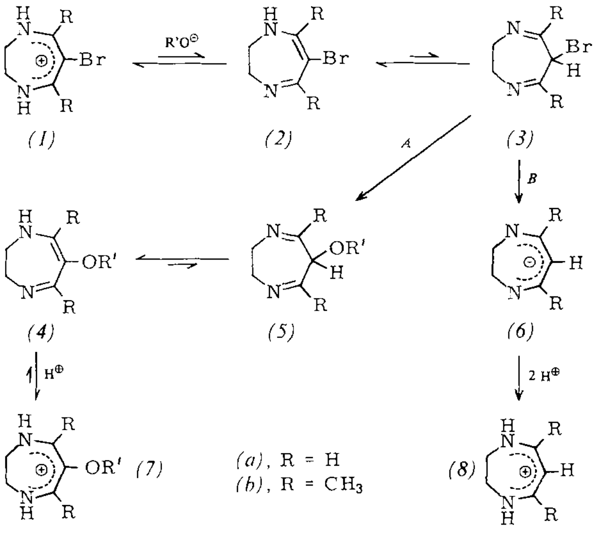
[9] *P. Bischof, J. A. Hashmall, E. Heilbronner, V. Hornung*, Helv. Chim. Acta *52*, 1745 (1969); *E. Haselbach, E. Heilbronner, G. Schröder, ibid. 54*, 153 (1971).

---

## An Onium Anion

By *Douglas Lloyd, Raymond K. Mackie, Glynis Richardson,* and *Donald R. Marshall*[*]

When 6-bromodihydrodiazepinium salts *(1)* react with alkoxides they may undergo either nucleophilic substitution to give 6-alkoxy-derivatives (route A) *(7)*, or protodebromination to give the products *(8)* (route B)[1]. It has been suggested that both of these reactions involve initial formation of the dihydrodiazepine base *(2)*, which can tautomerize to provide a bisimine species *(3)* very susceptible to nucleophilic attack[1]. The type of product which results seems to be determined largely by steric factors[1].



The tautomerization of *(2)* to *(3)* involves the loss of a considerable amount of resonance energy[1b], but there is some energetic compensation in the loss of vicinal crowding between the 5-, 6- and 7-substituents[1c].

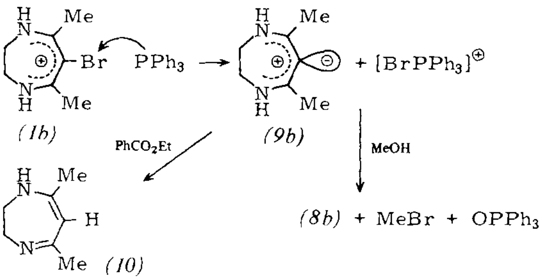
Evidence in favor of this mechanism is provided by the following facts: (a) the bromine atom of *(1a)* is immune to attack by alkoxide ion (save for conversion into the corre-

---

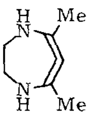
[*] Dr. D. Lloyd [+], Dr. R. K. Mackie, Dr. G. Richardson
Department of Chemistry, Purdie Building
University of St. Andrews
St. Andrews, Fife KY16 9ST (Scotland)
Dr. D. R. Marshall
School of Physical and Molecular Sciences
University College of North Wales
Bangor, Gwynedd LL57 2UW (Wales)
[+] Author to whom correspondence should be addressed.

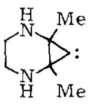
sponding dihydrodiazepine base), presumably because in *(2a)* there is minimal crowding between the 5-, 6- and 7-positions in the conjugated form of the base and hence no steric factor to assist change to the bisimine form[1c]; (b) *N,N'*-disubstituted 6-bromodihydrodiazepinium salts such as *(13)* do not undergo reactions of types *A* or *B*[1a].

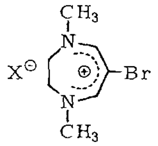
When the salt *(1b)* is heated with a molar equivalent of triphenylphosphane in methanol, the product *(8b)* is formed in high yield. The $pK_a$ for the acid-base equilibrium involving *(1b)* is 11.8[2]. It seems very unlikely, therefore, that in the presence of triphenylphosphine in methanol there could be sufficient base form present to sustain the protodebromination reaction proceeding *via* this base as intermediate. An alternative mechanism, in keeping with the known reactivity of triphenylphosphane towards bromine[3a], could involve the following sequence of reactions[3].



The postulated intermediate species *(9b)* is remarkable in that it is at the same time an onium ion and a carbanion. Alternative forms which might be considered for this species, but which would involve substantial distortion of the geometry of the ring[4] are the allene *(11)* (by analogy with structures considered for cycloheptatrienylidene[5]) or the carbene *(12)*. However contributions from either of these structures would involve considerable increase in geometric strain in the molecule, coupled with loss of the delocalization energy (*ca.* 20 $\mathrm{kcal \cdot mol^{-1}}$ [1b]) of the vinamidinium system[6].


*(11)*


*(12)*


*(13)*

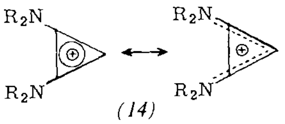
In the onium ion *(9b)* the anionic lone-pair is orthogonal to the delocalized system, which adds further complication by being an electron-rich cation[7].

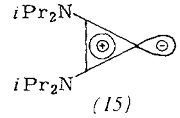
A variety of evidence is available in support of this mechanism, and, consequently, of the postulate of this *onium anion (9b)*.

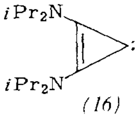
- If perdeuteriomethanol is used as solvent a 6-deuteriodihydrodiazepinium salt is formed.
- The cation *(1a)*, which will not undergo protodebromination with alkoxides[1c], is protodebrominated by triphenylphosphane, although a higher boiling solvent, 1-pentanol, is required to promote the reaction.
- The salt *(13)*, which cannot form a dihydrodiazepine base, also undergoes protodebromination when heated with triphenylphosphane in 1-pentanol.
- Protodebromination of *(1b)* in 1-propanol provided the other expected products, triphenylphosphane oxide and 1-bromopropane, which were isolated and characterized.
- The higher temperatures required for *(1a)* and *(13)* may be associated with the diminished crowding between the 5-, 6- and 7-positions in these molecules, making the C—Br bond slightly stronger and/or raising the energy of the transition state because of diminished steric assistance. The 6-chloro-analogue of *(1b)* likewise undergoes protodechlorination in refluxing 1-propanol but not in refluxing methanol. The higher temperature required is similarly reasonable.

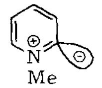
It seemed possible that in an aprotic solvent such an onium anion *(9)* might gain a proton at the 6-position by transfer from a nitrogen atom.

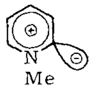
The *N,N'*-disubstituted dihydrodiazepinium species *(13)* could not provide a proton in this way. In accord with this proposition, *(1b)* underwent protodebromination when heated in dry ethyl benzoate but similar treatment of *(13)* only produced polymeric material, presumably resulting from alternative reactions of the intermediate species.


*(14)*


*(15)*


*(16)*

*(17)*



*(18)*

There is other evidence for the formation of onium anions in the literature even although they have not been formulated as such.

Bisaminocyclopropenium salts *(14)* and the vinamidinium system in *(1)*[6], are electronically similar and reactivity in keeping with this has been reported[8a]. It has been postulated that the onium ion *(15)* is formed as an intermediate in a number of reactions[8b,c], but it has been described as a carbene *(16)*, which can be another contributing form.

Also the ready decarboxylation of 2-pyridine carboxylic acids has for some time been attributed to the formation of the intermediate pyridinium ylid *(17)*[9]. If the pyridinium cation is regarded as a delocalized system, this species *(17)* provides another example of an onium anion *(18)*.

Received: August 6, 1980 [Z 685 IE]
German version: Angew. Chem. *93*, 193 (1981)

---

[1] a) *A. M. Gorringe, D. Lloyd, F. I. Wasson, D. R. Marshall, P. A. Duffield*, J. Chem. Soc. *C 1969*, 1449; b) *D. Lloyd, D. R. Marshall*, Chem. Ind. (London) *1972*, 335; c) *D. Lloyd, H. McNab, D. R. Marshall*, J. Chem. Soc. Perkin Trans. I 1975, 1260.

[2] *R. P. Bell, D. R. Marshall*, J. Chem. Soc. *1964*, 2195.

[3] a) See *J. I. G. Cadogan, R. K. Mackie*, Chem. Soc. Reviews *3*, 87 (1974); b) cf. *A. J. Burn, J. I. G. Cadogan*, J. Chem. Soc. *1963*, 5788.

[4] For the normal geometry see *G. Ferguson, W. C. Marsh, D. Lloyd, D. R. Marshall*, J. Chem. Soc. Perkin Trans. II *1980*, 74.

[5] *Inter alia W. M. Jones, L. Ennis*, J. Am. Chem. Soc. *89*, 3069 (1967); *R. L. Tyler, W. M. Jones, Y. Öhrn, J. R. Sadin, ibid. 96*, 3765 (1974).

[6] *D. Lloyd, H. McNab*, Angew. Chem. *88*, 496 (1976); Angew. Chem. Int. Ed. Engl. *15*, 459 (1976).

[7] *D. Lloyd, R. K. Mackie, H. McNab, K. S. Tucker, D. R. Marshall*, Tetrahedron *32*, 2339 (1976).

[8] a) *R. Weiss, C. Priesner*, Angew. Chem. *90*, 484 (1978); Angew. Chem. Int. Ed. Engl. *17*, 445 (1978); *R. Weiss, H. Wolf*, Chem. Ber. *113*, 1746 (1980). b)

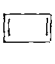
*R. Weiss, C. Priesner, H. Wolf*, Angew. Chem. *91*, 505 (1979); Angew. Chem. Int. Ed. Engl. *18*, 472 (1979). c) *R. Weiss, M. Hertel, H. Wolf*, Angew. Chem. *91*, 506 (1979); Angew. Chem. Int. Ed. Engl. *18*, 473 (1979).

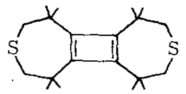
[9] a) *H. Quast, E. Frankelfeld*, Angew. Chem. *77*, 680 (1965); Angew. Chem. Int. Ed. Engl. *4*, 691 (1965); *K. W. Ratts, R. K. Howe, W. G. Phillips*, J. Am. Chem. Soc. *91*, 6115 (1969); *H. Quast, E. Schmitt*, Justus Liebigs Ann. Chem. *732*, 43 (1970). b) A similar species has also been postulated in reactions of pyridine-*N*-oxides: *R. A. Abramovitch, M. Saha, E. M. Smith, R. T. Couts*, J. Am. Chem. Soc. *89*, 1537 (1967).

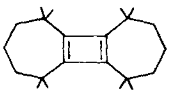
# The Electronic Triplet State of a Peralkylated Cyclobutadiene[**]

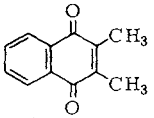
By *Jakob Wirz, Adolf Krebs, Hermann Schmalstieg* and *Herbert Angliker*[*]

In accordance with the results of *ab initio* calculations, recent experiments have established that the ground state of cyclobutadiene *(1)* is a singlet ($S_0$) and that its geometry is probably rectangular[1]. In contrast, the energy level and geometry of the triplet state ($T_1$) have not yet been determined. All efforts to detect ($^3$*1*) existing in thermal equilibrium with *(1)* have been unsuccessful. Even the use of derivative *(2)*, stabilized by sterically demanding substituents, produced no ESR signal in solution or solid state studies at temperatures up to +100 °C[2]. It is therefore probable that the triplet excitation energy of *(2)* exceeds 40 kJ/mol.


*(1)*


*(2)*


*(3)*


*(4)*

We report here that we have generated and observed the triplet state of the isolable, alkyl-substituted cyclobutadiene *(3)*[3] using the technique of flash photolysis (Nd laser at 353 or 530 nm, pulse duration 20 ns, kinetic measuring configuration). The direct excitation of *(3)* produced no short or long term changes in its absorption spectrum in the range 250 to 820 nm. This was anticipated, since we had found earlier[4a] that electronically excited [4n]annulenes undergo very rapid radiationless decay, so that fluorescence emission or intersystem crossing to the $T_1$ state is effectively prevented. We therefore determined the bimolecular rate constants $k_{et}$ for the quenching of several excited triplet sensitizers ($^3S$) by *(3)* in degassed benzene (25 °C). For this purpose we used polycyclic arenes which have characteristic triplet absorption bands[5a] and the triplet energies of which are known[5b-e].

The decay kinetics of the ($^3S$) state in the absence of *(3)* in a time range >10 μs was dominated by ($^3S$)—($^3S$) annihilation. For this reason the concentration (0.001 to 0.1 M)[6] of the quenching agent *(3)* was chosen such that the lifetime of the ($^3S$) state was reduced to about 0.5 μs. The decay then followed pseudo first-order kinetics, and hence the observed decay rate of ($^3S$), $k_{obs}$, could be equated to the rate of the quenching process, $k_{et}$ [*(3)*].

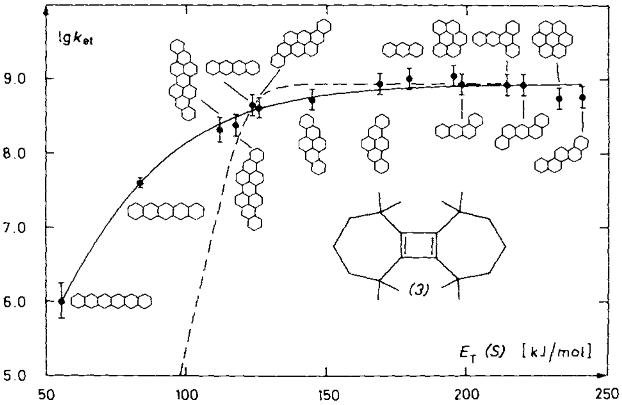


Fig. 1. Logarithmic plot of the rate constants $k_{et}$ for triplet energy transfer from several sensitizers *(S)* to the cyclobutadiene derivative *(3)*, against the triplet energy $E_T$ of the sensitizers *(S)*. For the sake of clarity, only the carbon framework of the benzene rings is shown.

Figure 1 shows $k_{et}$ plotted logarithmically against the triplet energy $E_T$ of the sensitizers *(S)*. The hypothesis that the quenching of ($^3S$) by *(3)* can be assigned to a triplet energy transfer process is decisive for the interpretation of the results. Since the sensitizers ([*(S)*] ≈ $10^{-4}$ to $10^{-5}$ M) were not consumed, even upon prolonged irradiation, the process of quenching must regenerate the starting materials. A reversible electron transfer (*via* a triplet exciplex) is improbable on energetic grounds. Furthermore, all solutions immediately returned to their original absorbance in the visible region after the absorption of ($^3S$) was quenched; if ion-pair intermediates of the type $^3(S^{\dot{+}}\cdots 3^{\dot{-}})$ or $^3(S^{\dot{-}}\cdots 3^{\dot{+}})$ having $\tau \gtrsim 20$ ns had been involved, they would have produced a strong transient absorption in the visible region. On the basis of semiempirical calculations on cyclobutadiene *(1)*[7], we anticipated that ($^3$*3*) would exhibit a relatively weak, broad (*Franck-Condon*-forbidden) absorption band in the near UV. In most cases, measurements could not be made in this spectral region due to the strong background absorption of the parent solutions. A suitable sensitizer, by means of which the UV region became accessible, proved to be 2,3-dimethyl-1,4-naphthoquinone *(4)*. Its absorption maximum lay close to the laser wavelength of 353 nm and because *(4)* had a very high rate of quenching, $k_{et} = 7 \times 10^9$ $\mathrm{M}^{-1}\,\mathrm{s}^{-1}$, a concentration of [*(3)*] = 0.01 M was sufficient to quench ($^3$*4*) within *ca.* 20 ns. Under these conditions we were able to observe a short-lived product ($\tau = 240$ ns, 1st order decay) of the quenching process which exhibited a weak absorption band increasing gently in intensity from 400 to 300 nm. The spectrum of this sequential product corresponds qualitatively to that expected for ($^3$*3*), but is not consistent with the assignment $^3(3^{\dot{+}}\cdots 4^{\dot{-}})$.

A section through the energy surfaces of $S_0$ *(3)* and $T_1$ *(3)* is shown in Figure 2; the diagram displays the consistent results of numerous *ab initio* calculations on *(1)*[1], and qualitatively takes account of the asymmetric steric interaction arising from the α-methyl groups of *(3)*. The equilibrium geometries shown for $S_0$ *(3)* and $T_1$ *(3)* differ considerably; accordingly the vertical excitation energy $E_T^{\mathrm{v}}$ is much larger than

---

[*] Priv.-Doz. Dr. J. Wirz [+], Dr. H. Angliker
Physikalisch-chemisches Institut der Universität
Klingelbergstrasse 80, CH-4056 Basel (Switzerland)

Prof. Dr. A. Krebs, Dipl.-Chem. H. Schmalstieg
Institut für Organische Chemie und Biochemie der Universität,
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[+] Author to whom correspondence sould be sent.

[**] Part 4 of "Electronic structure and photophysical properties of planar, conjugated hydrocarbons with a 4n-membered ring". Part 5 of "Isolable cyclobutadienes". This work was supported by the Swiss National Science Foundation (Project Nr. 2.211-0.79), the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Parts 2 and 3 [4], Part 4 [3a], resp.

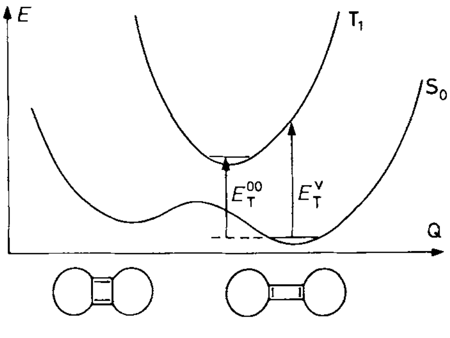


Fig. 2. Qualitative energy diagram for the double bond isomerization process in *(3)* (Q is reaction coordinate). The X-ray structural analysis of *(3)* [8] has yielded a planar 4-membered ring having bond lengths 133.9 (C=C) and 159.7 pm (C—C), corresponding to the right hand structural formula.

the "adiabatic" or "nonvertical" value $E_T^{00}$. In fact the smooth descent of the quenching curve for $E_T$ *(S)* values <120 kJ/mol is characteristic of a "nonvertical" energy transfer process[9]. For example, for $E_T^v = E_T^{00} = 120$ kJ/mol the dashed curve in Figure 1 would be expected. Moreover, it is striking that the plateau region of quenching rates for energy-rich sensitizers is reached at $k_{et} \cong 10^9$ M$^{-1}$ s$^{-1}$, which is approximately an order of magnitude less than the normally observed diffusion controlled limit. This presumably arises from the steric screening of the π-system by the alkyl substituents in *(3)*, since an exchange mechanism for the transfer of triplet energy[10] requires the chromophores to overlap. It should be noted that fluorenone and 2,3-dimethylnaphthoquinone *(4)* ($E_T = 213$ and 220 kJ/mol, resp.; $\pi\pi^*$) are quenched by *(3)* at a rate close to the diffusion controlled limit ($k_{et} = 9\times10^9$ and $7\times10^9$ M$^{-1}$ s$^{-1}$, resp.). This may be a consequence of the increased electron affinity[10b] and/or the modest spacial requirements of the carbonyl groups.

Based on a semi-classical model for the triplet energy transfer process in solution, *Balzani et al.*[9] recently suggested a general relationship between $k_{et}$ and $E_T^{00}$ *(S)* which makes use of several spectroscopic, kinetic and thermodynamic parameters and which satisfactorily describes both "vertical" and "nonvertical" quenching processes. *Balzani's* function (equation 29 in [9]) was fitted to the measured values of $k_{et}$[11] by application of the method of least squares[12]. The solid line shown in Figure 1 was obtained with the following values for the adjustable[13] parameters; $E_T^{00}$ *(3)* = 50±5 kJ/mol, $k_{en}^0 = (1.1\pm0.1)\times10^9$ s$^{-1}$ (rate constant for the energy-transfer in an activated encounter complex) and $\Delta G^{+}(0) = 1700\pm300$ cm$^{-1}$ [free energy of activation for a thermoneutral energy transfer from ($^3S$) to *(3)*]. From $\Delta G^{+}(0)$ and $E_T^{00}$ *(3)*, a lower limit of 120 kJ/mol for $E_T^v$ *(3)* can be estimated. A decrease in the energy transfer rates of the high-energy sensitizers is barely observable (picene and coronene, Fig. 1), although the energy of the $T_2$-state of *(3)* is very high (*ca.* 300 kJ/mol above $T_1$)[7]. An "inverted region", in the sense of the *Marcus* theory (equation 10 in [9]), accordingly does not appear even in this rather sensitive case.

*Conclusions:* Using flash spectroscopic sensitization of the cyclobutadiene derivative *(3)*, we were able to observe a short-lived (240 ns) intermediate which absorbed at wavelengths less than 400 nm. This species was assigned to the lowest triplet state of *(3)*. From the observed relation between the rate constant $k_{et}$ and the triplet energy $E_T^{00}$ *(S)* of the sensitizers used, the following estimates for the adiabatic and vertical triplet energies of *(3)* have been obtained: $E_T^{00} = 50\pm5$ kJ/mol, $E_T^v \geq 120$ kJ/mol.

Received: September 8, 1980 [Z 687 IE]
German version: Angew. Chem. 93, 192 (1981)

CAS Registry numbers:
*(1)*, 1120-53-2; *(2)*, 40219-42-9; *(3)*, 72931-47-6; *(4)*, 2197-57-1

---

[1] *T. Bally, S. Masamune*, Tetrahedron *36*, 343 (1980); *D. W. Whitman, B. K. Carpenter*, J. Am. Chem. Soc. *102*, 4272 (1980).

[2] *A. Krebs, H. Kimling, R. Kemper*, Justus Liebigs Ann. Chem. *1978*, 431 (footnote 29).

[3] a) *A. Krebs, H. Schmalstieg, O. Jarchow, K.-H. Klaska*, Tetrahedron Lett. *1980*, 3171; b) *J. Pocklington*, Dissertation, University of Hamburg, 1979.

[4] a) *J. Wirz* in *B. Pullman, N. Goldblum:* Excited States in Organic Chemistry and Biochemistry. Vol. *10*. Reidel, New York 1977, p. 283; b) *R. Gygax, J. Wirz, J. T. Sprague, N. L. Allinger*, Helv. Chim. Acta *60*, 2522 (1977).

[5] a) *H. Labhart, H. Heinzelmann* in *J. B. Birks:* Organic Molecular Photophysics. Vol. *1*. Wiley, New York 1973, p. 297; b) *J. B. Birks:* Photophysics of Aromatic Molecules. Wiley, New York 1970; c) *S. P. McGlynn, T. Azumi, H. Kinoshita:* Molecular Spectroscopy of the Triplet State. Prentice-Hall, Englewood Cliffs 1969; d) The photophysical properties of hexacene, which for reasons of solubility was used in 1,2,4-trichlorobenzene at 90 °C, are: $\lambda_{max}$ (T−T) = 550 nm, $E_T = 53\pm5$ kJ/mol, $^3\tau = 10$ μs; *H. Angliker, E. Rommel, J. Wirz*, unpublished results; e) *W. Leupin, J. Wirz*, J. Am. Chem. Soc. *102*, 6068 (1980).

[6] The concentration of *(3)* was determined by weighing and checked by monitoring the decrease in absorbance at 400 nm ($\Delta\varepsilon = 30$ M$^{-1}$ cm$^{-1}$) upon air oxidation of *(3)* after the measurements.

[7] a) *N. L. Allinger, C. Gilardeau, L. W. Chow*, Tetrahedron *24*, 2401 (1968); b) *M. Nakayama, M. Nishihira, Y. J. I'Haya*, Bull. Chem. Soc. Jpn. *49*, 1502 (1976); c) *M. Gisin, J. Wirz*, unpublished results.

[8] *A. Krebs, J. Pocklington, H. Schmalstieg, H. Irngartinger, N. Riegler*, unpublished results.

[9] *V. Balzani, P. Bolletta, F. Scandola*, J. Am. Chem. Soc. *102*, 2152 (1980).

[10] a) *D. L. Dexter*, J. Chem. Phys. *21*, 836 (1953); b) *M. F. Mirbach, V. Ramamurthy, M. J. Mirbach, N. J. Turro, P. J. Wagner*, Nouv. J. Chim. *4*, 471 (1980).

[11] The measured value for the quenching of $^3$(hexacene) (lg $k_{et} = 6.5$ in 1,2,4-trichlorobenzene, 90 °C) needed to be reduced for comparison with the other data (benzene, 25 °C). The applied correction of 0.5 units is self-consistent with the fitted *Balzani*-equation.

[12] *P. R. Bevington:* Data Reduction and Error Analysis for Physical Sciences. McGraw Hill, New York 1969.

[13] The following parameters have been determined elsewhere [9] and were not varied: $k_d = 10^{10}$ M$^{-1}$s$^{-1}$ (benzene, 25 °C), $k_d = 1.2\times10^{10}$ s$^{-1}$, $\Delta G^{+}_{(S)}(0) = 500$ cm$^{-1}$ (polycyclic arenes).

## Addition of Carbenes to Reactive Metal-Metal Bonds — A Simple Synthetic Method for μ-Methylene Complexes[**]

By *Wolfgang A. Herrmann, Christine Bauer, Johann Plank, Willibald Kalcher, Dieter Speth,* and *Manfred L. Ziegler*[*]

Following the synthesis of the first μ-methylene complex[1a], this class of compounds was rapidly extended, for which purpose diazoalkanes[1] and dihaloalkanes[2] were recognized as the most efficient carbene transfer reagents[3]. Apart from their well-documented synthetic use in organometallic chemistry, μ-methylene complexes are evidently also of interest for mechanistic studies concerning the *Fischer-Tropsch* process, not least because of their high reactivity with small molecules such as hydrogen and carbon monoxide[2b].

---

[*] Prof. Dr. W. A. Herrmann[+], Dipl.-Chem. Ch. Bauer, Dr. J. Plank, W. Kalcher
Institut für Anorganische Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg 1 (Germany)

Prof. Dr. M. L. Ziegler, Dipl.-Chem. D. Speth
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[+] Author to whom correspondence should be addressed.

[**] Transition Metal Methylene Complexes, Part 16. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, Degussa Hanau, BASF AG, and Hoechst AG. Part 15: *W. A. Herrmann, J. Plank, M. L. Ziegler, P. Wülknitz*, Chem. Ber., *114*, 716 (1981).

Subsequent to our work on dimetallacyclopropanes[1,4] we have found a further simple, generally applicable synthetic method which implies clean carbene addition to reactive metal-metal bonds. For example, the diazoalkanes *(2a)—(2g)* react with solutions of the binuclear rhodium compound *(1)*[5] in tetrahydrofuran (THF) to give near quantitative yields of the novel, easily crystallizable, nitrogen-free μ-methylene complexes *(4a)—(4e)* or *(5f)* and *(5g)*, respectively, which are air-stable in the solid state (Table 1). The extremely high reactivity of the starting compound *(1)*[6] even with the most stable diazoalkanes is evidenced by immediate [*(2a)—(2e)*] or smooth nitrogen elimination [*(2f)* and *(2g)*] at $-80\,^{\circ}C$ from these and many other diazo precursors. Carbene addition to the metal-metal bond (possibly *via* [2+3]-cycloaddition between *(1)* and *(2)*) first gives the triply bridged μ-methylene complexes of type *(3)* which, under certain steric conditions, can be isolated and characterized at room temperature as stable intermediates; the compounds resulting from tetrabromo-diazocyclopentadiene and 9-diazofluorene[7] may be quoted as well-characterized examples of this general observation. In boiling THF, however, the primary products *(3)* rapidly undergo CO-elimination, with the final compounds *(5)* being formed in practically quantitative yields.

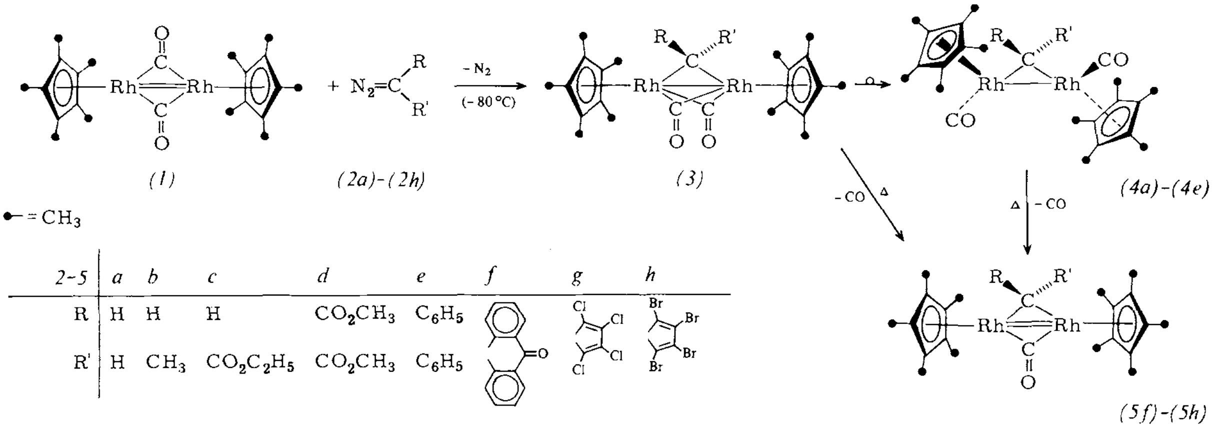


Table 1. Selected spectroscopic and physical data of the novel μ-methylene rhodium complexes *(4a)—(4e)*, *(5f)* and *(5g)*. Composition and constitution were verified by total elemental analysis, IR, $^1H$-NMR, $^{13}C$-NMR, mass spectroscopy (EI or FD); in addition, molecular weights were determined by osmometry.

| Comp. | IR (νCO) [$cm^{-1}$] [a] | $^1H$-NMR<br>(δ-value, 90 MHz, $CDCl_3$, int. TMS, 29 °C) [b] | Color and M. p. [c] |
|---|---|---|---|
| *(4a)* [d] | 1933 vs, 1901 sh [KBr])<br>1941 vs [THF]; 1948 vs [$C_5H_{12}$] | 1.95 [30 H, $^2J_{Rh,H} \approx 0.35$ Hz]; 5.97 [pseudotriplet, 2 H] | bright red prisms; above: *ca.* 50 °C dark colored (169 °C decomp.) |
| *(4b)* | 1953 sh, 1933 vs [KBr]<br>1937 vs [THF] | 1.98 [30 H]; 7.09 [m, 1 H; $^2J_{H,H} = 7.23$ Hz]; 2.28 [d, 3 H] | deep-red prisms;<br>162—163 °C (decomp.) |
| *(4c)* | 1974 s, 1951 vs, 1671 s [KBr]<br>1953 vs, 1677 w [THF] | 1.91 [30 H]; 1.23 [t, 3 H, $^2J_{H,H} = 7.20$ Hz]; 4.10 [q, 2 H]; 5.78 [t, 1 H, $^2J_{Rh,H} = 1.71$ Hz] | red plates;<br>148—149 °C |
| *(4d)* | 1965 vs, 1925 sh, 1682 vs [KBr]<br>1964 vs, 1682 s [THF] | 1.82 [30 H]; 3.62 [s, 6 H] | red, refractive plates;<br>187—188 °C |
| *(4e)* | 1938 vs [KBr]; 1941 vs [THF] | 1.62 [30 H]; 6.2–7.2 [m, 10 H] | carmine red, microcrystalline;<br>145—146 °C (decomp.) |
| *(5f)* | 1765 vs, 1623 s [KBr]<br>1778 vs, 1625 s [THF] | 1.15 [30 H]; 8.37 [m, 2 H]; 7.1–7.2 [m, 6 H] | steel blue needles; no M.p. <250 °C |
| *(5g)* | 1796 vs [KBr]; 1795 vs [THF] | 1.59 | blue-black lustrous microcrystals;<br>no M.p. <250 °C |

[a] Beckmann 4240: Reproducibility. ±1 $cm^{-1}$. [b] The $C_5(CH_3)_5$ signals appear as pseudo-singlets: the Rh—H couplings (<0.5 Hz) were only determined in a few cases. [c] After re-crystallization from *n*-pentane, *(4a)—(4e)*, or $CH_2Cl_2$/ether, *(5f)* and *(5g)*. [d] $^{13}C$-{$^1H$} NMR data ($CDCl_3$; int. TMS; 32 °C; ≈10% $^{13}CO$ enrichment): $\delta = 196.64$ [t: CO, $^1J_{Rh,C} = 44$ Hz], $\delta = 111.36$ [t; $CH_2$, $^1J_{Rh,C} = 29$ Hz], $\delta = 100.06$ [s, $C_5Me_5$], $\delta = 10.60$ [s, $CH_3$]. The multiplicity of the CO resonance proves that, in contrast to the $C_5H_5$ compounds [9b], rapid intramolecular CO exchange occurs on the NMR time scale (racemization of the chiral metal centers); at $-40\,^{\circ}C$ ($CD_2Cl_2$) only a doublet appears ($^1J_{Rh,C} = 89.7$ Hz).

Apart from CO-elimination, the carbene addition products *(3)* also provide the possibility of intramolecular carbonyl bridge opening. The isomers *(4a)—(4d)* thus accessible, resist decarbonylation under both thermal and photochemical conditions (THF, 66 °C, 5 h). By way of contrast, the μ-diphenylmethylene derivative *(4e)* is slowly converted to *(5e)* in the dark (THF, 25 °C). The complexes *(5f)* and *(5g)*, formed through consecutive carbene addition[8] and CO-elimination, exhibit the structural characteristics of *(1)*; comparison of *(1)* and *(5)* once again emphasizes the close electronic[9a] and structural[9b] analogies between carbonyl and methylene bridges.

The above-mentioned striking dependence of the product pattern upon the constitution of the diazo substrates predominantly arises from steric factors. The isomers of type *(4)* cannot be formed if sterically demanding cyclic carbenes are present in the immediate precursors *(3)* (*e.g.*, 9-fluorenylidene, 10-oxo-9,10-dihydro-9-anthrylidene, or cyclopentadienylidenes flanked by halogen substituents, *etc.*) since there is no way of further approaching the bulky pentamethylcyclopentadienyl groups. The molecular structures of the typical examples *(4d)* and *(3h)* nicely amplify on this statement (Fig. 1 and Table 2). While on the one hand, the small steric requirements of the methoxycarbonyl substituents in *(4d)* can tolerate consid-

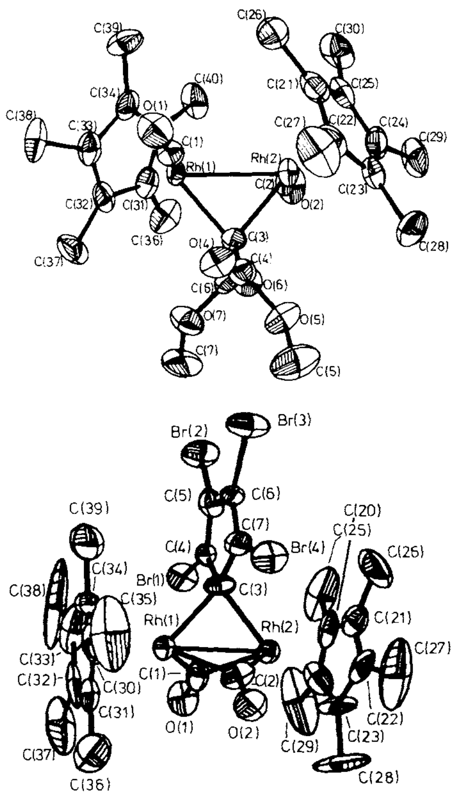


Fig. 1. ORTEP-Drawing of the μ-bis(methoxycarbonyl)methylene complex *(4d)* (above) as well as the μ-tetrabromocyclopentadienylidene complex *(3h)* (below). Scale models show that the planar, rigid α-bromo substituted five membered ring in *(3h)* cannot accept the structure type *(4)* because of considerable steric interaction with the $CH_3$ groups. *(4d)*: triclinic (from *n*-pentane/ether), space group $C_i^1$-$P\bar{1}$, $a=939.4(5)$, $b=1000.3(3)$, $c=1678.0(4)$ pm: $\alpha=76.67(2)$, $\beta=76.86$ *(3)*, $\gamma=68.80(3)°$, $Z=2$; 3815 non-zero reflections ($I>3\sigma(I)$; LP and absorption correction: $2\leq 2\theta\leq 60°$; $R_w=0.039$. *(3h)*: triclinic (from $CH_2Cl_2$/ether), space group $C_i^1$-$P\bar{1}$, $a=893.1(4)$, $b=1093.8(3)$, $c=1689.3(3)$ pm; $\alpha=76.37(2)$, $\beta=78.25(3)$, $\gamma=67.08(3)°$, $Z=2$; 2377 non-zero reflections ($I>3\sigma(I)$); $R_w=0.042$. Both structures were determined conventionally using a computer-controlled Syntex single crystal diffractometer and the SHELXTL program (P3, Data General Nova 3 System). — The structures of *(4a)* and *(4b)* show the same general features as found for *(4d)* (W. A. Herrmann, M. L. Ziegler, et al., unpublished results).

erable tilting of the $C_5Me_5$-rings towards the plane of the dimetallacyclopropane system and thus permit terminal coordination of the carbonyl functionalities, the strictly planar tetrabromo-cyclopentadienylidene bridge in *(3h)* forces the CO ligands into bridging positions, because it repels the two parallel $C_5Me_5$ rings towards each other. The unsubstituted $C_5H_5$ ligand, as a result of its far smaller size, still accepts the structure type *(4)*[10], even with extended planar cyclic carbene ligands present in such molecules. Both the synthetic routes and the structural influence of the methylene ligands described in this paper also hold for the nitrosyl complex $[(\eta^5\text{-}C_5H_5)Fe(\mu\text{-}NO)]_2$ which is a congener of the rhodium dimer *(1)*[11].

## *Procedure*

All operations were carried out under $O_2$ and $H_2O$ free conditions (Schlenk technique).

*(4a)*: A solution of *(1)* (532 mg, 1.0 mmol) in 80 $cm^3$ THF is treated with 10 $cm^3$ of a 0.2 M solution of $CH_2N_2$ in diethyl ether at −80 °C. Nitrogen is evolved and the deep blue solution becomes red within 1-2 min. The mixture is then allowed to warm up to room temperature, the solvent removed using an oil pump and the product recrystallized from the brick-red residue using *n*-pentane (−25 °/−80 °C); yield 514 mg (94%). The compound *(4a)*, which is stable in air, is very soluble in all common organic solvents.

Table 2. Selected bonding parameters of the μ-methylene complexes *(4d)* and *(3h)*.

| | *(4d)* | *(3h)* |
|---|---|---|
| Bond lengths [pm] | | |
| Rh(1)—Rh(2) | 266.3(1) | 261.2(2) |
| Rh(1)—C(3) | 208.3(6) | 210.3(15) |
| Rh(2)—C(3) | 207.6(6) | 211.8(11) |
| Rh(1)—C(1) | 183.3(9) | 203.4(18) |
| Rh(2)—C(1) | — | 205.5(14) |
| Rh(1)—C(2) | — | 202.3(14) |
| Rh(2)—C(2) | 183.7(10) | 201.1(20) |
| C(1)—O(1) | 115.5(12) | 117.7(9) |
| C(2)—O(2) | 115.1(13) | 116.8(21) |
| Bond angles [°] | | |
| Rh(1),C(1),O(1) | 166.6(6) | 138.5(9) |
| Rh(1),C(3),Rh(2) | 79.6(2) | 76.5(4) |
| Rh(1),C(2),Rh(2) | — | 80.7(7) |
| Rh(1),C(1),Rh(2) | — | 80.1(4) |
| C(4),C(3),C(7) | — | 101.6(9) |
| C(4),C(3),C(6) | 108.2(5) | — |
| Interplanar angles [°] [a] | | |
| Cp(C20—24)/Cp(C30—34) | 47.6 | 7.2 |
| Cp(C30—34)/$CR_2$ | 129.4 | 6.6 |
| Cp(C20—24)/$CR_2$ | 129.9 | 0.7 |
| Cp/Rh(1),Rh(2),C(3) | 55.9 | 90.3 |
| Cp′/Rh(1),Rh(2),C(3) | 55.8 | 90.3 |
| Rh(1),Rh(2),C(3)/$CR_2$ | 82.1 | 90.6 |

[a] The interplanar angles are calculated from the best planes of the $C_5Me_5$ ligands, the methylene bridges $CR_2$ [*(4d)*: C(3), C(4), C(6); *(3h)*: C(3—7), Br (1—4)] and from the Rh(1), C(3), Rh(2) plane. The strictly planar tetrabromocyclopentadienylidene ligand of *(3h)* exhibits alternating C—C bond lengths typical of a 1,3-diene system. The $C_6Me_5$ rings form angles of 41.2 and 89.6° resp., with the Rh(1), Rh(2)-vector.

*(5f)*: A solution of *(1)* (266 mg, 0.5 mmol) in 60 $cm^3$ THF at −80 °C, is treated dropwise with a solution of 10-diazoanthrone (110 mg, 0.5 mmol) in 15 $cm^3$ THF. $CO/N_2$ are evolved and the color changes from deep blue to blue-green. Finally the solution is stirred for 30 mins at 25 °C, concentrated using a water aspirator and the residue chromatographed on Florisil (10 × 1 cm column, water-cooled jacket). Using *n*-pentane/benzene (5:1) and benzene as eluents, small amounts of $[\eta^5\text{-}C_5(CH_3)_5]Rh(CO)_2$ or *(1)*, respectively, are eluted. *(5f)* appears in a deep blue band (benzene/diethyl ether 5:2). The eluent is removed *in vacuo*. The residue is recrystallized from $CH_2Cl_2$/diethylether (−80 °C). Yield 334 mg (96%); very soluble in $CH_2Cl_2$, moderately soluble in ether, practically insoluble in *n*-hexane.

Received: September 19, 1980,
supplemented November 11, 1980 [Z 693 IE]
German version: Angew. Chem. *93*, 212 (1981)

CAS Registry numbers:
*(1)*, 69728-34-3; *(2a)*, 334-88-3; *(2b)*, 1117-96-0; *(2c)*, 623-73-4; *(2d)*, 6773-29-1; *(2e)*, 883-40-9; *(2f)*, 1705-82-4; *(2g)*, 21572-61-2; *(2h)*, 38123-55-6; *(3a)*, 76550-26-0; *(3b)*, 76550-27-1; *(3c)*, 76550-28-2; *(3d)*, 76550-29-3; *(3e)*, 76550-30-6; *(3f)*, 76550-31-7; *(3g)*, 76550-32-8; *(3h)*, 76550-33-9; *(4a)*, 76582-86-0; *(4b)*, 76582-87-1; *(4c)*, 76582-88-2; *(4d)*, 76550-34-0; *(4e)*, 76582-89-3; *(5f)*, 76550-35-1; *(5g)*, 76550-36-2; *(5h)*, 76550-37-3; *(6)*, 76584-34-4; $\mu\text{-}SO_2[\{\eta^5\text{-}C_5\text{-}(CH_3)_5\}Rh(CO)]_2$, 76550-06-6; $(\mu\text{-}C_{13}H_8)(\mu\text{-}Co)_2[\{\eta^5\text{-}C_5(CH_3)_5\}Rh]_2$, 76550-38-4; $[\eta^5\text{-}C_5(CH_3)_5]Rh(CO)_2$, 32627-01-3; $(CH_3)_3NO$, 1184-78-7; 9-diazofluorene, 832-80-4

---

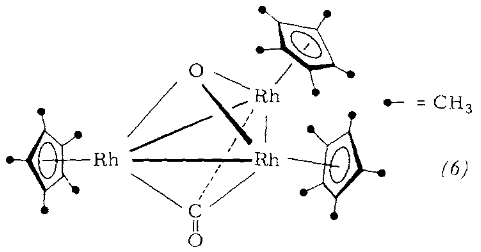
[1] a) *W. A. Herrmann, B. Reiter, H. Biersack*, J. Organomet. Chem. *97*, 245 (1975); b) Review: *W. A. Herrmann*, Angew. Chem. *90*, 855 (1978); Angew. Chem. Int. Ed. Engl. *17*, 800 (1978); c) More recent examples are cited by: *W. A. Herrmann, J. Plank, D. Riedel, M. L. Ziegler, K. Weidenhammer, E. Guggolz, B. Balbach*, J. Am. Chem. Soc. *103*, 63 (1981); *W. A. Herrmann*, Advan. Organomet. Chem., in press.

[2] a) *K. H. Theopold, R. G. Bergman*, J. Am. Chem. Soc. *102*, 5694 (1980); b) *Ch. E. Sumner, Jr., P. E. Riley, R. E. Davis, R. Pettit, ibid. 102*, 1752 (1980); *R. C. Brady III, R. Pettit, ibid. 102*, 6181 (1980).

[3] A further synthetic procedure of general applicability is the addition of carbene complexes $L_xM = CRR'$ to organometallic fragments; see *e.g.* *T. V. Ashworth, J. A. K. Howard, M. Laguna, F. G. A. Stone*, J. Chem. Soc. Chem. Commun. *1979*, 43. $CH_2$-derivatives have however not yet proved accessible by this method.

[4] *W. A. Herrmann, J. Plank, E. Guggolz, M. L. Ziegler*, Angew. Chem. *92*, 660 (1980); Angew. Chem. Int. Ed. Engl. *19*, 651 (1980); *W. A. Herrmann, J. Plank, M. L. Ziegler, B. Balbach*, J. Am. Chem. Soc. *102*, 5906 (1980).

[5] The synthesis of *(1)* on a 6g-scale can be carried out by reaction of $[\eta^5\text{-}C_5(CH_3)_5]Rh(CO)_2$ [5b] with $(CH_3)_3NO\cdot 2H_2O$ [boiling acetone, 3h; yield 80-90%]. Column chromatography of the crude material on $SiO_2$ also resulted in the isolation of the novel, trinuclear $\mu_3$-oxo-complex *(6)* in 7–10%



*(6)*

yield. This compound forms deep purple, air-stable crystals (from $CH_2Cl_2$/ether), which are thermally stable up to temperatures >265 °C (sealed capillary); very soluble in THF, methanol and dimethylformamide, moderately soluble in acetonitrile and diethylether, practically insoluble in *n*-pentane. IR: 1661 vs, 1654 vs, 1648 s (sh) $cm^{-1}$ [$\nu$CO, KBr]; 1655 vs, 1649 vs, 1643 vs (sh) $cm^{-1}$ [$\nu$CO, $CH_2Cl_2$]; $^1$H-NMR: (90 MHz, $CDCl_3$, 33 °C, int. TMS) $\delta = 1.81$; field desorption mass spectrum (from acetone): $m/e = 758$ ($M^+$); correct elemental analysis. b) *J. W. Kang, P. M. Maitlis*, J. Organomet. Chem. *26*, 393 (1971).

[6] The application of the EAN-rule to *(1)* leads to the formulation of a Rh=Rh double bond [cf. *A. Nutton, P. M. Maitlis*, J. Organomet. Chem. *166*, C21 (1979)] which suggests an analogy between carbene-addition and the cyclopropanation of alkenes. However, since considerable uncertainties exist over metal-metal multiple bonds and since bond orders are rarely well defined, we stress caution in over-evaluation of such formalisms [cf. *e.g.* *I. Bernal, J. D. Korp, M. G. Reisner, W. A. Herrmann*, *ibid.* *130*, 321 (1977)].

[7] This compound (yield 100%), forms black, completely air-stable needles which have a metallic luster (M. p. 179 °C, decomp.). IR($\nu$CO): 1842 vs, 1788 vs [KBr]; 1846 s, 1792 vs [THF]. $^1$H-NMR ($CDCl_3$, int. TMS, 33 °C): $\delta = 1.36$ ["s", 30H], $\delta = 7.0$–7.8 [m, 8H].

[8] We have also observed smooth additions with $CH_2$-analogous molecules. For example, *(1)* gives the deep red, air-stable complex $(\mu\text{-}SO_2)[\{\eta^5\text{-}C_5(CH_3)_5\}Rh(CO)]_2$ in 98% yield, when treated with $SO_2$. IR ($\nu$CO): 1980 vs [KBr]; 1985 vs [THF]. $^1$H-NMR ($CDCl_3$, int. TMS, 29 °C): $\delta = 2.00$ ["s"]; FD mass spectrum (from acetone): $m/e = 596$ ($M^+$).

[9] a) *P. Hofmann*, Angew. Chem. *91*, 591 (1979); Angew. Chem. Int. Ed. Engl. *18*, 554 (1979); cf. *A. R. Pinhas, T. A. Albright, P. Hofmann, R. Hoffmann*, Helv. Chim. Acta *63*, 29 (1980); b) *W. A. Herrmann, C. Krüger, R. Goddard, I. Bernal*, J. Organomet. Chem. *140*, 73 (1977).

[10] *M. Creswick, I. Bernal, W. A. Herrmann, I. Steffl*, Chem. Ber. *113*, 1377 (1980).

[11] *W. A. Herrmann, Ch. Bauer*, J. Organomet. Chem. *204*, C21 (1981); *ibid.*, in press. In the meantime *(4a)* has also been synthesized by other workers: *A. D. Clauss, P. A. Dimas, J. R. Shapley*, *ibid.* *201*, C31 (1980); *F. G. A. Stone et al.*, J. Chem. Soc. Chem. Commun. *1980*, 1171.

## Tetrafluoroboric Acid-Methanol (1/2), Cyclic Molecules by Hydrogen Bonds between Ions[**]

By *Dietrich Mootz* and *Michael Steffen*[*]

We have been able to characterize the phase $HBF_4\cdot 2CH_3OH$[1] which melts congruently at −41 °C in the system $HBF_4\cdot CH_3OH$—$CH_3OH$ by its crystal structure analysis as an oxonium salt $[(CH_3OH)_2H]BF_4$ with molecular structure.

Samples of corresponding composition have been prepared by passage of boron trifluoride[2] into a mixture of hydrogen fluoride and methanol in the ratio 1:2. Growth of a single crystal on a diffractometer in a teflon tube sealed at both ends was achieved by slow cooling in a stream of cold gas at −50 °C. The X-ray measurements were also carried out at this temperature. They showed[3] the monoclinic space group $P2_1/c$, the lattice constants $a = 5.197$, $b = 14.458$, $c = 9.318$ Å and $\beta = 94.61°$, four formula units per unit cell, and the atomic arrangement shown in Figure 1[4].

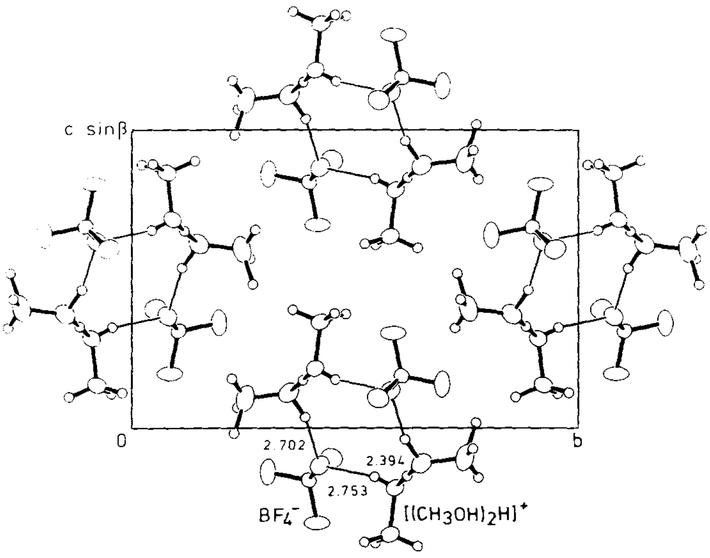


Fig. 1. Crystal structure of $C_2H_9O_2BF_4$. Projection down the *a*-axis, with O...O and O...F distances of the hydrogen bonds in Å.

The acid proton links two methanol molecules by a very short hydrogen bond (O....O distance 2.394 Å) to give a bis(methanol)hydrogen cation $[(CH_3OH)_2H]^+$, which can also be regarded as a methyl-substituted $H_5O_2^+$ ion, and which to our knowledge has hitherto not been observed in a crystal structure. Its two terminal OH protons are oriented *cis* to each other. Cations of this type and $BF_4^-$ anions are coupled by hydrogen bonds O—H···F with O....F distances of 2.702 and 2.753 Å to give molecular cyclic dimers of the formula unit with centrosymmetric $O_4F_2$ six-membered rings planar within 0.13 Å. Both independent hydrogen bonds involve the same F atom of the four independent ones; its B—F distance of 1.407 Å is markedly longer than those of the other three between 1.356 and 1.365 Å.

We have also been able to obtain single crystals of the "parent compound" (without methyl-substitution) $H_5O_2BF_4$ (m.p. −34 °C) and to determine its structure. The O....O distance in the $H_5O_2^+$ ion is 2.412 Å; owing to the greater number of protons capable of forming hydrogen bonds, the cations and anions are cross-linked in a three-dimensional network. The structure is not an isotype of $H_5O_2ClO_4$[5].

Received: June 9, 1980 [Z 641 IE]
German version: Angew. Chem. *93*, 211 (1981)

CAS Registry numbers:
$[(CH_3OH)_2H]BF_4$, 2088-66-6; $BF_3$, 7637-07-2; HF, 7664-39-3; $CH_3OH$, 67-56-1

---

[*] Prof. Dr. D. Mootz, Dipl.-Chem. M. Steffen
Institut für Anorganische Chemie und Strukturchemie der Universität
Universitätsstr. 1, D-4000 Düsseldorf (Germany)

[**] Crystal Structures of Acid Hydrates and Oxonium Salts, Part 17. — Part 16: *D. Katryniok, R. Kniep, D. Mootz*, Z. Anorg. Allg. Chem. *461*, 96 (1980).

[1] *S. Pawlenko*, Z. Anorg. Allg. Chem. *332*, 149 (1964).

[2] For a recently determined crystal structure of boron trifluoride itself, see *D. Mootz, M. Steffen*, Angew. Chem. *92*, 481 (1980); Angew. Chem. Int. Ed. Engl. *19*, 483 (1980).

[3] Single-crystal diffractometer Syntex $P2_1$ with modified cooling unit LT-1; $Mo_{K\alpha}$, ω-scan $2\theta_{max} = 60°$; 1064 significant reflections, program system E-XTL, $R = 0.066$.

[4] *C. K. Johnson*: ORTEP II program, ORNL-5138. Oak Ridge National Laboratory, Oak Ridge, Tenn. 1976.

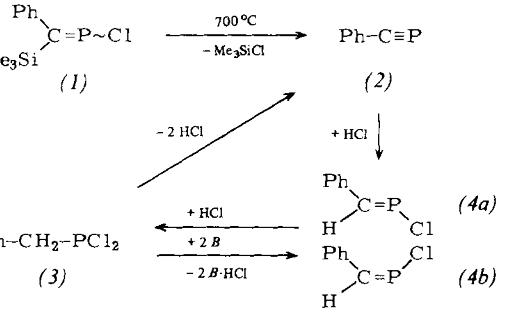
[5] *I. Olovsson*, J. Chem. Phys. *49*, 1063 (1968).

## Elimination and Addition at the Phosphorus-Carbon pπ-pπ Bond[**]

By *Rolf Appel, Günther Maier, Hans Peter Reisenauer,*
and *Axel Westerhaus*[*]

The existence of three phosphaalkynes has so far been reported: Besides the parent compound, phosphaacetylene HCP, which was first obtained as long ago as 1961 on passage of $PH_3$ through an electric arc generated between graphite electrodes[1a,b], the fluoro- and the methyl-derivative (1-phosphapropyne) could later also be prepared and characterized, in particular by microwave and photoelectron spectroscopy[1c]. In both cases the method employed for the synthesis was the elimination of hydrogen halide, from trifluoromethylphosphane and dichloro(ethyl)phosphane, respectively. The pyrolysis of dichloro(ethyl)phosphane, however, does not proceed uniformly; ethylene, $PCl_3$, ethane and acetylene are formed as well as HCl, and the 1-phosphapropyne obtained in only low yield is contaminated with difficultly separable byproducts.

We have now found that when chloro[phenyl(trimethylsilyl)methylene]phosphane *(1)*[2] is heated to 700 °C under vacuum (Hg-diffusion pump), chlorotrimethylsilane is selectively cleaved and phenylmethylidynephosphane (2-phenylphosphaacetylene) *(2)* is formed in almost quantitative yield. The elimination process was optimized by means of a mass spectrometer coupled directly to the pyrolysis apparatus and *(2)* was collected in a cold trap cooled to −196 °C.



The P≡C triple-bond structural element in *(2)* is detectable by the characteristic $^{13}C$- and $^{31}P$-NMR data[3] and is confirmed by stepwise HCl-addition; initially the phosphaalkene *(4a)* is formed, which reacts with a second equivalent of HCl to give the benzyldichlorophoshane *(3)*. It can be shown by $^{31}P$-NMR spectroscopic measurements that *(3)* can also be dehydrochlorinated with tertiary amines *(B)*, with reversal of this formation reaction[2]. However, the *Z*-isomer *(4b)* is formed concomitantly besides *(4a)*. Owing to a stereospecific *cis*-addition at the triple bond, *(4b)* is not obtained on addition of HCl to *(2)*.

In contrast to the halosilane-elimination, direct vacuum pyrolysis of *(3)* affords numerous unidentified by-products and only very small amounts of *(2)*.

*(2)* exists in the monomeric state only at low temperatures; slow decomposition sets in above −50 °C. According to $^{31}P$-NMR spectroscopic measurements its half-life at 0 °C is 7 min. The silyl compound $Me_3SiCP$[4] is much more stable.

### *Experimental*

A quartz tube (25 mm diameter) packed with quartz wool in the hot zone is preheated in a controllable 10 cm-long ring oven at 750 °C. Approximately 0.5 g of an excess supply of *(1)* (room temperature) is thermolyzed under vacuum (Hg-diffusion pump) for 12 h and the condensate collected in cold-trap at −196 °C. The condensate is taken up in a small amount of $CD_2Cl_2$ and rapidly filtered at −78 °C; the filtrate contains only $(CH_3)$ SiCl and *(2)*.

*(3)* is thermolyzed analogously at 800 °C. According to $^{31}P$-NMR measurements the condensate consists mainly of unreacted *(3)* together with small amounts of *(2)* and a series of unidentified by-products.

Received: July 28, 1980 [Z 642 IE]
German version: Angew. Chem. *93*, 215 (1981)

CAS Registry numbers:
*(1)*, 74483-17-3; *(2)*, 76684-21-4; *(3)*, 4545-85-1; *(4a)*, 76684-22-5; *(4b)*, 76684-23-6.

---

[1] a) *T. E. Gier*, J. Am. Chem. Soc. *83*, 1769 (1961); b) *S. P. Anderson, H. Goldwhite, D. Ko, A. Letsou*, J. Chem. Soc. Chem. Commun. *1975*, 744; c) *H. W. Kroto, J. F. Nixon, N. P. C. Simmons, N. P. C. Westwood*, J. Am. Chem. Soc. *100*, 446 (1978); *M. J. Hopkinson, H. W. Kroto, J. F. Nixon, N. P. C. Simmons*, Chem. Phys. Lett. *42*, 460 (1976).

[2] *R. Appel, A. Westerhaus*, Angew. Chem. *92*, 578 (1980); Angew. Chem. Int. Ed. Engl. *19*, 556 (1980).

[3] $^{13}C\{^1H\}$-NMR ($CD_2Cl_2$, 22.6 MHz, TMS int.): $\delta = 164.9$ [d, $J(PC) = 48.3$ Hz, PC]; $^{31}P\{^1H\}$-NMR (32.2 MHz, $H_3PO_4$ ext.): $\delta = -32.0$, cf. also [1b].

[4] *R. Appel, A. Westerhaus*, Tetrahedron Lett., in press.

---

[*] Prof. Dr. R. Appel, Dipl.-Chem. A. Westerhaus
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)
Prof. Dr. G. Maier, Dr. H. P. Reisenauer
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)

[**] Phosphorus-Carbon-Halogen Compounds, Part 26.—Part 25: *R. Appel, J. Peters, R. Schmitz*, Z. Anorg. Allg. Chem., in press.

## $Ba_4SiAs_4$ and $Ba_4GeAs_4$, Zintl Phases with Isolated $SiAs_4^{8-}$ and $GeAs_4^{8-}$ anions[**]

By *Brigitte Eisenmann, Hanna Jordan,*
and *Herbert Schäfer*[*]

Zintl phases are intermetallic compounds which display a pronounced heteropolar bonding contribution and whose anionic partial lattices, in agreement with an ionic formulation, obey the $(8-N)$ rule. A classification according to this Zintl-Klemm concept[1] embraces the majority of compounds of the alkali and alkaline-earth metals which contain, in particular, the semimetals of the 4th and 5th main group as anionic partners. Only such compounds have so far been systematically characterized whose anionic partial lattice is made up of merely one element. No comprehensive investigations have been carried out on compounds with binary anions which may also be interpreted as Zintl phases and which represent bridging members between ternary intermetallic compounds and salts with complex anions.

Particularly impressive examples for such an extension of the Zintl-Klemm concept are the isotypic compounds $Ba_4SiAs_4$ and $Ba_4GeAs_4$ reported here for the first time, which contain "isolated" $SiAs_4$- and $GeAs_4$-tetrahedra, *i.e.*

---

[*] Prof. Dr. H. Schäfer, Dr. B. Eisenmann, Dipl.-Ing. H. Jordan
Abteilung II für Anorganische Chemie im
Eduard-Zintl-Institut der Technischen Hochschule
Hochschulstrasse 4, D-6100 Darmstadt (Germany)

[*] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

surrounded only by Ba counterions. The atomic arrangement determined by complete X-ray structure analyses[2] is perspectively reproduced in Figure 1. The Si—As and Ge—As distances of 239.3 and 240.7 pm and of 246.4 and 248.1 pm, respectively, are in very good agreement with the sums of the radii of the elements of 240.1 (Si—As) and 248.3 pm (Ge—As).

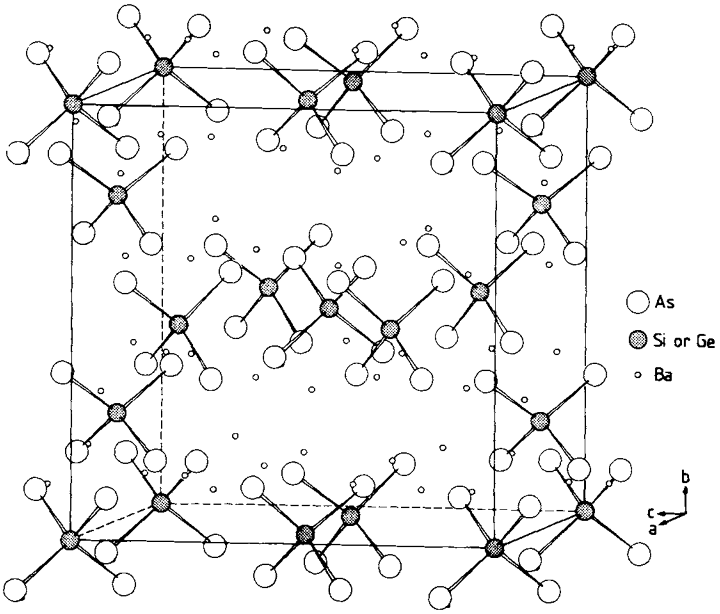


Fig. 1. Unit cell of $Ba_4SiAs_4$ and $Ba_4GeAs_4$.

Corresponding to the observed bonds between the electronegative elements (Si and Ge with four bonds $\hat{=}$ formal charge 0. As with one bond $\hat{=}$ formal charge 2—[1]), $Ba_4SiAs_4$ and $Ba_4GeAs_4$ can be ionically formulated according to $4\,Ba^{2+} + SiAs_4^{8-}$ or $GeAs_4^{8-}$. Hence, the principle already found for the previously described[3] compounds containing polyanions is preserved. That is the semimetal of lower electronegativity is saturated by covalent bonds and the charges provided by the alkaline-earth metal are to be ascribed to the more electronegative partner.

## *Experimental*

Stoichiometric amounts of the elements were heated under argon in a quartz ampoule within 8 h to 1000 °C, kept at this temperature for 1.5 h, and then slowly cooled to 600 °C. The product is annealed at this temperature for 12 h and the furnace then switched off.—Both compounds form lustrous, dark metallic, cubic shaped crystals which become covered with dark decomposition products of unknown composition on exposure to a moist atmosphere.

Received: May 30, 1980 [Z 643 IE]
German version: Angew. Chem. *93*, 211 (1981)

---

[1] Cf. *H. Schäfer, B. Eisenmann, W. Müller,* Angew. Chem. *85*, 742 (1973); Angew. Chem. Int. Ed. Engl. *12*, 694 (1973).

[2] $Ba_4SiAs_4$: cubic, space group $P\bar{4}3n$, $Z=8$, $a=1330.7(9)$ pm, $\varrho_{calc}=4.822$ g/cm$^3$; two-circle diffractometer Stoe Stadi II (MoKα, graphite monochromator, ω-scan), $R=0.095$ (574 symmetry independent reflections, isotropic temperature factors).
$Ba_4GeAs_4$: cubic, space group $P\bar{4}3n$, $Z=8$, $a=1341.9(2)$ pm, $\varrho_{exp}=5.04$, $\varrho_{calc}=5.065$ g/cm$^3$; four-circle diffractometer PW 1100 (MoKα, graphite monochromator, ω-scan), $R=0.099$ (643 symmetry independent reflections, isotropic temperature factors).
Solution of structure with MULTAN 78, A system of computer programs (*P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, M. M. Woolfson,* University of York 1978); calculation of structural factors and Fourier syntheses with SHEL-X-76 program system (*G. M. Sheldrick,* University of Cambridge, 1976).

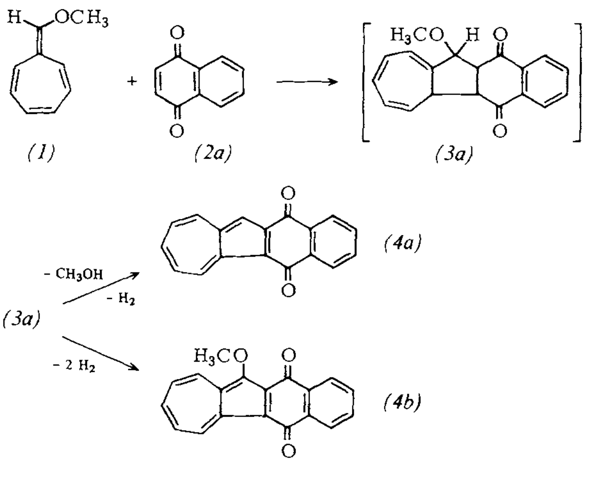
[3] *B. Eisenmann, H. Schäfer,* Angew. Chem. *92*, 480 (1980); Angew. Chem. Int. Ed. Engl. *19*, 490 (1980).

---

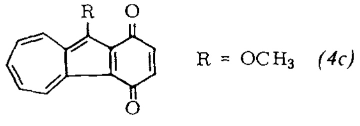
# Acenazulenediones: Synthesis, Spectroscopy, Electrochemical Detection of a Double Redox Cycle[**]

By *Margarete Baier, Jörg Daub, Adelheid Hasenhündl, Andreas Merz,* and *Knut M. Rapp*[*]

8-Methoxyheptafulvene *(1)* adds compounds containing electron-deficient multiple bonds with formation of hydroazulenes[1]. Hence, reaction with *p*-quinones *(2)* should lead, *via* hydroacenazulenediones *(3)* to diones *(4)*.



Reaction of *(1)* with 1,4-naphthoquinone *(2a)* in the molar ratio 1:2 affords naphth[2,3-*a*]azulene-5,12-dione *(4a)* and the methoxy compound *(4b)* in a ratio of 65:35 in 67% overall yield. If the reaction is carried out in a ratio of 1:1 the proportion of *(4a)* increases to >95% with a total yield of *(4)* of 34%. This is consistent with favored cleavage of $CH_3OH$ from the non-isolable intermediate *(3a)* at small quinone concentration. *(4a)* and *(4b)* were separated by column chromatography (low-pressure, Merck pre-packed column, silica gel, dichloromethane). Reaction of 1,4-benzoquinone with *(1)* affords 10-methoxybenz[*a*]azulene-1,4-dione *(4c)* in only 9% yield; a product with R = H was not found. The low yield of *(4c)* is attributed to polymerization of *(1)*.



The spectra of *(4)* show characteristic features of the individual structural moieties (Table 1). Typical for the azulene moiety is the longest-wave band in the electronic spectrum

---

[*] Prof. Dr. J. Daub, Prof. Dr. A. Merz, Dr. K. M. Rapp, M. Baier, A. Hasenhündl
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg (Germany)

[**] Fulvenes with Inverse Ring Polarization, Part 5. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and BASF.—Part 4: [1].

[*(4a)*: $\lambda_{max} = 655$ nm]; the hydrocarbon naphth[2,3-*a*]azulene absorbs in the same region ($\lambda_{max} = 647$ nm)[2]. A pronounced solvatochromism is determinable for the long-wave bands of *(4)* [*(4a)*: $\lambda_{max}(CH_3CN)$: 655 nm, $\lambda_{max}$(benzene): 672 nm]. The quinones *(4)* can thus be compared with merocyanines in which the quinone moiety has acceptor properties and the cycloheptatriene moiety has donor properties.

Table 1. Some physical data of acenazulendiones *(4)*.

*(4a)*: M.p. = 279—280 °C; IR (KBr): 1668 (CO), 1634 (CO), 740, 710 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 7.5$—8.0 (m, 5H), 8.1—8.35 (m, 2H), 8.6 (d, $J = 9.5$ Hz, H-6), 9.9 (d, m, $J = 9.5$ Hz, H-10); UV-VIS ($CH_3CN$): $\lambda_{max}$ ($\log\varepsilon$) = 248 (4.1), 308 (4.3), 415 (3.6), 585 (2.8), 610 (2.9), 655 nm (2.7); MS (70 eV): $m/e = 258$ ($M^+$, 100%), 230 (20), 202 (31), 176 (4), 129 ($M^{2+}$); redox potentials in $CH_3CN$: reduction −0.69 V, −1.39 V; oxidation +1.28 V (irrev.)

*(4b)*: M.p. = 217—220 °C; IR (KBr): 1665 (CO), 1625 (CO), 730, 705 $cm^{-1}$. $^1H$-NMR($CDCl_3$): $\delta = 4.3$ (s, $OCH_3$), 7.2—8.3 (m, H-1,2,3,4,7,8,9), 8.6 (d, t, $J = 9.8$ Hz, H-6), 9.9 (d, m, $J = 10$ Hz, H-10); UV-VIS ($CH_3CN$): $\lambda_{max}$ ($\log\varepsilon$) = 253 (3.9), 312 (4.0), 454 (3.5), 678 nm (2.6); MS (70 eV): $m/e = 288$ ($M^+$, 87%), 273 (100), 260 (11), 245 (20), 144 ($M^{2+}$, 4), 136.5 (<2); redox potentials in $CH_3CN$: reduction −0.69, −1.39 V, oxidation +1.11, +1.50 V (irrev.)

*(4c)*: M.p. = 191 °C (dec.); IR (KBr): 1650 (CO), 1622 (CO), 850, 735 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 4.2$ (s, $OCH_3$), 6.75, 6.83 (d, AB-part, $^3J = 4.4$ Hz, H-2, H-3), 7.42—7.82 (m, H-6,7,8), 8.65, 9.63 (d,d, $J = 10.2$ Hz, H-5, H-9); UV-VIS ($CH_3CN$): $\lambda_{max}$ ($\lg\varepsilon$) = 265 (4.3), 315 (4.3), 472 (3.8), 690 nm (3.2); MS (70 eV): $m/e = 238$ ($M^+$, 82%), 223 (100), 210 (5); redox potentials in $CH_3CN$: reduction −0.62, −1.32 V; oxidation +1.15, +1.55 V (irrev.)

The unusual electrochemical behavior of the quinones *(4a)* and *(4b)* in aprotic medium ($CH_3CN$ or dimethylformamide (DMF), 0.1 M $Bu_4N^{\oplus}ClO_4^{\ominus}$) is demonstrated in the following by example of the cyclic voltammetry of *(4a)* (Fig. 1a): The reversibility of the one-electron reduction to the radical anion *(4a⁻̇)* (signals I and I′) is curtailed by an homogeneous secondary reaction (complete reversibility at $v \geq 5$ $Vs^{-1}$). Consequently, an additional redox pair of peaks III and III′ occurs besides the signals for the formation of the dianion ($4a^{2\ominus}$) (II and II′) as well as an additional signal IV for the irreversible oxidation, which is not observed, for example, in the case of anthraquinone. In the direct current polarogram, only the reduction steps quoted in Table 1 are observed at the mercury dropping electrode[3]. The complete reduction (1F/mol) at −0.8 V leads to a deep-red solution ($\lambda_{max}(CH_3CN) = 470$ nm, broad band), whose cyclic voltammogram now only shows the peaks III/III′ and IV (Fig. 1b). The red species is re-converted into the educt *(4a)* both by the electrolysis at +1.0 V as well as by oxidation with atmospheric oxygen.

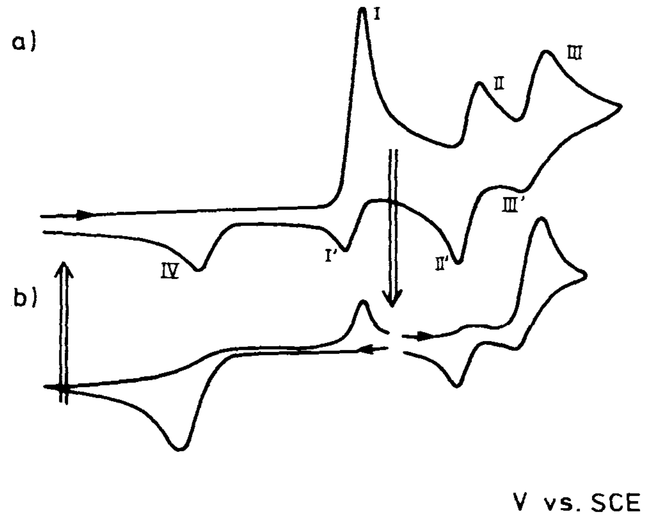
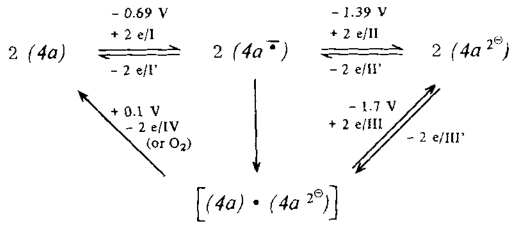


Fig. 1. Cyclic voltammograms of naphth[2,3-*a*]azulene-5,12-dione *(4a)* (in $CH_3CN$/0.1 M $Bu_4N^{\oplus}ClO_4^{\ominus}$, Pt-disk electrode, scanning rate $v = 0.1$ $Vs^{-1}$). a) $2 \times 10^{-3}$ M *(4a)*; b) after complete reduction of this solution at −0.8 V. I,I′,II,II′,III,III′,IV, see text and Scheme 1.

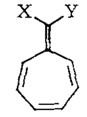
We interpret this behavior in terms of an association of the radical anions *(4⁻̇)* formed in the primary step to give quinhydrone-like EDA complexes [quinone × quinone$^{2\ominus}$]. These complexes are more difficult to reduce as well as more difficult to oxidize than the radical ions *(4⁻̇)* (Scheme 1).



Scheme 1. Redox cycle on uptake of electrons by *(4a)*. I,I′,II,II′,III,III′,IV, see Fig. 1.

In acid medium (0.05 M $HClO_4$ in 95% aqueous DMF, glassy-carbon electrode) the quinones show the usual reversible two-electron reduction, even though marked deviations of the cyclovoltammogram from the ideal shape here also indicate the participation of association.

The behavior in the redox process is consistent with the concept of "heptafulvenes with normal and inverse electron distribution"[4]. The quinones *(4)* correspond to heptafulvenes *(5)* with normal electron distribution (*i.e.* X and Y are acceptors—the system is stable). The monoanions *(4⁻̇)* and dianions ($4^{2\ominus}$) formed in the reduction correspond to the heptafulvenes *(5)* with inverse electron distribution (*i.e.* X and Y are donors—the system is destabilized. ($4^{2\ominus}$) can be stabilized as the EDA complex [*(4)*·*($4^{2\ominus}$)*].



*(5)*

Received: August 1, 1980 [Z 677 IE]
supplemented: December 19, 1980
German version: Angew. Chem. 93, 196 (1981)

CAS Registry numbers:
*(1)*, 71133-64-7; *(2a)*, 130-15-4; *(4a)*, 76319-75-0; *(4b)*, 76319-76-1; *(4c)*, 76-319-77-2

---

[1] *A. Hasenhündl, K. M. Rapp, J. Daub*, Chem. Lett. *1979*, 597.

[2] *M. Yasunami, P. W. Yang, Y. Kondo, Y. Noro, K. Takase*, Chem. Lett. *1980*, 167.

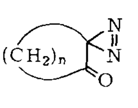
[3] The azulene moiety of the quinones *(4)* makes itself noticeable by the easy electrochemical oxidizability (on Pd or C); for oxidation potentials, see Table 1).

[4] *J. Daub*, lecture at the International Symposium on Aromaticity, Dubrovnik 1979; *K. M. Rapp, J. Daub*, Tetrahedron Lett. *1977*, 227.

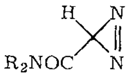
# 3,3-Diazirinedicarboxylic Acid ("Cyclodiazomalonic Acid") and Some of Its Derivatives

By *Gennady V. Schustov, Nina B. Tavakalyan,*
and *Remir G. Kostyanovsky*[*]

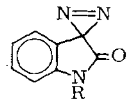
Compounds *(1)-(4)*, 3,3-disubstituted diazirines having a carbonyl group at a position α to the three membered ring, have hitherto been synthesized by oxidation of the corresponding alcohols (α-azicycloalkanones *(1)*)[1], or more frequently by photoisomerization of α-diazocarbonyl compounds, (3*H*-diazirinecarboxylic acid dialkylamides *(2)*[2], *N*-alkyl-3-azi-2-indolinone *(3)*[3], isopropylidene-3,3-diazirinedicarboxylate *(4)*[4]).



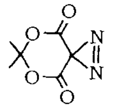
*(1)*, n = 4,5



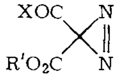
*(2)*



*(3)*



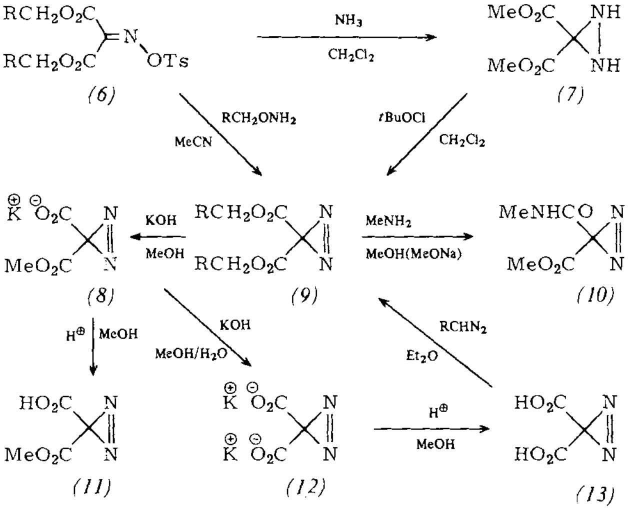
*(4)*



*(5)*, X = RO, $R_2N$

All attempts to photocyclize diesters and amidoesters of diazomalonic acid have been unsuccessful due to the spontaneous isomerization of the diazirines *(5)* to the educts. This has been attributed to the steric effects of the two carbonyl substituents[2]. Indeed, within a few weeks, *(4)* undergoes spontaneous isomerization at room temperature to the diazo compound[4]. This fact, the low thermal stability of the spiranes *(1)* $n=4$[1] and *(3)*[3], and the lability of *(1)* in acidic media[1] may be attributed to the favorable interaction (pseudoconjugation[3]) between the diazirine ring and the $C{=}O$ group in the five and six membered rings. (cf. spiro-activation[5]). We therefore believed that a study of the synthesis of diazirines *(5)*, with conformationally mobile $C{=}O$ groups, would provide a route to their stable derivatives.

We have found that the 3,3-diazirinedicarboxylates *(9)* are readily accessible by reaction of the tosyloximes *(6)* with *O*-alkylhydroxylamines[6] or by oxidation of the 3,3-diaziridinedicarboxylic dimethyl ester *(7)* with *tert*-butylhypochlorite[7]. The esters *(9)*, thus obtained, are colorless and stable at 0 °C; after being stored for a month at 20 °C, crystals of *(9a)* were unchanged and a solution of *(9a)* in trifluoroacetic acid was unchanged after 2 hours ($^1$H-NMR investigation). Mild amidation and alkaline hydrolysis of *(9a)* (0 to −5 °C) yielded the monamide *(10)*, which was stable at 0 °C, and the salts *(8)* and *(12)* respectively. While crystals of the dipotassium salt *(12)* were also unchanged after storage for two months at 20 °C, the monopotassium salt *(8)* decomposed within a few hours at 0 °C. Both salts exploded when triturated!



*(a)*, R = H; *(b)*, R = Me

The monoacid *(11)* and diacid *(13)* are colorless stable crystalline substances at 0 °C; the structure of *(13)* was confirmed by conversion to the diesters *(9)*. The UV-spectra of all the diazirine products obtained displayed a shoulder around the 240–250 nm region and a band at 286–300 nm (see Table 1). We have assigned this band to a $\pi\rightarrow\pi^*$ transition[8], since its position was almost identical in the esters *(9)*, amide *(10)*, and acids *(11)* and *(13)*. Furthermore when methanol was substituted for heptane as solvent, and when $HClO_4$ was added to a solution of *(9a)* in methanol, no hypsochromatic shift was observed.

Table 1. Yields and some characteristic physical data of compounds *(8)*, *(9a)*, *(9b)*, *(10)*, *(11)*, *(12)*, and *(13)*.

| Comp. [a] | Yield [%] | M.p. [°C] | IR $\nu_{C=O}$ [cm$^{-1}$] | $^1$H-NMR (δ values, $C_6D_6$) | UV (π−π*) $\lambda_{max}$ [nm] (lg ε) | Solvent |
|---|---|---|---|---|---|---|
| *(8)* | 90 | 104 [b] | — | 4.02 s [c] | 300 (1.59) [d] | MeOH |
| *(9a)* | 39 [e] | 50–51 (Decomp.) | 1730, 1750 | 3.21 s | 289 (1.66) | MeOH |
| | 81 [f] | | | | 289 (1.63) | heptane |
| | 99 [g] | | | | | |
| | 98 [h] | | | | | |
| *(9b)* | 70 [i] | [j] | 1740, 1760 | 0.78 t, 3.75 q ($J$=7.0 Hz) | 289 (1.89) | MeOH |
| | 98 [k] | | | | 289 (1.89) | heptane |
| *(10)* | 92 | 25–27 | 1740, 1680 | 2.37 d ($J$=4.5 Hz), 2.95 s | 292 (1.67) | MeOH |
| *(11)* | 73 | 49–51 (Decomp.) | 1720 | 3.19 s, 10.49 s | 289 (1.63) | MeOH |
| *(12)* | 79 | 195 [b] | 1610 | — | 298 (1.94) [d] | $H_2O$ |
| *(13)* | 90 | 76 [b] | — | 9.37 s [l] | 286 (1.92) [d] | MeOH |

[a] Correct elemental analysis results were obtained for *(9a)*, *(9b)*, *(10)*, *(11)* and *(12)*. [b] Decomposition temperature. [c] Solvent: $D_2O$. [a] Shoulder [e] From *(6a)* and $MeONH_2$. [f] From *(6a)* and $EtONH_2$. [g] From *(7)* and *t*BuOCl. [h] From *(13)* and $CH_2N_2$. [i] From *(6b)* and $EtONH_2$. [j] $n_D^{20}=1.4248$. [k] From *(13)* and $CH_3CHN_2$. [l] Solvent: $(CD_3)_2CO$.

### *Experimental*

*(9a)* *O*-Ethylhydroxylamine (3.66 g, 60 mmol) was added dropwise to a stirred, cooled (−10 to −15 °C) solution of

---

[*] Prof. Dr. R. G. Kostyanovsky, Dr. G. V. Shustov, N. B. Tavakalyan,
Institute of Chemical Physics
Academy of Sciences of the USSR
Vorobievskoye shosse 2b, 117334 Moscow (USSR)

*(6a)* (7.88 g, 25 mmol) in 30 cm$^3$ dry acetonitrile. The mixture was stirred for 4 h, left *ca.* 12 h at 0 °C and the solvent removed *in vacuo*. The residue was recrystallized from absolute MeOH (−20 to −30 °C) and sublimed at 20 °C/1 Torr. Yield 3.22 g (82%).

*(8)* A solution of KOH (0.42 g, 7.50 mmol) in 5 cm$^3$ absolute methanol was added dropwise to a stirred, cooled solution of *(9a)* (1.26 g, 7.86 mmol) in 8 cm$^3$ absolute methanol. The mixture was left *ca.* 12 h at −10 °C, the precipate of *(8)* filtered off, washed with ether and dried *in vacuo*. Yield 1.6 g (90%).

*(11)* A suspension of *(8)* (0.25 g, 1.45 mmol) and 1 g of Dowex 50 W × 12 ($H^{\oplus}$) in 5 cm$^3$ absolute methanol was stirred for 1 hr at 0 °C. After separation from the cation exchanger, the solution was evaporated *in vacuo* and the residue sublimed at 20 °C/1 Torr. Yield 0.15 g (73%).

*(12)* 2 cm$^3$ of water and a solution of KOH (0.38 g, 6.8 mmol) in 3.5 cm$^3$ methanol were added to a suspension of *(8)* (0.81 g, 4.7 mmol) in 12 cm$^3$ methanol at 10 °C and the mixtured left *ca.* 12 h at 0 °C. The salt crystals which had formed were filtered off, washed with absolute MeOH and dried *in vacuo*. Yield 0.77 g (79%).

*(13)* The carboxylic acid *(13)* was obtained from *(12)* in an analogous manner to *(11)* from *(8)*, but with omission of the sublimation step. Yield 85%.

Received: July 7, 1980 [Z 686 IE]
German version: Angew. Chem. 93, 206 (1981)

CAS Registry numbers:
*(6a)*, 54972-12-2; *(6b)*, 20893-05-4; *(7)*, 54972-13-3; *(8)*, 76429-92-0; *(9a)*, 76429-93-1; *(9b)*, 76429-94-2; *(10)*, 76429-95-3; *(11)*, 76429-96-4; *(12)*, 76429-97-5; *(13)*, 76429-98-6; *O*-methylhydroxylamine, 67-62-9; *O*-ethylhydroxylamine, 624-86-2

---

[1] *E. Schmitz, A. Stark, Ch. Hörig*, Chem. Ber. *98*, 2509 (1965); *E. Schmitz, Ch. Hörig*, Chem. Ber. *100*, 2101 (1967).

[2] *G. Lowe, J. Parker*, J. Chem. Soc. Chem. Comm. *1971*, 1135; *R. A. Franich, G. Lowe, J. Parker*, J. Chem. Soc. Perkin Trans. I, *1972*, 2034.

[3] *E. Voigt, H. Meier*, Angew. Chem. *87*, 109 (1975); Angew. Chem. Int. Ed. Engl. *14*, 103 (1975) *idem*, Chem. Ber. *108*, 3326 (1975).

[4] *T. Livinghouse, R. V. Stevens*, J. Am. Chem. Soc., *100*, 6479 (1978). See also: *R. V. Stevens, G. S. Bisacchi, L. Goldsmith, C. E. Strouse*, J. Org. Chem. *45*, 2708 (1980).

[5] *H. McNab*, Chem. Soc. Rev. *17*, 345 (1978); *S. Danishefsky*, Acc. Chem. Res. *12*, 66 (1979).

[6] A mixture of *O*-Tosyloxime hexafluoroacetone oxime and *O*-methylhydrocylamine yield 3,3-bis(trifluoromethyl)diazirine: *R. G. Kostyanovsky, A. E. Polyakov, G. V. Shustov, K. S. Zakharov, V. I. Markov*, Dokl. Akad. Nauk SSSR *219*, 873 (1974).

[7] *R. G. Kostyanovsky, G. V. Shustov, V. I. Markov*, Izv. Akad. Nauk SSSR. Ser. Khim. *1974*, 2923.

[8] *M. Kasha*, Discuss. Faraday Soc., 9, 14 (1950); *H. McConnel*, J. Chem. Phys. *20*, 700 (1952). *J. W. Sidman*, Chem. Rev. *58*, 689 (1958).

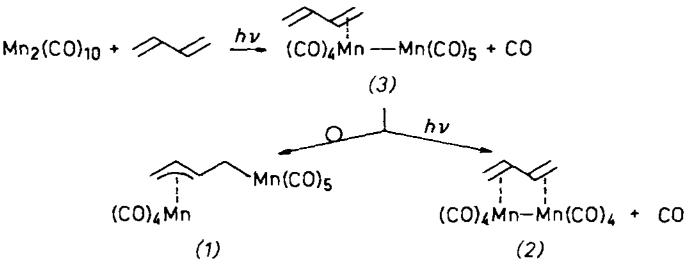
---

## Cleavage of a Metal-Metal Bond by 1,3-Butadiene under Photochemical Conditions[**]

By *Cornelius G. Kreiter* and *Wolfgang Lipps*[*]

Carbonyl-transition metal compounds usually react with olefins on irradiation with cleavage of carbon monoxide to give olefin complexes[1]. Application of this reaction principle to a carbonyl complex containing a metal-metal single bond, such as $Mn_2(CO)_{10}$, and 1,3-butadiene leads within 10 minutes irradiation to formation of the complexes $Mn_2(CO)_9C_4H_6$ *(1)* and $Mn_2(CO)_8C_4H_6$ *(2)* as main products, which can be separated from each other by HPLC. The complex *(2)* is the already well-known μ-(η-1,3-butadiene)octacarbonyldimanganese(0), in which the *trans*-1,3-butadiene ligand on both manganese atoms of $Mn_2(CO)_{10}$ replaces an equatorial CO ligand[2]. Complex *(1)*, however, is not the expected precursor *(3)*; the IR and NMR spectroscopic data would rather indicate cleavage of the Mn—Mn bond and formation of a 2—4-η$^3$-1-σ-2-butenylene bridge between two separated $Mn(CO)_5$- and $Mn(CO)_4$-moieties.

*(1)* and *(2)* could be formed *via* a common precursor, the aforementioned $Mn_2(CO)_9C_4H_6$ *(3)*. This complex, however, cannot be detected directly: the IR spectrum of the reaction solution contains the νCO bands of $Mn_2(CO)_{10}$, *(1)* and *(2)*, but no intense bands that would be expected for *(3)*. *(1)* is formed from the postulated *(3)* with cleavage of the Mn—Mn bond by the η$^2$-1,3-butadiene ligand, while *(2)* is formed from *(3)* by photochemical displacement of a second CO ligand.



In the $^{13}$C-NMR spectrum of *(1)* (Table 1) the $C_4H_6$ ligand gives rise to two methine and two methylene signals. Their upfield shift compared to the signals of free 1,3-butadiene[3]

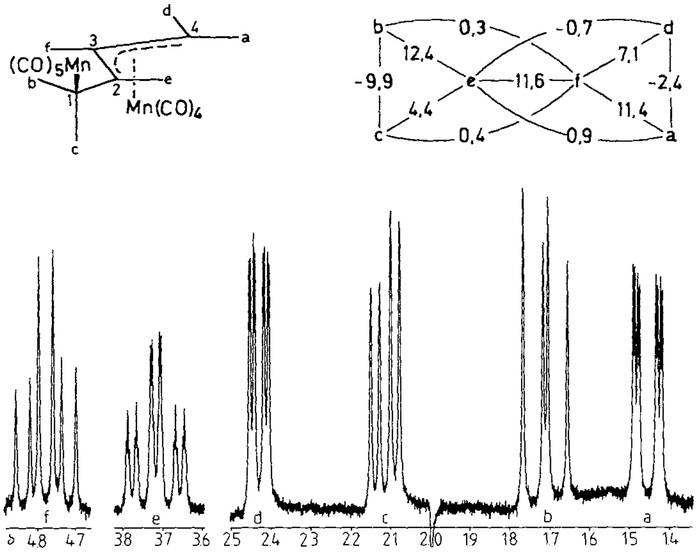


Fig. 1. $^1$H-NMR spectrum and δ-*J* diagram of *(1)* in $CD_2Cl_2$.

Table 1. NMR parameters of $(CO)_4Mn—C_3H_4—CH_2—Mn(CO)_5$ *(1)*. δ rel. int. TMS. $^{13}$C-NMR in [D$_6$]-acetone, $^1$H-NMR in $CD_2Cl_2$.

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| δ($^{13}$C) | 14.18 | 88.74 | 89.51 | 34.23 |
| $^1J_{^{13}C\ ^1H}$ [Hz] | 140.4 | 153.8 | 158.7 | 161.13 |
| δ($^1$H) | 1.71 *(Re)* [a]<br>2.12 *(Si)* [a] | 3.71 | 4.78 | 1.45 *(Z)*<br>2.43 *(E)* |

[a] For an explanation of the stereochemical designations *Re* and *Si*, see [6].

---

[*] Prof. Dr. C. G. Kreiter, Dipl.-Chem. W. Lipps
Fachbereich Chemie der Universität
Paul-Ehrlich-Str., D-6750 Kaiserslautern (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

and the $^{1}J_{^{13}C,\,^{1}H}$-coupling constants indicate $sp^2$ character[4] of the methine groups and one of the methylene groups and their π-bonding to manganese. The $^{1}J_{^{13}C,\,^{1}H}$-coupling indicates an $sp^3$ hybridization for the second methylene group.

Four (a, d, e, f) of six $^{1}$H-NMR multiplets (Fig. 1) of *(1)* are typical for an $\eta^3$-enyl ligand with a methylene group in *E* position[5]. Since formally three electrons to a $Mn(CO)_4$ group and one electron to a $Mn(CO)_5$ group are lacking for the 18-electron occupation, $Mn(CO)_4$ must be bound to an enyl system, $Mn(CO)_5$ to the $sp^2$ methylene group. Complexes with unsymmetrical enyl ligands are chiral, as follows from the signal splitting of the diastereotopic protons (b, c) of the *E*-$sp^3$ methylene group. The magnitude of the splitting and the extremely different vicinal coupling constants suggest preferred orientation in the complex *(1)* with maximum separation of the carbonylmanganese groups. This might best be explained in terms of spatial requirements.

### *Experimental*[7]

All operations were carried out under an inert gas ($N_2$, He). 1,3-Butadiene (25 $cm^3$) is allowed to condense into a solution of $Mn_2(CO)_{10}$ (750 mg, 1.92 mmol) in *n*-hexane (225 $cm^3$) and the mixture is irradiated for 10 min at 253 K. After filtration of the solution through filter flocs the solvent is removed by evaporation; the residue is taken up in *n*-hexane (20 $cm^3$) and separated into 2 $cm^3$-fractions by HPLC with *n*-hexane. Zone 1: $Mn_2(CO)_{10}$ (50%); Zone 2: *(1)*; Zone 3: $Mn_2(CO)_8(C_4H_6)_2$, rejected; Zone 4: *(2)*. After removal of solvent, *(1)* is recrystallized from *n*-hexane, *(2)* from ether at 240 K; *(1)*, yellow platelets, yield 240 mg (30%), m.p. 104 °C (dec.); IR: $Mn(CO)_4$: 2060, 1989, 1972, 1958; $Mn(CO)_5$: 2105, 2011, 1998 $cm^{-1}$. *(2)*, fine, orange crystals, yield 55 mg (7.4%), m.p. 146 °C (dec.).

Received: July 10, 1980 [Z 688 IE]
German version: Angew. Chem. *93*, 191 (1981)

CAS Registry numbers:
*(1)*, 76430-74-5; *(2)*, 38999-17-6; *(3)*, 76430-75-6; $Mn_2(CO)_{10}$, 10170-69-1

---

[1] *M. Herberhold:* Metal π-Complexes. Vol. II. Complexes with Mono-Olefinic Ligands. Elsevier, Amsterdam 1972, p. 34ff.

[2] a) *M. L. Ziegler, H. Haas, R. K. Sheline*, Chem. Ber. *98*, 2454 (1965); b) *H. E. Sasse, M. L. Ziegler*, Z. Anorg. Allg. Chem. *392*, 167 (1972); c) *M. Zöller, M. L. Ziegler*, *ibid. 425*, 265 (1976).

[3] In $[D_6]$-acetone: $\delta = 118.02$ (156.9 Hz, C-1, C-4), 138.46 (150.2 Hz, C-2, C-3); see also *D. E. Dorman, M. Jautelat, J. D. Roberts*, J. Org. Chem. *35*, 2757 (1971).

[4] *M. D. Newton, J. M. Schulman, M. M. Manus*, J. Am. Chem. Soc. *96*, 17 (1974).

[5] a) *M. L. Maddox, S. L. Stafford, H. D. Kaesz*, Adv. Organomet. Chem. *3*, 1 (1965); b) *B. Henc, P. W. Jolly, R. Salz, G. Wilke, R. Benn, E. G. Hoffmann, R. Mynott, G. Schroth, K. Seevogel, J. C. Sekutowski, C. Krüger*, J. Organomet. Chem. *191*, 425 (1980).

[6] *V. Prelog, G. Helmchen*, Helv. Chim. Acta *55*, 2581 (1972).

[7] A mercury vapor lamp TQ 150 (Original Hanau Heraeus GmbH) was used as light source in Duran reactors. The yields are not optimized. IR: Perkin-Elmer 297; NMR: Bruker WP 200; HPLC: Spectra Physics SP 8000; column: Knauer Si 60/16 mm ID.

## 9,9′-Bianthryl-10,10′-dicarbonitrile, An Aromatic π-System with Six One-electron Redox Steps[**]

By *Jürgen Heinze*[*]

The chemical and physical properties of electrochemically generated radical ions of aromatic hydrocarbons have long been investigated in detail[1]; studies on electrochemically stable di- and trications or anions on the other hand, are limited to but a few examples[2]. Aromatic systems, which exhibit more than four reversible one-electron redox steps have hitherto not been described in the literature[3]. The difficulties encountered in the electrochemical generation of multiply-charged organic ions are often due to the reactivity of impurities which remain in the solvent during usual work-up of the sample[4] or stem from competing reactions of the solvent-electrolyte system, whereby the electroactive species is trapped by electrophilic or nucleophilic addition reactions[5].

In the group of arenes, we have observed for the first time *six* reversible one-electron redox steps; namely, in 9,9′-bianthryl-10,10′-dicarbonitrile, whose ions are adequately stabilized by the two cyanide groups. The success of the experiment rested on a special working technique which enabled total exclusion of water and other protic impurities[6]. The measurements were carried out in propionitrile with tetrabutylammonium hexafluorophosphate ($TBAPF_6$, 0.1 M) as supporting electrolyte. A platinum disk electrode fused in soft glass served as working electrode. The electrochemical behavior of the compound was investigated by cyclic voltammetry (CV) (see Fig. 1 and Table 1).

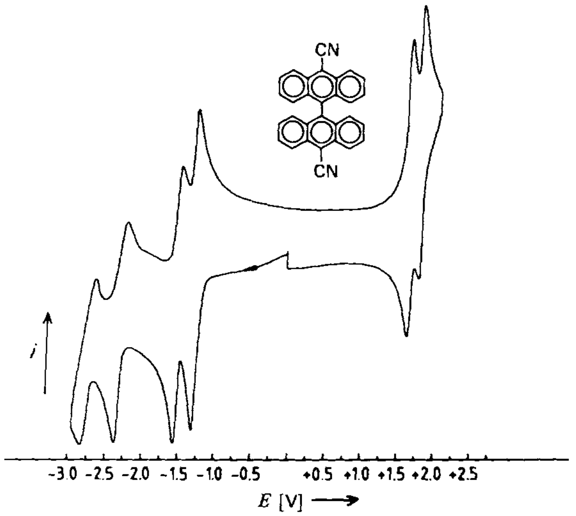


Fig. 1. Cyclovoltammogram of 9,9′-bianthryl-10,10′-dicarbonitrile in super-pure propionitrile/0.1 M $TBAPF_6$ at a Pt-disk electrode *vs.* Ag/AgCl, $v = 300$ mV/s.

Table 1. Standard potentials and heterogeneous rate constants $k_s$ of the cathodic and anodic redox steps of 9,9′-bianthryl-10,10′-dicarbonitrile in propionitrile/0.1 M $TBAPF_6$ *vs.* Ag/AgCl.

| Redox steps | $E^0$ [mV] | $\Delta E_n$ [mV] [a] | $k_s$ [cm/s] |
|---|---|---|---|
| 1 red | −1270 | — | 0.25 |
| 2 red | −1538 | 268 | 0.10 |
| 3 red | −2328 | — | 0.039 |
| 4 red | −2712 | 384 | 0.015 |
| 1 ox | 1702 | — | 0.044 |
| 2 ox | 1878 | 176 | 0.027 |
| 3 ox | (2700) | — | — |

[a] $\Delta E_n = E^0_{2n} - E^0_{2n-1}$ $(n = 1, 2)$.

The molecule (A) can be reduced in four successive one-electron transfer reactions up to the tetraanion [eq. (a)]. Surprisingly, in the anodic direction successive reversible oxidation takes place up to the dication. Above +2.7 Volt a further wave becomes visible, indicating transition to the trication. Since the electrode is passivated in this region, and,

---

[*] Priv.-Doz. Dr. J. Heinze
Institut für Physikalische Chemie der Universität
Albertsstrasse 21, D-7800 Freiburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

$$\begin{array}{ccccccccccccccc} (A^{3\oplus}) & \overset{-e}{\leftrightarrows} & A^{2\oplus} & \overset{-e}{\leftrightarrows} & A^{\oplus} & \overset{-e}{\leftrightarrows} & A & \overset{+e}{\rightleftarrows} & A^{\ominus} & \overset{+e}{\rightleftarrows} & A^{2\ominus} & \overset{+e}{\rightleftarrows} & A^{3\ominus} & \overset{+e}{\rightleftarrows} & A^{4\ominus} \\ & (E^0_{3\,\mathrm{ox}}) & & E^0_{2\,\mathrm{ox}} & & E^0_{1\,\mathrm{ox}} & & E^0_{1\,\mathrm{red}} & & E^0_{2\,\mathrm{red}} & & E^0_{3\,\mathrm{red}} & & E^0_{4\,\mathrm{red}} & \end{array} \qquad (a)$$

moreover, the solvent attacks the trication *via* a CE mechanism, this wave was not investigated. All six steps are stable in the time-scale of the electrochemical experiment. In the case of the tetraanion and the dication, however, with longer measuring times ($v < 200$ mV/s) secondary products appear, as a result of reaction with the solvent-electrolyte system.

Since the molecule is made up of two equal moieties, between which weak interactions occur, the redox potentials of the two mono- and di-ions and of the tri- and tetraanions lie relatively close to one another[7]. From the different intervals $\Delta E_{2\,\mathrm{red}} > \Delta E_{1\,\mathrm{red}} > \Delta E_{1\,\mathrm{ox}}$ a decrease in the Coulomb interaction between the centers with equal charge can be observed along the series tetraanion, dianion, and dication. On transition from the monocation to the dication the redox potential separation is only 176 mV—a finding indicative of a strong mutual twisting of the two halves of the molecule.

9,9′-Bianthryl-10,10′-dicarbonitrile is an excellent model system for the study of solvation effects in organic molecules. CV measurements in the temperature range between 20 and −60 °C showed that the $\Delta E$ value markedly diminishes with decreasing temperature. In agreement with the Born model, this supports the assumption of an enhanced solvation of the species in the higher charged states[8]. The changes in $k_s$ (Table 1), whose values are significantly smaller in the formation of the di-, tri- and tetraion, point in the same direction.

Received: April 21, 1980 [Z 689 IE]
German version: Angew. Chem. *93*, 186 (1981)

CAS Registry number:
9,9′-Bianthryl-10,10′-dicarbonitrile, 1467-03-4

---

[1] *N. L. Holy*, Chem. Rev. *74*, 243 (1974); *A. J. Bard, A. Ledwith, H. J. Shine*, Adv. Phys. Org. Chem. *13*, 156 (1966).

[2] *A. J. Bard, J. Phelps*, J. Electroanal. Chem. *25*, App. 2 (1970); *K. Deuchert, S. Hünig*, Angew. Chem. *90*, 927 (1978); Angew. Chem. Int. Ed. Engl. *17*, 875 (1978); *O. Hammerich, V. Parker*, Electrochim. Acta *18*, 537 (1973); *W. Kaim, H. Bock*, J. Am. Chem. Soc. *100*, 6504 (1978).

[3] *T. Saji, S. Aoyagui*, J. Electroanal. Chem. *102*, 139 (1979); *J. Rieser, G. Abou-Elenien, K. Wallenfels, H. Baumgärtel*, Tetrahedron Lett. *1976*, 2363.

[4] *M. M. Baizer:* Organic Electrochemistry. Marcel Dekker, New York 1973.

[5] *O. Hammerich, V. D. Parker*, J. Chem. Soc. Chem. Commun. *1974*, 245.

[6] *J. Heinze, C. Heyne*, unpublished results.

[7] *K. Itaya, A. J. Bard, M. Schwarz*, Z. Phys. Chem. N. F. *112*, 1 (1978).

[8] *F. Ammar, J. M. Saveant*, J. Electroanal. Chem. *47*, 115 (1973).

---

## Novel Method for the Phase-Transfer Catalyzed Sulfodechlorination of 1-Chloro-2,4-dinitrobenzene[**]

By *Markus Gisler* and *Heinrich Zollinger*[*]

*Dedicated to Professor Robert Schwyzer on the occasion of his 60th birthday*

The replacement of chlorine by a sulfonic acid residue in arenes activated by -M-substituents is an important industrial reaction. Sulfite serves as nucleophilic reagent. If the arene derivative is insoluble in water then sulfodehalogenation takes place as a two-phase reaction only at the phase boundary between the arene, usually employed as melt, and an aqueous solution of $Na_2SO_3$. The reactions are consequently slow and require seemingly drastic conditions; undesirable side reactions, *e.g.* reduction of nitro groups by sulfite, lower the yield. The yields can be improved by carrying out the reactions in boiling aqueous alcohol; thus, *Lunt*[2] achieved yields of 81% in the sulfodechlorination of 1-chloro-2,4-dinitrobenzene.

Under the usual phase-transfer conditions (reagents: tetra-*n*-butylammonium sulfate and $K_2SO_3$; $CH_2Cl_2/H_2O$ two-phase system) we did not obtain higher yields than when using the conventional method[2-4].

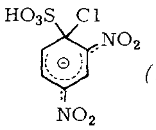
We report here on the use of protonated *tertiary* amines as phase-transfer catalysts for the sulfodechlorination. In some representative cases of one series of tri-*n*-alkylamines considerably better yields and higher purity of product were obtained on reaction of 1-chloro-2,4-dinitrobenzene with potassium disulfite ($K_2S_2O_5$) (Table 1).

Table 1. Yield and purity of 2,4-dinitrobenzenesulfonic acid in the phase-transfer catalyzed sulfodechlorination of 1-chloro-2,4-dinitrobenzene with potassium disulfite in the presence of tertiary amines (3 h, 0–8 °C).

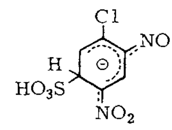
| Amine | Yield [%] [a] | Purity [%] [a] |
|---|---|---|
| Tri-*n*-propylamine | 81 | 96 |
| Tri-*n*-butylamine | 97 | 96 |
| Tri-*n*-pentylamine | 95 | 99 |
| Tri-*n*-hexylamine | 85 | 78 |
| Tri-*n*-octylamine | 76 | 87 |

[a] Yield and purity were determined UV spectroscopically.

A further series of tertiary amines proved ineffective[5]. Apparently the lipophilicity of the tertiary amines concerned plays an important role: In the case of tri-*n*-butylamine and tri-*n*-pentylamine it is apparently optimal under the reaction conditions employed. Tri-*n*-butylamine has the additional advantage that it can be readily regenerated by liquid/liquid extraction. Tri-*n*-hexylamine and tri-*n*-octylamine molecules are too large for the sulfodechlorination of 1-chloro-2,4-dinitrobenzene; the yield decreases with increasing length of the alkyl chain of the amine, and the purity of the product is reduced by irremovable amine. The organic phase turns red-violet in color during the reaction. This coloration also occurs on using quaternary ammonium compounds or crown ethers as phase-transfer catalysts. This coloration, as we have been able to establish by $^1$H-NMR spectroscopy, is caused by the Meisenheimer complex *(1)* or *(2)*[5].



*(1)*



*(2)*

*Procedure*

A solution of $K_2S_2O_5$ (2.27 g, 0.01 mol) in cold water (10 cm$^3$) is treated with $CH_2Cl_2$ (10 cm$^3$) and tri-*n*-butylamine (4.9 cm$^3$, 0.02 mol) and the mixture cooled to 0 °C. A freshly prepared solution of 1-chloro-2,4-dinitrobenzene (2.03 g, 0.01 mol) in $CH_2Cl_2$ is then added at 0 °C and the final mixture stirred for 3 h. The organic phase momentarily turns wine-red to red-violet in color and then pale yellowish-orange. After removal of the cooling-bath the reaction mixture is treated with 25 cm$^3$ of 0.8 M KOH. The precipitated product is filtered off, washed with $CH_2Cl_2$ (25 cm$^3$) and

---

[*] Prof. Dr. H. Zollinger, Dipl.-Chem. M. Gisler
Technisch-Chemisches Laboratorium,
Eidgenössische Technische Hochschule
Universitätsstrasse 6, CH-8092 Zürich (Switzerland)

[**] Nucleophilic Aromatic Substitution, Part 13.—Part 12: [1]

dried by suction. The aqueous phase is extracted with hexane (25 cm$^3$), salted-out with KCl (7 g) and filtered; total yield of dried product: 2.87 g (97%).

Received: September 8, 1980 [Z 692]
German version: Angew. Chem. *93*, 184 (1981)

CAS Registry numbers:
1-chloro-2,4-dinitrobenzene, 97-00-7; 2,4-dinitrobenzoic acid, 89-02-1; tri-*n*-propylamine, 102-69-2; tri-*n*-butylamine, 102-82-9; tri-*n*-pentylamine, 621-77-2; tri-*n*-hexylamine, 102-86-3; tri-*n*-octylamine, 1116-76-3

---

[1] *H. Eggimann, P. Schmid, H. Zollinger*, Helv. Chim. Acta *58*, 257 (1975).
[2] *E. Lunt*, J. Appl. Chem. *7*, 446 (1957).
[3] *H. E. Fierz-David, L. Blangey:* Grundlegende Operationen der Farbenchemie. 8th Edit. Springer, Wien 1952, p. 99.
[4] *O. Lange:* Die Zwischenprodukte der Teerfarbenfabrikation. O. Spamer, Leipzig 1920, p. 137.
[5] *H. Zollinger, M. Gisler*, unpublished results. We thank Prof. *J. F. Bunnett*, University of California, Santa Cruz, for pointing out the possible occurrence of *(2)*.

## Trinuclear Clusters from $HCo(CO)_4$ Solutions[**]

By *Giuseppe Fachinetti*, *Laura Balocchi*, *Fernando Secco*, and *Marcella Venturini*[*]

Since its discovery by *Hieber et al.*[1a], $HCo(CO)_4$ *(1)* has been the subject of very extensive spectroscopic[1b], catalytic[1c] and kinetic studies[1d].

Surprisingly, it has now been found that, by carefully removing the gas evolved at the appropriate temperature (see *Experimental*), the trinuclear electronically unsaturated hydrido cluster $HCo_3(CO)_9$ *(3)* is the product of the thermal decomposition of *(1)* in pentane solution, together with the expected $Co_2(CO)_8$ *(2)*[1d] [eq. (a) and (b)].

$$\underset{(1)}{HCo(CO)_4} \rightarrow 1/2\,H_2 + 1/2\,\underset{(2)}{Co_2(CO)_8} \tag{a}$$

$$\underset{(1)}{HCo(CO)_4} + \underset{(2)}{Co_2(CO)_8} \rightleftarrows \underset{(3)}{HCo_3(CO)_9} + 3\,CO \tag{b}$$

This finding, and the earlier observation[2,4a] that *(3)* reacts rapidly and quantitatively with CO to give equimolar quantities of *(1)* and *(2)* (or $Co_4(CO)_{12}$ *(7)*, depending on the CO partial pressure) bring us to the important conclusion that the carbonyl species of equation (b) are in equilibrium.

*(3)* is the first hydrido-carbonyl cluster of cobalt to be *isolated* from *(1)*. The isolation of $HCo_3(CO)_9$ *(3)* may be interpreted in terms of the thermodynamically less unfavorable[3] 18e→46e transformation of *(1)* into *(3)*, as compared with the 18e→16e conversion of *(1)* into $HCo(CO)_3$. Since *(3)* can also be obtained from $Co_3(CO)_9C{-}OH$ *(4)* [eq. (c)][4a] it was suggested, by analogy with the recently demonstrated[4b] "redox condensation"[5] with $LiCo(CO)_4$ *(5)* [eq. (d)], to assume *(4)* as an intermediate in the formation *(3)* from *(1)* [eq. (e)].

Several experiments carried out between 0 and 40 °C at different concentrations of *(1)* and CO pressures between 0 and 1 bar failed to yield the thermally unstable *(4)* in observable concentrations; under these conditions *(3)* was obtained, and at higher temperatures *(7)* was the sole reaction product.

$$\underset{(4)}{Co_3(CO)_9C{-}OH} \longrightarrow CO + \underset{(3)}{HCo_3(CO)_9} \tag{c}$$

$$\underset{(5)}{LiCo(CO)_4} + \underset{(2)}{Co_2(CO)_8} \rightleftarrows \underset{(6)}{LiCo_3(CO)_{10}} + 2\,CO \tag{d}$$

$$\begin{tikzcd} \underset{(1)}{HCo(CO)_4} + \underset{(2)}{Co_2(CO)_8} \arrow[r, "-2\,CO"'] & \underset{(4)}{Co_3(CO)_9C{-}OH} \arrow[dl, "-CO"] \\ \underset{(3)}{HCo_3(CO)_9} \arrow[u, "+3\,CO"] \arrow[r, "Ar", "20\,^{\circ}C"'] & H_2 + \underset{(7)}{Co_4(CO)_{12}} \end{tikzcd} \tag{e}$$

In order to gather experimental evidence about the validity of the mechanism suggested in eq. (e), *(1)* was allowed to react with one equivalent of triethylamine and an excess of *(2)* [toluene, 40 min, 10 °C, vacuum]; the triethylamine-adduct *(8)* was formed as main product, which could also be obtained independently from *(4)* and $NEt_3$ [eq. (f) and (g)].

$$\underset{(4)}{Co_3(CO)_9C{-}OH} + NEt_3 \rightarrow \underset{(8)}{Co_3(CO)_9C{-}OH \cdot NEt_3} \tag{f}$$

$$\underset{(9)}{NEt_3 \cdot HCo(CO)_4} + \underset{(2)}{Co_2(CO)_8} \rightarrow \underset{(8)}{Co_3(CO)_9C{-}OH \cdot NEt_3} + 2\,CO \tag{g}$$

According to an X-ray structure analysis *(4)* contains an approximately sp$^3$-hybridized apical carbon atom carrying the alcoholic OH-group[6]. The reaction described in equation (g) is the first example of an amine-assisted transformation of a metal-bonded hydridic hydrogen atom into an *O*-bonded hydrogen atom. Moreover, the O-atom of a terminal CO ligand becomes an alcoholic O-atom.

To conclude: (*i*) solutions of *(1)* yield trinuclear clusters—presumably *via* attack of the proton of *(1)* at a CO-group in *(2)*[7]. It is plausible that other conditions could permit low-nuclearity clusters to exist as intermediate species in homogeneous processes such as hydroformylation or the reduction of CO to methanol[1c]. (*ii*) Reaction (d) corresponds to a cluster-assisted four-electron reduction of carbon. On a model system we have therefore observed some of the stoichiometric steps required for the reduction of CO to methanol. (*iii*) *(1)* can function as a proton- or hydride-donor[8], depending on the solvent and reaction partners. In solvents of low polarity, such as the ones used in this study, tertiary amines and edge-bridging CO-groups are believed to enhance the proton activity of *(1)*.

### *Experimental*

Unless otherwise stated, all the operations reported in this study were carried out under an atmosphere of purified argon.

*(5):* The reagent was obtained by stirring a tetrahydrofuran solution of *(2)* with anhydrous LiOH at room temperature under an atmosphere of CO for several (1—4) days until a colorless solution was obtained. After filtration, the solvent was evaporated under reduced pressure and the residue was heated to 140 °C for 1 h at *ca.* 0.05 torr. The solid residue was dissolved in ether (CAUTION: strongly exothermic reaction!), the solvent evaporated, and the residue heated again under the conditions specified above. Dissolution in a toluene/ether mixture yielded a colorless solution which was filtered. Evaporation to dryness, heating of the solid residue at 130° *in vacuo*, and washing with toluene afforded the ivory-colored, microcrystalline, pyrophoric *(5)* (70% yield; correct elemental analysis).

---

[*] Dr. G. Fachinetti [+], L. Balocchi
Istituto di Chimica Generale dell'Università
Via Risorgimento, 35, I-56100 Pisa (Italy)
Dr. F. Secco, Dr. M. Venturini
Istituto di Chimica Analitica ed Elettrochimica dell'Università
Via Risorgimento, 35, I-56100 Pisa (Italy)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the C.N.R. (Rome). We thank Professor *F. Calderazzo* for helpful discussions.

*(1)*: As stable 0.04 M solution in pentane: Solvent-free *(5)* was treated with the stoichiometric amount of dry HCl. Afterwards, pentane was added.

*(3)*: A 0.04 M pentane solution of *(1)* was maintained at 20 °C and intermittently connected to a vacuum line in order to evacuate the gaseous reaction products. After about 45 min the solution was cooled to −78 °C and the resulting green-maroon solid filtered off. Sublimation at 18°/0.05 torr afforded *(2)* and a green residue, which was identified by IR comparison with an authentic sample as *(3)* ($\nu_{CO}$: 2054, 2037, 1879 cm$^{-1}$ in hexane).

*(8)*: This was prepared in essentially quantitative yields from *(4)*[6] and the stoichiometric amount of $NEt_3$ at *ca.* −30° in a hexane/toluene mixture. The adduct is a dark violet solid, stable at 0 °C under an Ar atmosphere, and is extremely sensitive to moisture and air. Its IR spectrum ($\nu_{CO}$: 2063 w, 2000 vs, 1990 s, 1985 sh cm$^{-1}$, toluene solution) is similar to that of *(4)* ($\nu_{CO}$: 2095 w, 2038 vs, 2022 s, 2005 sh cm$^{-1}$ in the same solvent), except for the shift to lower wavenumbers. *(8)* gave a correct elemental analysis for cobalt. Its thermal decomposition at room temperature in toluene gave *(7)* and *(9)* according to *(8)* → 1/2 *(7)* + *(9)*.

*(9)*: Reaction of stoichiometric amounts of *(1)* and $NEt_3$ in hexane at −80 °C gave *(9)* as a colorless solid soluble in aromatic solvents. IR (toluene): $\nu_{CO}$ = 2005 w, 1950 s, 1890 vs cm$^{-1}$; $^1$H-NMR ($C_6D_6$): δ = −8.1 (s, 1 H), −2.0 (q, 6 H); −0.5 (t, 9 H).

Received: August 27, 1980 [Z 694 IE]
German version: Angew. Chem. *93*, 215 (1981)

CAS Registry numbers:
*(1)*, 16842-03-8; *(2)*, 10210-68-1; *(3)*, 71204-90-5; *(4)*, 71032-29-6; *(5)*, 15616-75-8; *(7)*, 17786-31-1; *(8)*, 76550-40-8; *(9)*, 76550-41-9; $NEt_3$, 121-44-8

---

[1] a) *W. Hieber, H. Schulten*, Z. Anorg. Allg. Chem. *232*, 29 (1937); b) *M. L. H. Green*, Angew. Chem. *72*, 719 (1960); *F. A. Cotton, G. Wilkinson:* Advanced Inorganic Chemistry. 4th edit., Wiley, New York 1980, p. 1114; c) For a recent review on catalytic properties of *(1)* see *P. Pino, F. Piacenti, M. Bianchi* in *I. Wender, P. Pino:* Syntheses *via* Metal Carbonyls. Vol. 2, Wiley, New York 1977, pp. 43—231; see also *J. W. Rathke, H. M. Feder*, J. Am. Chem. Soc. *100*, 3623 (1978); d) *F. Ungváry, L. Markó*, J. Organomet. Chem. *20*, 205 (1969); *R. W. Wegman, T. L. Brown*, J. Am. Chem. Soc. *102*, 2494 (1980).

[2] *G. Fachinetti*, J. Chem. Soc. Chem. Commun. *1979*, 397.

[3] *P. Chini, B. T. Heaton*, Top. in Curr. Chem. *71*, 1 (1977); *J. A. Connor, ibid. 71*, 71 (1977).

[4] a) *G. Fachinetti, S. Pucci, P. F. Zanazzi, U. Methong*, Angew. Chem. *91*, 657 (1979); Angew. Chem. Int. Ed. Engl. *18*, 619 (1979); b) *G. Fachinetti*, J. Chem. Soc. Chem. Commun. *1979*, 396.

[5] *P. Chini, G. Longoni, V. G. Albano*, Adv. Organomet. Chem. *14*, 98 (1976).

[6] *H.-N. Adams, G. Fachinetti, J. Strähle*, Angew. Chem. *93*, 94 (1981); Angew. Chem. Int. Ed. Engl. *20*, 125 (1981).

[7] *J. S. Kristoff, N. J. Nelson, D. F. Shriver*, J. Organomet. Chem. *49*, C 82 (1973), and references cited therein.

[8] *W. C. Trogler*, J. Am. Chem. Soc. *101*, 6459 (1979).

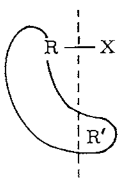
---

# Functional Groups at Concave Sites: Asymmetric Diels-Alder Synthesis with Almost Complete (Lewis-Acid Catalyzed) or High (Uncatalyzed) Stereoselectivity[**]

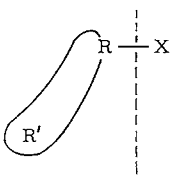
By *Günter Helmchen* and *Roland Schmierer*[*]

*Dedicated to Professor Gerhard Pfleiderer on the occasion of his 60th birthday*

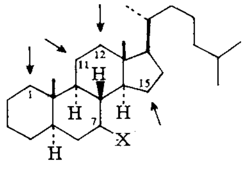
The terms concave/convex have been used casually for the characterization of molecular morphological aspects of intermolecular interactions[1]. They also enable a useful description of intramolecular spatial relationships, *e.g.* of a substituent X relative to the rest of the molecule or a further group R′ in the molecule. As illustrated by the two-dimensional "molecules" *(1)* and *(2)*, X is at a concave/convex site relative to the rest of the molecule or to R′ when X and one or more atoms ≠ H of the rest of the molecule or of R′ lie in the same half-space/different half-spaces defined by[2] the plane (– – –) dividing the X—R bond at its midpoi[3].



*(1)*



*(2)*

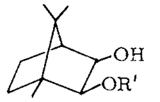


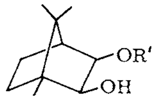
*(3a)*, X = α-OH
*(3b)*, X = β-OH

We have taken this classification, unambiguous for rigid and conformationally established structures, as a basis for the development of new alcohol reagents (R—X···C—OH) for diastereoface-differentiating asymmetric syntheses[4] with esters (X = planar prochiral acyloxy group); we assumed that alcohols of type *(1)* are better suited for this purpose than are those of type *(2)* (*e.g.* menthol, borneol, 2-octanol) which have generally been used so far. Thus, of a large number of chiral alcohols used in the atrolactic acid synthesis according to the McKenzie-Prelog method[5] (assignment of configuration) only in a few cases were enantiomeric yields (e.e.[4]) of >50% achieved[6]; these were unequivocally, or potentially (in the case of several possible conformers), compounds of type *(1)*. This is particularly clear in the case of the epimeric 7-cholestanols *(3)*, of which *(3a)*, e.e. = 13%, belongs to the type *(2)*, and *(3b)*, e.e. = 69%, to the type *(1)* (R′ = $C^{15}H_2$). Analogous conditions should exist for X at the positions of the steroid moiety marked by arrows[7].

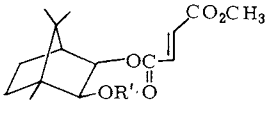
The alcohols *(4)* and *(5)* are presented here as new reagents of type *(1)*. They are distinguished, apart from by their

*(4)*

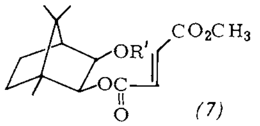




*(5)*

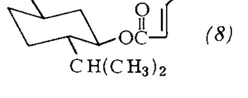


*(6)*



*(7)*

*(a)*, R′ = $CH_2Ph$
*(b)*, R′ = $CHPh_2$
*(c)*, R′ = CONHPh



*(8)*

(11*S*, 12*S*)    (11*R*, 12*R*)

*(9)*, $R^1$ = $CO_2CH_3$, $R^2$ = $CO_2R^3$[$R^3$–OH = *(4)*, *(5)* or (1*R*)-Menthol]
*(10)*, $R^1$ = $R^2$ = $CH_2OH$

---

[*] Priv.-Doz. Dr. G. Helmchen, Dr. R. Schmierer
Institut für Organische Chemie, Biochemie und Isotopenforschung
der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by Thomae, Biberach (Germany).

morphology, by the following properties: a) The group R can be readily varied. b) Their diastereomeric esters can usually be separated by liquid chromatography (LC). This enables a precise analysis and preparative purification of mixtures of the diastereomers. c) The alcohols are readily accessible as pure enantiomers from (+)-camphor[8]. d) Although *(4)* and *(5)* are constitutional isomers they yield inversely configurated products, since the "convex" methyl group at C-1 exerts only a small effect.

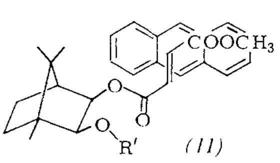
We report here[9] on the cycloaddition of the methyl fumarates *(6)* and *(7)* obtained from *(4)* and *(5)*, and (comparison with results quoted in the literature) of the menthyl ester *(8)* with anthracene (for reaction conditions, see Tables 1 and 2)[10]. The configuration of products *(9)* was determined *via* the optical rotation of the diols *(10)*[11a], prepared by reduction with $LiAlH_4$ and purified *only by LC*. In this way[11b], or still better by HPLC or $^1$H-NMR analysis (signal of the $COOCH_3$ group) of the crude product *(9)*, the diastereoselectivity was determined.

Table 1. Uncatalyzed asymmetric cycloaddition of *(6)*, *(7)* and *(8)* to anthracene [toluene, 110 °C, 5d, *c* (anthracene) = 0.1 mol/dm$^3$, *c* (dienophile) = 0.05 mol/dm$^3$, *c* (hydroquinone) = 0.005 mol/dm$^3$]. d.e. = diastereomeric yields (definition analogous to e.e. [4]).

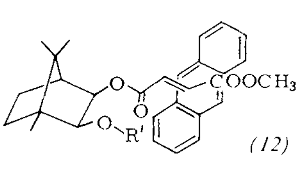
| Dienophile | Yield [%] *(9)* [a] | α [b] | d.e. [%] $^1$H-NMR/HPLC |
|---|---|---|---|
| *(8)* | 47 | 1.08 (98:2) | /<10 |
| *(6a)* | 30 | [c] (98:2) | <10/ |
| *(6b)* | 68 | 1.6 (95:5) | <10/<10 |
| *(6c)* | 90 | 1.4 (9:1) | 60/58 [d] |
| *(7c)* | 68 | 1.07 (9:1) | 34/ [e] |

[a] The products were isolated by medium-pressure chromatography: For apparatus see *G. Helmchen, G. Nill, D. Flockerzi, W. Schühle, M. S. K. Youssef*, Angew. Chem. *91*, 64 (1979); Angew. Chem. Int. Ed. Engl. *18*, 62 (1979). [b] α = chromatographic separation factor, determined by HPLC (apparatus, see [a]); eluent: petroleum ether/low boiling ethyl acetate in the ratio given in brackets. [c] No separation of the diastereomers. [d] Absolute configuration of the preferred diastereomer: 11*S*, 12*S*. [e] Absolute configuration of the preferred diastereomer: 11*R* 12*R*.

With one exception[12a], e.e. = 39%, only a small e.e. has so for been achieved (normal pressure: <13%; high pressure: <21%)[5, 12b] in the uncatalyzed Diels-Alder reaction. This is also true (Table 1) for *(6a)* and *(6b)* and, as expected, for *(8)*. Thus, anthracene is not an atypical diene. It would seem significant that in the case of *(6c)*, high diastereoselectivity is accompanied by increased reactivity. Assuming transition states with the topography *(11)* (preferred) and *(12)*[13] this points both to effective diastereoface-differentiated[4] shielding as well as to electronic and conformational influence of the enone system by the *N*-phenylcarbamoyl group (for an analogous observation see[7a]). As expected, with *(7c)* the inversely configurated product is obtained, but in poorer yields and with lower diastereoselectivity.



*(11)*



*(12)*

The Lewis acid-catalyzed reaction of fumarates and acrylates with butadiene or cyclopentadiene is already fairly stereoselective, d.e. ≅ 50–80%[5], in the case of menthyl esters, so that here too the reaction of *(8)* with anthracene (Table 2) is typical. With *(6a)* and *(6c)*, complete or almost complete asymmetric induction, respectively, is achieved[14]; once again, *(6c)* is particularly reactive. Temperature-dependence of the diastereomeric yields[4] observed here—it is greater at −30 °C or at −78 °C than at 0 °C [the small variation in the case of *(6a)* is significant]—has hitherto not been reported. The configurational relationships are the same for the uncatalyzed and the catalyzed reaction.

Table 2. Lewis acid-catalyzed cycloaddition of *(6)*, *(7)* and *(8)* to anthracene [$CH_2Cl_2$, 1d, 1 equivalent $AlCl_3$ (with respect to the dienophile); for concentrations see Table 1]: absolute configuration of the preferred diastereomer: 11*S*, 12*S*.

| Dienophile | *T* [°C] | Yield [%] *(9)* [b] | d.e. [%] $^1$H-NMR/HPLC/o.p. [c] |
|---|---|---|---|
| *(6a)* | 0 | 74 | 98/—/— |
| | −30 | 96 | >99/—/97 |
| | −78 | 58 | 98/—/— |
| | −78 [a] | [d] | |
| *(6b)* | 0 | [d] | |
| *(6c)* | 0 | 0 | |
| | 0 [a] | 100 | 86/86/— |
| | −30 [a] | 100 | 99/—/— |
| | −78 [a] | 96 | 66/—/— |
| *(7c)* | 0 | 0 | |
| | 0 [a] | 100 | 92/—/94 [e] |
| | −30 [a] | <10 | |
| *(8)* | +25 | 92 | —/—/62 |
| | 0 | 90 | —/76/82 |
| | −30 | 21 | —/—/76 |

[a] 2 equivalents $AlCl_3$. [b] See footnote [a] in Table 1. [c] d.e. of *(9)* = optical purity (o.p.) [4] of the diol *(10)* obtained by reduction of the unseparated diastereomers *(9)*. This value is less accurate than the other two, since the optical rotation of *(10)* is relatively small [11b]. [d] Reaction products: *(9)*, R′ = H. [e] Absolute configuration of the preferred diastereomer: 11*R*, 12*R*.

Received: September 24, 1980 [Z 695a IE]
German version: Angew. Chem. *93*, 208 (1981)

CAS Registry numbers:
*(3a)*, 19031-34-4; *(3b)*, 19031-34-4; *(6a)*, 76550-02-2; *(6b)*, 76529-70-9; *(6c)*, 76529-71-0; *(7c)*, 76529-72-1; *(8)*, 76529-73-2; (11*S*, 12*S*)-*(9)* (R$^3$OH = (1*R*)-menthol), 76529-74-3; (11*S*, 12*S*)-*(9)* (R$^3$OH = *(4a)*), 76529-75-4; (11*S*, 12*S*)-*(9)* (R$^3$OH = *(4b)*), 76529-76-5; (11*S*, 12*S*)-*(9)* (R$^3$OH = *(4c)*), 76529-77-6; (11*R*, 12*R*)-*(9)* (R$^3$OH = *(5c)*), 76529-78-7; (11*S*, 12*S*)-*(10)*, 33216-02-3; (11*R*, 12*R*)-*(10)*, 41063-84-7

---

[1] *V. Prelog*, quoted in Nachr. Chem. Tech. *23*, 461 (1975).

[2] For the term "half-space" („Halbraum") see: *V. Prelog, G. Helmchen*, Helv. Chim. Acta *55*, 2581 (1972).

[3] This definition can be generalized or modified, *e.g.* by choosing another surface instead of the plane or another point of intersection instead of the middle of the bond.

[4] Definition, see: *Y. Izumi, A. Tai* Stereo-differentiating Reactions. Academic Press, New York 1977.

[5] *J. D. Morrison, H. S. Mosher:* Asymmetric Organic Reactions. Prentice-Hall, Englewood Cliffs 1971.

[6] Cf. [5], Table 2—5, No. 28, 39, 41—44.

[7] For other examples which can be interpreted analogously see: a) *E. J. Corey, K. B. Becker, R. K. Varma*, J. Am. Chem. Soc. *94*, 8616 (1972); b) *J.-M. Vanest, R. H. Martin*, Recl. Trav. Chim. Pays-Bas *98*, 113 (1979); c) on the structural aspect cf. also Figure 1 in *H. Nozaki, A. Matsuo, Y. Kushi, M. Nakayama, S. Hayashi, D. Takaoka, N. Kamijo*, J. Chem. Soc. Perkin Trans. II *1980*, 763.

[8] *R. Schmierer*, Dissertation, Universität Stuttgart 1980.

[9] One other example: *R. Schmierer, G. Grotemeier, G. Helmchen, A. Selim*, Angew. Chem. *93*, 209 (1981); Angew. Chem. Int. Ed. Engl. *20, 207* (1981). Furthermore, in a kinetic resolution according to *Horeau* [8] diastereomeric α-phenylbutyrates have been obtained from *(4c)* with a selectivity of 93:7 (HPLC). Phenylsulfenylchloride adds to the acrylate of *(4c)* with the diastereoselectivity 95:5: *T. Beisswenger, F. Effenberger*, unpublished.

[10] All the new compounds gave correct analyses and characteristic spectra.

[11] a) Absolute configuration of *(10)*: (+)-(11*S*, 12*S*), *M.-J. Brienne, J. Jacques*, Bull. Soc. Chim. Fr. *1974*, 2647; b) As reference for the o.p. determination we used a sample of *(10)* obtained by reduction of HPLC-pure (11*S*, 12*S*)-*(9c)*: $[\alpha]_{578}^{22} = +10.7$ ($c = 1.9$, methanol) [R$^3$—OH in (11*S*, 12*S*)-*(9c)* is *(4c)*]. Ethanol [11a] is not a suitable solvent, since (±)-*(10)* is considerably less soluble than (+)-*(10)*.

[12] a) *H. Nitsch, G. Kresze*, Angew. Chem. *88*, 801 (1976); Angew. Chem. Int. Ed. Engl. *15*, 760 (1976); b) *J. Jurczak, M. Tkacz*, J. Org. Chem. *44*, 3347 (1979), and references cited therein.

[13] This suggestion, which is fully discussed in [8], differs from those presented previously [5], [12b] regarding the conformation of the ester group (cf. [9]).

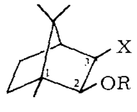
[14] Similarly good results (e.e. = 94 and 99%) were achieved with the acrylates of 7-phenylmenthol, likewise a reagent of type *(1)*: *E. J. Corey, H. E. Ensley*, J. Am. Chem. Soc. *97*, 6908 (1975).

---

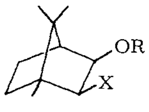
## Functional Groups at Concave Sites: Asymmetric Alkylation of Esters with Very High Stereoselectivity and Reversal of Configuration by Change of Solvent[**]

By *Roland Schmierer, Gregor Grotemeier, Günter Helmchen*, and *Adel Selim*[*]

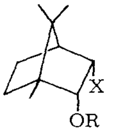
A new concept for the development of reagents for asymmetric syntheses first proved successful in the case of Diels-Alder reactions[1]. We report here on experiments with reagents *(1)*—*(3)*, which are closely related to those quoted in[1], in the α-alkylation of the esters *(4)*—*(6)* to products *(7)*—*(9)* *via* lithium enolates. An asymmetric induction in this important C—C coupling was previously achieved in enantiomeric yields (e.e.) of 7 to 50%[2] only for the very special case of esters *(10)*.



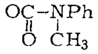
*(1)*, R = H
*(4)*, R = $COCH_2R^1$
*(7)*, R = $COCHR^1R^2$

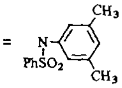


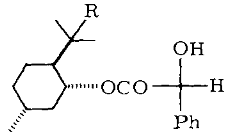
*(2)*, R = H
*(5)*, R = $COCH_2R^1$
*(8)*, R = $COCHR^1R^2$



*(3)*, R = H
*(6)*, R = $COCH_2R^1$
*(9)*, R = $COCHR^1R^2$

*(a)*, X =

$OC(=O)-N(CH_3)Ph$

*(b)*, X =




*(10a)*, R = H
*(10b)*, R = Ph

The esters *(4)*—*(6)*[3] were metalated with lithium cyclohexylisopropylamide (LiCHIPA) at −78 °C in tetrahydrofuran (THF) or THF/hexamethylphosphoric triamide (HMPT) 4:1[4]. In all cases, clear, colorless or lemon-yellow colored (sulfonamides) solutions were formed. These were allowed to react with alkylating agents $R^2$—X′ (X′ = Br or I, addition of 1 equivalent of HMPT) by warming to −40 °C and maintaining the mixture at this temperature (TLC control). The products *(7)*—*(9)* were isolated by extraction and analyzed by HPLC and/or $^1$H-NMR. Despite only moderate separation factors (α ≅ 1.1—1.3)[5], esters *(7)*—*(9)* could by obtained pure on a gram scale by preparative medium-pressure liquid chromatography because of initially high enrichment. On reduction [$Ca(BH_4)_2$[6a] or $LiAlH_4$[6b]] they gave enantiomerically pure alcohols $R^1R^2CH—CH_2OH$[7], which are valuable chiral synthons, particularly for the synthesis of natural products[8].

The α-alkylation proceeds in very good yields and with excellent diastereoselectivities (Table 1). In THF as solvent a diastereoselectivity of ≥ 90:10 is achieved with the urethanes *(4a)*, independent of the nature of groups $R^1$ and $R^2$. Other than in the case of the Diels-Alder reactions[1], a greater selectivity is achieved in these alkylations with the 2- than with the 3-acyloxybornanes.

Table 1. Reaction of the lithium enolates of the esters *(4)*—*(6)* with alkylating reagents $R^2$—X′ to give esters *(7)*—*(9)*; solvent: THF (A) or THF-HMPT 4:1 (B) [a].

| No. | Educt $R^1$ | $R^2X'$ | Solvent | Diastereoselectivity HPLC/ $^1$H-NMR | Configuration [b] | Yield [c] [%] |
|---|---|---|---|---|---|---|
| 1 *(4a)* | $CH_2Ph$ | $CH_3I$ | A | >95:5 [d] | *R* | 95 |
| 2 *(4a)* | $CH_3$ | $PhCH_2Br$ | A | —/94:6 | *S* | 96 |
| 3 *(4a)* | $CH_2Ph$ | $CH_2CHCH_2Br$ | A | 93:7/91:9 | *R* | 78 (92) |
| 4 *(4a)* | $CH_2CHCH_2$ | $PhCH_2Br$ | A | 93:7/94:6 | *S* | 90 |
| 5 *(4a)* | $CH_2Ph$ | $nC_4H_9I$ | A | 89:11/90:10 | *R* | 93 |
| 6 *(4a)* | $nC_4H_9$ | $PhCH_2Br$ | A | 93:7/94:6 | *S* | 90 |
| 7 *(4a)* | $CH_2CHCH_2$ | $CH_3I$ | A | 90:10/— | *R* | 88 |
| 8 *(4a)* | $CH_3$ | $CH_2CHCH_2Br$ | A | 93:7/— | *S* | 92 |
| 9 *(4a)* | $CH_3$ | $iC_4H_9I$ | A | 93:7/— | *S* | 78(90) |
| 10 *(4a)* | $nC_{16}H_{33}$ | $CH_3I$ | A | 90:10/— | *R* | 93 |
| 11 *(4a)* | $CH_3$ | $nC_{16}H_{33}I$ | A | 93:7/— | *S* | 88 |
| 12 *(4a)* | $CH_3$ | $PhCH_2Br$ | B | —/70:30 | *R* | 96 |
| 13 *(4a)* | $CH_3$ | $iC_4H_9I$ | B | 72:28/— | *R* | 60(90) |
| 14 *(4a)* | $CH_2Ph$ | $nC_4H_9I$ | B | 85:15/85:15 | *S* | 36(90) |
| 15 *(5a)* | $CH_2Ph$ | $CH_3I$ | A | —/81:19 | *S* | 93 |
| 16 *(5a)* | $CH_3$ | $PhCH_2Br$ | A | —/86:14 | *R* | 91 |
| 17 *(5a)* | $nC_{16}H_{33}$ | $CH_3I$ | A | 83:17/— | *S* | 94 |
| 18 *(5a)* | $CH_3$ | $nC_{16}H_{33}I$ | A | 94:6/— | *R* | 89 |
| 19 *(4b)* | $CH_3$ | $nC_{14}H_{29}I$ | A | 98.5:1.5/— | *S* | 84 |
| 20 *(4b)* | $CH_3$ | $nC_{14}H_{29}I$ | B | 94:6/— | *R* | 75 |
| 21 *(6b)* | $CH_3$ | $nC_{14}H_{29}I$ | A | 97.5:2.5/— | *R* | 74(91) |
| 22 *(6b)* | $CH_3$ | $nC_{14}H_{29}I$ | B | 98:2/— | *S* | 77(93) |

[a] The solvent contained *ca.* 5% hexane. [b] Absolute configuration of the chirality center of the acyl group of *(7)*—*(9)* determined *via* the optical rotation of the alcohols $R^1R^2CH—CH_2OH$ obtained by reduction; No. 1—9, 12—6: [3a]; No. 10, 11, 17, 18: [8]; No. 19—22: Assumption of same absolute configuration for 2-methyl-1-octadecanol and -hexadecanol of the same sign of rotation. [c] Total yield of pure, chromatographically isolated esters *(7)*—*(9)*. Values in brackets: yields corrected with respect to recovered educt. [d] Determined *via* the optical rotation of 2-methyl-3-phenyl-1-propanol obtained by reduction: $[\alpha]_D^{22} = +9.9°$ ($c = 3.7$, $CHCl_3$); the reference sample was prepared by reduction of (+)-2-benzylpropionic acid [5b] with $LiAlH_4$: $[\alpha]_D^{22} = -10.0°$ ($c = 4.1$, $CHCl_3$).

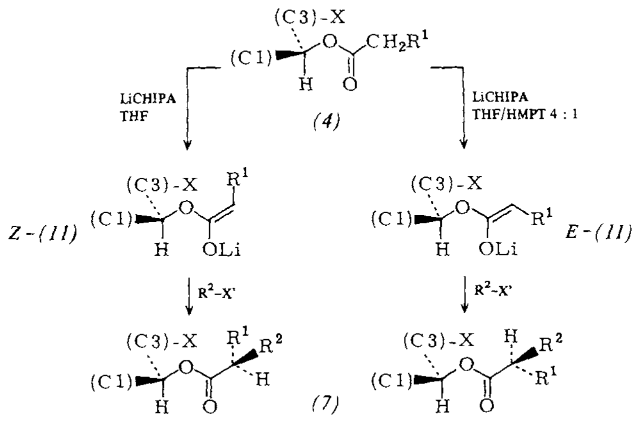
The sulfonamides *(4b)* and *(6b)* show particularly remarkable properties (cf. Table 1, Nos 19—22): *In THF and in THF-HMPT (4:1) as solvent, products with inverse configuration are obtained, with almost complete asymmetric induction in each case.* Thus, it was possible, to our knowledge for the first time in this way, to prepare both enantiomers from one compound. The same solvent effect also occurs, albeit to a lesser extent, in the case of the urethanes *(4a)* and *(5a)* (Table 1). Corresponding experiments have already been carried out with chiral oxazolines[9a] and hydrazones[9b]; addition of HMPT led to considerable reduction in the selectivity, and only in one case to reversal of configuration; however, the diastereoselectivity (58:42) was not significant[9b].

---

[*] Priv.-Doz. Dr. G. Helmchen[+], Dr. R. Schmierer, G. Grotemeier, A. Selim, M.Sc.
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Suttgart 80 (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft (Project He 880/7) and by Thomae, Biberach (Germany). *A. S.* was awarded a grant by the Deutsche Akademische Austauschdienst. We thank Frl. Dipl.-Chem. *G. Heiligenmann* for the examples No. 10, 11, 17, 18 (Table 1). Part of this work was presented in lectures at the Universities of Göttingen (June 2, 1980), Freiburg (June 9, 1980), and München (July 25, 1980).



Scheme 1. Configurations of educt, intermediates and products in the asymmetric alkylation of the esters *(4)*.

The configurational relationships can all be explained on the basis of the following *hypotheses* (cf. Scheme 1):

1) According to *Ireland* and *Willard* the esters Alkyl-$CH_2$—COOR are deprotonated with lithium amides in THF preferably to *Z*-, in THF-HMPT (4:1) preferably to *E*-enolates (selectivity in each case$\geq$4:1)[10]; thus, *Z*- or *E-(11)* can be generated selectively from *(4)*.

2) The conformation of the H—C—O—C—OLi group parallels that of the corresponding H—C—O—C=O group of esters[11] (torsional angle about the bold bonds $\cong 0°$).

3) Attack of the electrophile $R^2$—X at the enolate is blocked by the group X; that is in the case of *(11)* it takes place from the front side. Under otherwise equal conditions, therefore, *Z*- and *E*-enolates are alkylated to inversely configurated products.

4) The esters *(4)* and *(5)* as well as *(4)* and *(6)* are heterochiral[12] with respect to the X—C—$\overset{\bullet}{C}$H—O group ($\overset{\bullet}{C}$ = C-2 or C-3), and therefore under the same conditions give products with inverse configuration of the acyl group.

5) Inversely configurated products are also formed in the reactions of *(4)*—*(6)*with $R^2$—X′ when $R^1 = R^a$, $R^2 = R^b$ and $R^1 = R^b$, $R^2 = R^a$ (cf. references cited in[9a]).

Other than in the case of the systems described in[9], complexation of the lithium by X in *(4)*—*(6)* does not seem to play an important role. This is supported by results obtained with esters of 2-aminoalcohols [*(1)*, X = *N*(alkyl)aryl; *N*-alkylephedrine] and 1,2-diols and their derivatives [*(1)*, *(2)*, X = *O*-alkyl and $O(CH_2)_2OCH_3$, 2,2′-binaphthol, *trans*-1,2-cyclohexandiol][13].

Received: September 24, 1980 [Z 659b IE]
German version: Angew. Chem. *93*, 209 (1981)

CAS Registry numbers:
*(4a)* (R′ = $CH_2Ph$), 76529-52-7; *(4a)* (R′ = $CH_3$), 75817-71-9; *(4a)* (R′ = $CH_2CHCH_2$), 76529-53-8; *(4a)* (R′ = $nC_4H_9$), 76529-54-9; *(4a)* (R′ = $nC_{16}H_{33}$), 76529-55-0; *(5a)* (R′ = $CH_2Ph$), 76529-56-1; *(5a)* (R′ = $CH_3$), 76529-57-2; *(5a)* (R′ = $nC_{16}H_{33}$), 76529-58-3; *(4b)* (R′ = $CH_3$), 76529-59-4; *(6b)* (R′ = $CH_3$), 76529-60-7; (*R*)-*(7a)* (R′ = $CH_2Ph$, $R^2 = CH_3$), 76529-61-8; (*S*)-*(7a)* (R′ = $CH_3$, $R^2 = PhCH_2$), 76582-32-6; (*R*)-*(7a)* (R′ = $CH_2Ph$, $R^2 = CH_2CHCH_2$), 76529-62-9; (*S*)-*(7a)* (R′ = $CH_2CHCH_2$, $R^2 = PhCH_2$), 76582-33-7; (*R*)-*(7a)* (R′ = $CH_2Ph$, $R^2 = nC_4H_9$), 76529-63-0; (*S*)-*(7a)* (R′ = $nC_4H_9$, $R^2 = PhCH_2$), 76582-34-8; (*R*)-*(7a)* (R′ = $CH_2CHCH_2$, $R^2 = CH_3$), 76529-64-1; (*S*)-*(7a)* (R′ = $CH_3$, $R^2 = CH_2CHCH_2$), 76582-35-9; (*S*)-*(7a)* (R′ = $CH_3$, $R^2 = iC_4H_9$), 76529-65-2; (*R*)-*(7a)* (R′ = $nC_{16}H_{33}$, $R^2 = CH_3$), 75879-21-9; (*S*)-*(7a)* (R′ = $CH_3$, $R^2 = nC_{16}H_{33}$), 75817-73-1; (*R*)-*(7a)* (R′ = $CH_3$, $R^2 = iC_4H_9$), 76582-36-0; (*S*)-*(8a)* (R′ = $CH_2Ph$, $R^2 = CH_3$), 76529-66-3; (*R*)-*(8a)* (R′ = $CH_3$, $R^2 = PhCH_2$), 76582-84-8; (*S*)-*(8a)* (R′ = $nC_{16}H_{33}$, $R^2 = CH_3$), 76529-67-4; (*R*)-*(8a)* (R′ = $CH_3$, $R^2 = nC_{16}H_{33}$), 76582-37-1; (*S*)-*(7b)* (R′ = $CH_3$, $R^2 = C_{14}H_{29}$), 76529-68-5; (*R*)-*(7b)* (R′ = $CH_3$, $R^2 = nC_{14}H_{29}$), 76582-38-2; (*R*)-*(9b)* (R′ = $CH_3$, $R^2 = nC_{14}H_{29}$), 76582-85-9; (*S*)-*(9b)* (R′ = $CH_3$, $R^2 = nC_{14}H_{29}$), 76582-39-3

---

[1] *G. Helmchen, R. Schmierer*, Angew. Chem. *93*, 208 (1981); Angew. Chem. Int. Ed. Engl. *20*, 205 (1981).

[2] *T. Kaneko, D. L. Turner, M. Newcomb, D. E. Bergbreiter*, Tetrahedron Lett. *1979*, 103.

[3] a) Preparation of the esters *(4a)* and *(5a)*: *R. Schmierer*, Dissertation, Universität Stuttgart 1980; b) preparation of the esters *(4b)* and *(6b)*: *G. Helmchen, G. Grotemeier, A. Selim*, unpublished.

[4] *M. W. Rathke, A. Lindert*, J. Am. Chem. Soc. 93, 2318 (1971); for optimum yields the base must be present in excess (in the case of urethanes 2 equivalents, in the case of sulfonamides 1.5 equivalents).

[5] a) Apparatus, see *G. Helmchen, G. Nill, D. Flockerzi, W. Schühle, M. S. K. Yousef*, Angew. Chem. *91*, 64 (1979); Angew. Chem. Int. Ed. Engl. *18*, 62 (1979); petroleum ether (low-boiling)/ethyl acetate mixtures of suitable eluotropy were used as eluents; b) *G. Helmchen, G. Nill, D. Flockerzi, M. S. K. Youssef*, Angew. Chem. *91*, 65 (1979); Angew. Chem. *91*, 65 (1979); Angew. Chem. Int. Ed. Engl. *18*, 63 (1979).

[6] a) Ethanol (95%), 0 °C, only applicable in the case of *(8a)*; b) the urethanes *(7a)* and *(8a)* yield 2,3-bornanediol; in the case of the sulfonamides *(7b)* and *(9b)*, *(1b)* and *(3b)* are reobtained.

[7] All the new compounds gave correct analyses and characteristic spectra.

[8] An example: *E. Ade, G. Helmchen, G. Heiligenmann*, Tetrahedron Lett. *1980*, 1137.

[9] a) *A. I. Meyers, E. S. Snyder, J. J. H. Ackerman*, J. Am. Chem. Soc. *100*, 8186 (1978); b) *K. G. Davenport, H. Eichenauer, D. Enders, M. Newcomb, D. E. Bergbreiter*, J. Am. Chem. Soc. *101*, 5654 (1979).

[10] *R. E. Ireland, A. K. Willard*, Tetrahedron Lett. *1975*, 3975; *R. E. Ireland, R. H. Mueller, A. K. Willard*, J. Am. Chem. Soc. 98, 2868 (1976).

[11] Cf. *G. Helmchen*, Tetrahedron Lett. *1974*, 1527; *L. Golka*, Dissertation, Universität Stuttgart 1980.

[12] *E. Ruch*, Acc. Chem. Res. *5*, 49 (1972).

[13] *G. Helmchen et al.*, unpublished results.

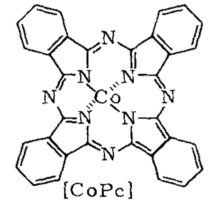
# Selective Reduction of the Nitro to the Amino Functional Group by means of the Phthalocyaninecobalt (I) Anion; Synthesis of N-Heterocycles and Alkaloids

By *Heiner Eckert*[*]

The directed transformation of functional groups, while other functionalties with similar reaction specifity are retained intact, is one of the most frequently encountered problems in synthetic organic chemistry. The reduction of nitro to amino groups is the best route to the important aromatic amine class of compounds; it is however well known[1a] that this is often accompanied by reactions of other functional groups (C=C, >C=O, —C≡N, aryl halides)[1]. Under basic reaction conditions rearrangement products and products arising from *N*-coupling are often produced in considerable amounts[1a,2]. The reduction of unsaturated compounds in the presence of metallic macrocycles of the vitamin $B_{12}$ structure type, although not with stable phthalocyaninemetal anions, has already been described[3].

Aromatic and aliphatic nitro compounds *(1)* can be reduced to primary amines *(2)* at room temperature using weakly basic conditions in protic solvents *e.g.* alcohols, in the presence of the phthalocyaninecobalt (I) anion$[Co^IPc]^{\ominus}$. The reaction proceeds cleanly and selectively: the following functional groups do not react; arenes and aryl halides, C=C double bonds even when activated, cyanides and isocyanides, aldehydes and ketones, carboxylic acid esters and am-

$$\underset{(1)}{O_2N{-}R{-}X} \xrightarrow[\text{MeOH}]{6\,[Co^IPc]^{\ominus}} \underset{(2)}{H_2N{-}R{-}X}$$



[CoPc]

$NC{-}(CH_2)_4{-}CN$ *(3)*

$Ph{-}CH{=}CH{-}CO_2Et$ *(4)*

---

[*] Dr. H. Eckert
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

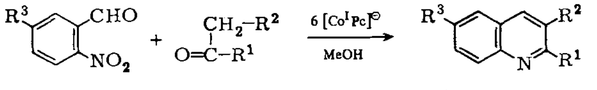
ides (see Table 1). The high yields, in particular with *(1g)* and *(1i)* which have a strong tendency to form side products, indicate the extremely high selectivity[4a] of the stable phthalocyaninecobalt (I) anion. Apart from its role in reduction reactions $[Co^IPc]^\ominus$ only participates in substitution reactions[4a] with alkyl[4b] or acyl halides[4a]. Control experiments indicated that even at long reaction times, hexanedinitrile *(3)* and ethyl cinnamate *(4)* were not attacked by $[Co^IPc]^\ominus$; only the transesterification of *(4)* was observed. Both the characteristic selectivity and reactivity parameter "supernucleophilicity relative to alkyl halides" ($n_{CH_3I} = 10.8$)[5a] and low reduction potential (−0.37 V)[5b] of the phthalocyaninecobalt(I)anion, have been determined in preliminary investigations of its mechanism of action[6] and for reduction processes.

Table 1. Selective reduction of nitro compounds *(1)*, which contain other reactive functional groups, to amines *(2)* by means of $[Co^IPc]^\ominus$ at 20–25 °C in methanol.

| | R | X | t [h] | Yield [%] |
|---|---|---|---|---|
| a | $nC_3H_7$ | | 95 | 66 |
| b | α-Naphthyl | | 48 | 70 |
| c | $C_6H_4$ | p-Cl | 80 | 91 |
| d | $C_6H_4$ | p-F | 26 | 63 |
| e | $C_6H_4$ | p-$CH_2$—CN | 62 | 95 |
| f | $C_6H_4$ | p-NC | 72 | 76 |
| g | $C_6H_4$ | p-CH=CH—$CO_2$Et | 65 [a] | 82 |
| h | $C_6H_4$ | p-CO—$CH_3$ | 90 | 78 |
| i | $C_6H_4$ | o-CHO | 90 | 96 |

[a] EtOH as Solvent.

As a result of its high selectivity and mild conditions of reaction, this reduction method is highly suitable for use in the synthesis of *N*-heterocycles by the Friedländer reaction[7]. The nitroaldehydes *(1i)* or *(1k)* were reduced in this way in a one-pot reaction and, without being isolated, the sensitive aldehydes produced were condensed with the ketones *(5)*; it was therefore unnecessary to protect the reactive functional groups in the intermediates (Table 2). The synthesis of the alkaloid comptothecine *(9)* and its derivatives[8], which are powerful antitumor agents, was successfully carried out by condensing *(1i)* or *(1k)* with *(7)* to give the tetracyclic systems *(8a)* or *(8b)* respectively (A-B-C-D) with yields of 62 and 51% respectively; it is particularly noteworthy that *(7)* contains groups which can be further reduced. The classic, base catalyzed Friedländer reaction using freshly prepared *(2i)* and *(7)* proceeds in only 20% yield and leads to the formation of side products which are difficult to separate[8a].

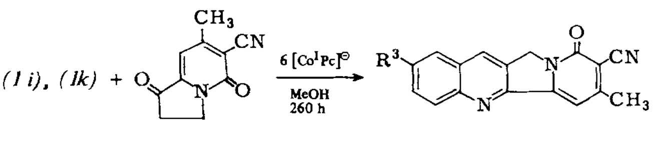


*(1i)*, *(1k)* *(5a)*-*(5c)* *(6a)*-*(6d)*

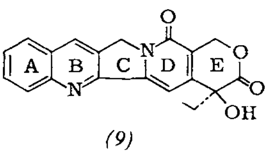
Table 2. Synthesis of N-heterocycles *(6)* from nitro compounds using the onepot procedure in methanol at 20–25 °C.

| Educts | R¹ | R² | R³ | t [h] | Products | Yield [%] |
|---|---|---|---|---|---|---|
| *(1i)* + *(5a)* | $CH_3$ | H | H | 63 | *(6a)* | 77 |
| *(1k)* + *(5a)* | $CH_3$ | H | Cl | 160 | *(6b)* | 87 |
| *(1i)* + *(5b)* | $CH_3$ | $CH_3$ | H | 49 | *(6c)* | 71 [a] |
| *(1i)* + *(5c)* | $C_6H_5$ | H | H | 96 | *(6d)* | 88 |

[a] No isomeric 2-Ethylquinoline.



*(7)* *(8a)*, R³ = H(62%)
*(8b)*, R³ = Cl(51%)



*(9)*

### *Procedure*

*(2)*: Under a nitrogen atmosphere, Li[CoPc]·4.5 tetrahydrofuran (THF)[9] (17–18 g, 19–20 mmol) is dissolved in 100 cm³ $N_2$-saturated methanol. The deep green solution is treated with 3.0 mmol *(1)* and stirred at 20–25 °C (Table 1). 10 cm³ $H_2O$ is then poured into the reaction mixture, $CO_2$ and air passed in for 5 min and the mixture centrifuged to separate the deep blue precipitate (5 min; 3000 rpm) which is then washed twice with methanol. The combined centrifugates are then concentrated and the residue distributed between ether and water. The organic phase is dried over $Na_2SO_4$ and the solvent evaporated; compound *(2)* remains. For compound *(2a)* the mixture is not treated with $H_2O$, but with 50 cm³ of 1 N hydrochloric acid and centrifuged. The centrifugate is then made alkaline with NaOH and extracted with ether. The ether phase is extracted with 10 cm³ of 1 N hydrochloric acid and water and the combined aqueous extracts concentrated, by means of which *(2a)*·HCl remains.

*(6)*: Under a $N_2$ atmosphere, Li[CoPc]·4.5 THF[9] (12–13 g, 13–14 mmol) is dissolved in 70 cm³ $N_2$-saturated methanol. The deep green solution is treated with an excess of *(6)* (*ca.* 50 mmol), 2.0 mmol *(1i)* or *(1k)* and stirred at 20–25 °C (see Table 2). Following this, 5 cm³ of $H_2O$ is added to the green reaction mixture, $CO_2$ and air passed into the mixture for 5 min, before being centrifuged (5 min; 3000 rpm) from the deep blue precipitate, which is then washed once with ethanol and twice with ether. The combined centrifugates are concentrated, the still damp residue distributed between 0.5 N hydrochloric acid and hexane, and the hexane phase extracted twice with water. The combined aqueous phases are washed with hexane, neutralized with 5 N NaOH and extracted with ether. The ether extract is dried over KOH and concentrated; *(6)* remains behind.

*(8a)*: Under a nitrogen atmosphere, Li[CoPc]·4.5 THF[9] (11.9 g, 13.2 mmol) is dissolved in 70 cm³ methanol which had been saturated with $N_2$. The deep green solution is treated with *(1i)* (302 mg, 2.0 mmol) and *(7)* (376 mg, 2.0 mmol)[8a] and stirred at 20–22 °C for 260 h. Following this, 5 cm³ $H_2O$ is added to the reaction mixture, $CO_2$ and air passed in for 5 mins and the mixture then centrifuged (5 min, 3000 rpm) from the deep blue precipitate; the latter is washed with warm (50 °C) nitrobenzene (5 × 40 cm³). Further washing with methanol (3 × 40 cm³) and ether (2 × 40 cm³) and drying at 60 °C yields $Co^{II}Pc$ (7.35 g, 98%). Solvent is removed from the combined nitrobenzene centrifugates and the residue triturated in methanol and filtered. Yield 340 mg (62%) *(8a)*. M.p. = 340 °C (decomp.).

Received: May 19, 1980, supplemented
October 6, 1980 [Z 696 IE]
German version: Angew. Chem. 93, 216 (1981)

CAS Registry numbers:
*(1a)*, 108-03-2; *(1b)*, 86-57-7; *(1c)*, 100-00-5; *(1d)*, 350-46-9; *(1e)*, 555-21-5; *(1f)*, 619-72-7; *(1g)*, 953-26-4; *(1h)*, 100-19-6; *(1i)*, 552-89-6; *(1k)*, 6628-86-0; *(2a)*, 107-10-8; *(2b)*, 134-32-7; *(2c)*, 106-47-8; *(2d)*, 371-40-4; *(2e)*, 3544-25-0; *(2f)*, 873-74-5; *(2g)*, 5048-82-8; *(2h)*, 99-92-3; *(2i)*, 556-18-3; *(5a)*, 67-64-1; *(5b)*, 78-93-3; *(5c)*, 98-86-2; *(6a)*, 91-63-4; *(6b)*, 92-46-6; *(6c)*, 1721-89-7; *(6d)*, 612-96-4; *(7)*, 58610-63-2; *(8a)*, 66911-21-3; *(8b)*, 76529-26-5; Li[CoPc], 14516-90-6

---

[1] a) *Houben-Weyl:* Methoden der Organischen Chemie. Bd. 11/1. Thieme, Stuttgart 1957; b) *R. A. Egli*, Helv. Chim. Acta *51*, 2090 (1968); c) *T. R. Lewis, S. Archer*, J. Am. Chem. Soc. *71*, 3753 (1949); d) *T. Satoh, S. Suzuki*, Tetrahedron Lett. *1969*, 4555.

[2] a) *Y. Maki, A. Sugijama, K. Kikuchi, S. Seto*, Chem. Lett. *1975*, 1093; b) *H. J. Barber, E. Lunt*, J. Chem. Soc. *1960*, 1187.

[3] a) *A. Fischli*, Helv. Chim. Acta *62*, 882 (1979); b) *N. M. Ricroch, A. Gaudemer*, J. Organomet. Chem. *67*, 119 (1974); c) *Y. Ohgo, S. Takeuchi, J. Yoshimura*, Bull. Chem. Soc. Jpn. *44*, 282 (1971).

[4] a) *H. Eckert, A. Schier*, Angew. Chem. *91*, 841 (1979); Angew. Chem. Int. Ed. Engl. *18*, 794 (1979); b) *R. Taube, H. Drevs, T. Duc-Hiep*, Z. Chem. *9*, 115 (1969); c) *H. Eckert, I. Lagerlund, I. Ugi*, Tetrahedron *33*, 2243 (1977).

[5] a) *H. Eckert, I. Ugi*, Angew. Chem. *87*, 847 (1975); Angew. Chem. Int. Ed. Engl. *14*, 825 (1975); b) *D. W. Clack, N. S. Hush, J. S. Woolsey*, Inorg. Chim. Acta *19*, 129 (1976).

[6] *H. Eckert*, unpublished results

[7] a) *J. Eliasberg, P. Friedländer*, Ber. Dtsch. Chem. Ges. *25*, 1752 (1892); b) *W. Borsche, F. Sell*, Chem. Ber. *83*, 78 (1950).

[8] a) Shanghai No. 5 Pharmaceutical Plant, Shanhai No. 12 Pharmaceutical Plant, Shanghai Institute of Pharmaceutical Industrial Research, and Shanghai Institute of Materia Medica, Scientia Sinica *21*, 87 (1978); b) *P. C. Pan, S. Y. Pan, Y. H. Tu, S. Y. Wang, T. Y. Owen*, Acta Chim. Sinica *33*, 71 (1975); c) *H. Eckert, C. Stangl, Y. Kiesel, M. Listl*, unpublished results.

[9] *H. Eckert, I. Ugi*, Justus Liebigs Ann. Chem. *1979*, 278.

---

## "Magnetochemical Series" for Lanthanoid Compounds[**]

By *Werner Urland*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

*Klemm* was the first to make use of magnetic measurements to determine the "valence" of rare earth elements in compounds where this was not immediately apparent from their composition (*e.g.* $Ce^{IV}O_2$, $Ce^{III}S_2$)[1]. In this article it will be shown that magnetochemistry also enables statements to be made about the chemical bonding in lanthanoid compounds.

Powdered samples of NT-$CsTmO_2$[2a] (NT ≙ low temperature form), NT-$CsYbO_2$[2b], $CsAPrF_6$ (A = K, Rb)[2c], $Cs_2AHoF_6$ (A = Na,K, Rb)[2d], $Cs_2LiTmX_6$ (X = Cl, Br, I)[2e], $Cs_2NaTmI_6$[2e], $Cs_2KTmX_6$ (X = Cl, Br)[2f], $CsATmF_6$ (A = Na, K, Rb)[2f], $Cs_2AYbF_6$ (A = Na, K, Rb)[2g] and $Cs_2NaYbBr_6$[2g] were studied over the temperature range of 3–250 K using the Faraday method. Their magnetic behaviour could be explained applying a model of paramagnetism[3a] in which the influence of the crystal field was treated by the Angular Overlap (AO) model[3b]. The conventional crystal field parameters can be expressed in terms of the AO parameters, $e_\sigma(R)$ and $e_\pi(R)$, which are directly related to the $\sigma$- and $\pi$-covalent contribution to the chemical bonding and should be proportional to the square of the respective overlap integral[3b]. If it is assumed, on the basis of earlier investigations[4], that the value of the ratio, $e_\sigma(R)/e_\pi(R)$, lies between 2 and 6 for all the compounds considered here, then the values of $e_\sigma(R)$ for the alkali metal thulium halides can be determined unequivocally from measurements of the magnetic susceptibility. From these considerations, a ligand "magnetochemical series" can be drawn up. Table 1 shows values of $e_\sigma(R)$ compared with those of the overlap integrals $S_\sigma^2(R)$. The values of $S_\sigma^2(R)$ for the quaternary sodium compounds[2e,f] were calculated from[5] using the 4f-$Er^{3+}$ and 4f-$Yb^{3+}$ functions[6a] respectively, and the corresponding np-ligand function of $X^-$ [6b] (for NT-$CsTmO_2$ of $O^{2-}$, 2p solution function for the +2 potential well[6c]) for the respective $Tm^{3+}$-ligand ion distance $R$. Then the average value was formed. Since the Hartree-Fock 5p-function for $I^-$ could not be found in the literature, the calculation of the respective overlap integrals was not performed in this case.

Table 1. AO parameters $e_\sigma(R)$, overlap integrals $S_\sigma^2(R)$ and $Tm^{3+}$ ligand ion distances $R$, for NT-$CsTmO_2$ and $Cs_2NaTmX_6$ (X = F, Cl, Br, I).

| Compound | $e_\sigma(R)$ [$cm^{-1}$] | $S_\sigma^2(R) \cdot 10^4$ | $R$ [pm] | Ref. |
|---|---|---|---|---|
| NT-$CsTmO_2$ | 450 [a] | 2.47 | 219.8 | [2a] |
| $Cs_2NaTmF_6$ | 450 ± 10 | 2.36 | 217 [b] | [2f] |
| $Cs_2NaTmCl_6$ | 215 ± 10 [c] | 0.81 | 269 [d] | [2e,f] |
| $Cs_2NaTmBr_6$ | 145 ± 8 [c] | 0.60 | 284 [d] | [2e,f] |
| $Cs_2NaTmI_6$ | 125 ± 5 | — | 308 [d] | [2e] |

[a] Without determination of the errors involved. [b] cf. [7]. [c] Average value, including the values for lithium and potassium compounds. [d] Sum of the ionic radii of $Tm^{3+}$ and ligand ion for the coordination number 6: *R. D. Shannon*, Acta Crystallogr. *A 32*, 751 (1976).

With the exception of NT-$CsYbO_2$[2b] the unequivocal determination of $e_\sigma(R)$ from magnetic studies of this type did not prove possible for the remaining compounds. As an approximation a value of $e_\sigma(R)/e_\pi(R) = 3$ can be used for the halides[4a]. The values of $e_\sigma(R)$ for the ratio $e_\sigma(R)/e_\pi(R) = 3$ also allow the ligands to be arranged in a "magnetochemical series" (Table 2).

Table 2. AO parameters $e_\sigma(R)$ for $e_\sigma(R)/e_\pi(R) = 3$, overlap integrals $S_\sigma^2(R)$, and $Yb^{3+}$-ligand ion distances $R$ for NT-$CsYbO_2$ and $Cs_2NaYbX_6$ (X = F, Cl, Br).

| Compound | $e_\sigma(R)$ [$cm^{-1}$] | $S_\sigma^2(R) \cdot 10^4$ | $R$ [pm] | Ref. |
|---|---|---|---|---|
| NT-$CsYbO_2$ | 360 ± 30 | 2.18 | 219 | [2b] |
| $Cs_2NaYbF_6$ | 360 ± 30 | 2.11 | 216 | [2g] |
| $Cs_2NaYbCl_6$ | 252 [a] | 0.72 | 267 [b] | [2g,8] |
| $Cs_2NaYbBr_6$ | 160 ± 10 | 0.59 | 278 | [2g] |

[a] For $e_\sigma(R)/e_\pi(R) = 1.62$. [b] *G. Meyer*, personal communication.

When the ligands are ordered according to increasing $e_\sigma(R)$ values, (cf. Tables 1 and 2), the following "magnetochemical series" arises:

$$I^- < Br^- < Cl^- < F^- \approx O^{2-}$$

Table 3. AO parameters $e_\sigma(R)$ for $e_\sigma(R)/e_\pi(R) = 3$, overlap integrals $S_\sigma^2(R)$ and $M^{3+}$—$F^-$ distances $R$ for $Cs_2AMF_6$ (A = K, Rb; M = Pr, Ho, Tm, Yb).

| Compound | $e_\sigma(R)$ [$cm^{-1}$] | $S_\sigma^2(R) \cdot 10^4$ | $R$ [pm] | Ref. |
|---|---|---|---|---|
| $Cs_2KPrF_6$ | 720 ± 30 | 6.90 | 227 [a] | [2c] |
| $Cs_2RbPrF_6$ | 690 ± 30 | | | |
| $Cs_2KHoF_6$ | 420 ± 30 | 2.88 [b] | 219 | [2d] |
| $Cs_2RbHoF_6$ | | | | |
| $Cs_2KTmF_6$ | 420 ± 10 | 2.36 | 217 [a] | [2f] |
| $Cs_2RbTmF_6$ | 390 ± 10 | | | |
| $Cs_2KYbF_6$ | 360 ± 30 | 2.11 | 216 [a] | [2g] |
| $Cs_2RbYbF_6$ | | | | |

[a] Cf. [7]. [b] Average value including functions for 4f-$Dy^{3+}$ and 4f-$Er^{3+}$ [6a].

---

[*] Priv. Doz. Dr. W. Urland
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

From Table 3 it can be seen that the values of $e_\sigma(R)$ decrease with increasing atomic number of the lanthanoid element, and in this way a similar "magnetochemical series" for the central ions also follows, which corresponds to the pattern of the "lanthanoid contraction".

Received: September 26, 1980 [Z 697 IE]
German version: Angew. Chem. 93, 205 (1981)

---

[1] *W. Klemm:* Magnetochemie. Akademische Verlagsgesellschaft, Leipzig 1936.

[2] a) *W. Urland,* Z. Naturforsch. *A 34,* 997 (1979); b) *ibid. A 35,* 247 (1980); c) *W. Urland, K. Feldner, R. Hoppe,* Z. Anorg. Allg. Chem. *465,* 7 (1980); d) *W. Urland,* Z. Naturforsch. *A 35,* 403 (1980); e) Ber. Bunsenges. Phys. Chem. *84,* 484 (1980); f) *ibid. 83,* 1042 (1979); g) Z. Naturforsch. *A 34,* 1507 (1979).

[3] a) *W. Urland,* Chem. Phys. Lett. *46,* 457 (1977); b) Chem. Phys. *14,* 393 (1976).

[4] a) *W. Urland,* Chem. Phys. Lett, *53,* 296 (1978); *ibid.,* in press; b) Chem. Phys. *38,* 407 (1979).

[5] *W. Urland,* J. Chem. Phys. *70,* 5335 (1979); correction in [2g].

[6] a) *A. J. Freeman, R. E. Watson,* Phys. Rev. *127,* 2058 (1962); b) *E. Clementi,* Tables of Atomic Functions, Supplement to IBM J. Res. Dev. *9,* 2 (1965); c) *R. E. Watson,* Phys. Rev. *111,* 1108 (1958).

[7] Dissertation *K. Feldner,* Universität Giessen 1979; *K. Feldner, R. Hoppe, Z.* Anorg. Allg. Chem., in press.

[8] *B. Kanellakopulos, H.-D. Amberger, G. G. Rosenbauer, R. D. Fischer,* J. Inorg. Nucl. Chem. *39,* 607 (1977).

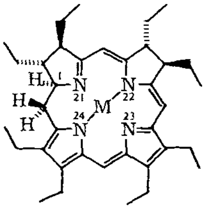
---

## Conformational Coupling between Ring A and Ring B in Isobacteriochlorins[**]

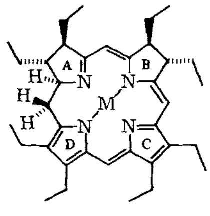
By *Christoph Kratky, Christof Angst,* and *Jon Eigill Johansen*[*]

Of the 16 possible isomers of nickel(II)octaethyl-1,2,3,7,8,20-hexahydroporphyrinate *(1),* almost exclusively the diastereomers *tttt-(1)* and *ttct-(1)* were obtained from complexation and tautomerization reactions[1a]. Their crystal structures revealed a conformational coupling between rings A and B: The ethyl substituents on both ring A, as well as on ring B, have diequatorial conformation in the *ttct*-isomer, whereas in *tttt-(1)* the substituents on ring A are diequatorial, those on ring B diaxal. At first we assumed that the conformational coupling is a result of the perturbation in the planarity of the porphyrin system (due to $sp^3$-hybridization of C-1 in ring A), which propagates *via* the coordinated nickel(II) ion to ring B.

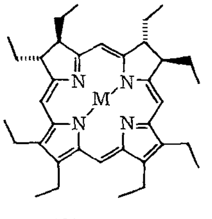
At the tetrahydro stage predominantly isobacteriochlorins and nickel(II) isobacteriochlorinates also having *trans* oriented vicinal ethyl groups on rings A and B were observed[1]. Octaethylisobacteriochlorin *(2)* and its metal complexes, *e.g. (3),* have been proposed as synthetically convenient models for the natural product sirohydrochlorin[2], with previous experiments being restricted to mixtures of the *ttt*- and *tct*-isomers[3]. In the case of the nickel complexes *(3),* the separation of the mixture was achieved by HPLC[1a]. We have now been able to separate the (HPL chromatographically inseparable) mixture of the free ligands *(2)* by fractional crystallization[4].



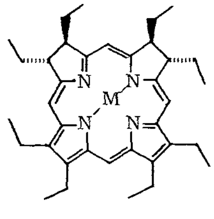
*tttt-(1),* M = Ni



*ttct-(1),* M = Ni



*ttt-(2),* M = 2 H
*ttt-(3),* M = Ni



*tct-(2),* M = 2 H
*tct-(3),* M = Ni

Remarkably, the crystal structures of the nickel complexes *ttt-(3)* and *tct-(3)* show the substituents on rings A and B (Fig. 1) in a surprisingly similar conformation to *tttt-(1)* and *ttct(1),* respectively. In the free ligands *ttt-(2)* and *tct-(2)* (Fig. 1), *trans* vicinal ethyl groups always have diaxial conformation and thus, in contrast to *(3),* show no conformational coupling.

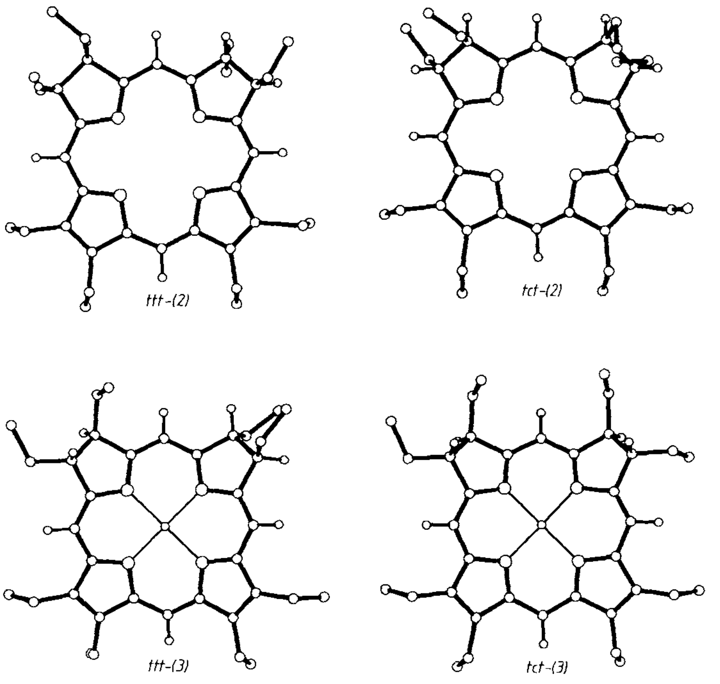


Fig. 1. Crystal structures of some isobacteriochlorins. Projection into the plane of the atoms N-21—N-22—N-23. *ttt-(2):* from ether/methanol, monoclinic, $P2_1/c$, $a=16.43$, $b=8.16$, $c=24.67$ Å, $\beta=97.68°$, $Z=4$, $\varrho_x=1.10$ g cm$^{-3}$, 4564 reflections refined (1001 with $I>2.5\sigma(I)$), $R=0.14$; *tct-(2):* from ether/methanol, orthorhombic, Pbca, $a=12.38$, $b=22.14$, $c=24.69$ Å, $Z=8$, $\varrho_x=1.06$ g cm$^{-3}$, 5310 reflections refined (1213 with $I>2.5\sigma(I)$), $R=0.13$; *ttt-(3):* from ether/hexane, triclinic, $P\bar{1}$, $a=8.73$, $b=13.12$, $c=15.27$ Å, $\alpha=105.79$, $\beta=102.52$, $\gamma=101.31°$, $Z=2$, $\varrho_x=1.26$ g cm$^{-3}$, 5578 reflections refined (4481 with $I>2.5\sigma(I)$), $R=0.05$. *tct-(3):* from ethyl acetate, monoclinic, $P2_1/c$, $a=9.66$, $b=20.89$, $c=15.92$ Å, $\beta=99.97°$, $Z=4$, $\varrho_x=1.26$ g cm$^{-3}$, 5765 reflections refined (1019 with $I>2.5\sigma(I)$), $R=0.10$ (see [5]).

---

[*] Dr. Ch. Kratky
Institut für Physikalische Chemie der Universität
Heinrichstrasse 28, A-8010 Graz (Austria)
Dipl. Naturwiss. ETH Ch. Angst, Dr. J. E. Johansen
Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

[**] This work was supported by the Österreichische Fonds zur Förderung der wissenschaftlichen Forschung (Project No. 3763), the Österreichische Akademie der Wissenschaften, the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung, and the Norwegian Research Council of Science and Technology (Travelling scholarship for *J. E. J.*). We thank Prof. *A. Eschenmoser* for stimulating advice and support of this work.

On incorporation of nickel(II) into the isobacteriochlorin ligand system the macrocycle collapses into a strongly contracted conformation. The "closing up" of the four nitrogen atoms, enforced by the coordinative requirements of the small nickel(II) central atom, effects considerable deformation of the entire porphyrin ring: Oppositely situated five-membered rings are mutually twisted by *ca.* 50° with respect to an axis through their nitrogen atoms[5], leading to the formation of a strongly puckered macrocycle with approximate $D_{2d}$ symmetry (Fig. 2). The conformational coupling between rings A and B observed in the nickel complexes *(1)* and *(3)* is an immediate manifestation of this $D_{2d}$-deformation, which is not observed [*ttt-(2)*] or, if so, only to a very slight extent [*tct-(2)*] in the free ligands[5].

This $D_{2d}$-type deformation with small central atoms[6] (nickel(II)[7], low spin cobalt[8a] and iron[8b]) was occasionally observed, though without such far-reaching stereochemical consequences, in unhydrogenated metal porphyrinates.

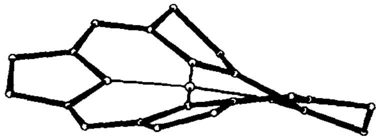


Fig. 2. Conformation of the hydroporphyrin system in the crystal structure of *ttt-(3)*.

The crystal structures[1a] (Fig. 1) suggest that a *diequatorial* conformation of *trans* vicinal ethyl groups is energetically preferred over a diaxial conformation in the (contracted) nickel complexes *(1)* and *(3)*, since the maximum number of diequatorial pairs of ethyl substituents consistent with the overall conformation of the macrocycle is always found. This is in excellent agreement with the observed relative thermodynamic stabilities: *tttt-(1)* and *ttt-(3)* can epimerize to over 50% into *ttct-(1)*[1a] and *tct-(3)*, respectively, whereas *ttct-(1)* and *tct-(3)* are hardly converted under the same conditions[9]. In the conformationally unfixed[10] free ligands *(2)*, on the other hand, the vicinal ethyl groups always have *diaxial* conformation. This could explain the difficulties encountered on attempting a separation of *ttt-(2)* and *tct-(2)* by HPLC.

Received: June 30, 1980 [Z 690 IE]
German version: Angew. Chem. *93*, 204 (1981)

CAS Registry numbers:
*tttt-(1)*, 76529-80-1; *ttct-(1)*, 76582-40-6; *ttt-(2)*, 76582-28-0; *tct-(2)*, 76582-29-1; *ttt-(3)*, 72880-99-0; *tct-(3)*, 72881-00-6

---

[1] a) *J. E. Johansen, Ch. Angst, Ch. Kratky, A. Eschenmoser*, Angew. Chem. *92*, 141 (1980); Angew. Chem. Int. Ed. Engl. *19*, 141 (1980); b) *Ch. Angst, M. Kajiwara, E. Zass, A. Eschenmoser, ibid. 92*, 139 (1980) and *19*, 140 (1980).

[2] Cf. footnote [12] in [1a], and *P. F. Richardson, C. K. Chang, L. K. Hanson, L. D. Spaulding, J. Fajer*, J. Phys. Chem. *83*, 3420 (1979); *C. K. Chang, J. Fajer*, J. Am. Chem. Soc. *102*, 848 (1980).

[3] *A. M. Stolzenberg, L. O. Spreer, R. H. Holm*, J. Chem. Soc. Chem. Commun. *1979*, 1077; J. Am. Chem. Soc. *102*, 364 (1980).

[4] Recrystallization of a *ttt-(2)/tct-(2)* mixture (55:45, for preparation cf. [1b]) from ether/methanol concentrates *tct-(2)* in the precipitate; eleven-fold recrystallization afforded 97% *tct-(2)*. Crystals with 94% *ttt-(2)* were obtained from a three-fold concentrated mother liquor. The *ttt/tct* ratio was determined at each step by HPLC after transformation into the nickel complex *(3)* [1a]. *ttt-(2)*: m.p. 151 °C; *tct-(2)*: m.p. 168—168.5 °C; cf. also [3].

[5] Distances N-21—N-23 and N-22—N-24, respectively: *ttt-(2)*: 4.11 and 4.12 Å; *tct-(2)*: 4.06 and 4.16 Å; *ttt-(3)*: 3.86 and 3.84 Å; *tct-(3)*: 3.89 and 3.83 Å; angle between rings A and C and between rings B and D, respectively: *ttt-(2)*: 2.4 and 8.5°; *tct-(2)*: 17.2 and 16.17°; *ttt-(3)*: 49 and 48°; *tct-(3)*: 48.5 and 48°; mean deviation of the atoms 1—24 from their best plane: *ttt-(2)*: 0.073 Å; *tct-(2)*: 0.163 Å; *ttt-(3)*: 0.455 Å; *tct-(3)*: 0.428 Å.

[6] See also *J. L. Hoard* in *K. M. Smith:* Porphyrins and Metaloporphyrins. Elsevier, Amsterdam 1975, p. 317ff.

[7] In the (unhydrogenated) porphyrin ring system, the tendency of "smaller" central atoms towards optimum coordination and that of the π-system towards optimum conjugation appear to be of about the same order of magnitude. Besides the tetragonal nickel(II) octaethylporphyrinate crystal structure with a strongly twisted porphyrin ring (*E. F. Meyer Jr.*, Acta. Crystallogr. *B 28*, 2162 (1972)), there also exists a triclinic modification with practically planar macrocycle (*D. L. Cullen, E. F. Meyer, Jr.*, J. Am. Chem. Soc. *96*, 2095 (1974)).

[8] a) *P. Madura, W. R. Scheidt*, Inorg. Chem. *15*, 3182 (1976); *J. A. Kaduk, W. R. Scheidt, ibid. 13*, 1875 (1974); b) *J. P. Collman, J. L. Hoard, N. Kim, G. Lang, C. A. Reed*, J. Am. Chem. Soc. *97*, 2676 (1975); *D. M. Collins, R. Countryman, J. L. Hoard, ibid. 94*, 2066 (1972).

[9] Epimerization of *(3)*: *(3)* ($1.7 \times 10^{-3}$ M) in THF/1 M *t*BuOK in *t*BuOH (1:2), *ca.* 20 °C, 53d, under argon. After work-up, determination of the content of nickel chlorinates by UV/VIS, and of the isomeric ratio by HPLC. Starting from *ttt-(3)*: *ttt-(3)* (9%), *tct-(3)* (55%), other isomers of *(3)* (6%), Ni-chlorinates (30%). Starting from *tct-(3)*: *ttt-(3)* (3%), *tct-(3)* (69%), other isomers of *(3)* (2%), Ni-chlorinates (26%). Epimerization of *(1)*, cf. [1a].

[10] The $^1H$- and $^{13}C$-NMR spectra of *ttt-(3)* and *tct-(3)* differ markedly [1a], while the corresponding spectra of the free ligands *(2)* are very similar [1b].

---

## Chalcogenide Iodides of Arsenic[**]

By *Rüdiger Kniep* and *Horst Dieter Reski*[*]

*Dedicated to Professor Wilhelm Klemm on the occasion of his 85th birthday*

Investigations in ternary systems As-(S,Se,Te)-I have hitherto been decided, in particular, by the interest attached to relatively stable semiconducting chalcogenide iodide *glasses;* data on the composition and structure of *crystalline* phases are sparse and by no means free of inconsistencies[1]. It seemed worthwhile to us to narrow this "gap" regarding the well-documented and still topical class of compounds comprising the Sb- and Bi-chalcogenide halides of the SbSI-type[2a] (ferro- and photoelectric properties[2b]).

According to our thermoanalytical and X-ray crystallographic findings (cf. Table 1) the quasibinary sections $As_2Te_3$-$AsI_3$ and $As_2Se_3$-$AsI_3$ of the respective ternary systems contain the thermodynamically stable phases: $As_4Te_5I_2$ (m.p. incongruent 303 °C), α-AsTeI[3a] (m.p. incongruent 281 °C), and α-AsSeI (m.p. incongruent 221 °C); in addition, the metastable phases β-AsTeI and β-AsSeI could also be isolated. The existence of the stable phase AsSI[3b] is confirmed by us.

The growth of single crystals of the above mentioned arsenic chalcogenide iodides is rendered difficult by the tendency of such systems to form relatively stable glasses; success was achieved as follows: α-AsTeI, black metallic, monoclinic-prismatic crystals; hydrothermally[4a] (HI 67%, 65% packing, 155 → 145 °C, 42d)[4b]. β-AsTeI, black metallic, compact crystals; primary crystallizate on cooling from melts ("$As_8Te_7I_5$") from *ca.* 330 °C (4d); shortest possible post-annealing phase, since β-AsTeI is already completely transformed into α-AsTeI after, 18 h at *e.g.*, 180 °C. $As_4Te_5I_2$, metallic (somewhat like $As_2Te_3$), platelike crystals with prominent laminar cleavage; on cooling of melts (60 mol-% $As_2Te_3$/40 mol-% $AsI_3$) from *ca.* 320 °C (7d). α-AsSeI, in transmitted light dark-red, in reflected light metallic, needle-shaped with pronounced fibrillar cleavage; after cooling (7—8d) of AsSeI melts (320 °C), incorporated in a wax-like ma-

---

[*] Prof. Dr. R. Kniep, Dipl.-Chem. H. D. Reski
Institut für Anorganische Chemie und Strukturchemie der Universität
Universitätsstr. 1, D-4000 Düsseldorf (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

trix at room temperature. β-AsSeI, in transmitted light dark-red, in reflected light metallic, rectangular platelets; after cooling (7—8d) of a AsSeI melt (280 °C), which is in contact with partially recrystallized selenide iodide glass. AsSI, orange-yellow needle-shaped crystals, microcrystalline; after annealing (6 weeks) of AsSI glasses at 150 °C, incorporated in a wax-like matrix at room temperature. Reaction of $AsI_3$ with thioacetic acid[5] does not lead to AsSI, but unexpectedly to molecular adducts of $AsI_3$ with tetramethylhexathiaadamantane.

Table 1. Crystallographic data of chalcogenide iodides of arsenic (β-phases metastable).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| α-AsTeI [a] | mcl. | $P2_1$ | $a = 8.965(2)$, | $b = 4.042(1)$,<br>$\beta = 90.75(2)°$ | $c = 10.341(2)$ Å | $Z = 4$ | $\varrho_c = 5.84$ gcm$^{-3}$ |
| β-AsTeI [a] | cub. | Fm3m | $a = 5.791(8)$ Å | | | $Z = 2$ | $\varrho_c = 5.63$ gcm$^{-3}$ |
| $As_4Te_5I_2$ [b] | mcl. | C2, Cm,<br>C2/m | $a = 14.58$, | $b = 4.00$,<br>$\beta = 95.0°$ | $c = 12.26$ Å | $Z = 2$ | $\varrho_c = 5.51$ gcm$^{-3}$ |
| α-AsSeI [a] | mcl. | $P2_1$ | $a = 8.855(2)$, | $b = 4.194(1)$,<br>$\beta = 93.74(1)°$ | $c = 9.792(1)$ Å | $Z = 4$ | $\varrho_c = 5.14$ gcm$^{-3}$ |
| β-AsSeI [b] | cub. | $F4_132$ | $a = 11.05$ Å | | | $Z = 16$ | $\varrho_c = 5.53$ gcm$^{-3}$ |
| AsSI [c] | mcl. | $P2_1$ | $a = 8.61$, | $b = 4.22$,<br>$\beta = 97.2°$ | $c = 9.95$ Å | $Z = 4$ | $\varrho_c = 4.33$ gcm$^{-3}$ |

[a] Crystal structure analysis: MoKα, Syntex $P2_1$, ω-scan, $F_0 > 3.92\sigma_F$, E-XTL program system *α-AsTeI:* 2563 symmetry independent reflections, 1219 significant, $2\theta_{max} = 80°$, $R = 8.7\%$ (with empirical absorption corrections); *β-AsTeI:* 40 symmetry independent reflections, 39 significant $2\theta_{max} = 75°$, $R = 8.9\%$ (without absorption corrections); *α-AsSeI:* 1474 symmetry independent reflections, 865 significant, $2\theta_{max} = 65°$, $R = 6.8\%$ (with empirical absorption corrections). [b] Photographic investigations on single crystals. [c] Lattice constants from X-ray powder data (isotypic relation with α-AsSeI).

The crystal structures of α-AsTeI, β-AsTeI and α-AsSeI were determined (cf. Table 1). Figure 1 shows the macromolecular (1/∞) structural units of α-AsTeI and α-AsSeI. α-AsTeI shows the same double chain structure as is found in SbSI[2a] and corresponding isotypic 5B-6B-7B-compounds[1]. The $[As_2Te_2I_2]_\infty$ double chain in α-AsSeI is degenerated to an AsSe spiral with $2_1$ symmetry and still only terminal iodine atoms; the coordination and bond geometries change on (formal) transition from the α-AsTeI to the α-AsSeI structural unit as follows (cf. also caption to Fig. 1): chalcogen (C.N.3, trig. pyr) → (C.N.2, angular[6]); arsenic (C.N. 5, tetrag. pyr.) → (C.N. 3, trig. pyr.); iodine (CN. 2, bridging) → (C.N. 1, terminal). Figure 2 shows the projections of the structural assemblies of α-AsTeI and α-AsSeI in the direction of view of the (1/∞) structural units in comparison with the corresponding projection on the SbSI structure[2a]. SbSI and α-AsTeI show different packing of the same macromolecular structural units in the structural assemblies, while α-AsTeI and α-AsSeI show a comparable packing of different (modified) structural units; in general the crystal structures of α-AsTeI and α-AsSeI can thus be regarded as "variations of the SbSI type".

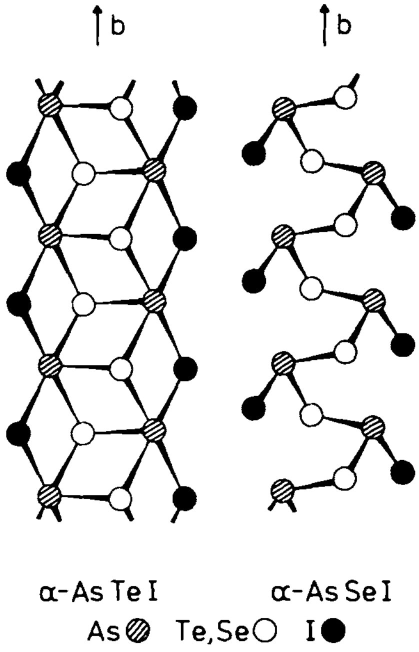


Fig. 1. Macromolecular structural units of α-AsTeI (left) and α-AsSeI (right). Bond lengths and angles (averaged values: standard deviations 0.01 Å and 0.4°, respectively): *α-AsTeI:* As—I 3.089, As—Te 2.741 Å; AsIAs 81.8, AsTeAs 91.5, IAsI 81.8, IAsTe 92.2, TeAsTe 90.5°. *α-AsSeI:* As—I 2.680 [8]; As—Se 2.430 Å; AsSeAs 97.4, IAsSe 97.1, SeAsSe 96.2°. Intramolecular interactions take place between As atoms and each of the neighboring Se and I atoms in the b direction (lying above in the figure): 3.079 and 3.518 Å (sum of the corresponding van-der-Waals radii: As...Se 4.00, As...I 4.15 Å [9]).

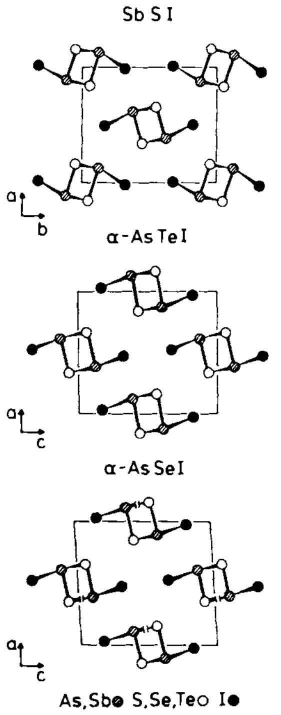


Fig. 2. Arrangement of the structural units of SbSI [2a], α-AsTeI and α-AsSeI in the structural assemblies. Projections in the direction of the macromolecular structural units. In α-AsTeI and α-AsSeI the shortest intermolecular interactions in each case are between As atoms of a structural unit and the bridging or terminal I atoms of the neighboring structural unit in the (101) direction (average value: 3.777 and 3.668 Å, respectively; standard deviations, see caption to Fig. 1).

*0570-0833/81/0202-0213 $ 02.50/0*

On crystallization of arsenic chalcogenide iodide glasses, particular importance attaches to the metastable ternary β-phases (Table 1). Thus, *e.g.*, in each case the ternary crystalline phase initially formed during the ordering processes on thermal treatment of glasses of the $As_2Te_3$-$AsI_3$ section is the cubic (metastable) β-AsTeI[7]. In this crystal structure (AB-type, fcc) tellurium and iodine are randomly distributed at positions of a partial lattice, while the As partial lattice—likewise random—is only 50% occupied. In the course of further ordering (annealing; β-AsTeI → α-AsTeI) the randomly semi-occupied As positions separate into ordered vacancies and fully-occupied lattice sites parallel to the (111) faces of the cubic system and thus contribute to approximation to the structural assembly of the monoclinic thermodynamically stable α-AsTeI. The As—(Te,I) distance of 2.895 Å in β-AsTeI is of the same order of magnitude as the averaged value 2.915 Å for all As—(Te,I) bond lengths of the macromolecular (ordered) structural element of α-AsTeI. Similar structural and phase relationships can be expected for α-AsSeI and β-AsSeI[10]; a metastable AsSI phase has not been observed by us.

Received: October 29, 1980 [Z 698 IE]
German version: Angew. Chem. *93*, 218 (1981)

---

[1] Review: *J. Fenner, A. Rabenau, G. Trageser*, Adv. Inorg. Chem. Radiochem. *23*, 329 (1980).

[2] a) *E. Dönges*, Z. Anorg. Allg. Chem. *263*, 112 (1950); b) *M. E. Lines, A. M. Glass:* Principles and Applications of Ferroelectrics and Related Materials. Clarendon Press, Oxford 1977, p. 513.

[3] a) The X-ray powder diagram of α-AsTeI is identical with that for a phase reported as $As_8Te_7I_5$ cf. *A. P. Chernov, S. A. Dembovskii, N. P. Luzhnaya*, Zh. Neorg. Khim. *20*, 2174 (1975); b) *A. P. Chernov, S. A. Dembovskii, I. A. Kirilenko*, Izv. Akad. Nauk SSSR, Neorg. Mater. *6*, 262 (1970; *L. M. Agamirova, E. G. Zhukov, V. T. Kalinnikov*, Russ. J. Inorg. Chem. *24*, 1430 (1979).

[4] a) *A. Rabenau, H. Rau*, Inorg. Synth. *14*, 160 (1973); b) by reducing the amount of solid used ("$As_8Te_7I_5$") by 80%, and under otherwise the same conditions, a hitherto unknown tellurium subiodide [cf. *R. Kniep, D. Mootz, A. Rabenau*, Z. Anorg. Allg. Chem. *422*, 17 (1976)] of the composition $Te_3I$ was obtained in almost quantitative yield.

[5] *N. Tarugi*, Gazz. Chim. Ital. *27*, 153 (1897).

[6] Elemental structure: *P. Cherin, P. Unger*, Inorg. Chem. *6*, 1589 (1967).

[7] The occurrence of a chemically not fully characterized cubic fcc-phase ($a = 5.778$ Å) on crystallization of $As_{50}Te_{50-x}I_x$ glasses ($x \leq 37$) has also been described [*R. K. Quinn, R. T. Johnson*, J. Non-Cryst. Solids *7*, 53 (1972)]. An fcc-phase ($a = 5.782$ Å) identified by X-ray powder methods is characterized as $As_4Te_5I_2$ in [3a] (see, on the other hand, the data in Table 1).

[8] $As{-}I_{terminal}$ in $AsI_3 = 2.591$ Å: *R. Enjalbert, J. Galy*, Acta Crystallogr. *B 36*, 914 (1980).

[9] *L. Pauling:* The Nature of the Chemical Bond, 3rd Ed. Cornell University Press, Ithaca, N. Y. 1960.

[10] *Note added in proof:* In the meantime a crystal structure analysis of AsSeI has been published whose accuracy is comparable with the analysis described here for α-AsSeI: *A. S. Kanishcheva, Yu. N. Mikhailkov, A. P. Chernov*, Sov. Phys. Dokl. *25*, 234 (1980).

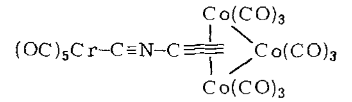
## Permetalated Methyl Isocyanide[**]

By *Wolf Peter Fehlhammer, Fritz Degel,*
and *Heribert Stolzenberg*[*]

α-Metalated isocyanides such as M—CX(H)—NC (X = H, $CO_2R$, $SO_2$aryl; M = Li,Na,Cu) have recently become important as versatile synthons in preparative organic chemistry[1]. Except for the silylated species $H_{3-n}(SiR_3)_nCNC$[2], however, these main group metal-organic isocyanides in general are poorly characterized, occurring only at low temperatures and in low concentrations, respectively.

We now present a stable transition metal derivative *(1)*, in which the CNC-skeleton functions as a $\mu_4$-bridge between a chromium atom and three cobalt atoms.

Compound *(1)*, which can be synthesized in 24% yield from $Cr(CO)_5CNCCl_3$[3] and $Co_2(CO)_8$ (molar ratio 4:9) is of interest for at least two reasons: *(i)* as the first functional isocyanide with an α-acetylenic C-atom, and *(ii)* as the first nonacarbonyltricobalt cluster containing a *functional* nitrogen-grouping on the methylidyne C-atom[4].



$$(OC)_5Cr{-}C{\equiv}N{-}C\begin{array}{l}Co(CO)_3\\Co(CO)_3\\Co(CO)_3\end{array}$$

*(1)*

As expected, the IR spectrum of *(1)* consists of the ν(CO) pattern of the $Co_3(CO)_9$ and $Cr(CO)_5$ moieties (cyclohexane: 2110 vw, 2062 s, 2044 m, 1980 s, 1969 vs, 1945 vs $cm^{-1}$) which presumably masks the weak intensity ν(CN) band. In the mass spectrum of *(1)* the molecular ion and all CO-deficient molecular fragments down to the base peak of CO-free $[CrCNCCo_3]^+$ appear as 15 equidistant groups of lines.

According to X-ray structure analysis[5], the molecule in the solid state has a crystallographic plane of symmetry which contains 13 of the total of 35 atoms (Fig. 1). The structural dimensions in the $CCo_3(CO)_9$ cluster compare well with those reported for other representatives of this cluster family[6]. In the $Cr(CO)_5$ moiety, the *trans* CO ligand with $d(Cr{-}C11) = 1.860(4)$ and $d(C11{-}O11) = 1.159(6)$ Å as against $\bar{d}(Cr{-}C_{cis}) = 1.892(9)$ and $\bar{d}(C{-}O)_{cis} = 1.140(6)$ Å reflects the *trans*-influence of a typical *C*-isocyanide, having a linear structure (CNC angle = 176.0(3), CrCN = 177.7(3)°).

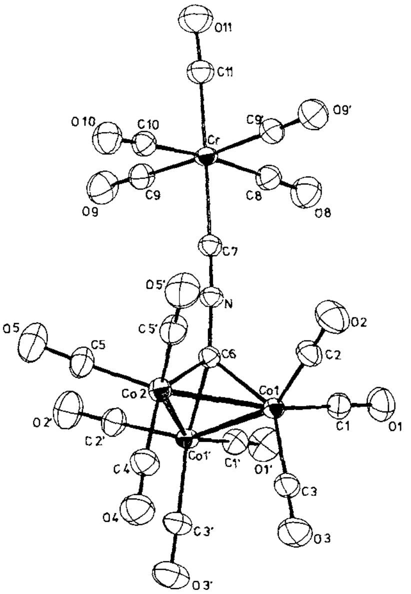


Fig. 1. ORTEP diagram of $(CO)_5CrCNCCo_3(CO)_9$ *(1)* showing 30% probability ellipsoids [5].

A normal C≡N bond length (1.160(5) Å) coupled with a markedly short N—C6 bond (1.354(5) Å), however, clearly demonstrates the sp character of the methylidyne C-atom.

Particular attention has been paid to the X-ray structural assessment of the *isocyanide* nature of *(1)*, since we had observed isocyanide → cyanide isomerization in a number of

---

[*] Prof. Dr. W. P. Fehlhammer, Dipl.-Chem. F. Degel,
Dipl.-Chem. H. Stolzenberg
Institut für Anorganische Chemie der Universität Erlangen-Nürnberg
Egerlandstrasse 1, D-8520 Erlangen (Germany)

[**] Metal Complexes of Functional Isocyanides, Part 5. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Bayer AG for supplying the isocyanide dichloride.—Part 4: [7a].

cases, even under very mild conditions[7]. Least-squares refinement calculations on the isocyanide and cyanide isomers and a comparison of their thermal parameters, however, left no doubt as to the correctness of the assignment.

The perchlorinated trichloromethyl isocyanide dichloride *(2)*[8a] would appear to provide a direct entry to metal-rich, CNC-bridged systems such as *(1)*. Indeed, it reacts with excess $Co_2(CO)_8$ immediately and cleanly to give *(3a)*, but there is no further reaction. The much higher reactivity of the chlorine atoms in the α-position with respect to the isocyanide dichloride function thus is also established for reactions with organometallic nucleophiles[8]. Attempted dehalogenation by conventional methods[9] of *(3a)* to give the parent isocyanide has so far failed. "Oxidative three-fragment addition" of *(3a)* to $Pt(\eta^2\text{-}C_2H_4)(PPh_3)_2$ under very mild conditions yields a second permetalated methyl isocyanide species *(4)* exhibiting a weak IR absorption at 2170 $cm^{-1}$ [$\nu(CN)$][10]. On reaction with $Pt(PPh_3)_3$, on the other hand, *(3a)* only undergoes substitution to give *(3b)*.

$Cl_3C{-}N{=}CCl_2$

*(2)*

$L(CO)_8Co_3{\equiv}C{-}N{=}CCl_2$

*(3a)*, L = CO
*(3b)*, L = PPh₃

$(CO)_9Co_3{\equiv}C{-}N{\equiv}C{-}Pt(Cl_2)PPh_3$

*(4)*

$Cl_2C{=}N{-}CCl_2CCl_2{-}N{=}CCl_2$

*(5)*

Interestingly, reaction of *(2)* with $Fe_2(CO)_9$ (molar ratio 1:1, tetrahydrofuran) proceeds by a completely different route: at room temperature, C—C coupling takes place with formation of metal-free *(5)*, which is also accessible by high-temperature chlorination of tetramethylethylenediamine or dimethylformamide[8a].

Received: August 18, 1980 [Z 691 IE]
German version: Angew. Chem. *93*, 184 (1981)

CAS Registry numbers:
*(1)*, 76346-71-9; *(2)*, 29164-55-4; *(3a)*, 76346-72-0; *(3b)*, 76346-73-1; *(4)*, 76346-74-2; *(5)*, 29164-57-6; $Cr(CO)_5CNCCl_3$, 68927-87-7; $Co_2(CO)_8$, 10210-68-1; $Pt(\eta^2\text{-}C_2H_4)(PPh_3)_2$, 12120-15-9; $Fe_2(CO)_9$, 15321-51-4

---

[1] a) *U. Schöllkopf*, Angew. Chem. *82*, 795 (1970); Angew. Chem. Int. Ed. Engl. *9*, 763 (1970); Pure Appl. Chem. *51*, 1347 (1979); *D. Hoppe*, Angew. Chem. *86*, 878 (1974); Angew. Chem. Int. Ed. Engl. *13*, 789 (1974); *T. Saegusa, Y. Ito*, Synthesis *1975*, 291; b) *A. M. van Leusen, J. Wildeman, O. H. Oldenziel*, J. Org. Chem. *42*, 1153, 3114 (1977); Synthesis *1977*, 501.

[2] *R. West, G. A. Gornowicz*, J. Organomet. Chem. *25*, 385 (1970).

[3] *W. P. Fehlhammer, F. Degel*, Angew. Chem. *91*, 80 (1979); Angew. Chem. Int. Ed. Engl. *18*, 75 (1979).

[4] Only the dimethylamino derivatives $Co_3(CO)_9CN(CH_3)_2$ and $[Co_3(CO)_9CNH(CH_3)_2]PF_6$ have previously been mentioned: *D. Seyferth, I. E. Hallgren, P. L. K. Hung*, J. Organomet. Chem. *50*, 265 (1973).

[5] Monoclinic, $P2_1/m$, $Z=2$, $a=11.683(5)$, $b=10.919(8)$, $c=8.997(6)$ Å, $\beta=89.70(3)^\circ$. Philips PW 1100 automated four-circle diffractometer, $Ag_{K\alpha}$ radiation (0.5614 Å), 1701 independent reflections, $R=3.51\%$ ($R_w=3.41\%$).

[6] *D. C. Miller, R. C. Gearhart, T. B. Brill*, J. Organomet. Chem. *169*, 395 (1979), and references cited therein.

[7] a) *B. Weinberger, W. P. Fehlhammer*, Angew. Chem. *92*, 478 (1980); Angew. Chem. Int. Ed. Engl. *19*, 480 (1980); b) *F. Beck*, Dissertation, Universität Erlangen-Nürnberg 1980.

[8] a) *H. Holtschmidt, E. Degener, H.-G. Schmelzer, H. Tarnow, W. Zecher*, Angew. Chem. *74*, 848 (1962), *80*, 942 (1968); Angew. Chem. Int. Ed. Engl. *1*, 632 (1962); *7*, 856 (1968); b) *E. Kühle, ibid. 81*, 18 (1969) and *8*, 20 (1969), respectively.

[9] Cf. *e.g. I. Ugi:* Isonitrile Chemistry. Academic Press, New York 1971.

[10] *W. P. Fehlhammer, A. Mayr, B. Olgemöller*, Angew. Chem. *87*, 290 (1975); Angew. Chem. Int. Ed. Engl. *14*, 369 (1975).

## BOOK REVIEWS

**Reaction Rates of Isotopic Molecules.** By *L. Melander* and *H. W. Saunders, Jr.*, Wiley, New York 1980. xiv, 391 pp., bound, £ 16.30.

This is a completely new and extended edition of *Melander's* "Isotope Effects on Reaction Rates" (Ronald, New York 1960). A short introduction is followed in turn by the mathematical foundations for the description and calculation of isotope effects from molecular data, an explanation of the measurement techniques, and the evaluation of experimental data. The special section deals with the measurements of primary and secondary kinetic hydrogen isotope effects and also solvent isotope effects and their interpretations. After a description of the isotope effects of carbon and other nonmetals, the book concludes with a discussion of the techniques for, and results from, measurements of the isotope effects in complex reaction systems, including enzymatic reactions. A three-part appendix provides instructions for calculations and tables.

Particular stress is placed on detailed mathematical treatment of the isotope effect, which is used to derive reaction-kinetic interpretations and mechanistic applications. The examples given have been chosen as a means of explaining the theory. The arrangement and presentation are clear, making it easy for the less initiated. The consistent and complete treatment of the entire field distinguishes this book from its competitors, which all too often concentrate on individual aspects. Since much of the relevant work is nowadays taking place in biochemistry, we might have expected a rather greater emphasis on this area, *e.g.* a description of some relevant procedures and concepts (equilibrium perturbation method, partitioning factor). All in all, this is currently the most authoritative book for anyone concerned with the theory, application, and interpretation of kinetic isotope effects.

*F. J. Winkler* [NB 534 IE]

**Recent Books**

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Metal Ions in Biological Systems.** Vol. 11. Metal Complexes as Anticancer Agents. Edited by *H. Sigel*. Marcel Dekker, New York 1980. xx, 440 pp., bound, SFr. 115.00.—ISBN 0-8247-1004-5

**Fuels and Fuel Technology.** By *W. Francis* and *M. C. Peters.* Pergamon Press, Oxford 1980, x, 716 pp., bound, Flexi \$ 34.50.—ISBN 0-08-02524-8; bound, Hard \$ 95.00.—ISBN 0-08-025249-4

**Hydroboration.** By *H. C. Brown.* Benjamin Cummings, Menlo Park, 1980. xiii, 321 pp., bound, \$ 19.50.—ISBN 0-8053-1501-2

**Umwelt und Energie.** Handbuch für die betriebliche Praxis. R. Haufe Verlag, Freiburg 1980. 650 pp., loose-leaf, DM 48.00.

**Transition Metal Clusters.** Edited by *B. F. G. Johnson.* John Wiley & Sons, New York 1980. 681 pp., bound, £ 33.00.—ISBN 0-471-27817-3

**Microbiological Aspects of Pollution Controll.** 2nd Edition. By *R. K. Dart* and *R. J. Stretton.* Elsevier, Amsterdam 1980. ix, 265 pp., bound, \$ 53.75.—ISBN 0-444-41918-7

**Cement and Mortar Technology and Additives.** Edited by *M. H. Gutcho.* Noyes Data, Park Ridge 1980. xvi, 540 pp., bound, \$ 54.00.—ISBN 0-8155-0822-0

**Modern Synthetic Methods.** Edited by *R. Scheffold.* Salle, Frankfurt a. M. und Sauerländer, Aarau. Vol. 1: 1976. 300 pp., bound, DM 48.00.—ISBN (Salle) 3-7935-5521-6, (Sauerländer) 3-7941-2146-3; Vol. 2: 1980. 358 pp., bound, DM 38.00.—ISBN (Salle) 3-7935-5522-4, (Sauerländer) 3-7941-2148-1

**Lebensmittel- und Bedarfsgegenstände-Gesetz.** By *K.-H. Nüse* and *R. Franck.* Carl Heymanns Verlag, Köln 1980. v, 125 pp., bound, DM 32.80.—ISBN 3-452-18812-4

**Chemistry of the Moon.** Physics and Chemistry of the Earth. Edited by *L. H. Ahrens, F. Press,* and *S. K. Runcorn.* Pergamon Press, Oxford 1980. 264 pp., bound, \$ 97.00.—ISBN 0-08-020287X

**Comprehensive Treatise of Electrochemistry.** Vol. 1. Edited by *J. M. Bockris, B. E. Conway,* and *E. Yeager.* Plenum Press, New York 1980. xix, 553 pp., bound, \$ 49.50.—ISBN 0-306-40275-0

**Molecular Interactions.** Vol. 1. Edited by *H. Ratajczak* and *W. J. Orville-Thomas.* John Wiley & Sons, New York 1980. xxi, 415 pp., bound, \$ 84.00.—ISBN 0-471-27664-2

**Optimierungsmethoden in der Wirkstofforschung—Quantitative Wirkungs-Analyse.** By *R. Franke.* Akademie-Verlag, Berlin 1980. xvi, 454 pp., bound, *ca.* DM 50.00

**Mechanismen und Theorie in der Organischen Chemie.** By *Th. H. Lowry* and *K. Schueller-Richardson.* Verlag Chemie, Weinheim 1980. xxiii, 831 pp., bound, DM 98.00.—ISBN 3-527-25795-0

**Allgemeine Chemie.** By *J. A. Campbell.* Verlag Chemie, Weinheim 1980. 2nd Edit. xxiv. 1223 pp., bound, DM 78.00.—ISBN 3-527-25856-6

**Arzneistoffe.** By *W. Schunack, K. Mayer,* and *M. Haake.* Vieweg, Braunschweig 1980. xi, 608 pp., bound, DM 68.00.—ISBN 3-528-08405-7

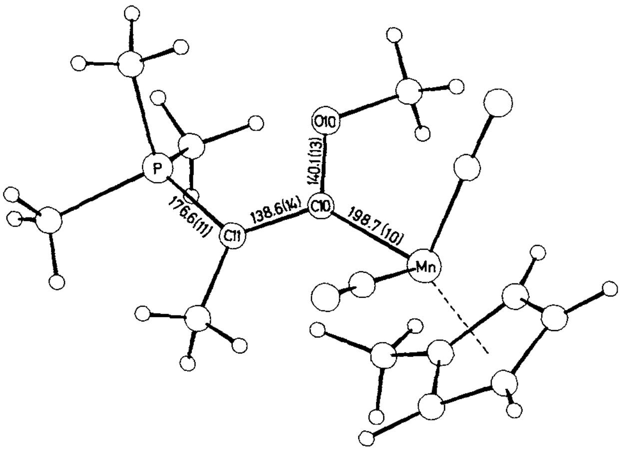
**Notices and Group Exemptions in EEC Competition Law.** By *Ch. Harding.* ESC Publishing, Oxford 1980. xvi, 259 pp., loose-leaf, £ 25.00.

**Organische Synthesen mit Cyansäureestern.** By *D. Martin* and *R. Bacaloglu.* Akademie-Verlag, Berlin 1980. 227 pp., bound, *ca.* DM 55.00.

---

### Erratum

In the short communication entitled "Phosphorus Ylide Carbene Complexes of Manganese – Synthesis and Structure" by *Wolfgang Malisch, Herbert Blau,* and *Ulrich Schubert* (Angew. Chem. Int. Ed. Engl. *19,* 1020 ... 1021 (1980)) the following figure should be inserted between formula *(2c)* and the figure caption on p. 1021.



**Editorial office:** Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

**Editor:** *O. Smrekar,* **Translation Editors:** *I. G. Neil* and *A. Stimson.*

**Publishers:** Verlag Chemie, GmbH. (Managing Directors Dr. *Helmut Grünewald* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE
CHEMIE
International Edition in English

Volume 20 · Number 3
March 1981
Pages 217–302

# Target Directed Drug Synthesis: The Aminoacyl-tRNA Synthetases as Possible Targets

**By Friedrich von der Haar, Hans-Joachim Gabius and Friedrich Cramer**[*]

*Dedicated to Prof. Dr. Hans Herloff Inhoffen on the occasion of his 75th birthday*

The "tailor-made" pharmaceutical has been an old dream ever since *Paracelsus'* days. His saying *"Dosis sola facit venenum"* is still valid. The ideal pharmacon should inhibit the pathological process or the parasitical organism to a maximum while causing as little harm as possible to the human organism. In order to achieve this goal one must try to make use of metabolic differences between the metabolism of the pathological organism and normal human metabolism in a rational way. With today's improved knowledge of enzymatic processes this seems to be a possible and highly promising approach. The pharmaceutical should act upon a process of central importance, such as the process of protein biosynthesis, where the required highly accurate construction of the macromolecules is achieved by a "proofreading" process. It is shown that this "proofreading" mechanism exhibits specific difference in different species.

## 1. Introduction: Is Target Directed Drug Synthesis Feasible?

"... here one is dealing with the problem of curing an organism which is infected by certain parasites by killing these parasites within the organism. That is to say: the organism must be sterilized with the aid of substances that have been produced in the retort of the chemist[1]".

"If one wants to study this question experimentally one must look for substances which firstly in the test tube act in an inhibitory manner or by killing the bacteria, which secondly are virtually undangerous for the organism, which thirdly preserve the disinfecting action even within the organism[2]".

This was written by *Paul Ehrlich* 75 years ago, in the same year when *H. H. Inhoffen,* to whom this article is dedicated, was born. *Ehrlich* postulates, at that time highly advanced, have only been fulfilled to a very limited extent to date. The pharmaceutical industry has created a vast number of highly efficient drugs, in a rather non-rational approach, however. Most pharmaceuticals have been discovered by vast screening programs involving thousands of compounds, or owe their discovery to the "trial and error" method[3]. Furthermore, the mode of action of many active drugs was initially unknown, a situation which continues even today. A good example of this is "Aspirin" (acetylsalicylic acid), by far the most widely used drug. While aspirin was registered in 1899, its mode of action, the inhibition of the synthesis of prostaglandins or of the prostaglandin cyclooxygenase, was only explained in 1971 and 1975, respectively[4,5].

Biochemical and molecular biological research in recent years has been able to clarify essential pathways in cells and organisms and thereby has opened possibilities for the more rational synthesis of pharmaceuticals. In spite of this, however, satisfactory drugs exist for only one third of all diseases, as *König* has demonstrated[3,6].

When the mode of action for a specific drug has been elucidated in a model organism or an experimental animal, one

---

[*] Priv.-Doz. Dr. F. von der Haar, Dipl.-Biochem. H.-J. Gabius, Prof. Dr. F. Cramer
Max-Planck-Institut für experimentelle Medizin, Abteilung Chemie
Hermann-Rein-Strasse 3, D-3400 Göttingen (Germany)

*0570-0833/81/0303-0217 $ 02.50/0*

can expect that the mode and the intensity of action will vary in different organisms. Thus, for example, it is known that pyrimethamine, trimethoprim and methotrexate are inhibitors of the essential enzyme dihydrofolate reductase. It has been observed that pyrimethamine is 3600 times more effective against this enzyme from plasmodia than against the enzyme from human tissue. Pyrimethamine can therefore be used as an antimalarial drug against plasmodia. Trimethoprim is 60000 times more effective against dihydrofolate reductase from bacteria in comparison with the human enzyme and is therefore an antibacterial drug. Methotrexate also has a strong general activity against dihydrofolate reductase from human tissue and can therefore be used as an antineoplastic drug[7]. If the precise inhibition kinetics of these three substances with regard to the different enzymes had been known, the specific mode of action of pyrimethamine, trimethoprim and methotreaxate could in principle have been predicted. In theory, a target directed drug synthesis would have been possible if biochemical studies of the *in vitro* situation had resulted in complete understanding of the mode of action of the enzymes involved. The structure of a drug fulfilling *Ehrlich's* postulate, that drugs should be "strongly inhibitory for parasites in the test tube, but practically harmless towards the organism" could in principle be predicted from an understanding of the enzymatic properties of the parasite and the host *in vitro*. Without doubt such differences exist which will be more effective when the enzymes involved occupy a key position in metabolism. Here an important task for the biochemist in the pharmaceutical industry can be identified: to elucidate differences in the mechanisms of key enzymes so that preferential inhibition can be achieved by the synthesis of specific antimetabolites. This approach has been recently proposed in a highly interesting article by *Cohen*, who termed this "target directed drug synthesis"[8].

## 2. Aminoacyl-tRNA Synthetases as Target Enzymes

With infectious diseases, an invading pathogen has to be affected without harming the host. A potential target enzyme must play such a crucial role in the life-cycle of the pathogen, that perturbation of its action is sufficient to inhibit growth of the pathogen to such an extent that the self-defense mechanism of the host can control the infection. One possible way of achieving this is to administer an enzyme inhibitor for a key enzyme involved in metabolism. Perhaps a more efficient technique would be the use of substrate analogs, which are processed by the enzyme into erroneous products. In an ideal case these erroneous products should be of importance in additional processes thus resulting, independent of the action of the target enzyme itself, in perturbing the metabolism in many places. It is this latter aspect which led us to consider aminoacyl-tRNA synthetases as potential candidates for target directed drug design.

Aminoacyl-tRNA synthetases are a group of at least 20 enzymes corresponding to the 20 amino acids commonly found in proteins. Each enzyme selects its amino acid from the cellular pool, activates it by consumption of an equivalent adenosine triphosphate (ATP), and esterifies it to the 3'-terminal adenosine of its corresponding transfer ribonucleic acid (tRNA). The aminoacylated tRNA is complexed with an elongation factor and channeled into the ribosomal system where peptidization takes place (Fig. 1, upper part). Since the specific position of a particular amino acid within the growing protein chain is determined solely according to the well known codon-anticodon interaction between mRNA and tRNA, aminoacyl-tRNA synthetases must verify that a particular amino acid is linked exclusively to the tRNA with the corresponding anticodon. This is not a trivial problem, since in several cases amino acids have very similar structure (e.g. tyrosine and phenylalanine or isoleucine and valine).

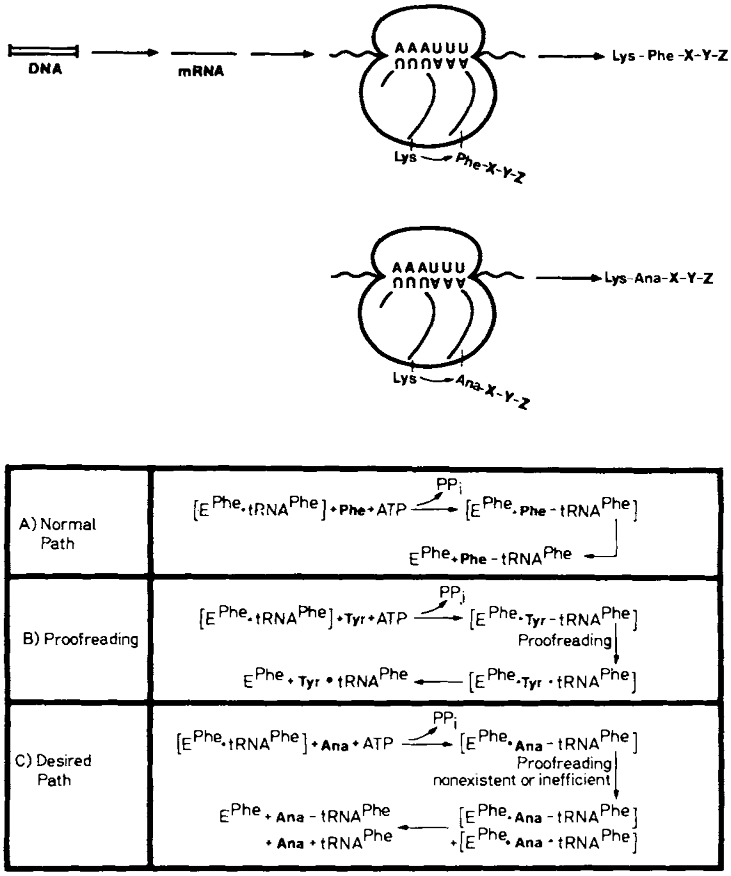


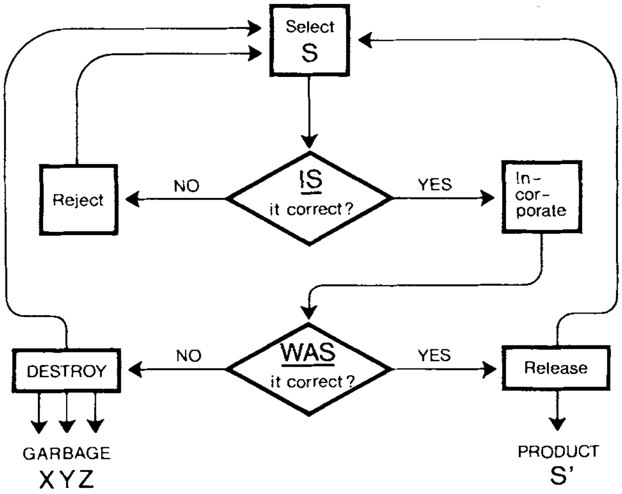
Fig. 1. Schematic representation of phenylalanine activation and incorporation into a growing protein chain. A) Normally, phenylalanine is esterified to $tRNA^{Phe}$—C—C—A. The Phe—$tRNA^{Phe}$—C—C—A is transferred into the ribosomal machinery and phenylalanine is incorporated into any position determined by the codon UUU due to interaction with the anticodon AAA (or AAG) of $tRNA^{Phe}$. B) To prevent misincorporation of misactivated amino acids such as Tyr, the proofreading was developed. C) If an analog (Ana) of Phe escapes the proofreading pathway it is incorporated into a growing peptide chain. In the example given above, a peptide ...Lys—Ana—X—Y—Z—$NH_2$ instead of ...Lys—Phe—X—Y—Z—$NH_2$ would be built up. ($NH_2$-groups have not been shown in order to improve clarity. E = phenylalanyl-tRNA synthetase, $PP_i$ = diphosphate; for other abbreviations see text.)

Research in our laboratory during recent years has provided information which indicates that the required accuracy is a result of a two-step mechanism consisting firstly of transfer of the amino acid to the tRNA and secondly a "proofreading" step[9,10] as exemplified for phenylalanyl-tRNA synthetase in Figure 1.

Phenylalanyl-tRNA synthetase from yeast normally binds phenylalanine, activates it by consuming one equivalent of ATP, and transfers it to the phenylalanine tRNA ($tRNA^{Phe}$). Subsequently, the product, Phe—$tRNA^{Phe}$, is released (Fig. 1, pathway A).

Occasionally the enzyme binds and activates tyrosine, and in this case, tyrosine is also transferred to the tRNA$^{Phe}$. However, this erroneous product Tyr—tRNA$^{Phe}$ is not released from the enzyme. In a control step, phenylalanyl-tRNA synthetase from yeast hydrolyzes the ester linkage between tyrosine and tRNA$^{Phe}$ and releases both substrates[11]. This correction step which we phrased "chemical proofreading"[12] prevents the misincorporation of a tyrosine in place of a phenylalanine in a growing peptide chain (Fig. 1, pathway B).

The essentials of this selection process are presented in a more generalized way in Scheme 1. Interacting with the 20 amino acids from the pool, the enzyme in each case asks: "Is this particular amino acid the right one?". If the answer is "no" the amino acid is rejected, if the answer is "yes" the amino acid will be processed further. The error rate of this first selection step is considerably reduced in the subsequent step. The enzyme now asks: "Was the first discrimination correct?". When the answer is "yes" the product is released, otherwise, the ester bond is hydrolyzed. For each amino acid incorrectly activated, the cell consumes one ATP molecule.



Scheme 1. Flow diagram for a two-step selection process. High specificity is obtained by an energy consuming proofreading process.

The mechanistic details of this correction step are still not known for the case of incorrect selection of tyrosine rather than phenylalanine by phenylalanyl-tRNA synthetase. In a further example, the misactivation of valine by isoleucyl-tRNA synthetase, we attempted to fit all experimental details into a mechanistic scheme[12] (Fig. 2). Valine (Val) differs from isoleucine (Ile) by the absence of one methyl group. Val—tRNA$^{Ile}$ becomes isosteric with Ile—tRNA$^{Ile}$ if in place of the missing methyl group a water molecule appears. Our results indicate that this water molecule is activated by the enzyme and used to split the ester bond in Val—tRNA$^{Ile}$[12]. Specificity in this case is due to self-protection of the correct product against hydrolysis, which can occur in the incorrect product. Since the difference is in chemical reactivity, we termed this mechanism "chemical proofreading"[12].

For an E$^{Phe}$ directed drug synthesis, it is desirable for the enzymes of the host and pathogen to differ to such an extent, that design of a phenylalanine analog, which is proofread by the host but not by the pathogen, is possible. In this ideal case the analog would be incorporated statistically into a number of enzymes in place of phenylalanine (Fig. 1, pathway C) leading to malfunctioning enzyme proteins. Due to the accuracy normally observed in protein synthesis[13,14], one would tend to extrapolate that even a relatively small number of misincorporated analogs would result in serious interference with the metabolism of the pathogen. This proposal applies not only for phenylalanyl-tRNA synthetase but for any aminoacyl-tRNA synthetase which follows an analog pathway, for instance isoleucyl- or valyl tRNA synthetase[12].

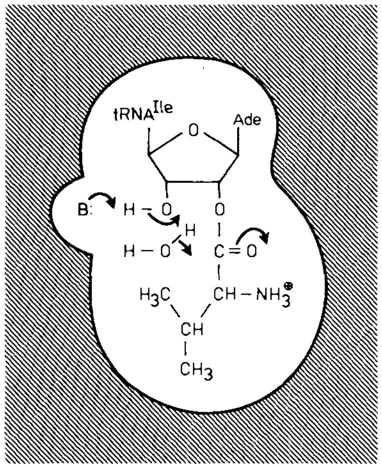


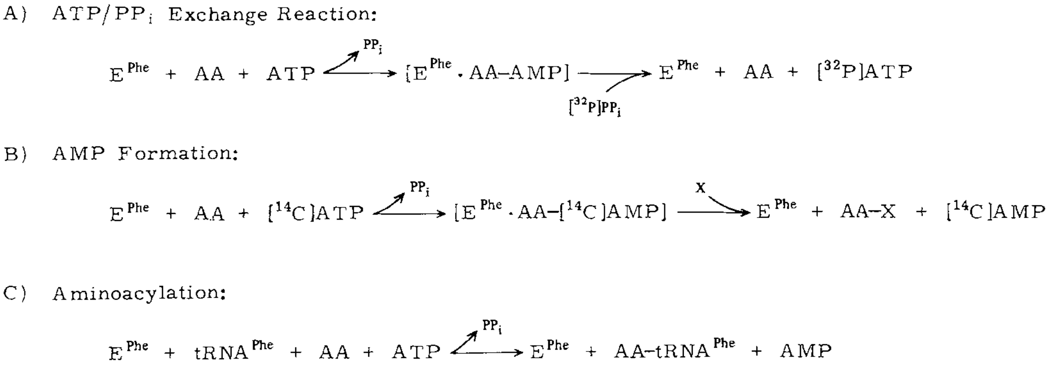
Fig. 2. Mechanism of proofreading Val—tRNA$^{Ile}$ by isoleucyl-tRNA synthetase from yeast.

## 3. Comparison of Proofreading Mechanisms of Phenylalanyl-tRNA Synthetases in Different Organisms

In order to examine differences in the proofreading mechanisms in a variety of enzyme sources, phenylalanyl-tRNA synthetases from *Escherichia coli*, *Saccharomyces cerevisiae* (bakers' yeast), *Neurospora crassa* and turkey liver were purified to homogeneity[15]. Subsequently, the interaction of these enzymes with eight different phenylalanine analogs was studied. Additionally, tyrosine, leucine and methionine, the natural amino acids known to be misactivated by the enzyme from bakers' yeast[11], were investigated. Prior to discussion of these results in summarized form, the methodology used to obtain them will be outlined.

Three different types of assay were used (Scheme 2). The so called ATP/PP$_i$ exchange assay (Scheme 2, reaction A) is based on the fact, that the amino acid is intermediately activated by splitting ATP into AMP and PP$_i$. If [$^{32}$P]PP$_i$ is added externally it will be incorporated into ATP due to the reversibility of the activation. If this test, which is independent of tRNA, is positive, an analog is undoubtedly a substrate.

The fate of the activated substrate can be followed by measuring the consumption of ATP or the formation of adenosine monophosphate (AMP) (Scheme 2, path B). This test is again based on the intermediate activation; every amino acid processed by an aminoacyl-tRNA synthetase involves the consumption of one equivalent of ATP, irrespective of subsequent reactions of the activated amino acid. Catalytic formation of AMP from ATP will be observed, if the activated amino acid is immediately hydrolyzed or if it is transferred to a tRNA and subjected to proofreading. With this reaction the influence of tRNA can be followed, even if no stable aminoacylated tRNA is formed. Pathway B in Figure 1 shows that no Tyr-tRNA$^{Phe}$ is released from the enzyme, but that one equivalent of AMP is formed, for every equivalent of Tyr—tRNA$^{Phe}$ formed intermediately. Thus, aminoacylation can be followed indirectly[12].



A) ATP/PP$_i$ Exchange Reaction:

$$E^{Phe} + AA + ATP \xrightarrow{PP_i} [E^{Phe} \cdot AA\text{–}AMP] \xrightarrow[{[^{32}P]PP_i}]{} E^{Phe} + AA + [^{32}P]ATP$$

B) AMP Formation:

$$E^{Phe} + AA + [^{14}C]ATP \xrightarrow{PP_i} [E^{Phe} \cdot AA\text{–}[^{14}C]AMP] \xrightarrow{X} E^{Phe} + AA\text{–}X + [^{14}C]AMP$$

C) Aminoacylation:

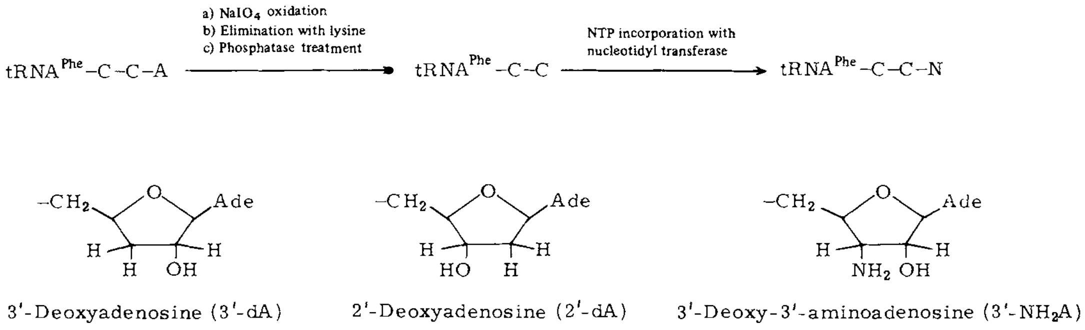
$$E^{Phe} + tRNA^{Phe} + AA + ATP \xrightarrow{PP_i} E^{Phe} + AA\text{–}tRNA^{Phe} + AMP$$

Scheme 2. Assays for substrate properties of phenylalanine and its analogs (AA = amino acid; X = tRNA$^{Phe}$ or other nucleophile).

Finally the transfer of a substrate to tRNA$^{Phe}$ can be measured, if a stable product is released from the enzyme (Scheme 2, path C). If a radioactively labeled substrate is available, its incorporation can be followed directly. Alternatively, unlabeled substrate can be incorporated into the tRNA and the amount of free tRNA$^{Phe}$ remaining after a certain reaction time back-titrated with [$^{14}$C] phenylalanine (see also Table 1).

Table 1: tRNA$^{Phe}$—C—C—N dependent [$^{14}$C]AMP formation *via* phenylalanyl-tRNA synthetase from turkey liver and *bakers'* yeast, $k_{cat}$ [min$^{-1}$].

| Enzyme | Source | Leu | Met | Tyr |
|---|---|---|---|---|
| $E^{Phe}$ | baker's yeast | <0.05 | <0.05 | <0.05 |
| | turkey liver | 0.75 | 1.35 | <0.1 |
| [$E^{Phe} \cdot$ tRNA$^{Phe}$—C—C] | baker's yeast | <0.05 | <0.05 | <0.05 |
| | turkey liver | 0.80 | 1.60 | <0.1 |
| [$E^{Phe} \cdot$ tRNA$^{Phe}$—C—C—3'-dA] | baker's yeast | <0.1 | <0.1 | <0.1 |
| | turkey liver | 0.64 | 1.13 | <0.1 |
| [$E^{Phe} \cdot$ tRNA$^{Phe}$—C—C—A] | baker's yeast | 0.64 | 2.03 | 6.80 |
| | turkey liver | 2.93 | 3.62 | 0.31 |
| [$E^{Phe} \cdot$ tRNA$^{Phe}$—C—C—2'-dA] | baker's yeast | <0.05 | <0.05 | <0.05 |
| | turkey liver | 2.50 | 3.57 | 0.27 |



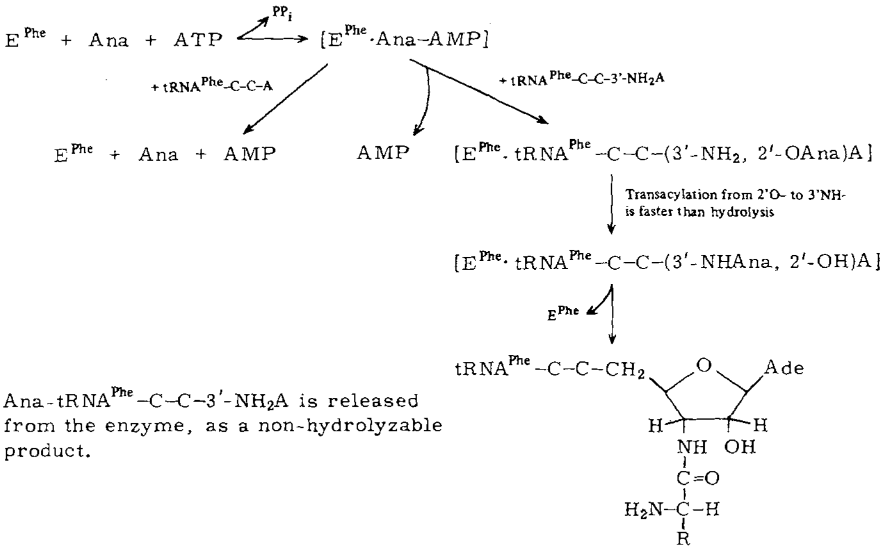
Scheme 3. Modification of the 3'-end of tRNA$^{Phe}$ (tRNA$^{Phe}$—C—C—3'dA and tRNA$^{Phe}$—C—C—3'NH$_2$A are substrates: tRNA$^{Phe}$—C—C—2'dA and tRNA-$^{Phe}$—C—C are not substrates).

In order to increase the information obtained from these tests we developed the following methodology. Normally the 3'-terminus of tRNA$^{Phe}$ consists of an adenosine, whose 2'-hydroxyl group is the acceptor for the activated phenylalanine. To study this transfer reaction in more detail, we removed the 3'-terminal adenosine and replaced it by adenosine analogs using the enzyme nucleotidyl transferase, which has a low specificity for the substrate adenosine triphosphate *in vitro*[16]. The analogs used for this investigation are given in Scheme 3. The prerequisite for the present investigation was the ability to modify tRNA$^{Phe}$ in such a way, that it was not longer susceptible to proofreading after esterification with misactivated phenylalanine analogs. In this respect the tRNA$^{Phe}$—C—C—3'NH$_2$A was of special importance. With this 3'-NH$_2$A group, phenylalanine or any misactivated analog is transferred to the 2'-OH. Subsequent nucleophilic attack of the 3'-NH$_2$ on the 2'-hydroxyl group ester bond and formation of a 3'-amide is more rapid than hydrolysis by proofreading. The stable amide cannot be hydrolyzed further by phenylalanyl-tRNA synthetase[9,14] (Scheme 4).

Using this methodology we obtained the results summarized as follows:

a) Phenylalanyl-tRNA synthetase from *E. coli*, bakers' yeast and *N. crassa* behave qualitatively the same. They activate all the phenylalanine analogs investigated.

b) The misactivated analogs are transferred to tRNA$^{Phe}$—C—C—3′NH$_2$A albeit that the efficiency is somewhat different for the respective analogs.



Scheme 4. Properties of tRNA$^{Phe}$—C—C—3′NH$_2$A upon transfer of phenylalanine analogs.

c) With natural tRNA$^{Phe}$—C—C—A the amino acid analogs were intermediately transferred to the tRNA$^{Phe}$ and, with one exception described below, subsequently hydrolyzed from the tRNA$^{Phe}$—C—C—A prior to release of erroneous product.

d) Only moderate quantitative differences were observed with respect to the extent with which these analogs could substitute for phenylalanine in the enzymatic reactions studied. These differences allow speculations regarding the nature of the binding site to be made[15].

The phenylalanyl-tRNA synthetase from turkey liver behaved markedly differently:

a) In the ATP/PP$_i$ exchange assay, all the phenylalanine analogs were active as well as the natural amino acids leucine, methionine and tyrosine. However, tyrosine was observed to be a very poor substrate for the turkey liver enzyme in contrast to *E. coli*, bakers' yeast and *N. crassa*[15].

b) In contrast to the enzymes from *E. coli*, bakers' yeast and *N. crassa*, none of the misactivated analogs could be esterified to a measureable extent to tRNA$^{Phe}$—C—C—3′NH$_2$A by the enzyme from turkey liver. Since, however, a tRNA$^{Phe}$-dependent AMP formation was observed with this enzyme, the analogs must have been processed by the phenylalanyl-tRNA synthetase from turkey liver.

This latter results suggests that with the enzyme from turkey liver, a proofreading mechanism operates without intermediary transfer of misactivated analog to tRNA$^{Phe}$—C—C—A. That this pathway does exist, can be observed from the tRNA$^{Phe}$—C—C—N-dependent AMP formation described in Table 1, in which enzymes from bakers' yeast and turkey liver are compared. For the free enzyme and the [E$^{Phe}$·tRNA$^{Phe}$—C—C] complex, the misactivated intermediates have significant stability in the presence of enzyme from bakers' yeast, whereas they are unstable in the presence of enzyme from turkey liver.

With the complex E$^{Phe}$·tRNA$^{Phe}$—C—C—3′dA we observe the same high rate of AMP formation as in the case of free enzyme. However, it must be restated that this modified tRNA$^{Phe}$—C—C—3′dA, in the presence of a phenylalanine analog, is a substrate for the yeast enzyme but not for the turkey liver enzyme. With this modified tRNA$^{Phe}$ proofreading in the yeast system does not occur owing to the absence of the 3′-hydroxyl group which is essential for this process[14], while with the turkey liver enzyme transfer of the amino acid does not appear to occur.

As expected, enhanced AMP production as a result of proofreading takes place with the [E$^{Phe}$·tRNA$^{Phe}$—C—C—A] complex with enzymes from both organisms. An unexpected result was observed using the [E$^{Phe}$·tRNA$^{Phe}$—C—C—2′dA] complex: the complexed tRNA$^{Phe}$—C—C—2′dA is neither a substrate for phenylalanylation in the yeast nor turkey liver systems, and does not result in proofreading with the yeast enzyme. However, a very efficient proofreading reaction takes place with the turkey liver enzyme, which is specific for misactivated amino acids. In the presence of phenylalanine, increased stability of the activated intermediate was observed[15].

The most likely explanation for this data is that with the turkey liver enzyme, a proofreading reaction takes place without transfer of the misactivated amino acid to the tRNA$^{Phe}$. The 3′-terminal adenosine, and in particular the non-accepting 3′-OH of this adenosine, plays an important role in this step in accordance with our suggestions regarding "reactive site triggering"[17].

A proofreading mechanism preventing transfer of the misactivated amino acid to the tRNA$^{Phe}$ is obviously safer than one operating after transfer. Without transfer to the tRNA, an incorrectly activated amino acid has no chance of being incorporated within a protein. In this instance, incorrectly activated amino acids can only inhibit an aminoacyl-tRNA synthetase and, unless this inhibition is very severe, should result in little harm to the cell. Whatever the implications of these mechanistic differences may mean to cell biology, it is only important for the present discussion that such differences exist, and that they are a prerequisite for target directed drug design. Finally the question arises as to whether or not these differences can be utilized.

## 4. *N*-Benzyl-L-phenylalanine

*N*-Benzyl-D,L-amphetamine has been shown to be a very potent inhibitor for the phenylalanyl-tRNA synthetase of *E. coli* but not for the rat liver enzyme in the ATP/PP$_i$ exchange assay[18]. Despite the close structural relationship, neither enantiomer of *N*-benzylphenylalanine is reported to be an inhibitor for the enzyme from *E. coli*[19]. This discrepancy suggests that the phenylalanine analog is a substrate; although previous authors[18,19] did not appear to take this into consideration, we have subsequently observed it to be the case[15].

Whereas *N*-benzyl-D,L-amphetamine shows a dramatic difference in inhibitory power for the *E. coli* and rat liver systems[18], the Michaelis-Menten ($K_m$) values for *N*-benzyl-L-phenylalanine in the ATP/PP$_i$ exchange assay are very similar in *E. coli*, bakers' yeast and turkey liver systems (Table 2). In accordance with the results described in the preceding section, the analog can be esterified to tRNA$^{Phe}$—C—C—3'NH$_2$A only by the *E. coli* and yeast enzyme but not by the turkey liver enzyme. The value of $K_m$ in this transfer reaction is about 17 fold higher for the *E. coli* enzyme and 38 fold higher for the yeast enzyme relative to the respective $K_m$ in the ATP/PP$_i$ exchange assay. A much higher value of $K_m$ in reactions involving tRNA complexed to the enzyme, as compared with reaction of free enzyme, is observed with all our analogs tested[15], and this observation substantiates earlier discussions regarding the influence of the tRNA on enzyme conformation[14,17]. It however puts question marks against interpretations which attempt to extrapolate results obtained from ATP/PP$_i$ exchange with free enzymes to reactions with enzyme·tRNA complexes[19].

Table 2: *N*-benzyl-L-phenylalanine as substrate for several phenylalanyl-tRNA-synthetases.

| | Source of enzyme: | | |
|---|---|---|---|
| | *E. coli* | Bakers' yeast | Turkey liver |
| $K_m$ in the ATP/PP exchange reaction [μM] | 85 | 157 | 205 |
| Esterification to tRNA$^{Phe}$—C—C—3'-NH$_2$A [%] [a] | 64 | 50 | 0 |
| $K_m$ for esterification to tRNA$^{Phe}$—C—C—3'-NH$_2$A [μM] | 1500 | 6000 | — |
| Esterification to tRNA$^{Phe}$—C—C—A [%] [b] | 6 | 0 | 0 |

[a] Determined by the method of back-titration: Enzyme, tRNA$^{Phe}$—C—C—3'-NH$_2$A, ATP and unlabeled analogs are incubated for 30 min. Then excess ATP, [$^{14}$C]phenylalanine and additional enzyme are added in order to determine the account of nonacylated tRNA$^{Phe}$. Amount of tRNA acylated with analog is the difference between the nonacylated tRNA and total tRNA present. [b] Determined by the method of back-titration as well as by direct incorporation of [$^{14}$C]*N*-benzyl-L-phenylalanine and subsequent product analysis.

The most important result in the context of our present discussion is, however, that *N*-benzyl-L-phenylalanine, to a low but measurable extent, escapes the proofreading process with the *E. coli* enzyme and stable *N*-benzyl-L-phenylalanyl-tRNA$^{Phe}$—C—C—A is released (Table 2). This fact was unequivocally confirmed as follows: [$^{14}$C]*N*-benzyl-L-phenylalanine was synthesized and incorporated into tRNA$^{Phe}$—C—C—A. The [$^{14}$C]*N*-benzyl-L-phenylalanyl-tRNA$^{Phe}$—C—C—A was isolated by column chromatography, subjected to hydrolysis with alkali and the only radioactive compound liberated shown to be *N*-benzyl-L-phenylalanine by thin layer chromatography[15].

## 5. Conclusions

In this article we have not described or proposed a new pharmaceutical, we have rather tried to demonstrate a principle by using an example: The principle of the target directed drug synthesis with the example of the proofreading in the protein biosynthesis as target.

The various branches of evolution have adopted, improved and diversified the biochemical pathways. Even such a central and universal process as protein biosynthesis, which is directed by the universal genetic code and which uses the same 20 amino acids in all organisms, exhibits important species-specific differences. These can be observed in the degree of fidelity of amino acid recognition. These differences might be used pharmacologically. Depending on their place in the tree of evolution, organisms should behave differently with respect to incorporation of incorrect amino acids. In support of this suggestion we have given experimental proof using the phenylalanyl-tRNA synthetase system. Amino acid analogs are antimetabolites, the mode of action of which is largely unknown. In addition to phenylalanyl-tRNA synthetase, there are at least 19 further aminoacyl-tRNA synthetases — a wide open field for future research.

*The authors are grateful to Prof. Dr. E. Holler, Regensburg, for a sample of partially purified phenylalanyl-tRNA synthetase from E. coli and to Fritz Benseler, Erika Graeser and Jörg Schischkoff for skilfull cooperation upon isolation of the enzyme from Neurospora crassa as well as with the synthesis of N-benzyl-L-phenylalanine.*

Received: January 30th 1981 [A 356 IE]
German version: Angew. Chem. *93*, 250 (1981)

---

[1] *P. Ehrlich*, on occasion of the official opening of the Georg-Speyer-Haus, Sept. 6, 1906. Cited by: *F. Himmelweit:* The Collected Papers of Paul Ehrlich, Vol. 3: Chemotherapy, Pergamon Press, New York 1960.

[2] *H. Bechhold, P. Ehrlich*, Interrelationship of chemical structure and desinfecting action. Citation source of [1].

[3] Cf. the excellent review of *H. König*, Angew. Chem. 92, 802 (1980); Angew. Chem. Int. Ed. Engl. *19*, 749 (1980).

[4] *J. R. Vane*, Nature New Biol. *231*, 232 (1971).

[5] *G. Roth, N. Stanford, P. Majerus*, Proc. Natl. Acad. Sci. USA *72*, 3073 (1975).

[6] *E. Wiekert:* Pharma-Dialog 54, Arzneimittelforschung 1978, publ. Bundesverband der Pharmazeutischen Industrie, Frankfurt/M. Germany 1978.

[7] *A. Albert:* Selective Toxicity. Chapman and Hall, London 1973.

[8] *S. S. Cohen*, Science *205*, 964 (1979).

[9] *F. von der Haar*, Naturwissenschaften *63*, 519 (1976).

[10] *F. von der Haar*, FEBS Lett. *79*, 225 (1977).

[11] *G. L. Igloi, F. von der Haar, F. Cramer*, Biochemistry *17*, 3459 (1978).

[12] *F. von der Haar, F. Cramer*, Biochemistry *15*, 4131 (1976).

[13] *M. Yarus*, Progr. Nucleic Acid Res. Mol. Biol. *23*, 195 (1979).

[14] *F. Cramer, F. von der Haar, G. L. Igloi* in *P. R. Schimmel, D. Söll, J. Abel-*

*son:* Transfer RNA: Structure, Properties and Recognition. Cold Spring Harbor Laboratory 1979, p. 267.

[15] *F. Cramer, F. von der Haar, H.-J. Gabius,* unpublished results. Work with *E.-coli-* and yeast enzyme: *H.-J. Gabius,* Diplomarbeit, Medizinische Hochschule Hannover 1980; work with turkey liver enzyme: *H.-J. Gabius,* part of Ph. D. thesis, unpublished results; work with *Neurospora crassa* enzyme: *F. von der Haar,* unpublished results.

[16] *M. Sprinzl, H. Sternbach, F. von der Haar, F. Cramer,* Eur. J. Biochem. *81,* 579 (1977).

[17] *F. von der Haar* in "Biological Implications of Protein-Nucleic Acid Interactions", *Augustyniak, J.,* ed., Elsevier/North-Holland, Amsterdam, 1980, p. 325.

[18] *D. V. Santi, R. W. Webster, Jr.,* J. Med. Chem. *19,* 1276 (1976).

[19] *D. V. Santi, P. V. Danenberg,* Biochemistry *10,* 4813 (1971).

---

# Advances in Organophosphorus Chemistry Based on Dichloro(methyl)phosphane

**By Klaus Weissermel, Hanns-Jerg Kleiner, Manfred Finke, and Utz-Hellmuth Felcht**[*]

*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

Besides phosphorus trichloride and phosphane, dichloro(methyl)phosphane is gaining importance as a starting material for the synthesis of organophosphorus compounds. It provides ready access to phosphonic, phosphinic and phosphonous acid derivatives, as well as their secondary products. The synthetic and application potential of organophosphorus compounds—based on industrially produced dichloro(methyl)phosphane—is illustrated by means of numerous examples.

## 1. Introduction

To comply with the definition of organophosphorus chemistry, at least one phosphorus-carbon bond must be present in a compound. There are several possibilities of achieving this. The reaction of methane with phosphorus trichloride has been realized on the industrial scale. At about 600 °C in the gas phase at short residence times it leads, smoothly to dichloro(methyl)phosphane *(1)*[1]

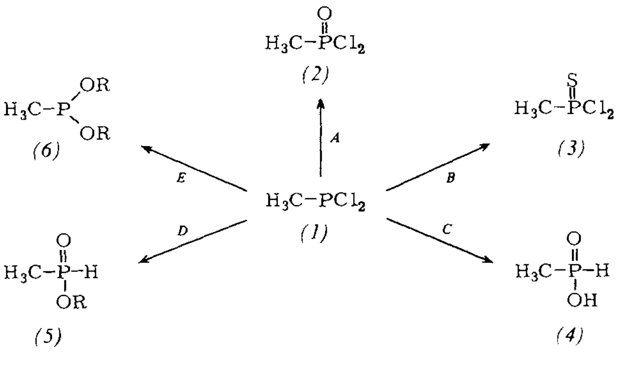
$$CH_4 + PCl_3 \longrightarrow \underset{(1)}{H_3C{-}PCl_2} + HCl$$

*(1)* is a colourless liquid which can be distilled without decomposition, but is extremely sensitive to moisture and is highly reactive. Many reactions of this simple "building block" have been investigated, and are described in a number of selected examples.

## 2. Reactions of Dichloro(methyl)phosphane *(1)* and its Most Important Secondary Products

Under optimized reaction conditions the simple reactions provide high yields.

The most important reactions of *(1)*[2,3] are shown schematically in Figure 1. Oxidation of *(1)* leads directly to methylphosphonic dichloride *(2)*[1]. Atmospheric oxygen, dinitrogen tetroxide[4] and chlorosulfuric acid[5] can be used as oxidizing agents, the latter method yielding especially pure products. With aluminum chloride catalysis, *(1)* reacts with elemental sulfur to form methylthiophosphonic dichloride *(3)*[1,6]. In the presence of excess water *(1)* reacts to form methylphosphinic acid *(4)*.



R = Alkyl

Fig. 1. Important reactions of dichloro(methyl)phosphane *(1)*. *A* Oxidation; *B* Sulfurization; *C* Hydrolysis; *D* Alcoholysis; *E* Alcoholysis in the presence of base.

Reaction of *(1)* with an excess of alcohols in the absence of bases, leads to the methylphosphinic esters *(5)*. For example, the isobutyl ester *(5)*, $R = iC_4H_9$[1] is obtained in good yield. In order to prevent acidolysis from *(5)* → *(4)*, hydrogen chloride liberated during the reaction *(1)* → *(5)* has to be removed in a current of nitrogen[7].

In contrast to the phosphinic esters *(5)*, the phosphonous diesters *(6)* can normally be produced only by alcoholysis in the presence of bases or other acid binders. Reaction of *(1)*

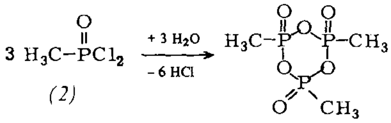
---

[*] Prof. K. Weissermel, Dr. H.-J. Kleiner, Dr. M. Finke, Dr. U.-H. Felcht
Hoechst Aktiengesellschaft
Postfach 800320, D-6230 Frankfurt am Main 80 (Germany)

with alcohols at −40 °C and subsequent neutralization of the hydrogen chloride formed in the process by ammonia has proved to be the simplest method[8]. A particularly suitable procedure for the preparation of the frequently used methylphosphonous diethyl ester *(6)*, $R = C_2H_5$, consists of reacting *(1)* with ethanol in the presence of dimethylaniline at 0 °C in *n*-pentane, and isolating the reaction product under mild conditions[9].

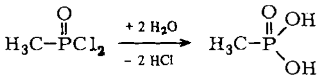
### 2.1. Reactions of Methylphosphonic Dichloride *(2)*

Methylphosphonic dichloride *(2)*, an important intermediate for the preparation of other derivatives of this acid, is only accessible, apart from the method starting from *(1)*, *via* multiple-step syntheses. *(2)*, for example, reacts with water in the molar ratio 1:1 to form methylphosphonic anhydride *(7)*[10] that is presumably present as the trimer.



(2) (7)

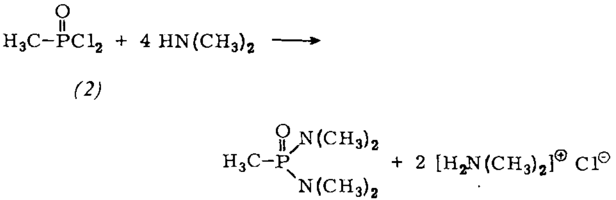
*(7)* can be stored without undergoing decomposition and is readily soluble in aprotic solvents. It is suitable, for example, as a condensation agent for peptide syntheses[11]. *(2)* also reacts readily with hydrogen sulfide to give the corresponding trimeric methylthiophosphonic anhydride[12]. As expected, complete hydrolysis of *(2)* leads to methylphosphonic acid *(8)*.



(2) (8)

$$H_3C{-}\overset{O}{\overset{\|}{P}}Cl_2 \xrightarrow[-2\,HCl]{+2\,H_2O} H_3C{-}\overset{O}{\overset{\|}{P}}(OH)_2$$

In addition, the bis(dialkylamides) of methylphosphonic acid are readily accessible from *(2)*; of these the tetramethyl derivative *(9)* is of interest as an aprotic solvent. In its possible applications it is similar to dimethyl sulfoxide and hexamethylphosphoric triamide. Because of its relatively good stability towards alkali metals and alkaline earth metals and its high basicity, *(9)* is especially suitable as a solvent for reactions with nucleophilic compounds[13].



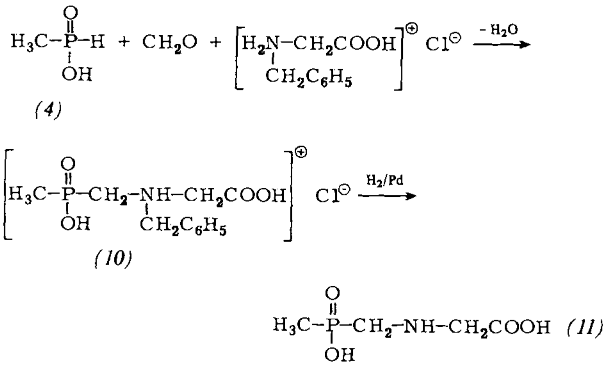
(2) (9)

$$H_3C{-}\overset{O}{\overset{\|}{P}}Cl_2 + 4\,HN(CH_3)_2 \longrightarrow H_3C{-}\overset{O}{\overset{\|}{P}}[N(CH_3)_2]_2 + 2\,[H_2N(CH_3)_2]^{\oplus}\,Cl^{\ominus}$$

Among other reactions of *(2)*, the reaction with aromatic Grignard compounds to form diaryl(methyl)phosphane oxides should be mentioned[14].

### 2.2. Reactions of Methylphosphinic Acid *(4)*

The acid *(4)* has so far only found limited preparative use; however, it serves as an intermediate.



(4) (10) (11)

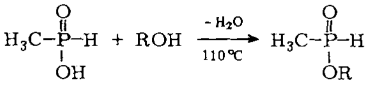
$$H_3C{-}\underset{OH}{\overset{O}{\overset{\|}{P}}}{-}H + CH_2O + \left[\underset{CH_2C_6H_5}{H_2N}{-}CH_2COOH\right]^{\oplus} Cl^{\ominus} \xrightarrow{-H_2O}$$

$$\left[H_3C{-}\underset{OH}{\overset{O}{\overset{\|}{P}}}{-}CH_2{-}\underset{CH_2C_6H_5}{NH}{-}CH_2COOH\right]^{\oplus} Cl^{\ominus} \xrightarrow{H_2/Pd} H_3C{-}\underset{OH}{\overset{O}{\overset{\|}{P}}}{-}CH_2{-}NH{-}CH_2COOH$$

Thus, in crude aqueous solutions, such as formed in the hydrolysis of *(1)*, *(4)* condenses with *N*-benzylglycine hydrochloride and formaldehyde, in the presence of concentrated hydrochloric acid, to the phosphinic acid derivative *(10)*[15].

*(10)* can be hydrogenated in 50% ethanol with palladium/activated charcoal to *N*-[hydroxy(methyl)phosphorylmethyl]glycine *(11)*[15].

Furthermore, with longer-chain alcohols, using toluene as a water entraining agent, the acid *(4)* can be converted without marked decomposition into the methylphosphinic esters *(5)*, $R \geqq C_4$[16].

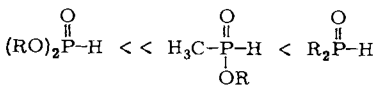


(4) (5), R = Alkyl ≧ C₄

$$H_3C{-}\underset{OH}{\overset{O}{\overset{\|}{P}}}{-}H + ROH \xrightarrow[110\,°C]{-H_2O} H_3C{-}\underset{OR}{\overset{O}{\overset{\|}{P}}}{-}H$$

### 2.3. Reactions of Methylphosphinic Esters *(5)*

Because of their reactive P—H bond, the esters *(5)* are of paramount importance as intermediates. Their reactivity exceeds that of phosphonic dialkylesters and approaches that of secondary dialkylphosphane oxides.

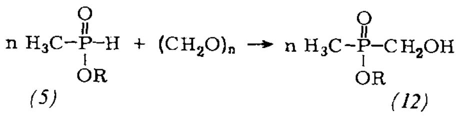


(5)

$$(RO)_2\overset{O}{\overset{\|}{P}}{-}H \ll H_3C{-}\underset{OR}{\overset{O}{\overset{\|}{P}}}{-}H < R_2\overset{O}{\overset{\|}{P}}{-}H$$

2.3.1. Addition of Methylphosphinic Esters *(5)* to Formaldehyde

In the simplest case the esters *(5)* can be added, without catalysis, to paraformaldehyde at 80–90 °C, to give hydroxymethyl(methyl)phosphinic esters *(12)*[17].

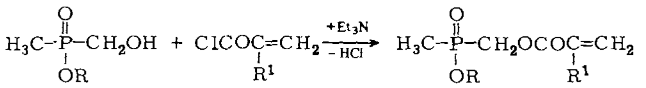


(5) (12)

R = Alkyl

$$n\,H_3C{-}\underset{OR}{\overset{O}{\overset{\|}{P}}}{-}H + (CH_2O)_n \rightarrow n\,H_3C{-}\underset{OR}{\overset{O}{\overset{\|}{P}}}{-}CH_2OH$$

Water-soluble phosphoryl-substituted acrylates *(13)*[18] which are suitable as comonomers, are obtained from *(12)* and either acryloyl or methacryloyl chloride.

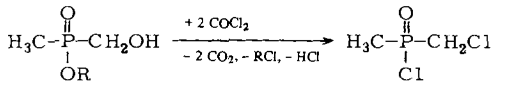


$$H_3C\text{-}P(O)(OR)\text{-}CH_2OH + ClCOC(R^1){=}CH_2 \xrightarrow[-HCl]{+Et_3N} H_3C\text{-}P(O)(OR)\text{-}CH_2OCOC(R^1){=}CH_2$$

*(12)* *(13)*

R = Alkyl; $R^1$ = H, $CH_3$

Reaction of *(12)* with phosgene at room temperature leads to chloromethyl(methyl)phosphinic chloride *(14)*[1,19] (see also Section 2.6.).



$$H_3C\text{-}P(O)(OR)\text{-}CH_2OH \xrightarrow[-2\,CO_2,\,-RCl,\,-HCl]{+2\,COCl_2} H_3C\text{-}P(O)(Cl)\text{-}CH_2Cl$$

*(12)* *(14)*

R = Alkyl

### 2.3.2. Addition of the Methylphosphinic Esters *(5)* to Compounds with Nonactivated Multiple Bonds

*(5)* can add to molecules which contain nonactivated double or triple bonds. A few typical examples are shown schematically in Figure 2.

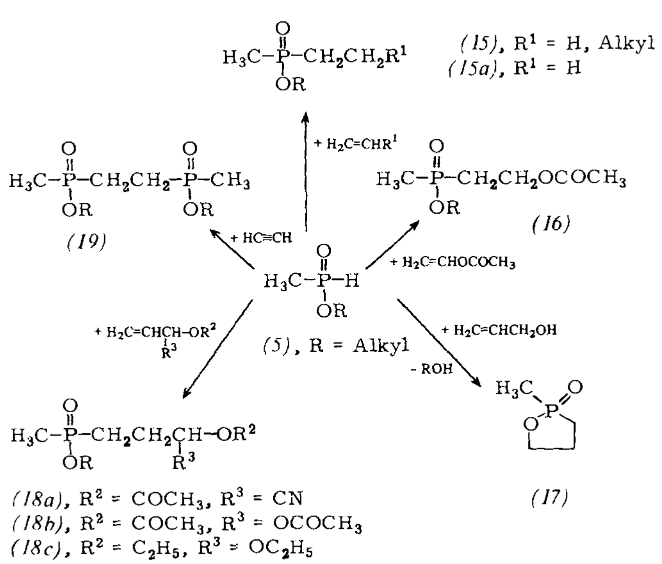


Fig. 2. Addition of *(5)* to compounds with nonactivated multiple bonds.

In the presence of peroxide-based catalysts the esters *(5)* react smoothly at about 150–170 °C with α-olefins to give alkyl(methyl)phosphinic esters *(15)*; the reaction is also catalyzed by UV-irradiation[20].

The addition of *(5)* to vinyl acetate in the presence of peroxides, particularly if an excess of *(5)* is used—leads to 2-acetoxyethyl(methyl)phosphinic esters *(16)*[21] in high yields.

The reaction with allyl alcohol proceeds analogously; 2-methyl-1,2-oxyphospholane 2-oxide *(17)* ("phostone") is formed directly *via* intramolecular alcohol cleavage[22]. Polycondensates formed simultaneously can to a large extent be cracked to monomeric phostone at high temperature *in vacuo*.

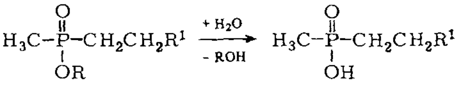
The addition compound *(18a)* is an important intermediate which is obtained from *(5)* and 1-cyanoallyl acetate (acroleincyanohydrin acetate)[23]. *(5)* also adds to the corresponding diacetate or diethyl acetal, the products *(18b)* or *(18c)*[24,25] being formed in high yields.

In the radical additions of *(5)* mentioned here, the phosphorus atom is almost exclusively linked to the carbon atom of the double bond which has the greater portion of hydrogen substituents.

The addition of *(5)* to acetylene at atmospheric pressure leads to the *P,P'*-ethylenebis(methylphosphinic) esters *(19)*[26].

#### *Alkyl(methyl)phosphinic Esters (15) and Secondary Products*

Hydrolysis of the phosphinic esters *(15)* at 160—200 °C leads to the phosphinic acids *(20)*[27].

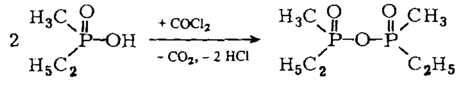


$$H_3C\text{-}P(O)(OR)\text{-}CH_2CH_2R^1 \xrightarrow[-ROH]{+H_2O} H_3C\text{-}P(O)(OH)\text{-}CH_2CH_2R^1$$

*(15)* *(20)*

R = Alkyl, $R^1$ = H, Alkyl

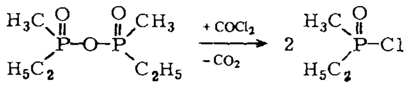
In the simplest case, ethyl(methyl)phosphinic acid *(20a)*[1] is obtained from *(15a)*; with phosgene in the molar ratio 2:1, phosphinic anhydride *(21)* is obtained almost quantitatively



$$2\,(H_3C)(H_5C_2)P(O)OH \xrightarrow[-CO_2,\,-2\,HCl]{+COCl_2} (H_3C)(H_5C_2)P(O)\text{-}O\text{-}P(O)(CH_3)(C_2H_5)$$

*(20a)* *(21)*

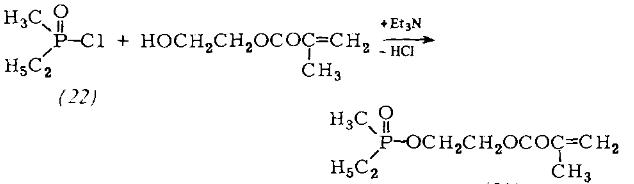
from *(20a)*[1,28]. Ethyl(methyl)phosphinic chloride *(22)*[1] is also readily accessible from the anhydride *(21)* by reaction with phosgene.



$$(H_3C)(H_5C_2)P(O)\text{-}O\text{-}P(O)(CH_3)(C_2H_5) \xrightarrow[-CO_2]{+COCl_2} 2\,(H_3C)(H_5C_2)P(O)Cl$$

*(21)* *(22)*

Alkyl(methyl)phosphinic chlorides, as monofunctional phosphoryl chlorides, are valuable intermediates. Thus from *(22)* and (2-hydroxyethyl)methacrylate the methacrylate *(23)* is obtained, the properties of which resemble those of the phosphorus containing acrylate *(13)*.

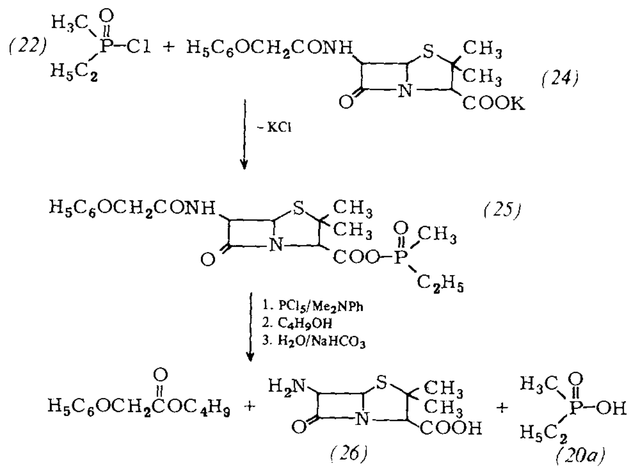


$$(H_3C)(H_5C_2)P(O)Cl + HOCH_2CH_2OCOC(CH_3){=}CH_2 \xrightarrow[-HCl]{+Et_3N} (H_3C)(H_5C_2)P(O)\text{-}OCH_2CH_2OCOC(CH_3){=}CH_2$$

*(22)* *(23)*

In addition, the alkyl(methyl)phosphinic chlorides enlarge the arsenal of protective group reagents. This may be illustrated by an example: from *(22)* and penicillin V, in the form of potassium salt *(24)* it is possible to prepare the mixed anhydride *(25)*.

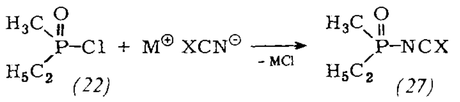
The carboxyamide group of the side chain is subsequently converted into the imide chloride by phosphorus pentachloride at about 0 °C, the anhydride function being preserved. By addition of butanol the imino ester is formed, which can



be smoothly hydrolyzed to 6-aminopenicillic acid *(26)*, an important intermediate for the synthesis of antibiotics.

Phosphinic chlorides can be used also for the synthesis of cephalosporin derivatives[30].

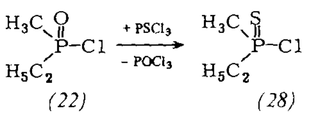
Among numerous further reactions, the reaction of *(22)* with cyanates and thiocyanates is of interest. It leads to the highly reactive phosphinic acid derivatives *(27)*[31], which have been used also to synthesize and modify natural products[32].



$$\underset{(22)}{\mathrm{H_3C(H_5C_2)P(=O)\!-\!Cl}} + M^{\oplus}\,XCN^{\ominus} \xrightarrow[-\,MCl]{} \underset{(27)}{\mathrm{H_3C(H_5C_2)P(=O)\!-\!NCX}}$$

M = Ag, Na, $NH_4$; X = O, S

Ethyl(methyl)thiophosphinic chloride *(28)* is formed by reaction of *(22)* with thiophosphoryl chloride at about 160 °C[33].

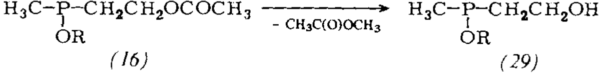


$$\underset{(22)}{\mathrm{H_3C(H_5C_2)P(=O)\!-\!Cl}} \xrightarrow[-\,POCl_3]{+\,PSCl_3} \underset{(28)}{\mathrm{H_3C(H_5C_2)P(=S)\!-\!Cl}}$$

Methylthiophosphinic chlorides are suitable educts for the preparation of methyldithiophosphinic acids, which form readily crystallizable metal complexes, some being intensely colored and many exhibiting extraordinary thermal stability[34].

### *2-Acetoxyethyl(methyl)phosphinic Esters (16) and Secondary Products*

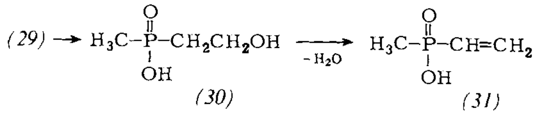
Transesterification of *(16)* with alcohols, preferably in the presence of bases, leads to formation of 2-hydroxyethyl-(methyl)phosphinic esters *(29)*; the yields being virtually quantitative[35].



$$\underset{(16)}{\mathrm{H_3C\!-\!P(=O)(OR)\!-\!CH_2CH_2OCOCH_3}} \xrightarrow[-\,CH_3C(O)OCH_3]{+\,CH_3OH/OH^{\ominus}} \underset{(29)}{\mathrm{H_3C\!-\!P(=O)(OR)\!-\!CH_2CH_2OH}}$$

R = Alkyl

The alcohols *(29)* provide the simplest access to methyl(vinyl)phosphinic acid *(31)*: hydrolysis to 2-hydroxyethyl(methyl)phosphinic acid *(30)* and subsequent dehydration of the latter *in vacuo*[36].



$$(29) \rightarrow \underset{(30)}{\mathrm{H_3C\!-\!P(=O)(OH)\!-\!CH_2CH_2OH}} \xrightarrow[-\,H_2O]{} \underset{(31)}{\mathrm{H_3C\!-\!P(=O)(OH)\!-\!CH\!=\!CH_2}}$$

### *Phostone (17) and Secondary Products*

As the "lactone" of 3-hydroxypropyl(methyl)phosphinic acid, phostone *(17)* is suitable for numerous reactions. Figure 3 shows several examples.

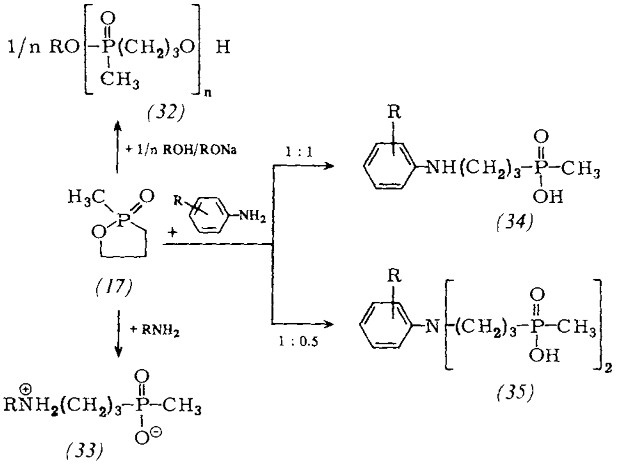
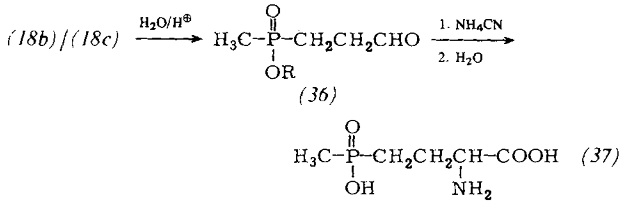


Fig. 3. Reactions of phostone *(17)*.

In the presence of catalytic quantities of the corresponding alcoholates, *(17)* reacts by oligoaddition to the adducts *(32)*[37]. Aliphatic amines form the internal salts *(33)* with *(17)*[38]. Depending on the molar ratio, either 3-anilinopropyl(methyl)phosphinic acids *(34)* or the corresponding *N,N*-disubstituted compounds *(35)* can be prepared from *(17)* and anilines, the yields being high[39].

### *2-Formylethyl(methyl)phosphinic Esters (36) and Secondary Products*

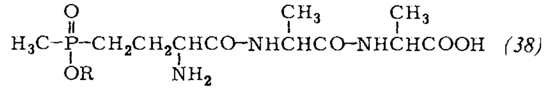
The esters *(18b)* and *(18c)* can be hydrolyzed in acidic media to 2-formylethyl(methyl)phosphinic esters *(36)*[24,25]. By means of a Strecker synthesis and subsequent hydrolysis, 2-amino-4-[hydroxy(methyl)phosphoryl]butyric acid *(37)* is obtained from *(36)*[25].



$$(18b)/(18c) \xrightarrow{H_2O/H^{\oplus}} \underset{(36)}{\mathrm{H_3C\!-\!P(=O)(OR)\!-\!CH_2CH_2CHO}} \xrightarrow[2.\ H_2O]{1.\ NH_4CN} \underset{(37)}{\mathrm{H_3C\!-\!P(=O)(OH)\!-\!CH_2CH_2CH(NH_2)\!-\!COOH}}$$

The amino acid *(37)*, also termed "phosphinothricin", was the first phosphinic acid derivative discovered in nature; it was isolated as the tripeptide *(38)* by *Bayer et al.*[40] in culture filtrates of *Streptomyces*[41].

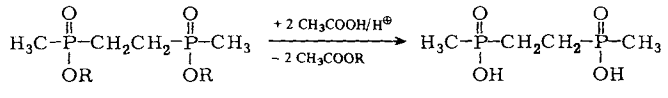
The route *via* cyanohydrin *(18a)* is the method of choice for the synthesis of phosphinothricin *(37)*.



$H_3C-P(=O)(OR)-CH_2CH_2CH(NH_2)CO-NHCH(CH_3)CO-NHCH(CH_3)COOH$ *(38)*

### *P,P'-Ethylenebis(methylphosphinic) Ester (19) and Secondary Products*

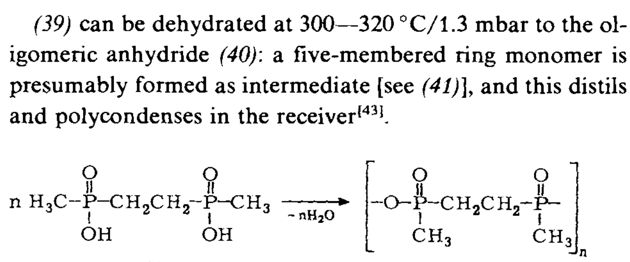
Cleavage of the ester *(19)* with acetic acid at about 140 °C in the presence of acid catalysts, preferably sulfuric acid, leads smoothly to *P,P'*-ethylenebis(methylphosphinic) acid *(39)*, m.p. = 190—191 °C[42]. This procedure is generally suitable for the preparation of high melting phosphinic acids which are readily soluble in hot and sparingly soluble in cold glacial acetic acid.



$H_3C-P(=O)(OR)-CH_2CH_2-P(=O)(OR)-CH_3 \xrightarrow[-2\,CH_3COOR]{+2\,CH_3COOH/H^{\oplus}} H_3C-P(=O)(OH)-CH_2CH_2-P(=O)(OH)-CH_3$

*(19)*, R = Alkyl *(39)*

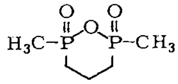
*(39)* can be dehydrated at 300—320 °C/1.3 mbar to the oligomeric anhydride *(40)*: a five-membered ring monomer is presumably formed as intermediate [see *(41)*], and this distils and polycondenses in the receiver[43].



$n\ H_3C-P(=O)(OH)-CH_2CH_2-P(=O)(OH)-CH_3 \xrightarrow{-nH_2O} [-O-P(=O)(CH_3)-CH_2CH_2-P(=O)(CH_3)-]_n$

*(39)* *(40)*

However, the anhydride *(41)*, which can be prepared in the same way at 250 °C from *P,P'*-trimethylenebis(methylphosphinic) acid is a six-membered ring compound (b.p. = 163 °C/0.3 torr, m.p. = 122—130 °C[43].



*(41)*

### 2.3.3. Addition of Methylphosphinic Acid Esters *(5)* to Compounds with Activated Double Bonds

The ester *(5)* adds to compounds with activated double bonds; in the presence of bases, derivatives of phosphinic acid esters are formed. Suitable unsaturated compounds, among others, are esters[44,45], amides[46] or α,β-unsaturated carbonitriles. A few selected reactions are compiled in Figure 4.

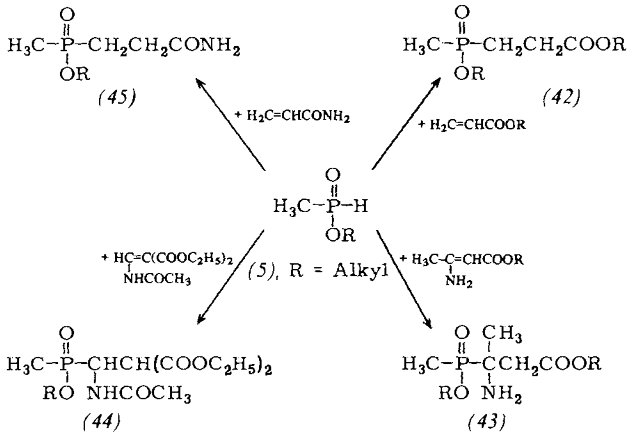
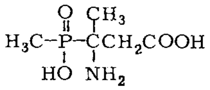
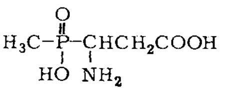


Fig. 4. Addition of *(5)* to compounds with activated double bonds.

The amino acids *(46)* or *(47)* are formed by hydrolysis of *(43)*[44] or hydrolysis and decarboxylation of *(44)*[45].



*(46)* $H_3C-P(=O)(HO)-C(CH_3)(NH_2)CH_2COOH$



$H_3C-P(=O)(HO)-CH(NH_2)CH_2COOH$ *(47)*

## 2.4. Reactions of the Methylphosphonous Diesters *(6)*

### 2.4.1. Arbusov reactions with Methylphosphonous Diesters *(6)*

In Arbusov reactions the diesters *(6)* are more reactive than trialkyl phosphites. A few selected reactions are given in Figure 5.

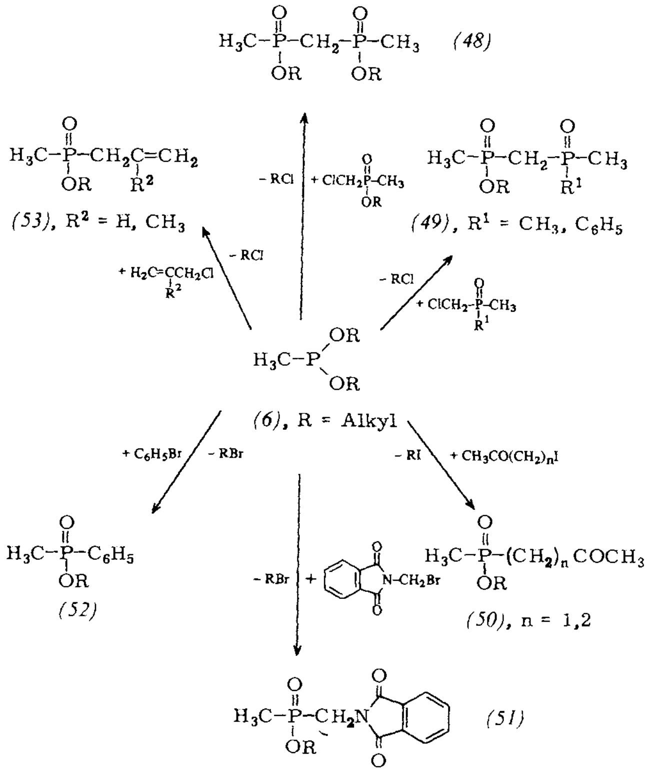
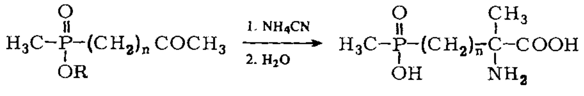


Fig. 5. Arbusov reactions of the methylphosphonous acid diesters *(6)*.

The *P,P'*-methylenebis(methylphosphinic) ester *(48)*, formed at 170—180 °C in almost quantitative yield, can be hydrolyzed to bisphosphinic acid, and the latter converted to polymeric titanyl complexes[47]. The phosphinic acids obtainable by hydrolysis of *(49)* form metal chelates having good thermal stability[48].

The phosphorus-containing amino acids *(54)* can, like *(37)*, be prepared by the Strecker synthesis[44].

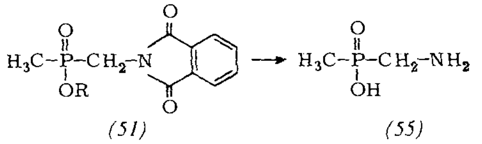


$H_3C-P(=O)(OR)-(CH_2)_nCOCH_3 \xrightarrow[2.\ H_2O]{1.\ NH_4CN} H_3C-P(=O)(OH)-(CH_2)_n-C(CH_3)(NH_2)-COOH$

*(50)* *(54)*

R = Alkyl, n = 1, 2

Aminomethyl(methyl)phosphinic acid *(55)* is accessible from *(51)* by hydrolysis[49]. In the presence of nickel halide catalysts *(6)* reacts with aryl halides, for example, bromobenzene, to give *(52)*[50]. Such catalysts, especially Raney nickel, have also been used for reactions of methallyl and allyl chloride with *(6)* to obtain the unsaturated phosphinic esters *(53)*[51].

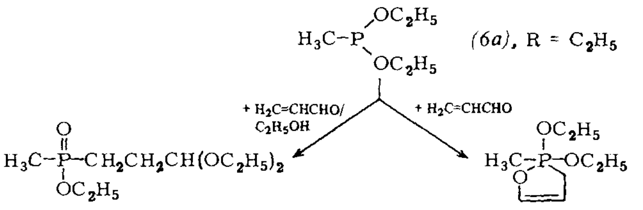


*(51)* *(55)*

R = Alkyl

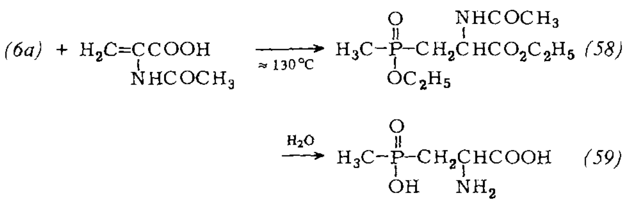
### 2.4.2. Addition of the Methylphosphonous Diesters *(6)* to Compounds with Activated Double Bonds

In contrast to the esters *(5)*, the diester *(6a)* in excess ethanol, adds smoothly to acrolein, to give diethylacetal *(56)*[52]. In the absence of ethanol, *(6a)* reacts with acrolein to give the pentacoordinate phosphorus compound *(57)*[53].



*(56)* *(57)*

The phosphonic ester *(58)* is obtained from *(6a)* and 2-acetamidoacrylic acid at about 130 °C; *(58)* can be hydrolyzed to a phosphorus-containing analogue of aspartic acid *(59)*.

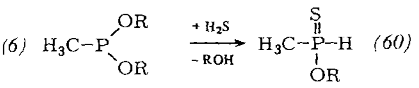


$$(6a) + H_2C{=}C(NHCOCH_3)COOH \xrightarrow[\approx 130\,^\circ C]{} H_3C{-}P(O)(OC_2H_5){-}CH_2CH(NHCOCH_3)CO_2C_2H_5 \quad (58)$$

$$\xrightarrow{H_2O} H_3C{-}P(O)(OH){-}CH_2CH(NH_2)COOH \quad (59)$$

### 2.4.3. Reaction of Methylphosphonous Diesters *(6)* with Hydrogen Sulfide

Of value in preparative chemistry is a procedure for the preparation of methylthiophosphinic ester *(60)*, in which the esters *(6)* are reacted with hydrogen sulfide at 50 °C under pressure in the presence of weakly basic amines, *e.g.* diethylaniline[54].



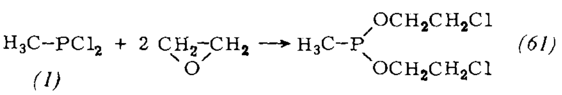
$$(6)\ H_3C{-}P(OR)_2 \xrightarrow[-\,ROH]{+\,H_2S} H_3C{-}P(S)(H)(OR) \quad (60)$$

R = Alkyl

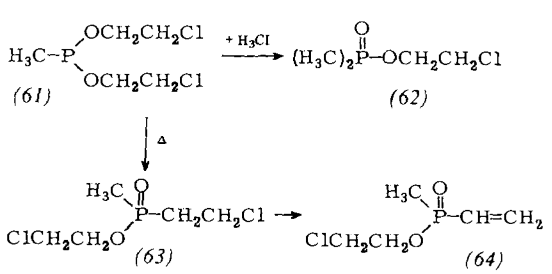
Methylthiophosphinic esters *(60)* have so far only rarely been used as synthetic building blocks. In the presence of radical initiators, compounds such as *(5)* can add smoothly to olefins; thus *via* addition to vinyl acetate, the 2-acetoxyethyl(methyl)thiophosphinic esters are obtained. The P=S group does not interfere with the radical addition.

### 2.5. Reaction of Dichloro(methyl)phosphane *(1)* with Ethylene Oxide

Reaction of *(1)* with ethylene oxide in the molar ratio 1:2 leads to methylphosphonous bis(2-chloroethyl) ester *(61)*, which occupies a special position among diesters of type *(6)*[55].



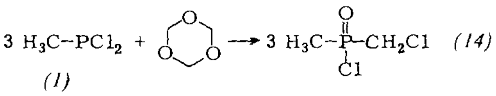
*(61)* reacts with methyl iodide, even at 30 °C, to form dimethylphosphinic 2-chloroethyl ester *(62)* and thus provides access to dimethylphosphoryloxy compounds[55].



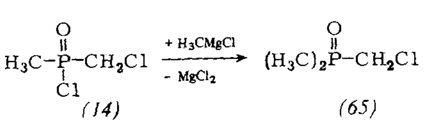
At 160 °C *(61)* reacts to form the phosphinic ester *(63)*, which eliminates HCl at 80 °C in the presence of triethylamine (molar ratio 1:1), the methyl(vinyl)phosphinic ester *(64)* being formed[55,56].

### 2.6. Reaction of Dichloro(methyl)phosphane *(1)* with Trioxane

The well known reaction of *(1)* with paraformaldehyde leads to chloromethyl(methyl)phosphinic chloride *(14)* in 70% yield[57]. *(14)* can also be obtained in almost quantitative yield from *(1)* and trioxane in the presence of Lewis acid catalysts in a current of hydrogen chloride at 130—150 °C[58] (see also Section 2.3.1.).



The phosphinic chloride *(14)* can be converted by Grignard reaction with methylmagnesium chloride to chloromethyl(dimethyl)phosphane oxide *(65)*[1,59].



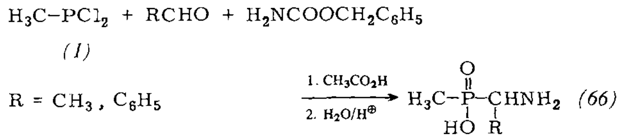
$$H_3C{-}P(O)(Cl){-}CH_2Cl \xrightarrow[-\,MgCl_2]{+\,H_3CMgCl} (H_3C)_2P(O){-}CH_2Cl$$

*(14)* *(65)*

Introduction of the tertiary phosphane oxide group into strongly hydrophobic compounds *via (65)* can considerably increase their water-solubility.

## 2.7. Reaction of Dichloro(methyl)phosphane *(1)* with Aldehydes and Carbamates or with Schiff's Bases

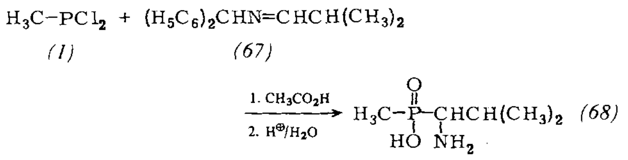
The direct preparation of 1-aminoalkyl(methyl)phosphinic acid is possible by condensation of *(1)* with aldehydes in the presence of carbamates. For example, if a mixture of *(1)*, benzylcarbamate and acetaldehyde or benzaldehyde is heated in glacial acetic acid and subsequently hydrolyzed with aqueous hydrochloric acid, 1-aminoalkyl(methyl)phosphinic acid *(66)* is obtained in 50—60% yield[60].



$$H_3C{-}PCl_2 + RCHO + H_2NCOOCH_2C_6H_5 \quad (1)$$

$$R = CH_3,\ C_6H_5 \quad \xrightarrow[2.\ H_2O/H^{\oplus}]{1.\ CH_3CO_2H} \quad H_3C{-}\underset{HO}{\overset{\overset{O}{\|}}{P}}{-}\underset{R}{C}HNH_2 \quad (66)$$

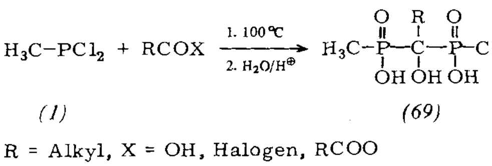
Phosphinic acids of this type are also obtained by reaction of *(1)* with Schiff's bases in glacial acetic acid and subsequent hydrolysis. Thus reaction of *(1)* with *(67)* and subsequent acidolysis, produces 1-amino-2-methylpropyl(methyl)phosphinic acid *(68)*[61].



$$\underset{(1)}{H_3C{-}PCl_2} + \underset{(67)}{(H_5C_6)_2CHN{=}CHCH(CH_3)_2} \quad \xrightarrow[2.\ H^{\oplus}/H_2O]{1.\ CH_3CO_2H} \quad H_3C{-}\underset{HO}{\overset{\overset{O}{\|}}{P}}{-}\underset{NH_2}{C}HCH(CH_3)_2 \quad (68)$$

## 2.8. Reaction of Dichloro(methyl)phosphane *(1)* with Aliphatic Carboxylic Acids

Dichloro(methyl)phosphane *(1)* reacts with aliphatic carboxylic acids — in the simplest case with glacial acetic acid — and also with their anhydrides and chlorides; hydrolysis of the primary products leads to derivatives of *P,P'*-(α-hydroxyalkylidene)bis(methylphosphinic) acid *(69)*[62].

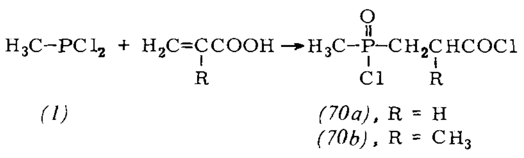


$$\underset{(1)}{H_3C{-}PCl_2} + RCOX \xrightarrow[2.\ H_2O/H^{\oplus}]{1.\ 100\,^{\circ}C} \underset{(69)}{H_3C{-}\underset{OH}{\overset{\overset{O}{\|}}{P}}{-}\underset{OH}{\overset{R}{C}}{-}\underset{OH}{\overset{\overset{O}{\|}}{P}}{-}CH_3}$$

R = Alkyl, X = OH, Halogen, RCOO

In contrast to the corresponding biphosphonic acids, compounds of type *(69)* do not exhibit any notable sequestering properties in aqueous systems.

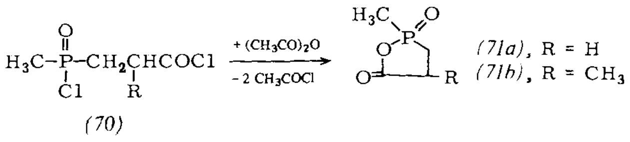
Acrylic acid reacts with *(1)* in a strongly exothermic reaction to form 3-[chloro(methyl)phosphoryl]propionyl chloride *(70a)*[63,64]. The reaction with methacrylic acid proceeds analogously to form *(70b)*.



$$\underset{(1)}{H_3C{-}PCl_2} + H_2C{=}\underset{R}{C}COOH \longrightarrow H_3C{-}\underset{Cl}{\overset{\overset{O}{\|}}{P}}{-}CH_2\underset{R}{C}HCOCl$$

*(70a)*, R = H
*(70b)*, R = $CH_3$

If the reaction is carried out continuously at 50—60 °C, the dichlorides *(70)* are obtained in almost quantitative yield[65]. They are smoothly cyclized by acetic anhydride to the 1,2-oxaphospholane-5-one 2-oxides *(71)*[1,63,64].



Numerous reactions of the phospholanes *(71)* (Fig. 6) proceed *via* ring opening. Thus the phosphinic acids are formed with water *(72)* and the phosphinic esters *(73)* are formed with alcohols such as ethanol. The reaction of *(71)* with aliphatic and aromatic amines leads to carboxamides, *e.g.* *(74)*[64], or with L-proline esters, after suitable isolation, to the compounds *(75)*[66].

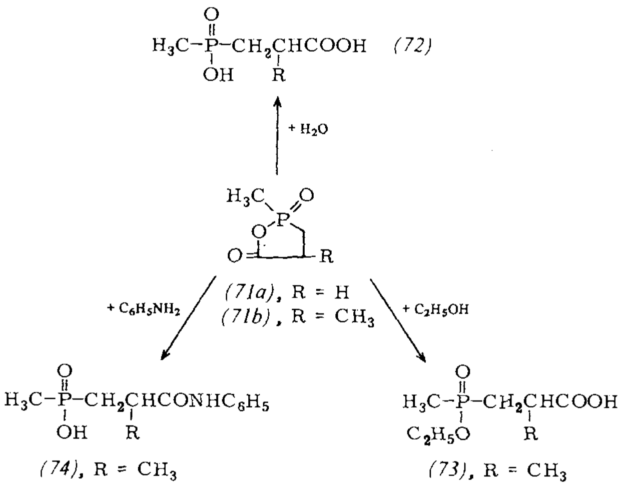
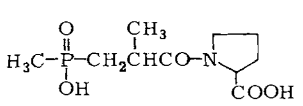
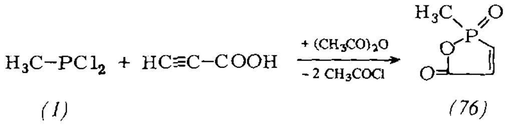


Fig. 6. Reactions of phospholanes *(71)*.



*(75)*

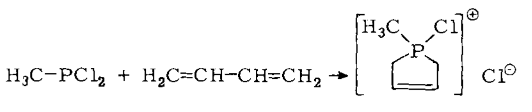
In a violent reaction with propiolic acid, *(1)* forms a phosphinic acid derivative which cyclizes when treated with acetic anhydride to form 2-methyl-Δ³-1,2-oxaphospholene-5-one 2-oxide *(76)*[64].



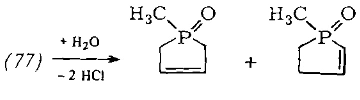
Reaction of *(1)* with *cis*-3-chloroacrylic acid[67], or preferably with 2-chloroacrylic acid[68], also leads to *(76)* using the same work-up procedure.

## 2.9. Reaction of Dichloro(methyl)phosphane *(1)* with 1,3-Dienes

[1+4]-Cycloaddition of *(1)* to 1,3-dienes, *e.g.* butadiene, leads to the phosphonium salt *(77)* which is readily converted by water into a mixture of the 1-methylphospholene oxides *(78)* and *(79)*[69,74].



(1) (77)

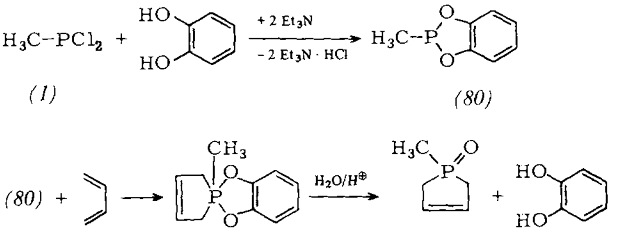


(77) (78) (79)

0.5 : 0.5

The extremely long reaction times can be shortened with the aid of solvents such as nitrobenzene, acyl chlorides and particularly phosphoryl chloride[75-78].

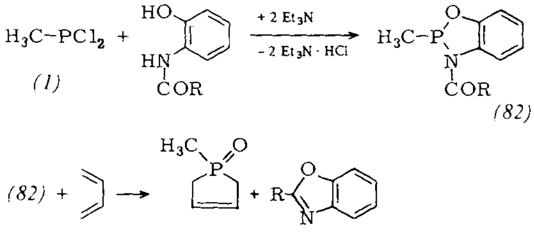
Two further syntheses of *(78)* proceed *via* benzoxaphospholenes. Benzodioxaphospholene *(80)*, obtainable from *(1)* and pyrocatechol cyclizes to the spiro compound *(81)* with butadiene and is hydrolyzed only very slowly to *(78)*[79].



(1) (80)

(80) + ... (81) (78)

Reaction of *(1)* with 2-(acylamino)phenols produces the isolable benzoxazaphospholenes *(82)*[80] in almost quantitative yield. The latter compounds react smoothly with butadiene to form *(78)* and 1,3-benzoxazoles *(83)*[81]. These compounds *(83)* can be readily split again into the 2-(acylamino)phenols. In both syntheses *(78)* is formed virtually free of isomers.

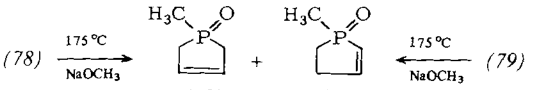


(1) (82)

(82) + (78) (83)

R = H, $CH_3$

Directed isomerization of *(78)* or *(79)* is possible above 150 °C in the presence of catalytic amounts of alkali metal alcoholates. The ratio 45:55 of *(78)* to *(79)* is always attained, regardless of whether *(78)* or *(79)* is used as starting material.



(78) (78) (79) (79)

0.45 : 0.55

## 2.9.1. Reactions of 1-Methyl-2-phospholene 1-Oxide *(78)*

Not only *(78)*, but also *(79)*, can react with a large number of compounds. Reactions of *(78)* are compiled in Figure 7.

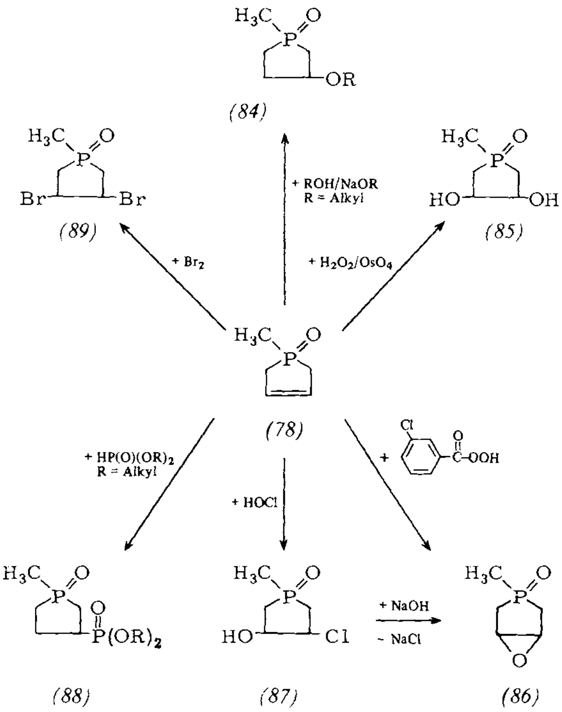


Fig. 7. Reactions of 1-methyl-phospholene 1-oxide *(78)*.

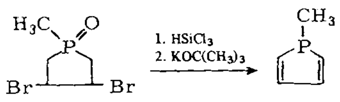
The addition of alcohols leads to 3-alkoxyphospholane 1-oxides *(84)*, good yields only being obtainable if alkali metal alcoholate (molar ratio approximately 1:1) is added[82].

In the presence of osmium tetroxide, *(78)* reacts with hydrogen peroxide to form 1-methyl-3,4-phospholanediol 1-oxide *(85)*[83].

The epoxide *(86)* is accessible either by reaction of *(78)* with *m*-chloroperbenzoic acid or—more advantageously—*via* the isolable 3-chloro-1-methyl-4-phospholanol 1-oxide *(87)*[84].

In the presence of radical initiators, the phosphonic diesters add to the double bond of *(78)* or *(79)*; the esters *(88)* being formed[85].

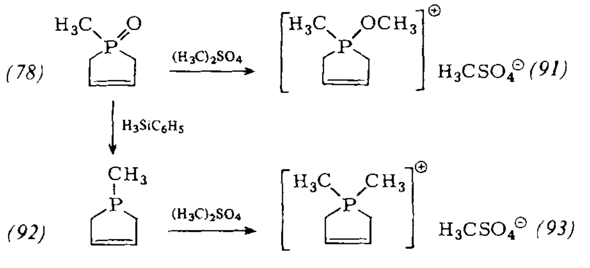
It is possible to brominate *(78)* to 3,4-dibromo-1-methylphospholane 1-oxide *(89)*, the reduction of which with trichlorosilane and subsequent dehydrobromination with potassium-*tert*-butoxide leads to 1-methylphosphole *(90)*. The spectroscopic data and reactivity of *(90)* are an indication of its aromatic character[86].



(89) (90)

*(78)* and *(79)* are readily quaternized by alkylation agents; thus the phosphonium salt *(91)* is obtained by reaction with dimethyl sulfate. The phospholene oxides *(78)* and *(79)* can

be reduced by organosilicon compounds to the phospholene *(92)*, which can be quaternized to the phosphonium salt *(93)*[87].



## 3. Fields of Application

### 3.1. Biocidal Compounds

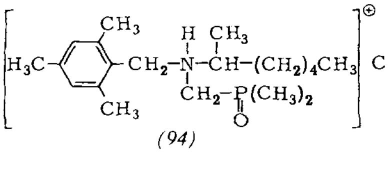
Because of their phosphorylating properties, methylphosphonic dichloride *(2)* and, in particular, methylthiophosphonic dichloride *(3)* are valuable starting materials for the synthesis of crop protection chemicals with biocidal properties[88-90]. The versatile synthetic potential of these acid dichlorides is supplemented by the alkyl(methyl)phosphinic chlorides and their thio-analogues, for example, ethyl(methyl)- *(22)* and chloromethyl(methyl)phosphinic chloride *(14)* or also ethyl(methyl)thiophosphinic chloride *(28)*[91].

Some derivatives of phosphinic acid exhibit biocidal properties. For example not only phosphinothricin *(37)*, but also its tripeptides *(38)* are suitable for use as herbicides[92,93]. Condensation products of the α-aminoalkyl(methyl)phosphinic acids *(55)*, *(66)* and *(68)* with one or more alanine residues exhibit herbicidal effects and plant growth regulating activity[61].

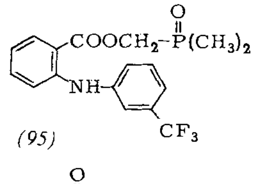
### 3.2. Pharmacologically Active Compounds

Starting from chloromethyl(dimethyl)phosphane oxide *(65)*, phosphane oxides having pharmacological activity can be obtained. Introduction of the phosphane oxide group into known active systems frequently improves solubility, while retaining the pharmacological activity. *(94)* is an antihistamine[94,95], *(95)* is of importance as an analgesic[96], and the phosphane oxides *(96)* are suitable as anti-hypertensives[97].

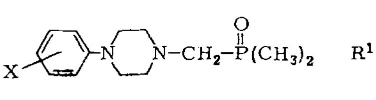
The benzodiazepines *(97)* are effective soporifics and have tranquilizing properties[98]; other 1,4-benzodiazepines with dimethylphosphoryl groups have been investigated in this connection[99]. The excellent water-solubility of the phosphane oxides *(97)* should be specially mentioned; the other benzodiazepine derivatives are far less soluble in water. The phosphinic acid derivative *(75)* has been found to be an active agent with hypotensive properties[6].



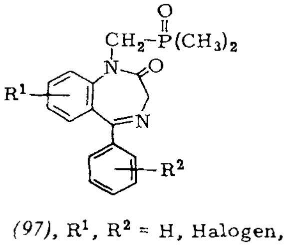
*(94)*



*(95)*



*(96)*, X = H, Cl, Alkyl



*(97)*, $R^1$, $R^2$ = H, Halogen, $CF_3$

### 3.3. Compounds Having Flame Retardant Activity

The well-known efficiency of numerous organophosphorus compounds as flame-retarding agents also extends to phosphinic acid derivatives and tertiary phosphane oxides. While derivatives of phosphonic acid are especially suitable for flame-retardant finishes of cellulosic fabrics, these same phosphorus compounds have also proved highly suitable, in this context, for polymers and polycondensates. They can be used in different ways:

a) *Introduction into the polymer chain:* by condensation of the oxaphospholane derivative *(71a)* into polyethyleneglycol terephthalates, polyesters are obtained which exhibit good permanent flame retardancy and can be made into flame-retardant fibers and filaments[100-102]. The phosphoryl acrylates *(13)* and *(23)* are monomers which, for example, can be used for terpolymerization with vinylidene chloride and acrylonitrile. Flame-retardant fibers having high luster and good lightfastness can be produced from the acrylonitrile polymers modified in this way[103-104].

b) *Use as additives:* because of their stability to hydrolysis and heat, phosphinic acids and their salts, as well as tertiary phosphane oxides, are particularly suitable as polymer additives. Thus, the alkali metal salts of the simple phosphinic acids *(20a)* or *(39)* can be used as additives for the production of flame-retardant polyamide molding compounds[105].

c) *Use as flame retardant textile auxiliaries:* textiles made from synthetic material can be rendered flame retardant by impregnation with phosphorus-containing compounds. Very high demands are made on these flame-retardant finishes; they should not adversely affect the properties of the textile material such as the "handle". Water-soluble products suitable for this purpose—*e.g.* the oligoadduct *(32)*, n = 11, ROH = glycerin[37]—are obtained by reacting phostone *(17)* with alcohols. Furthermore, polyadducts with similar properties *(71)* can also be obtained by reaction of the oxaphospholane derivatives with polyhydric alcohols and subsequent ethoxylation[106]. After cross-linking with "methylol-melamine esters", the products obtained with the aid of these—technically easy procedures—provide a washfast, flame-retardant finish on synthetic fibers.

A further possibility of achieving this consists of treating the textile material with a mixture of the water-soluble phosphoryl acrylates *(13)* or *(23)* and *N*-(hydroxymethyl)acrylamide in the presence of radical initiators. In this case the "methylol-melamine esters" can be completely dispensed with[107].

### 3.4. Metal Extraction Agents

Water-insoluble phosphinic esters *(15)*, for example, methyl(octyl)phosphinic acid isobutyl ester, are metal extraction agents. It has been suggested, for example, that they be used for the separation of zinc ions from aqueous $ZnCl_2$/$CdCl_2$ solutions[108] and also as additives in uranium(VI) extraction processes[109].

### 3.5. Further Uses

The phospholene oxides *(78)* and *(79)* can be used as catalysts for the preparation of flame-retardant polyurethane foams[110—114].

In alkaline media, hexyl(methyl)phosphinic and methyl(octyl)phosphinic acids exhibit outstanding wetting properties; consequently, they are suitable for the preparation of mercerizing solutions[115].

As an additive, *P,P'*-ethylenebis(methylphosphinic) acid *(39)* improves the heat and light stability of polyolefins[116].

## 4. Prospects

Owing to the intensive work being done in the field of organophosphorus compounds, and on their production on an industrial scale, it can be expected that they will find increasing use in many areas of application. Organophosphorus compounds can be both important starting materials and intermediates, as well as end products. The extraordinary multiplicity of reactions in which they can participate is due to a large number of intrinsic properties and the capacity of phosphorus to exist in several oxidation states. To utilize this possibility more than in the past in organic chemistry, is both an incentive and a challenge.

Received: January 12th, 1981 [A 353 IE]
German version: Angew. Chem. 93, 256, 1981

---

[1] Marketed product of Phosphororganische Chemikalien Hoechst.

[2] *H. Staendeke, H.-J. Kleiner,* Angew. Chem. *85*, 973 (1973); Angew. Chem. Int. Ed. Engl. *12*, 877 (1973).

[3] *H. Harnisch,* Angew. Chem. *88*, 517 (1976); Angew. Chem. Int. Ed. Engl. *15*, 468 (1976).

[4] *J. Deweerdt,* Fr. Pat. 2093256 (1970), État Francais.

[5] *J. Grosse,* Hoechst AG, unpublished results.

[6] *J. Longatte, R. Charles, J. Deweerdt,* Fr. Pat. 2064774 (1969), État Francais.

[7] *K. Gehrmann, E. Lohmar, A. Ohorodnik, H. Staendeke, P. Stutzke,* DOS 2415757 (1974), Hoechst AG; *E. Lohmar, H. Staendeke,* DOS 2519192 (1975), Hoechst AG.

[8] *B. M. Gladstein, L. N. Shitov,* Zh. Obshch. Khim. *39*, 1951 (1969).

[9] *J. A. Miles, T. M. Balthazor, H. L. Nufer, M. T. Beeny,* Org. Prep. Proced. Int. *11*, 11 (1979).

[10] *O. N. Grishina, M. A. Andreev, E. E. Sidorova,* Zh. Obshch. Khim. *46*, 1487 (1976).

[11] *H. Wissmann, H.-J. Kleiner,* Angew. Chem. *92*, 129 (1980); Angew. Chem. Int. Ed. Engl. *19*, 133 (1980).

[12] *L. Maier,* Phosphorus *1975*, 253.

[13] *H. Liebig,* Chem.-Ztg. *95*, 301 (1971).

[14] *E. L. Sukman,* DOS 2743848 (1977), M & T Chemicals Inc.

[15] *L. Maier,* EP-OS 0000767 (1978), Ciba-Geigy AG.

[16] *W. Dürsch,* Hoechst AG, unpublished results.

[17] *H.-J. Kleiner, H. Staendeke,* DAS 2226406 (1972), Hoechst AG.

[18] *H.-J. Kleiner,* DOS 2449466 (1974), Hoechst AG.

[19] *H.-J. Kleiner,* DBP 2259241 (1972), Hoechst AG.

[20] *H.-J. Kleiner, F. Landauer,* DOS 2100779 (1971), Hoechst AG.

[21] *M. Finke, H.-J. Kleiner,* DAS 2127821 (1971), Hoechst AG; *M. Finke, H.-J. Kleiner, S. Rösinger,* DOS 2208757 (1972), Hoechst AG.

[22] *M. Finke, H.-J. Kleiner,* DOS 2363852 (1973), Hoechst AG.

[23] *M. Finke, R. Mündnich,* DOS 2849003 (1978), Hoechst AG.

[24] *H.-D. Block,* DOS 2516341 (1975), Bayer AG; *H.-D. Block,* DOS 2516343 (1975), Bayer AG.

[25] *E. Gruszecka, M. Soroka, P. Mastalerz,* Pol. J. Chem. *53*, 937 (1979).

[26] *H.-J. Kleiner, W. Rupp,* DAS 2302523 (1973), Hoechst AG.

[27] *H.-J. Kleiner,* DBP 2441783 (1974), Hoechst AG; *W. Dürsch, H.-J. Kleiner, H.-D. Thamm,* DBP 2441878 (1974), Hoechst AG.

[28] *M. Finke, H.-J. Kleiner,* DBP 2129583 (1971), Hoechst AG.

[29] *D. Bormann, W. Schmitt, M. Schorr,* DOS 2222094 (1972), Hoechst AG.

[30] *W. H. W. Lunn,* US-Pat. 3980644 (1973), Eli Lilly and Co.

[31] *G. Tomaschewski, A. Otto, D. Zanke,* Arch. Pharm. *301*, 520 (1968).

[32] *J. K. van der Drift, C. A. Bruynes,* DOS 2405894 (1974), Gist-Brocades N.V.

[33] *M. Finke, H.-D. Thamm,* DOS 26233845 (1976), Hoechst AG.

[34] *W. Kuchen, H. Hertel,* Angew. Chem. *81*, 127 (1969); Angew. Chem. Int. Ed. Engl. *8*, 89 (1969).

[35] *H.-D. Block, R. Schliebs,* DOS 2313355 (1973), Bayer AG; *M. Finke, H.-J. Kleiner,* DAS 2335852 (1973), Hoechst AG.

[36] *H.-J. Kleiner,* DAS 2344332 (1973), Hoechst AG.

[37] *W. Dürsch, H.-J. Kleiner, F. Linke,* DOS 2841941 (1978), Hoechst AG.

[38] *W. Herwig,* DOS 2440239 (1974), Hoechst AG.

[39] *H.-J. Kleiner,* Liebigs Ann. Chem. *1980*, 324.

[40] *E. Bayer, K. H. Gugel, K. Hägele, H. Hagenmaier, S. Jessipow, W. A. König, H. Zähner,* Helv. Chim. Acta *55*, 224 (1972).

[41] *T. Niida, S. Inouye, T. Tsuruoka, T. Shomura, Y. Kondo, Y. Ogawa, H. Watanabe, Y. Sekizawa, T. Watanabe, H. Igarashi,* DBP 2236599 (1972), Meiji Seika Kaisha Ltd.

[42] *H.-J. Kleiner, H.-D. Thamm,* DOS 2719385 (1977), Hoechst AG.

[43] *W. Dürsch, H.-J. Kleiner,* EP-OS 0004323 (1978), Hoechst AG.

[44] *E. Gruszecka, M. Soroka, P. Mastalerz,* Pol. J. Chem. *53*, 2327 (1979).

[45] *M. Soroka, P. Mastalerz,* Rocz. Chem. *50*, 661 (1976).

[46] *C. Beermann, M. Reuter,* DBP 1946574 (1969), Hoechst AG.

[47] *B. P. Block, G. H. Dahl,* US-Pat. 3403176 (1966), Pennsalt Chemicals Corp.

[48] *B. P. Block, J. P. King, I. C. Popoff,* Inorg. Chem. *4*, 198 (1965).

[49] *O. Yasuaki, S. Inouye, H. Yamashina, T. Niida,* Meiji Seika, Kenkyu Nempo *1976*, 22; Chem. Abstr. *86*, 155917d (1977).

[50] *P. Tavs,* Chem. Ber. *103*, 2428 (1970).

[51] *G. Arend, H.-D. Block,* DOS 2601467, Bayer AG.

[52] *T. Tsuruoka, A. Suzuki, K. Tachibana, K. Mizutani, Y. Sekizawa, S. Inouye, T. Takematsu,* EP-OS 0009022 (1978), Meiji Seika Kaisha Ltd.

[53] *R. Mündnich,* Hoechst AG, unpublished results.

[54] *R. Schliebs,* DBP 1768503 (1968), Bayer AG.

[55] *I. A. Rogacheva, E. I. Gefter,* Zh. Obshch. Khim. *41*, 2634 (1971).

[56] *H. Gross, Th. Gnauk,* J. Prakt. Chem. *318*, 157 (1976).

[57] *L. C. D. Groenweghe, J. H. Payne,* J. Am. Chem. Soc. *83*, 1811 (1961).

[58] *H. Neumaier,* EP-OS 0005502 (1979), Hoechst AG.

[59] *H.-J. Kleiner, H. Neumaier, H.-D. Thamm,* Hoechst AG, unpublished results.

[60] *J. Oleksyszyn, R. Tyka, P. Mastalerz,* Synthesis *1978*, 479.

[61] *W. Hoyle, R. Vogel,* EP-OS 0010067 (1979), Ciba-Geigy AG.

[62] *H. W. Kranz, K.-H. Worms,* DOS 2153998 (1971), Henkel & Cie GmbH.

[63] *V. K. Khairullin, T. I. Sobčuk, A. N. Pudovik,* Zh. Obshch. Khim. *37*, 710 (1967).

[64] *V. K. Khairullin, R. M. Kondrat'eva, A. N. Pudovik,* Zh. Obshch. Khim. *38*, 288 (1968).

[65] *E. Lohmar, K. Gehrmann, A. Ohorodnik, P. Stutzke,* DBP 2529731 (1975), Hoechst AG.

[66] *E. W. Petrillo,* DOS 2942781 (1979), E. R. Squibb & Sons.

[67] *A. N. Pudovik, G. V. Dimitrieva, N. P. Anoshina, T. A. Zyablikova, V. K. Khairullin,* Izv. Akad. Nauk SSSR, Ser. Khim. *1972*, 1159.

[68] *E. Auer, A. Ohorodnik,* DOS 2609126 (1976), Hoechst AG.

[69] *L. D. Quin, J. P. Gratz, R. E. Montgomery,* Tetrahedron Lett. *1965*, 2187.

[70] *L. D. Quin, J. A. Caputo,* Chem. Commun. *1968*, 1463.

[71] *C. Symmes, L. D. Quin,* J. Org. Chem. *41*, 238 (1976).

[72] *L. D. Quin, E. D. Middlemas,* J. Am. Chem. Soc. *99*, 8370 (1977).

[73] *L. D. Quin, J. P. Gratz, T. P. Barket,* J. Org. Chem. *33*, 1034 (1968).

[74] *W. L. Orton, K. A. Mesch, L. D. Quin,* Phosphorus Sulfur *1979*, 349.

[75] *K. Moedritzer,* Synth. React. Inorg. Met.-Org. Chem. *5*, 299 (1975).

[76] *K. Moedritzer,* US-Pat. 3855186 (1972), Monsanto Co.

[77] *R. Schliebs, G. Jonas,* DBP 2036173 (1970), Bayer AG.

[78] *H.-D. Block, R. Schliebs,* DOS 2606682 (1976), Bayer AG.

[79] *N. A. Kurschakowa, N. A. Razumova,* Zh. Obshch. Khim. *46*, 1027 (1976).

[80] *U.-H. Felcht,* EP-OS 0006220 (1979), Hoechst AG.

[81] *U.-H. Felcht,* EP-OS 0006195 (1979), Hoechst AG.

[82] *H.-D. Block,* DOS 2552319 (1975), Bayer AG.

[83] *R. Schliebs, H.-D. Block,* DOS 2602646 (1976), Bayer AG.

[84] *F. Cavagna, U.-H. Felcht, E. F. Paulus,* Angew. Chem. *92*, 127 (1980); Angew. Chem. Int. Ed. Engl. *19*, 132 (1980).

[85] *R. Schliebs, H.-D. Block,* DOS 2504333 (1975), Bayer AG.

[86] *L. D. Quin, J. G. Bryson, C. G. Moreland,* J. Am. Chem. Soc. *91*, 3309 (1969).

[87] *K. Naumann, K. Sasse, K. Lürssen,* DOS 2503210 (1975), Bayer AG.

[88] *F. Mauer, H.-J. Riebel, R. Schröder, J. Hamann, B. Homeyer, W. Behrenz,* DOS 2702049 (1977), Bayer AG.

[89] *W. Sirrenberg, J. Hamann, B. Homeyer,* DOS 2420069 (1974), Bayer AG.

[90] *F. O'Melia,* US-Pat. 3911118 (1974), Dow Chemical Co.

[91] *L. Emmel, G. Stähler,* DOS 2227683 (1972), Hoechst AG.
[92] *W. Rupp, M. Finke, H. Bieringer, P. Langelüddeke,* DOS 2717440 (1977), Hoechst AG.
[93] *T. Takematsu, M. Konnai, T. Utsunomiya, T. Tsuruoka, S. Inouye, T. Watanabe,* DOS 2848224 (1978), Meiji Seika Kaisha Ltd.
[94] *A. Söder, R.-O. Weber, I. von Boksay, V. Bollmann,* DBP 2411406 (1974), Hoechst AG.
[95] *A. Söder, R.-O. Weber, I. von Boksay, V. Bollmann,* DBP 2428625 (1974), Hoechst AG.
[96] *A. Söder, K. Perrey,* DBP 2505415 (1975), Hoechst AG.
[97] *E. J. Glamkowski, J. T. Strupczewski, E. Wolf,* DOS 2322851 (1973), Hoechst AG.
[98] *E. Wolf, H. Kohl, G. Härtfelder,* DBP 2022503 (1970), Hoechst AG.
[99] *H. Kuch, I. Hoffmann,* DOS 2118262 (1971), Hoechst AG.
[100] *H.-J. Kleiner, M. Finke, U. Bollert, W. Herwig,* DBP 2346787 (1973), Hoechst AG.
[101] *H. Zimmermann,* Chemiefasern + Text. Anwendungstechn. Text. Ind. *28/80,* 1054 (1978).
[102] *S. Müller, H. Zimmermann,* Chemiefasern + Text. Anwendungstechn. Text. Ind. *30/82,* 38 (1980).
[103] *B. Huber, H.-J. Kleiner,* DBP 2449469 (1974), Hoechst AG.
[104] *B. Huber, H.-J. Kleiner,* DBP 2449468 (1974), Hoechst AG.
[105] *W. Herwig, S. Noetzel,* DOS 2447727 (1974), Hoechst AG.
[106] *W. Dürsch, F. Linke, M. Finke,* DOS 2556482 (1975), Hoechst AG.
[107] *W. Dürsch, F. Linke, H.-J. Kleiner,* DOS 2449465 (1974), Hoechst AG.
[108] *F.-J. Gohlke, H.-J. Kleiner, H. J. Morawietz, P. Pfüller,* DOS 2315849 (1973), Hoechst AG.
[109] *C. A. Blake, C. F. Baes, K. B. Brown, C. F. Coleman, J. C. White,* Proc. 2nd UN Int. Conf. Peaceful Uses Atomic Energy *28,* 289 (1958).
[110] *A. Ibbotson,* DOS 2614323 (1976), ICI Ltd.
[111] *K. Findeisen, K. Wagner, W. Schäfer, H.-J. Henning,* DOS 2537685 (1975), Bayer AG.
[112] *R. Lantzsch, H. Hoffmann,* DOS 2638453 (1976), Bayer AG.
[113] *K. B. Onder, C. P. Smith,* DOS 2801701 (1978), Upjohn Co.
[114] *A. Spina, W. Dietrich, R. Schliebs,* DAS 2245634 (1972), Bayer AG.
[115] *K.-H. Schneider, G. Schneider, H.-J. Kleiner,* DOS 2231147 (1972), Hoechst AG.
[116] *R. Heinrich, H.-J. Kleiner,* DBP 2442390 (1974), Hoechst AG.

---

# Darwin and Molecular Biology[**]

## By Manfred Eigen[*]

*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

*Darwin*'s "idea of the century", the principle of selection, is as important in the age of molecular biology as it was a hundred years ago. As a natural law it is open to rigorous physical proof, if certain prerequisites are met, and to quantitative experimental test—*in vitro* and *in vivo*—under defined laboratory conditions.

If we, living in the second half of the twentieth century, ask ourselves whose work has furthered our understanding of the phenomenon of "life" to the greatest extent, then the name *Darwin* springs at once to mind.

"If you ask whether we shall call this the century of iron, or of steam, or of electricity, then I can answer at once with complete conviction: it will be called the century of the mechanistic understanding of Nature—the century of Darwin", wrote his contemporary, *Ludwig Boltzmann,* in 1886[1].

It is scarcely possible that the founder of statistical physics, writing these lines, was referring to *Darwin* the observer, the botanist, the zoologist. It was *Darwin*'s perception to which he was paying tribute. Today, with the improved methods and profound insights of molecular biology, *Darwin*'s gigantic empirical opus has become a matter of historical interest only, an outstanding achievement of the last century—not out-of-date, but out of the front line of modern science. *Darwin*'s true legacy is an insight, which is as relevant in the twentieth century as in the nineteenth, even if today the emphasis is placed rather differently.

**The story** of this epoch-making idea began in 1831, when the twenty-two-year-old *Charles Robert Darwin* boarded the British Admiralty surveying ship H. M. S. Beagle. A graduate in theology, he was thoroughly convinced of the truth of the doctrine of creation. But he was also possessed by an unremitting desire to discover the natural world. He was open-minded and prepared to draw conclusions from what he saw. Returning five years later from his journey around the world, he still hesitated to unveil to the public the crux of his experiences and observations. *Darwin*'s diaries make it clear that he had already arrived at the basic concept of his principle of selection in 1838, when he first became acquainted with *Thomas Robert Malthus*' "Essay on the Principles of Population"[2], a work which had appeared in 1798 and provoked much discussion. It is uncertain when this idea took final form in *Darwin*'s mind. For twenty years he worked on, endeavouring to broaden the empirical basis of his work. It took the news that a fellow countryman, *Alfred Russel Wallace,* had independently come to similar conclusions and the receipt of a copy of an essay[3] from *Wallace,* to jolt him into putting his theory into the form of a book—planned initially to appear in several volumes. The findings of these two scientists were publicly presented at the memorable meeting of the Linnean Society of London on July 1st, 1858. *Darwin*'s fundamental work "The Origin of Species"[4] finally appeared on November 24th, 1859, put to press by the well-known London publisher *John Murray.* Here at least the

---

[*] Prof. Dr. M. Eigen
Max-Planck-Institut für Biophysikalische Chemie,
Abt. Biochemische Kinetik
Am Fassberg, D-3400 Göttingen (Germany)

[**] An abridged version of this article, entitled "Charles Darwin und die moderne Biologie", may be found in Meyers Großes Universallexikon, Bibliographisches Institut AG, Mannheim 1981.

*0570-0833/81/0303-0233 $ 02.50/0*

principle of selection, borne out by a mass of observations, was developed clearly as the basis of evolution.

It has recently been put forward by *Brackman*[5] that *Darwin* was only able to formulate his concept of selection and evolution after reading *Wallace*'s manuscript. This suggestion is refuted not only by entries in *Darwin*'s diary but also by a plan sketched out in 1842 and 1844, known today as the "Foundations of the Origins of Species"[6]. *Wallace* never challenged *Darwin*'s priority—just as *Darwin* never denied his debt to *Wallace.*

The presentation by *Wallace* is simple and straightforward—*Darwin*'s texts are harder to read. Although both reached the same conclusions, *Darwin*'s reasoning is more convincing. For *Wallace,* the form of the growth law of a population plays only a secondary role, because—as he states explicitly—the population is in any case constant, and because even minor differences in succeeding generations should suffice to cause weaker and less well-organized forms to die out.

This is a correct observation, but still not an explanation. For *Darwin,* selection arises only from the "enormous geometric power of increase" of organisms. He records this in 1842 and makes reference to *Malthus.*

**Growth** alone is indeed not sufficient to explain selection[7].

In Figure 1a, growth curves for three growing species are shown. It is assumed that each one reproduces itself at a linear rate in time, that is, new members are produced at constant speed. If we now impose competition upon the system by limiting the total population—this is done by making the rate of removal (*e. g.,* by death) of each species proportional to its population size—the result is a stable coexistence of all these species, in which the selective advantage of a particular one results solely in its population becoming greater than those of the other two (see Fig. 1b). It is immaterial whether this advantage is due to a higher birth rate, a lower death rate, or both.

Genuine selection does not appear until we assume exponential growth, a condition simulated in Figure 2a. If the population is again restricted by removal of total excess production - for each species proportional to its fraction of individuals - only the species with optimal birth and death rates survives. Selection is determined solely by the inherent properties of the species and not by its population size (which the chemist would call "concentration" or "mass action"). If a mutant individual with an evolutionary advantage arises some time after the others, its progeny can outgrow them, even though it starts with a numerical disadvantage (Fig. 2b). Again, "advantage" means higher rate parameters for growth (reproduction), lower rate parameters for decay (death), or both. The effect of "mass action" cancels out, as removal is also proportional to each particular population size.

"Mass-action" appears in selection when growth accelerates at a rate faster than exponential. The examples in Figures 3, based upon hyperbolic growth laws (quadratic dependence for population growth, linear for decay) show sharp and unambiguous selection as a consequence of competition. However, in this case, the result of selection is a once-and-for-all decision. This may at first seem surprising, since the hyperbolic growth curve approximates very well to an exponential in any restricted time interval below the singularity. Such a form, however, then depends upon the population size at any given moment ($e^{k'Nt}$ instead of $e^{kt}$). It is therefore not enough for a mutant to have a sufficiently high rate parameter $k'$, since it would still be at a disadvantage by a factor $N$—the number of individuals already present. Such a factor is extremely difficult to overcome in real situations by favourable kinetic properties.

Populations obeying all these three growth laws—linear, exponential and hyperbolic—may be found in the biological world. For example, if two species obtain nourishment from two independent but restricted sources, the result is a con-

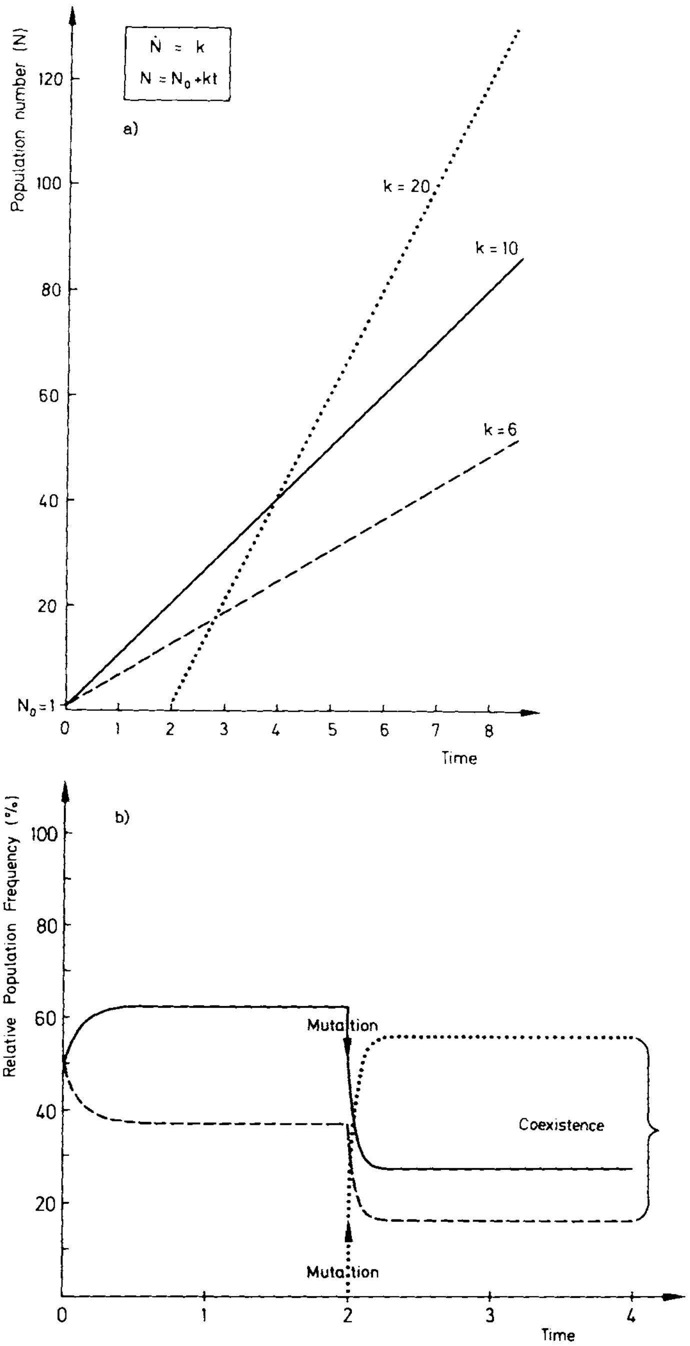


Fig. 1. a) A system with a constant rate of growth shows a linear growth law. b) Restriction of growth due to a first-order decay process results in coexistence of the competing species. The time required to reach a steady state depends on the number of individuals. The curves in this Figure and in Figures 2b and 3b are calculated on the basis of a total population $N = 10$.

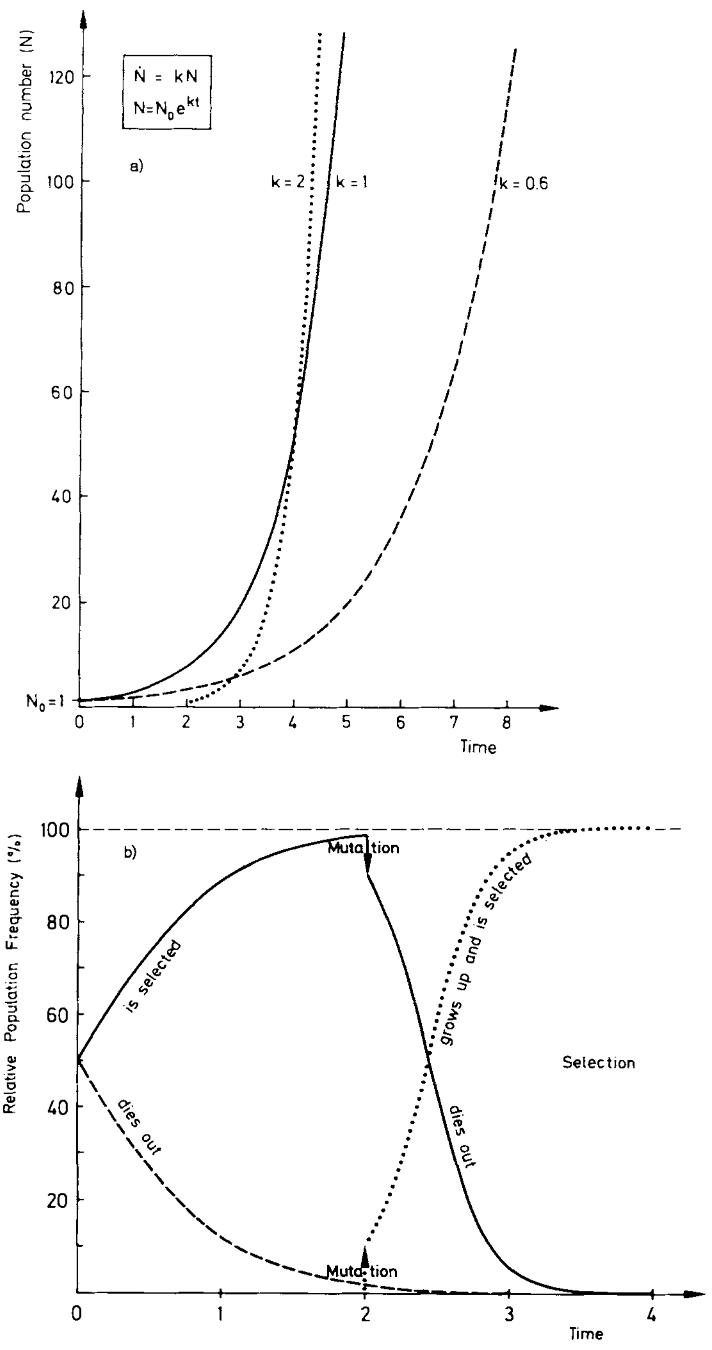


Fig. 2. a) A system with a linear autocatalytic rate term shows an exponential growth law. b) Limitation to a constant total population results in selection of the species with the highest effective growth rate. Mutants arising later grow successfully if they bear a selective advantage.

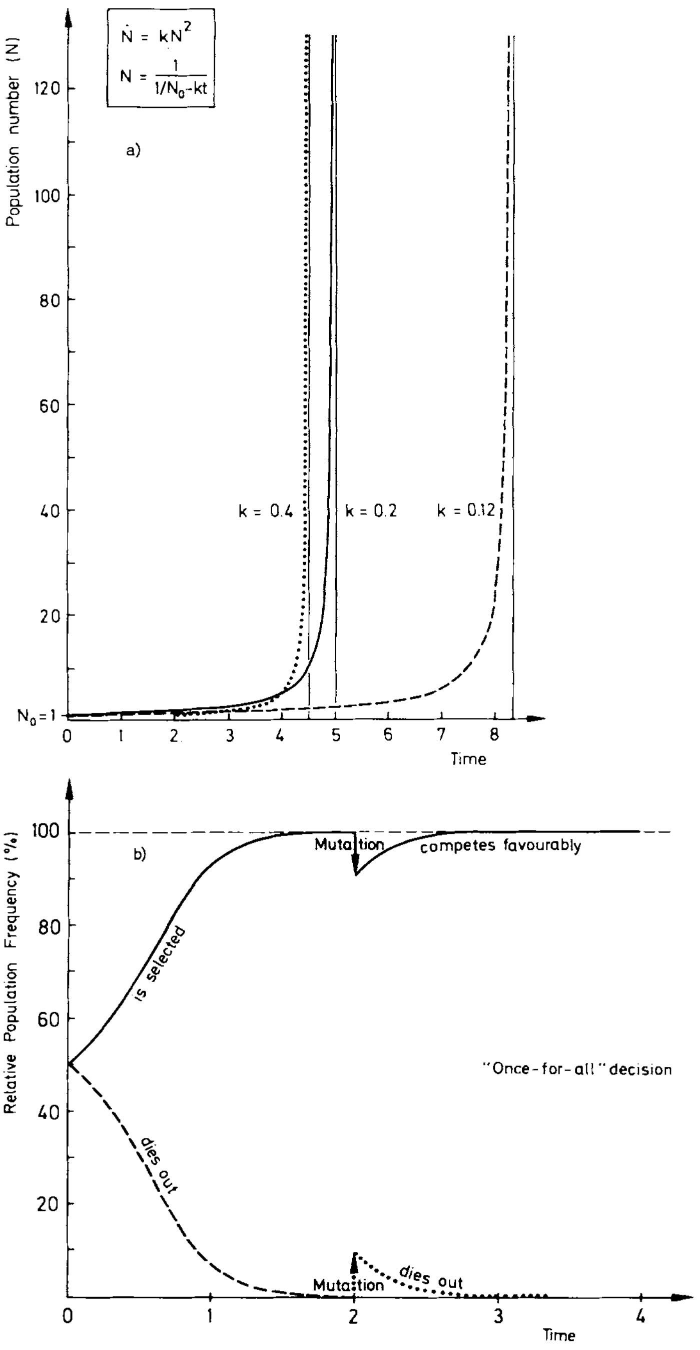


Fig. 3. a) Autocatalytic systems with a higher-order rate law show a hyperbolic growth law. b) Limitation of hyperbolic growth leads to selection with a "mass-action effect", which makes a once-and-for-all decision. The sharpness of selection in the course of time depends strongly upon the total population, *N*.

stant growth rate and thus a linear increase in population leading to coexistence of both species. Biologists call this niche formation. Selection then only takes place within each distribution of mutants. Niche formation has resulted in the coexistence of a great variety of species. However, these originally arose by selection on the basis of exponential growth laws. Hyperbolic growth limits the variety of species in an "all-or-none" way. Even the molecular self-organisation of life—as will be shown below—has passed through a phase of "co-operative" enhancement, in which the molecular machinery and a universal code for all posterity was laid down in a once-and-for-all decision.

It is futile to ask whether *Darwin* envisaged all this; however, his repeated reference to *Malthus* makes it clear that he was well aware of the significance of the form of the growth law.

Later, *Darwin* was to refine his ideas continually and to reexamine many details. His original work of 1859[4] was followed by five further editions during his lifetime, amid newer works on alterations to plants and animals caused by domestication, on the descent of Man, on the expressions of emotions, on geology and above all on botany.

What is the **essence of the principle of selection?** Both *Darwin* and *Wallace* treated the phenomenon of life for the first time as an object of scientific research, by assuming natural causes for its origin and its evolution, by setting up hypotheses which could be tested objectively, and, in *Darwin*'s case in particular, by showing many times over how such a test can be carried out using the methods of scrupulous observation. The palaeontologist *George Gaylord Simpson*[8] regarded this as the "most important accomplishment" of *Darwin*'s work, which "would have been revolutionary even if *Darwin* had been quite mistaken in the specific theories that he advanced" (*Simpson* adds: "As a matter of fact, he was not").

*Darwin* expended great effort on the minute analysis of all the facts which spoke for or against the assumption of an evolutionary development of living things. This assumption was by no means new; it was familiar to every natural scientist of the time. *Darwin* took the hypothesis from the work of *Jean Baptiste de Lamarck*[9], who had propounded it at the beginning of the nineteeth century. It seems, however, that *Darwin* begrudged *Lamarck* the credit for this. Although he described *Lamarck* as a "justly celebrated naturalist", he cannot resist mentioning[8] that his grandfather, Dr. *Erasmus Darwin,* had anticipated *Lamarck*'s opinions and "their erroneous grounds", and that in addition *Etienne Geoffroy Saint-Hilaire* in France and *Johann Wolfgang von Goethe* in Germany had already expressed similar opinions. *Goethe*'s works on morphology made a considerable contribution indeed to the doctrine of evolution, even though they were concerned with demonstrating its effects rather than postulating its causes.

Departing from *Lamarck, Darwin* postulated the descent of *all* living beings from a common ancestor, in agreement with *Goethe* and *Geoffroy Saint-Hilaire,* who took it that "what we call species are various degenerations of the same type". But only *Darwin,* dissatisfied with conjecture, assembled his evidence piece by piece. When in the end the burden of proof became crushing, and even mankind had to be included in his theory, *Darwin* became—and in some circles he still is today—an object of censure. In fact earlier research, such as *Goethe*'s discovery of the human intermaxillary jawbone, had already pointed towards this conclusion, for which *Darwin* simply had to provide the explanation. Modern molecular biology and the quantitative comparison of genetic information in different organisms has long since decided the issue in *Darwin*'s favour. Even when one can still read, "The theory of man's descent by natural selection from closely allied, preexisting species has never been proven, and probably never will be"[5], there is nonetheless no alternative "theory of man's descent" which can explain the phylogenetic family trees resulting from sequence homologies between individual RNA and protein molecules. Examples of these are shown in Figures 4 and 5 and in Table 1.

The stroke of genius consisted in tracing the process of evolution back to its natural cause. Reality is complex, but its principles are simple. *Darwin* had discovered a simple truth.

In the sixth edition of the "Origin of Species", which *Darwin* himself edited and which he saw as the final version, to be bequeathed to posterity, he wrote: "This preservation of favourable individual differences and variations, and the destruction of those which are injurious, I have called Natural Selection, or the Survival of the Fittest." *Darwin* uses several

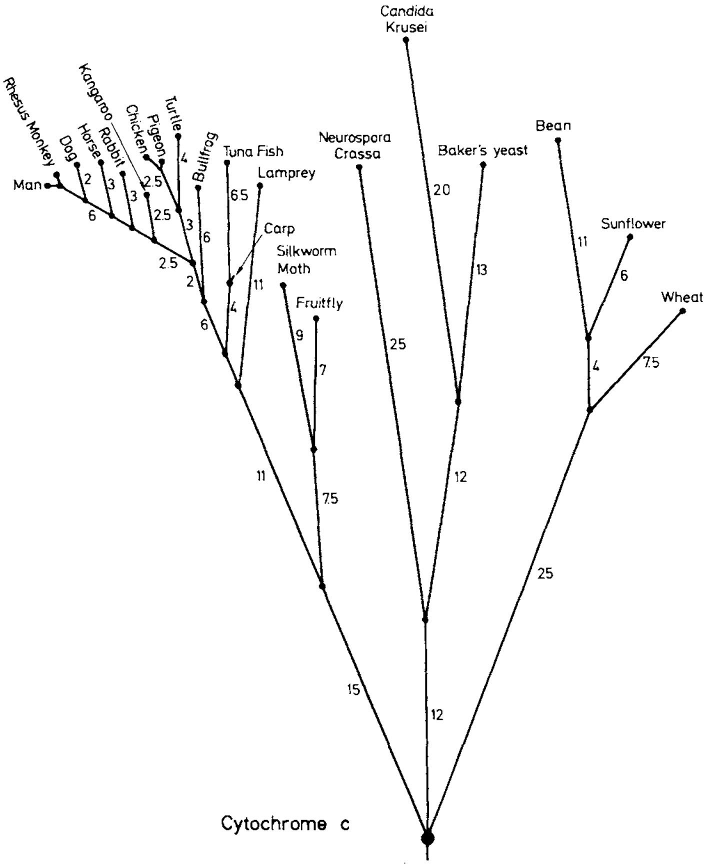


Fig. 4. Phylogenetic tree resulting from a sequence comparison of cytochrome c [10]. The distance reflects clearly the development of eucaryotes. Subtle branching effects among primates are more easily recognised in the haemoglobin sequences (Table 1).

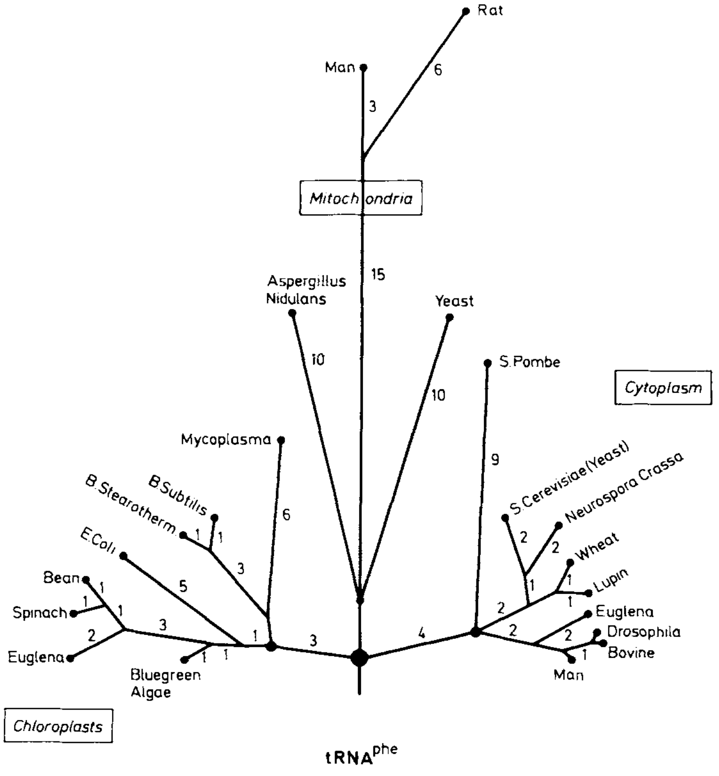


Fig. 5. Phylogenetic tree resulting from a comparison of transfer-RNA (isoacceptor for phenylalanine with the anticodon GAA) [11]. The conservative nature of this molecule conveys particularly clearly the effect of nearness of kin: division into pro- and eucaryotes, branching-off of mitochondria and chloroplasts, fanning-out among the procaryotes. Finer detail is on the other hand hardly visible for nearer kinship (*e.g.* difference from drosophila to man: one base pair).

expressions which he had taken from *Herbert Spencer*, such as "destruction", "struggle for existence" *etc.*, which today are somewhat misleading: they fail to express the passive nature of much of the competition, which indeed Darwin himself did not wish to deny. This is clear in his rejection of *Karl Marx*, who attempted to base his terminology on *Darwin*'s.

Table 1. Percentage differences between haemoglobin β-chains of various primates. Data from "Atlas of Protein Sequence and Structure" [10].

| | Man | Chimpanzee | Gorilla | Gibbon | Baboon | Spider Monkey | Tamarin | Squirrel Monkey | Rhesus Monkey | Japanese Macaque |
|---|---|---|---|---|---|---|---|---|---|---|
| Man | 0 | 0 | 1 | 1 | 5 | 4 | 5 | 6 | 5 | 5 |
| Chimpanzee | 0 | 0 | 1 | 1 | 5 | 4 | 5 | 6 | 5 | 5 |
| Gorilla | 1 | 1 | 0 | 2 | 5 | 5 | 6 | 7 | 5 | 4 |
| Gibbon | 1 | 1 | 2 | 0 | 5 | 3 | 4 | 5 | 4 | 3 |
| Baboon | 5 | 5 | 5 | 5 | 0 | 6 | 11 | 11 | 9 | 8 |
| Spider Monkey | 4 | 4 | 5 | 3 | 6 | 0 | 5 | 4 | 6 | 5 |
| Tamarin | 5 | 5 | 6 | 4 | 11 | 5 | 0 | 5 | 5 | 5 |
| Squirrel Monkey | 6 | 6 | 7 | 5 | 11 | 4 | 5 | 0 | 8 | 7 |
| Rhesus Monkey | 5 | 5 | 5 | 4 | 9 | 6 | 5 | 8 | 0 | 1 |
| Japanese Macaque | 5 | 5 | 4 | 3 | 8 | 5 | 5 | 7 | 1 | 0 |

*Darwin*'s view was that the total number of individuals in a population alters only very slowly in comparison with the rate at which new individuals are produced. This means that, on average, the number of deaths and the number of births are approximately equal. On account of the considerable inherited variation (which *Darwin* under- rather than overestimated), the individuals which are best suited to their environment ("fittest") will have the greatest probability of survival and will produce descendents with better genetic equipment than will the less fit. What the advantage—considered to be purely genetic in origin—consists of, whether it results in an active "struggle for existence" or a passive thinning-out of the less fit individuals, caused by differences in fertility and lifespan, is more or less immaterial. *Darwin* also left open the question of whether evolution takes place exclusively by a natural process of selection, and he was right to do so. Not because he thus left open a back door for purpose-directed evolution in the Lamarckian sense, but simply because he felt that a principle can only ever express a single aspect of reality and not reality *in toto.*

The laying of a quantitative foundation for *Darwin*'s theses had to wait for the population genetics of this century, represented by such names as *John B. S. Haldane*[12], *Ronald A. Fisher*[13] and *Sewall Wright*[14]. This science showed:

1. that natural selection may be derived rigorously—*i. e.*, mathematically—from the properties of populations of living individuals,
2. that various real situations can be described by alternative models which, while not disagreeing with the selection principle, have to take account of further factors, and
3. that the laws of sexual heredity, discovered by *Gregor Mendel*, can be integrated into the theory, but are then of decisive influence, above all in the question of genetic variation.

It is clear that Nature produces apparent deviations from strict "Darwinian" behaviour. An example of this is provided by the so-called neutral mutations. These are alterations in the genetic equipment which result in no advantage or disadvantage for the progeny, and so are selectively "neutral". The Japanese geneticist *Motoo Kimura*[15] has set up a theory of fluctuations, from which it emerges that neutral mutations of this kind can spread through a population and thus cause evolutionary drift which has no selective advantage. He came to the remarkable conclusion that in view of the complexity of the hereditary material of higher organisms the greater part of any alteration is to be attributed to a genetic drift of this kind. There has been controversy over the quantitative importance of this effect—an issue which could be decided by experimental test. Modern genetics has the means to do this. This kind of selection, which is not guided by a selective advantage, is sometimes referred to as "non-Darwinian"[16]. This could leave the impression that *Darwin* regarded his principle as a dogma. Let us read what he himself had to say about it: "Variations neither useful nor injurious would not be affected by natural selection, and would be left either a fluctuating element, as perhaps we see in certain polymorphic species, or would ultimately become fixed, owing to the nature of the organism and the nature of the conditions." This is precisely what the theory of neutral mutations lays down. *Darwin,* unacquainted with the mechanism of sexual recombination of chromosomes, could naturally never have guessed the extent of this process.

We now come to the central question: What **new perception** of Nature was encapsulated in the principle of selection? We do not mean here the actual biological process, with all its complicated superstructure—we want to understand the principle itself. What is it? An axiom, an underivable, fundamental law, to which all living matter is subject, which we simply have to observe and accept? Or is it a heuristic device, which simply describes a pattern of observations, but whose seeming regularity disappears when it is rigorously analysed?

It is neither the one nor the other. The principle of selection turns out to be a law which is rigorously derivable from physical premises.

To illustrate this, let us examine a physico-chemical law with which we are all familiar—the law of mass-action. It governs the distribution of chemical reactants in equilibrium. In thermodynamics, "equilibrium" is characterised by an extremum principle, which in this case means that in a system at constant temperature and pressure, which does not exchange matter with its surroundings (a "closed" system), the Gibbs' free energy tends towards a minimum, and the system is in equilibrium when this minimum is reached. At this point the distribution of reactants and product is determined, exclusively and therefore reproducibly, by the mass-action constant.

The selection principle may be approached in a very similar way. We are interested in the selection of a particular genotype which on the basis of its phenotypic properties may be summed up as "the fittest". The genotype, the genetic information of an organism, is represented by an enormous molecular chain, in which each monomeric subunit (nucleotide) corresponds to a "letter" of the genetic message. Even in the simplest, single-celled organisms, such as the *Coli* bacterium, this message consists of four million nucleotides, corresponding in letters to a 1000-page book. The human genome has three thousand million nucleotides—a respectable "library"! When a genetic message is reproduced, some letters are "read off" wrongly; we call these "mutations". They are the origin of evolutionary progress. Selection thus means two things:

1. The information representing the fittest phenotype has to be chosen, copied many times over, and made into the starting-point for further development.
2. The information for the fittest phenotype has to be stable enough to remain intact until a better mutant arises. In other words, mistakes must not accumulate but must remain below a critical threshold level.

One might formulate the physical problem which is to be solved by way of selection as follows:
What **mechanism** could guarantee the necessary but spontaneous origin of information?

The complexity of living organisms rules out any solution for this problem such as is offered by the law of chemical mass-action. Even a single gene, which encodes one of many thousand functions, has an inconceivably large number of possible arrangements of its elements, even if the total length and overall composition are known. Accumulation of errors could lead from a given sequence to any other one, and if thermodynamic equilibrium were to be reached all possible sequences would appear, with various probabilities. It is easy to estimate that if each possible sequence were represented by one molecule then the volume of the universe would not be sufficient for more than a tiny fraction of the material necessary.

Only selection can circumvent this dilemma. An essential prerequisite for this is the prevention of equilibrium, and this is only possible by continually supplying free energy to the system. In organisms this requirement is met by metabolism.

Natural selection rests on two further prerequisites: self-reproduction and variability. The self-reproduction of molecules in turn presupposes particular structural properties, which are fulfilled, for example, by the nucleic acids. It is these which endow all organisms with the ability to reproduce themselves. Variability is simply a consequence of "blurred" self-reproduction.

These three prerequisites suffice for the deduction of a governing **extremum principle,** valid for "open", self-reproducing systems and leading to selection as a regular feature of the behaviour of matter, appearing under defined conditions[17,18].

Let us define a population (or concentration) variable belonging to a reproductive unit "*i*" ("*i*" can be for example a DNA or RNA molecule, a cell, an organism, *etc.*) as $c_i$, and its proportion in a total population containing n species as $x_i$ $(=c_i/\sum_{k=1}^{n} c_k)$. The rate of variation in time of this component $(\dot{x} \equiv dx/dt)$ is then given by the differential equations

$$\dot{x}_i = (w_{ii} - \bar{E}(t))\,x_i + \sum_{l \neq i} w_{il}\,x_l \tag{1}$$

$$\sum_{k=1}^{n} \dot{c}_k = \bar{E}(t) \sum_{k=1}^{n} c_k - \phi \tag{2}$$

The individual terms have the following meanings:

Diagonal terms: $w_{ii}x_i$ (or $\sum_{k=1}^{n} w_{kk}x_k$) = first-order autocatalytic self-reproduction

Off-diagonal terms: $w_{ij}x_j$ (or $\sum_{l \neq i} w_{il}x_l$) = mutations; i arises through the incorrect reproduction of j or l

Sum term: $\bar{E}(t) = \sum_{k=1}^{n} w_{kk}x_k + \sum_{k=1}^{n} \sum_{l \neq k} w_{kl}x_l$ = average production rate

Flux term $\phi$: this describes regulable fluxes of dilution and wastage

This system of equations for the **"relative"** population variables applies to all possible time-dependent and -independent (stationary) conditions, with or without the imposition of fluxes, as long as the concentrations of the nutrients are kept constant (buffered).

The non-linear system of equations can be transformed into a diagonal form[19,20] and emerges as

$$\dot{y}_i = (\lambda_i - \bar{\lambda}(t))\,y_i \tag{3}$$

where $y_i$ is a composite population variable and $\lambda_i$ its corresponding eigenvalue. The transformation preserves the non-linear term $\bar{E}(t) = \bar{\lambda}(t)$, which can further be represented as the average of all the separate eigenvalues.

Thus the extremum principle emerges directly from the system of differential equations (3). All the population variables $y_s$ for which $\lambda_s < \bar{\lambda}(t)$ have a negative $\dot{y}_s$ value and thus die out, while all $y_g$ with $\lambda_g > \bar{\lambda}(t)$ increase. This however results in a continual displacement of $\bar{\lambda}(t)$, so that fewer and fewer eigenvalues can fulfil the threshold requirement. Finally $\bar{\lambda}(t)$ becomes equal to the highest eigenvalue $\lambda_{max}$.

The extremum principle thus runs:

$$\bar{E}(t) \equiv \bar{\lambda}(t) \rightarrow \lambda_m \tag{4}$$

$$y_m \rightarrow \sum_{k=1}^{n} x_k \tag{5}$$

This results in a self-organisation of the system, in which only that part of the population distribution with the highest $\lambda_m$ value survives. We call this a quasi-species. Second-order perturbation theory shows that the quasi-species selected will be dominated by one or several degenerate "master-types", which possess the highest diagonal term $w_{mm}$ within the distribution. Its proportion in the distribution may be relatively small, and can be calculated to be

$$\frac{x_m}{\sum_{k=1}^{n} x_k} = \frac{Q_m - \sigma_m^{-1}}{1 - \sigma_m^{-1}} \tag{6}$$

Here $Q_m$ is the quality of reproduction ($1 - Q_m$ is the error rate per replicative unit) and $\sigma_m$ the superiority of the master-type, which gives the factor by which the master-type is more efficiently reproduced than its mutational distribution.

In biology we refer to the master-type which is most suited to normal conditions as the wild-type. The target of selection is, however, not the wild-type alone, but a stationary distribution of mutants around it, whose relative frequencies are given by the off-diagonal terms $w_{im}$, divided by the differences between diagonal terms, $w_{mm} - w_{ii}$

$$\frac{x_i}{x_m} = \frac{w_{im}}{w_{mm} - w_{ii}} \tag{7}$$

The concentration ratios are reached independently of whether the system as a whole is growing or is in a stationary state.

The fact that this extremum principle is valid for Darwinian systems leads to the following **consequences:**

1) Selection of a distribution of mutants dominated by the best-fitted variant. This is stable as long (and only as long) as the conditions $\sigma_m > 1$ and $Q_m > \sigma_m^{-1}$ are fulfilled.
2) Evolution by selection of newly-appearing mutants which on account of a selective advantage violate the condition for stability $\sigma_m > 1$ and thus make the previous distribution unstable.
3) The second (and stronger) condition for stability, $Q_m > \sigma_m^{-1}$, can only be fulfilled by limiting the information content. If the master-type *m* is composed of $\nu_m$ units of information (*e.g.* nucleotides in a master sequence) and the average quality of reproduction is $\bar{q}_m$ ($1 - \bar{q}_m$ = average error rate per symbol), than the overall quality of a reproductive unit with $\nu_m$ symbols is given by $Q_m = \bar{q}_m^{\nu_m}$, where $Q_m$ is the probability that the entire unit will be copied correctly. For $1 - \bar{q}_m \ll 1$, since $Q_m > \sigma_m^{-1}$, we can write

$$\nu_m \leq \frac{\ln \sigma_m}{1 - \bar{q}_m} \tag{8}$$

The error thresholds applicable to biological evolution can be measured experimentally and are summarised in Table 2.

Table 2. Experimentally determined information thresholds of biological evolution.

| Process | Measured on | with Error rate | Upper limit of number of symbols (nucleotides) | Comparable linguistic unit |
|---|---|---|---|---|
| Base pairing (enzyme-free) | AU-polymers | 1:10 | 10 | syllable - word |
| | GC-polymers | 1:100 | 100 | word - sentence |
| Enzymic RNA replication | RNA viruses | 1:10000 | 10000 | essay |
| Enzymic DNA replication | procaryotes | 1:10000000 | 10000000 | book |
| Recombinative Reproduction | eucaryotes | 1:3000000000 | 3000000000 | library (containing ~ 10000 volumes) |

The two processes: selection as the stabilisation of a particular distrubution and evolution as the establishment of one new distribution after another (destabilisation of old and stabilisation of new distributions) are results of an "inner propensity", just as is the attainment of chemical equilibrium in a closed system. They can therefore be reproduced and quantitatively tested in the laboratory. The results of such experiments, using distributions of RNA molecules[21,22] or of viruses[23,24] in experiments *in vivo* and *in vitro*, yield information about the composition of the distribution of mutants, about the proportion of the "fittest" individual components and about the available storage capacity for information.

Thus we have the physical content of *Darwin*'s principle, a principle which shows how complex structures, with properties adapted to their environment, arise in a seemingly goal-directed way—although the goal is only defined by means of the process of evolution. This is equally true for organisms, for cells and for replicating molecules—and even finds its use in technology. *Rechenberg*[25] has invented a procedure for building complex structures suited to particular tasks. It emerges (and can also be shown mathematically) that for complex systems involving many parameters a succession of mutation and selection of the best-suited structure reaches the target more quickly than systematic, goal-directed optimisation.

Although *Darwin* cannot have foreseen such detailed extensions of his concept of selection and evolution, there is no doubt that he recognised its general implications. Thus he writes to *Nathaniel Wallich* in 1881:

"You expressed quite correctly my views where you said that I had intentionally left the question of the Origin of Life uncanvassed as being altogether *ultra vires* in the present state of our knowledge, and that I dealt only with the manner of succession. I have met with no evidence that seems in the least trustworthy, in favour of so-called Spontaneous Generation. I believe that I have somewhere said (but cannot find the passage) that the principle of continuity renders it probable that the principle of life will hereafter be shown to be a part, or consequence, of some general law."

It is clear that selection and evolution on a molecular scale, based on the self-reproduction of nucleic acids, is a **necessary** condition for the genesis of life. Does this further provide a **sufficient** explanation for the molecular organisation of the living cell, of which we now know so much?

The answer is: no.

The Darwinian principle contains the definition of its own limitation, which appears in the error threshold in equation (8). The reproduction of the original sequences was limited in its accuracy by the molecular forces of base-pairing. Even in the case of the stable G-C pair the length of a reproducible sequence is less than 100 nucleotides. This has been confirmed by measurements on model systems (cf. Table 2)[26,27]. Such an "information crisis" could only be overcome by the evolution of a mechanism of enzymic reproduction. Evolution requires the storage of information in reproducible sequences. To make the information available, a process of decoding is necessary. However, the simplest decoding equipment requires much more information than could ever have been accommodated in one of the primordial sequences[28]. Thus a further necessary condition was the functional integration of various replicative units. The various carriers of information could indeed all have emerged from a single, selected distribution of mutants, but they then had to adapt to their various functions. *Darwin*'s principle is not sufficient to account for this, for the following conditions must all have been fulfilled simultaneously:

1) Each replicative unit within the functionally integrated system must remain in continuous competition with its own mutants, and therefore work so well that no information is lost from one generation to another.
2) Competition between the replicative units (master sequences) belonging to the functional system must be abolished and replaced by a mutual regulation of concentration.
3) The functional unit must as a whole be able to compete successfully with alternative units.

Theory[18] tells us that a circular, closed network of coupled reactions—we call it a hypercycle—is the only system capable of fulfilling these three conditions simultaneously and thus of overcoming the **information crisis.**

A further problem arises in connection with the evolution of a translation apparatus. Let us call it the **Genotype-Phenotype-Dichotomy.** The information, which is later selected, resides in the genotype. However, its selection is based on the phenotypic properties displayed by the products of its translation. These must interact selectively with their "own" genotype, or otherwise the evolution of phenotypic properties will not be possible.

As an example, let us consider what happens when a bacterial cell is infected by RNA phage. In order to assure preferential reproduction of its genome, the virus codes for a protein which combines with proteins of the host cell to produce an RNA replicase; this recognises and reproduces the viral genome but not any of the RNA sequences of the host cell. Here again we encounter the hyperbolic growth law mentioned at the beginning. The rate of reproduction is on the one hand proportional to the number of templates (copies of the viral genome) and on the other to the number of functioning replicase units, which is itself proportional to the number of copies of the viral genome, since the replicase is a decoding product of the genome. The resulting quadratic, self-catalytic rate law gives rise to hyperbolic growth.

The origin of the translation apparatus poses problems of this kind, soluble only by postulating both hypercyclic organisation and compartmentation of the functionally integrated system[29]. The growth laws resulting from these necessitated a once-and-for-all decision on the organisation of the translation apparatus and the structure of the genetic code. The result of this decision has been binding on all living beings ever since.

If on the one hand *Darwin*'s principle is insufficient to account for the origin of life, it is on the other hand an essential premise for consequences whose importance reaches far **beyond the borders of biology.** Wherever there is natural selection, the result is self-organisation into sharply-differentiated, discrete states instead of the broad Gaussian distribution to which we are used in stochastic systems at thermodynamic equilibrium. The principle of natural selection could thus explain why sharply-defined states occur at all, instead of continua: why there is "something" and not "everything". It would be interesting to look for such applications in elementary-particle physics[30], neurobiology[31,32] or sociobiology; this means looking for the prerequisites of such behaviour in each case.

To end with, a comment on the many **misinterpretations** to which the Darwinian principle has time and again fallen victim. Physical principles indeed lie behind real processes, but reality, overspread by a myriad of extraneous influences, cannot be "reduced" to a single principle. Inattention to the difference between Principle and Reality is the sole cause of the fruitless wrangling between the so-called Holists and Reductionists.

Consider the wonderfully logical, self-consistent edifice of equilibrium thermodynamics. Its principles were developed in connection with a theory of the efficiency of the steam engine. None the less, one cannot even build a steam engine with their help, to say nothing of setting it in motion. To do this one has first to take the machine well away from a state of equilibrium.

History testifies to the misuses which have been made of *Darwin*'s doctrine outside of biological science. In biology, in any case, the idea of "Darwinism" is inappropriate. A law of Nature is not a *Weltanschauung*. If the requirements are fulfilled, the consequences will take place—predictably and inevitably. It is after all not customary to call an astronomer a "Newtonist".

Finally, the question **"Creation or Evolution?".** A believer in creation cannot evade including the natural laws in the creature. A God who contradicted His own laws would be contradicting Himself. So evolution, for the believer, is the mechanism of creation. God has not forbidden us to consider and to fathom His works. *Darwin* doing this, conquered a fresh summit of discovery.

*I am particularly grateful to Ruthild Winkler-Oswatitsch for her assistance in the drafting of the manuscript and the illustrations, and to Paul Woolley for his excellent translation of my paper into English.*

Received: February 9th, 1981 [A 359 IE]
German version: Angew. Chem. 93, 221 (1981)

---

[1] *L. Boltzmann:* "Der zweite Hauptsatz der mechanischen Wärmetheorie". Populäre Schriften, p. 28, J. A. Barth, Leipzig 1905.
[2] *Th. R. Malthus:* "Essay on the Principle of Population as it Affects the Future Improvement of Society, with Remarks on the Speculations of Mr. Godwin, Mr. Condorcet, and Other Writers" (1798).
[3] *A. R. Wallace:* "On the Tendency of Varieties to Depart Indefinitely from the Original Type". Manuscript sent to *Darwin* on March 9th, 1858, and read, together with *Darwin's* paper, to the Linnean Society of London on July 1st, 1858.
[4] *Ch. Darwin:* "The Origin of Species by Means of Natural Selection or the Preservation of Favoured Races in the Struggle for Life". J. Murray, London 1859.
[5] *A. C. Brackman:* "A Delicate Arrangement, The Strange Case of Charles Darwin and Alfred Russel Wallace". Times Books, New York 1980.
[6] *Ch. Darwin:* "The Foundations of the Origins of Species. Two Essays written in 1842 and 1844 by Charles Darwin". Cambridge 1904.
[7] *M. Eigen, R. Winkler-Oswatitsch:* "Das Spiel. Naturgesetze steuern den Zufall". Piper Verlag, München 1975. English Translation: "Rules of the Game". Knopf, New York 1981.
[8] *Ch. Darwin:* "The Origin of Species". Collier MacMillan, London 1962 containing a Foreword by G. G. Simpson and "An Historical Sketch" by *Charles Darwin.*
[9] *J. B. de Lamarck:* "Philosophie Zoologique". Paris 1809.
[10] *M. O. Dayhoff:* "Atlas of Protein Sequence and Structure", Vol. 5, p. 8 and D55. National Biomedical Research Foundation, Washington 1972.
[11] *M. Eigen, R. Winkler-Oswatitsch:* "Transfer RNA, The Early Adaptor". Naturwissenschaften *68* (1981), in press.
[12] *J. B. S. Haldane:* "The Causes of Evolution". Longmans, Green and Co., London 1932; Cornell University Press, Ithaca, N. Y. 1966.
[13] *R. A. Fisher:* "The Genetical Theory of Natural Selection". Clarendon Press, Oxford 1930.
[14] *S. Wright:* "Evolution in Mendelian Populations". Genetics *16*, 97 (1931).

[15] *M. Kimura, T. Ohta:* "Theoretical Aspects of Population Genetics". Princeton University Press, Princeton, N. Y. 1971.

[16] *J. L. King, T. H. Jukes:* "Non-Darwinian Evolution, Random Fixation of Selectively Neutral Mutations". Science *164*, 788 (1969).

[17] *M. Eigen:* "Selforganization of Matter and the Evolution of Biological Macromolecules". Naturwissenschaften *58*, 465 (1971).

[18] *M. Eigen, P. Schuster:* "The Hypercycle. A Principle of Natural Selforganization". Springer-Verlag, Berlin 1979.

[19] *B. L. Jones, R. H. Enns, S. S. Rangnekar:* "On the Theory of Selection of Coupled Macromolecular Systems". Bull. Math. Biol. *38*, 15 (1976).

[20] *C. J. Thompson, J. L. McBride:* "On Eigen's Theory of the Self-Organization of Matter and the Evolution of Biological Macromolecules". Math. Biosci. *21*, 127 (1974).

[21] *Ch. Biebricher, M. Eigen, R. Luce:* "Product Analysis of RNA Generated *de novo* by $Q_\beta$-Replicase". J. Mol. Biol. (1981), in press.

[22] *Ch. Biebricher, M. Eigen, R. Luce:* "Kinetic Analysis of Template-Instructed and *de novo* RNA Synthesis by $Q_\beta$-Replicase". J. Mol. Biol. (1981), in press.

[23] *E. Domingo, R. A. Flavell, C. Weissmann:* "In Vitro Site-Directed Mutagenesis, Generation and Properties of an Infectious Extracistronic Mutant of Bacteriophage $Q_\beta$". Gene *1*, 3 (1976).

[24] *E. Batschelet, E. Domingo, C. Weissmann:* "The Properties of Revertant and Mutant Phage in a Growing Population as a Function of Mutation and Growth Rate". Gene *1*, 27 (1976).

[25] *I. Rechenberg:* "Evolutionsstrategie. Optimierung technischer Systeme nach Prinzipien der biologischen Evolution". Fromman Verlag, Stuttgart-Bad Cannstatt 1973.

[26] *D. Pörschke:* "Elementary Steps of Base Recognition and Helix-Coil Transitions in Nucleic Acids". Mol. Biol. Biochem. Biophys. *24*, 191 (1977).

[27] *R. Lohrmann, P. K. Bridson, L. E. Orgel:* "Efficient Metal-Ion Catalyzed Template-Directed Oligonucleotide Synthesis". Science *208*, 1464 (1980).

[28] *M. Eigen, R. Winkler-Oswatitsch:* "Transfer RNA, An Early Gene?". Naturwissenschaften *68* (1981), in press.

[29] *M. Eigen, W. C. Gardiner Jr., P. Schuster, R. Winkler-Oswatitsch:* "The Origin of Genetic Information". Sci. Am. *244*, April (1981).

[30] *H. J. Queisser*, personal communication (Lecture at the 16th Winter Seminar, Klosters, 1981).

[31] *J. D. Cowan:* "Symmetry-Breaking in Embryology and in Neurobiology" in *B. Gruber, B. R. S. Millman:* "Symmetry in Sciences". Plenum Press, New York 1980.

[32] *Ch. von der Malsburg:* "Development of Ocularity Domains and Growth Behaviour of Axon Terminals". Biol. Cybernet. *32*, 49 (1979).

---

# Biliproteins

## By Hugo Scheer[*]

*Dedicated to Professor Hans-Herloff Inhoffen on the occasion of his 75th birthday*

Biliproteins, covalently bonded complexes of proteins and bile pigments, serve as light-harvesting pigments in photosynthesis and light-sensory pigments of photosynthetic organisms. Recent developments in the biochemistry and biophysics of these pigments are reviewed and an attempt is made to describe their functions of light-harvesting and of information transduction on a molecular level.

## 1. Introduction

Cyanobacteria, red algae, and cryptophytes contain large quantities of blue and red pigments, which essentially determine the color of these organisms and may amount to 40% of the protein[1]. *Engelmann*[2] was the first to relate these pigments to photosynthesis; *Haxo*[3], *Emerson*[4], and *Gantt*[5], among others, recognized their function as light-harvesting pigments, mainly of photosystem II. In 1928, *Lemberg*[6] demonstrated that they contain bile-pigment chromophores; in accord with their origin and composition, these chromoproteins are thus called *phycobiliproteins.*

Pigments of this structure, but having completely different functions, exist in many other organisms. The most important compound of this group is *phytochrome.* This sensory pigment of green plants was discovered in 1945 by action-spectroscopy[7]. Owing to its instability and low concentration, it was first enriched and characterized by absorption spectroscopy as late as 1959[8]. Phytochrome is a photoreversibly-photochromic pigment. The position of the equilibrium between its two forms (R- and FR-form), the total concentration, and other factors are fundamental in regulating the development of plants[9]. Another group of photoreversibly-photochromic pigments, the phycochromes, were isolated from various cyanobacteria[10], and at least one phycochrome was also related to developmental processes like chromatic adaption[1,11,12].

These three groups of pigments are referred to as biliproteins (Table 1). This contribution deals with recent developments in their biochemistry and biophysics. Since the last comprehensive survey in this field[13a] several different aspects have been reviewed[1,5,9,13-25,310]. It should be mentioned that besides these genuine biliproteins, there also exist bile pigment-protein aggregates lacking a covalent bond between both component parts. These include the physiologically important complex of bilirubin, which is only sparingly soluble in water, with serum albumin[26], and an increasing number of invertebrate pigments[13,27-30]. A selection of them is included in Table 1.

---

[*] Dr. H. Scheer
Botanisches Institut der Universität
Menzinger Strasse 67, D-8000 München 19 (Germany)

*0570-0833/81/0303-0241 $ 02.50/0*

Table 1. Natural occurrence and functions of biliproteins. The first three groups of pigments are the subject of this report.

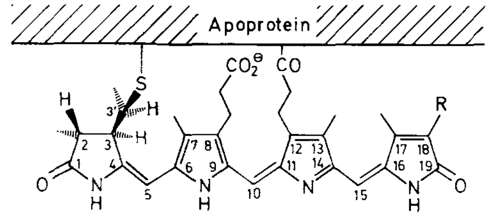
| Pigment | Occurrence | Function | Chromophore structure | Ref. |
|---|---|---|---|---|
| Phycobiliproteins (*e.g.* phycocyanin (PC) allophycocyanin (APC) phycoerythrin (PE)) | Cyanobacteria<br>Red algae<br>Cryptophytes | Antenna pigments of photosynthesis | Phycocyanobilin *(1a)*, phycoerythrobilin *(2) etc.* | see Text |
| Phytochrome | Higher green plants, certain algae, fungi (?), mosses, red algae (?) | Reaction-center pigments of photomorphogenesis | *(1b)*, *(3)* [a] | see Text |
| Phycochromes | Cyanobacteria, red algae | Possibly reaction center pigments of photomorphogenesis and chromatic adaption ("adaptachromes") | *(1a)* (?) | [1, 10–12] |
| Bilirubin-serum-albumin complexes | Vertebrates | Water-soluble transport form of bilirubin | — | [26] |
| Aplysioviolin | *Aplysia* (sea hare) | Defense excretion | Monoester of *(5)* | [29] |
| Turboverdin | *Turbo cornutus* (mussel) | Protective coloration (?) | [18-Ethyl]-[3-(2-hydroxyethyl)]-*(19)*, R=H | [30] |
| Pterobilin | Lepidoptera | Protective coloration (?) | IXγ-Isomer of *(19)*, R=H | [27] |
| Phorcabilins | Lepidoptera | Protective coloration (?) | Extended derivatives of pterobilin, similar to *(31)* | [27] |

[a] The substituents R, R′ und R″ in *(3)* suggest that the double bond between C-4 and C-5 present in $P_r$ is no longer noticeable in the absorption spectrum (see Section 2.3).

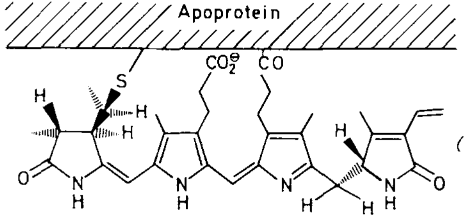
## 2. Structure of Chromophores

The two major chromophores of phycobiliproteins are *(1a)* (phycocyanobilin) and *(2)* (phycoerythrobilin)[*]. (In the formulas the bond to the protein is indicated.) *(1a)* is the blue chromophore of phycocyanins and allophycocyanins, *(2)* is the red chromophore of phycoerythrins. One or the other of them exists in each of the known phycobiliproteins, while R-phycocyanin (R-PC)[**] contains both. In addition, there occur several other chromophores with hitherto unknown structures, *e.g.* a phycourobilin in the γ-chain of B-phycoerythrin (B-PE)[**][31], the red chromophore in the α-chain of phycoerythrocyanin[32], the third chromophore ($P_{590}$) of PC from a *Hemiselmis species*[33] and the blue chromophore of PC from *Chroomonas*[34].

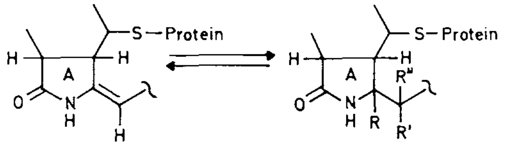
Strictly speaking, the structures *(1a)* and *(2)* have so far been unequivocally determined on only a few phycobiliproteins. Generally, they are identified by chromatographic comparison of the cleaved chromophores and spectroscopic investigations on denaturated biliproteins (see Section 2.3).



*(1a)*, R = $C_2H_5$ *(1b)*, R = $C_2H_3$



*(2)*



*(1b)* *(3)*

The chromophore *(1b)* of the R-form of phytochrome ($P_r$) is very similar to phycocyanobilin *(1a)*[35–38]. Instead of the ethyl-group it contains a vinyl-group at C-18[37,38], but the absolute configurations at C-2, C-3 and C-3′ are identical[39]. The structure of the $P_{fr}$-chromophore is still unclear; however, it is known that it contains a shorter conjugation-system than the $P_r$ chromophore[35] but the same β-pyrrolic substituents[37]. Comparative investigations on free bile pigments have currently led to two models which would account for the properties of the $P_{fr}$-chromophore. It could be a geometrical (*Z,E*)-isomer[40] or a substitution product of the $P_r$-chromophore[41] (see Section 2.4).

### 2.1. Cleavage of Chromophores

For a long time elucidation of the structures of biliprotein-chromophores was complicated by their covalent bonds to

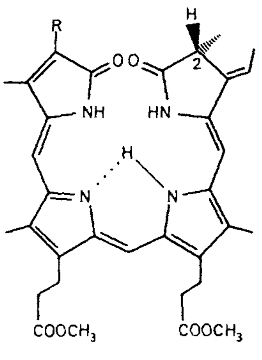
---

[*] The nomenclature of the bile-pigments has been modified several times in recent years. Four systems were and are used concomitantly. Trivial names and the numbering system of *H. Fischer*, which correlates the bile pigments with the porphyrins, are mainly used in the older literature [for example *(19)* = biliverdin IXα]. The numbering system, still used today and shown in formulas *(1)* and *(23)*, results from the first attempt of a rational nomenclature. It allows no direct correlation between the C-atoms of macrocyclic tetrapyrroles, and the linear tetrapyrroles derived therefrom. Apart from using a certain number of trivial-names, it is based on the completely saturated "bilan". An exchange-nomenclature is possible for both systems: A new substituent replacing the original one of a parent compound is placed in square brackets [*viz.* [*(18)*-vinyl]-*(1a)* = *(1b)*]. The nomenclature used in this article corresponds to the VIth Memorandum of the IUPAC Nomenclature Commission. Aside from a limited number of trivial-names [*e.g.* *(19)* = biliverdin] it is based on bilin which, ***in natural bile pigments***, contains the maximum number of non-cumulated double bonds [cf. *R. Bonnett*, in [24a], Vol. 1, 1978, p. 1; example: *(23)* = 2,3,7,8,12,13,17,18-octaethyl-2,3-dihydro-1,19[21*H*,24*H*]-bilindione]. The nomenclature recently proposed by the IUPAC (Pure Appl. Chem. *51*, 2251 (1979)) is similar.

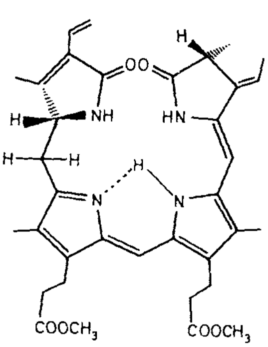
[**] Abbreviations: PC = phycocyanin, APC = allophycocyanin, PE = phycoerythrin, $P_r$, $P_{fr}$ = phytochrome in the R- or FR-form (see Sections 4.3 and 5.2). Prefixes indicate the parent organisms: C = cyanobacteria, R = red alga, B = *Bangiales* (an order of red alga), K = cryptophytes.

the proteins, which preclude a cleavage without chemical modification. Depending on the conditions of cleavage, different phycobilins result from one and the same pigment, so that the nomenclature became very complex (cf. [13,22,24]).

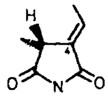
The best characterized products are the ethylidenebilins *(4a)* and *(5)*, which are formed as main products on treatment of the corresponding biliproteins with the chromophores *(1a)* and *(2)*, respectively, in refluxing methanol[42] or long chain alcohols[43], as well as by treatment with HBr/trifluoroacetic acid (TFA)[44]. The cleavage proceeds by stereoselective elimination of the C-3-thio ether[45]; in *(2)* and/or *(5)* the asymmetric C-16 can epimerize at the same time[46,47]. The structures, suggested originally from $^1$H-NMR and MS data[48-51] and from chromic acid degradation[13,52,53], have been confirmed by total syntheses[46,54].



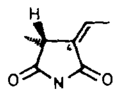
*(4a)*, R = $C_2H_5$
*(4b)*, R = $C_2H_3$



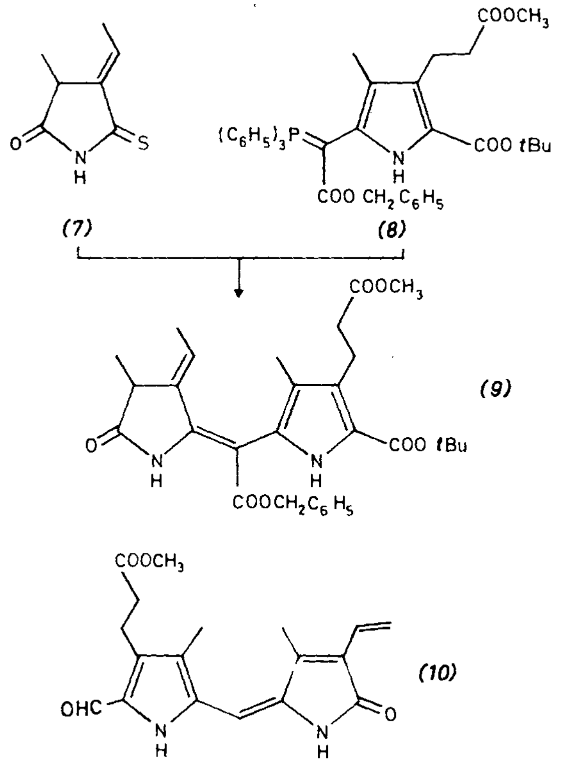
*(5)*



*(6a)*



*(6b)*

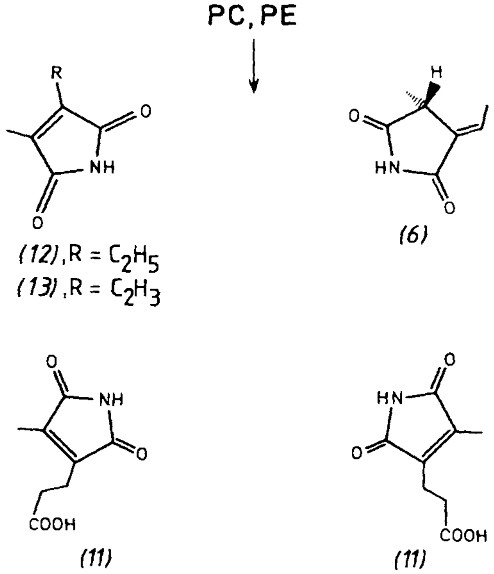


Scheme 1.

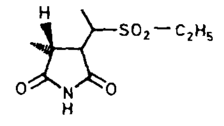
The key reaction in the synthesis is the regioselective coupling of rings A and B, which is possible in good yields by condensation of the monothioimide *(7)* with the pyrrole ylide *(8)*; condensation of the product *(9)* with the CD-fragment *(10)* yields *(4b)* (Scheme 1). For thermolabile substituents[54], sulfur-contraction[54a] can be used instead. By the first procedure the 18-vinylbilindione *(4b)* (= "P$_r$-bilin") was obtained[38]. It could be correlated with *(1b)* by treatment of the latter with HBr/TFA[55]. The stereochemistry of *(4a)* and *(5)* at C-2 was established by chromic acid degradation to the imide *(6)* with known absolute (4*R*)-configuration[56], while that of *(5)* at C-16 was established by asymmetric synthesis and correlation with (4*R*,16*R*)-urobilin[46,57].

## 2.2. Degradation Reactions of Biliproteins

On oxidation with chromic acid, tetrapyrroles are degraded to cyclic imides possessing (at least in principle) the same β-pyrrolic substituents. This method, originally introduced by *H. Fischer*, has in the meantime been improved several times and standardized, and has especially been applied to biliproteins by *Rüdiger et al.*[13,53]. The "hydrolytic" chromic acid degradation of phycocyanin (PC) at 100 °C yields the three imides *(6)*, *(11)* and *(12)*, while that of phycoerythrin (PE) and P$_r$[37] affords the imides *(6)*, *(11)* and *(13)*, the latter of which readily decomposes under the reaction conditions. On oxidation at ambient temperatures, no *(6)* is formed, and *(11)* can only be extracted in about 50% yield, thus indicating protein bonding to the respective rings[13].



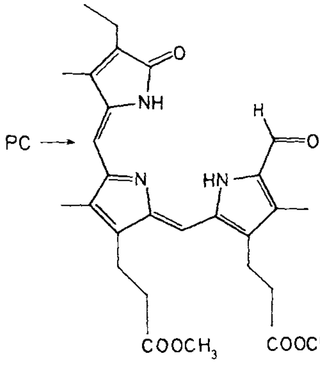
Under these conditions, the degradation of the tetrapyrrole is accompanied by oxidation of the thio ether to sulfone *(14)*, which eliminates —SO$_2$—C$_2$H$_5$ to give *(6)*[58] in the presence of aqueous ammonia. This reaction sequence not only demonstrates the protein-bond of ring A, it is also ste-



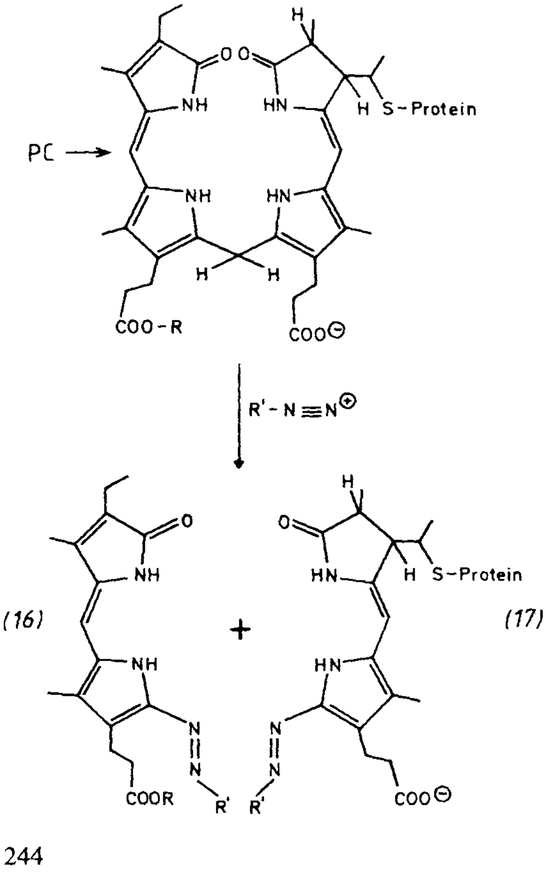
*(14)*

reoselective[45,58,59] and leads, with the well-known *4R,E*-configuration of the imide *(6a)*[56], to the *2R,3R;3'R*-configuration of *(1a)*, *(1b)*, *(2)* and *(3)*. A possible second binding site[13] is still controversial[22,60-65].

During chromic acid degradation the information concerning α-pyrrolic and methine-substituents is lost and, *e.g.*, hydrolysis of the β-pyrrolic substituents cannot be excluded. The milder degradation procedure with chromate yields imides of the terminal rings, whereas the inner ones yield pyrroledicarbaldehydes[13,53]. Thus, it is possible to differentiate, *e.g.*, between isomeric biliverdins, and to assign the IXα-type substitution to *(1)*-*(5)*. A recently developed milder method of oxidation enables regioselective cleavage of biliprotein chromophores like *(1a)* at the methine bridge next to ring A, to give formyltripyrrinones. The method is specific for A-dihydrobilindiones[66,67]. Thus, tripyrrinone *(15)* was obtained in this way from PC. Another selective cleavage reaction, in this case however between rings B and C, is the diazo reaction[68]. This reaction, important in the medical analysis of bilirubin[69], can be applied to the higher oxidized bilindiones present in the biliproteins, only after a pretreatment[70]. The protein first has to be unfolded by addition of urea, and then the central methine bridge of the chromophores has to be reduced by $NaBH_4$. The complete reaction sequence can be carried out under very mild conditions (4 °C, pH = 7). The fragments *(16)* and *(17)* were obtained from PC. *(17)* confirms again the binding of ring A to the protein; both of the last mentioned reactions also indicate the existence of a second bond at ring C, at least in PC of *Spirulina Platensis*, used in these studies. The proportion of free, extractable *(16)* is increased after hydrolytical pre-treatment; *(15)* is only obtainable in this way.



*(15)*

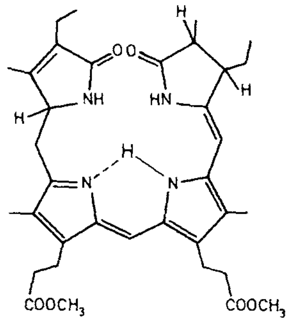


*(16)*

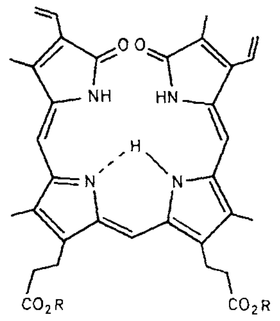
*(17)*

## 2.3. Spectroscopy of Denatured Pigments

A sensitive, non-destructive method for the analysis of biliprotein chromophores is UV-VIS absorption spectroscopy. In the native pigments the spectral properties are strongly dependent on the protein environment (see Section 3), but the non-covalent interactions responsible for these effects are decoupled by complete unfolding using urea, guanidinium chloride, or heat. Although still covalently bound to the protein, the chromophores can be correlated with free bile pigments of known structure. The identification is improved by measuring the free bases as well as the cations, anions, and metal-complexes; for an exact characterization the most suitable are cations and zinc-complexes[35,36,61,71,72]. The method has also been successfully applied for the quantitative determination of the number of chromophores (Table 3)[61,72]; and by acid-base titration the pK-values of protonation and deprotonation are available as additional important parameters[35,36].



*(18)*



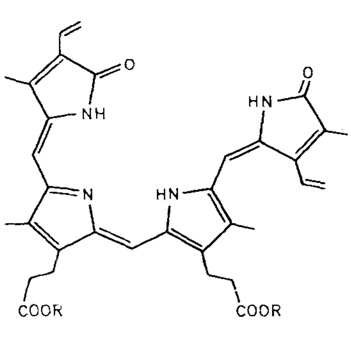
*(19)*

Denaturated PE is spectroscopically very similar to *(18)*; it contains the rhodin-chromophore *(2)*[71]. Denaturated PC and $P_r$ absorb at longer wavelengths than *(18)*, but at shorter wavelengths than bilindiones such as *(19)*. The spectroscopic similarities to *(23)* indicate the 2,3-dihydrobilindione conjugation system for the chromophores of both pigments. The 18-vinyl group of *(1b)* leads to a small red-shift of the absorption as compared to pigments containing *(1a)*[35]. At pH ≤ 5.2 denaturated $P_{fr}$ has an absorption maximum at 610 nm; thus, in contrast to native phytochrome the denaturated $P_{fr}$ absorbs at *shorter wavelengths* than denaturated $P_r$ under the same conditions ($\lambda_{max}^{cation}$ = 660 nm). Therefore, $P_{fr}$ has a shorter conjugation system than $P_r$[35]. Analogous results have been obtained when proteolytic digestion is used instead for the uncoupling of the chromophore[55]. The A-dihydrobilindione structure of the chromophores *(1a)* and *(1b)* and the thioether-bond have recently been proved, too, by NMR spectroscopy of the respective bilipeptides[38,65]. This method also afforded independent proof of the presence of the 18-vinyl group in *(1b)*[38].

### 2.4. Reactivity of Chromophores

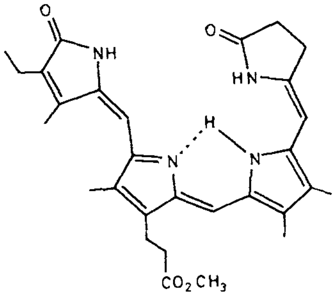
The different spectra of both forms of denaturated phytochrome ($P_{fr}$ and $P_r$) demonstrate that the chromophores have different molecular structures. Conformational[73] changes, protonation-deprotonation[74] and the like, can thus be excluded as the *sole* reactions during phytochrome-transformation, and photochemical reactions gain a special interest. The primary reaction of the phytochrome system is the photochemical transformation of $P_r$ into $P_{fr}$, or *vice versa.* The reaction has several spectroscopically well defined intermediates, which are different for the forward and back reactions, respectively. The structures of the intermediates are still unknown, but the results of flash[75-78] and of low-temperature spectroscopy[77,79-82] as well as of dehydration experiments[82-84] have shown, that only the first step(s) are photochemical one(s), followed by dark-reactions (cf. [18]). Owing to the formal analogy with the reactions of rhodopsin[85], an analogous nomenclature[84] has been used.

In the context of these results, photochemical reactions of free bile pigments[86] and especially of bilindiones related to the $P_r$-chromophore *(1b)* were investigated. From the criteria, determined by the natural system, it should be possible to obtain some evidence regarding the structure of $P_{fr}$, the reaction pathway, and the primary signal of the phytochrome system. There exist two well known photochemical reactions for the conversion $P_r \rightarrow P_{fr}$ which meet most criteria: 1. geometrical isomerization at the double-bond between C-4 and C-5 or C-15 and C-16; 2. oxidative substitution at the C-5 methine bridge. It has been known for some time that dipyrromethenones form stable geometric (*Z*,*E*)-isomers which are in photochemical equilibrium[87,88]. Photochemical studies on pterobilin ("biliverdin IXγ") gave first indications, that corresponding isomers also exist in the case of bilindiones[27]. The isomerization reactions have been investigated systematically by *Falk et al.* with partial structures and integral bile pigments. They could show that bilindiones isomerize at one or at both terminal methine bridges and they have isolated and characterized the resulting products, like *(20)*[40,88,89]. Starting with an *E*-configurated formylpyrromethenone *Gossauer et al.*[90] recently also achieved the total synthesis of (*E*,*Z*,*Z*)-bilindiones. In comparison to the (*Z*,*Z*,*Z*)-educts, the absorption maxima are displaced to shorter wavelengths, *e.g.* to regions expected for a $P_{fr}$-chromophore model. This shift has been rationalized in terms of a simultaneous change of the configuration at the double bond between C-4 and C-5 in *(20)* and of the conformation of the neighboring single bond between C-5 and C-6. By this mechanism the *E*-configurated double bond is partially uncoupled from the remaining π-system[91]. For the thermal reisomerization $\Delta G^0 = -20$ kJ/mol and $\Delta H^{\neq} = 105$ kJ/mol were determined[92]. Non-symmetrically substituted bilindiones yield two (*E*,*Z*,*Z*)-isomers[40]. A regioselective isomerization is observed with less symmetrical educts[93].

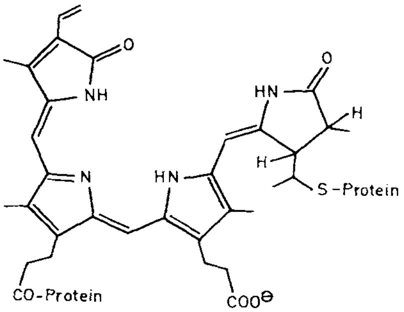


*(20)*

As a consequence of the hydrated ring A—and additionally of the 18-vinyl group in the case of $P_r$ [*(1b)*]—the chromophores of biliproteins are perturbed from symmetry. Ramachandran calculations indicate a preferred isomerization of the $\Delta^4$-bond next to the hydrogenated ring for steric reasons, thus products of the violin spectral type are expected[94]. This assumption has recently been confirmed experimentally[90b]. $\Delta^{15}$-*E*, but not $\Delta^4$-*E*-configurated 2,3 dihydrobilindiones are accessible by total synthesis, the former having a rhodin-type spectrum due to uncoupling of ring D[90b]. A violin-type spectrum is then expected for the hypothetical, less stable $\Delta^4$-*E*-isomer.

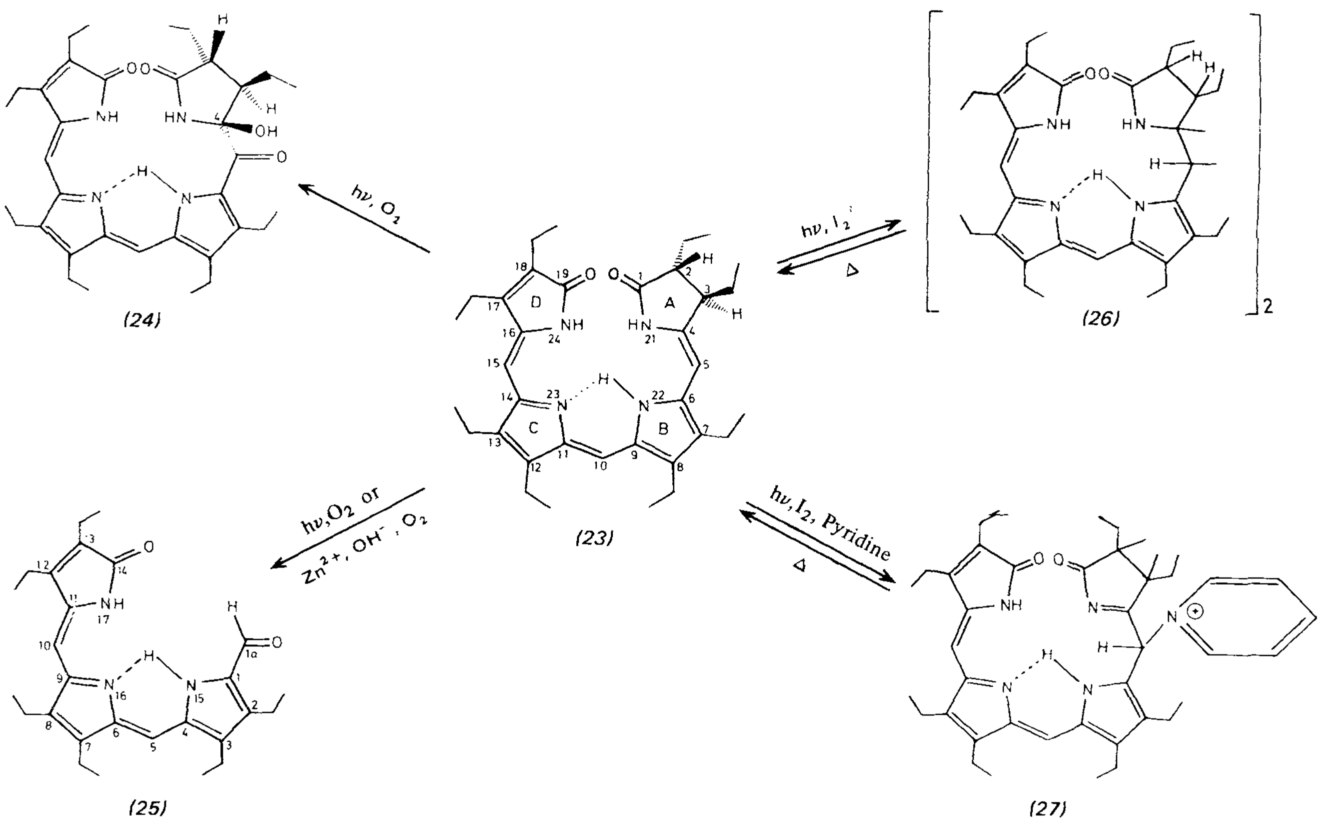


*(21)*



*(22)*

The hypothetical (*E*,*Z*,*Z*)-isomer of *(1b)* [cf. *(22)*] would be spectroscopically comparable with the $P_{fr}$-chromophore. The reaction mechanism is as yet only difficultly reconcilable with the properties of phytochrome. The photoisomerization of bilindiones does not proceed directly, but rather *via* intermediate rubinoid products formed in a dark reaction. Due to their low electron density at C-10[95], the bilindiones reversibly add nucleophiles[89b,96-99] and the yellow pigments thus formed are the substrates proper for isomerization[89b]. In accord with their absorption maximum at 450 nm, blue light is especially effective for isomerization[89b], whereas the action-spectrum of the $P_r \rightarrow P_{fr}$ transformation has its maximum at 660 nm in the red spectral region, the absorption-



Scheme 2.

maximum of the $P_r$-chromophore. The mechanism of reaction is, however, very dependent on the substrate structure, and direct photochemical reactions basically seem to be possible in all cases in which the geometry of the tetrapyrrole skeleton differs from the flat uniform helix. Examples are *N*-alkylated bilindiones[93] and non-(*Z,Z,Z*)-isomers[92]. It still remains open, how the asymmetry of the natural chromophores and their protein environment can affect the course of reaction.

The second model reaction for the $P_r \rightarrow P_{fr}$ transformation is a photochemical oxidation of the $P_r$-chromophore *(1b)*. Denaturated $P_r$ is oxidized by strong oxidizing agents ($Fe^{III}$, $Ce^{IV}$) to products, spectroscopically similar to denaturated $P_{fr}$[35]. The phytochrome transformation had already been correlated with redox-reactions[100-102]; and the spectra indicate a photochemical oxidation of the chromophore during $P_{fr}$-formation. This possibility was studied using *(23)* as a model for $P_r$. Comparison of *(23)* and *(19)* allows one to further analyze, whether a hydrogenated ring has similarly pronounced effects on the reactivity of bile pigments, as it has in the cyclic tetrapyrroles (cf. *e.g.* [103]). The products of photooxidation of *(23)* are summarized in Scheme 2. In presence of oxygen, the purpurins *(24)* and *(25)* are formed in a regioselective, self-sensitized singlet-$O_2$ reaction[66].

*(25)* is likewise accessible by a smooth dark-reaction[19], which is also suitable as a degradation reaction for biliproteins[67]. Spectroscopically similar products were observed during the dark reaction of *(19)* with singlet-$O_2$[104]; the typical spectrum with two bands[66], however, makes the proposed endoperoxide structure[104] unlikely and rather suggests the formation of purpurins as well. The influence of the hydrogenated ring on these reactions is very pronounced. *(23)* reacts much more rapidly than the fully unsaturated analogue and other bilindiones, and the reaction is regioselective at C-5. Although the spectroscopic characteristics of *(24)* and *(25)* correspond to denaturated $P_{fr}$, like other purpurins[109] they regenerate *(23)* in only small yields and under drastic conditions.

With regard to the reversion, especially the products *(26)* and *(27)*, derived from anaerobic photooxidation, seem attractive, because they correspond in their spectroscopic characteristics to denatured $P_{fr}$ and because they can regenerate *(23)*, at least thermally. These reactions, too, are specific for the A-dihydrobilindione *(23)* and are regioselective at the C-5 methine bridge; corresponding reactions at C-15 or with fully unsaturated bilindiones were only observed as rare exceptions[106]. The dimerization of *(23)* to *(26)* is reminescent of the reversible photodimerization of pyrimidines in nucleic acids (cf. *e.g.* [107]). In phytochrome, the presence of two chromophores would be a precondition, which seems unlikely from the known data[14,18,21,55]. The formation of the pyridiniobilindione *(27)* demonstrates, however, that in principle other partners may take place in the reaction besides a second bilindione[41]. Probably, the reaction proceeds in two steps. The educt is first oxidized in one or two one-electron steps. Such a series of oxidations has been established electrochemically with bilindiones[108] and is supported by observation of long-lived cation radicals during oxidation of Zn-*(23)*[109]. In the second step, the nucleophilic addition of pyridine at C-5 takes place. Obviously, the reactivity of the intermediates is reversed. The *(27)* that is formed, formally possesses the conjugation system of the educt *(23)*; but its absorption spectrum is shifted to shorter wavelengths, because the $\Delta^5$-bonding is twisted by the steric hindrance between the rings A, B and the bulky C-5 substituent[41,110].

Regarding the latter as a model reaction would require $P_r$ to contain both an oxidant and a nucleophile. According to present day knowledge, amino acid residues are the only candidates, because phytochrome is transformed in solution and contains only carbohydrates[111] besides the chromophore. For oxidation, cystine residues are possible candidates, for addition tryptophan, tyrosine, serine, cysteine and the like. There do in fact exist certain indications to this effect; thus, $P_{fr}$ contains one to two accessible SH-residues more than $P_r$[112,113], and *(23)* reacts with *e.g.* derivatives of tryptophan to give violins[106]; but here again a decision is not yet possible.

## 3. Chromophore-Protein Interactions

### 3.1. Molecular Ecology

The chromophores of native and denaturated biliproteins differ so conspicuously in their properties (Table 2) that a relationship between the two may seem unlikely. Phycobiliproteins can be denaturated reversibly and in excellent yields with urea or guanidinium chloride[22]. Since the covalent bonds between chromophore and protein are retained, the different properties of the chromophores in native and denatured pigments, respectively, are exclusively due to non-covalent interactions with the native protein. These interactions are essential in optimizing the chromophores for their function of photoreception. This includes (a) an increase in the extinction-coefficient by nearly one order of magnitude, leading to an increased light-absorption, (b) the suppression of radiationless deactivation to diminish energy losses in favor of fluorescence (phycobiliproteins) or of photochemical reactions (phytochrome), and (c) the chemical stabilization of chromophores (Table 2). In addition, also the positions of the absorption maxima of certain chromophores are variable between remarkable limits [*e.g.* 80 nm for *(1a)*] and thus permit a "fine tuning" of the energy transfer. The question as to the origin of these optimizations, which may be paraphrased under the heading "molecular ecology", is essential for an understanding of the function of biliproteins. Geometrical transformations, protonation-deprotonation, and a restricted flexibility of chromophores seem to be some of the essential factors.

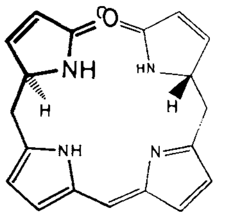
Table 2. Molecular ecology of the biliproteins. Comparison of the properties of native bilindiones, with those of denatured pigments and free bilindiones of similar structures.

| | Free bilindiones or denatured biliproteins | Native biliproteins |
|---|---|---|
| UV/VIS absorption spectra (see Fig. 1) | Broad bands, intense ($\varepsilon \approx 35000$) [a] in the near UV, weak ($\varepsilon \approx 15000$) [a] in the visible range | Narrow bands, weak ($\varepsilon \approx 15000$) [a] in the near UV, intense ($\varepsilon \approx 100000$) [a] in the visible range |
| Photochemistry | Mainly radiationless deactivation, low quantum yields ($\leq 10^{-3}$) for fluorescence or photochemical reactions | High quantum yields for fluourescence ($\geq 0.6$ in phycobiliproteins) or photochemical reactions ($\approx 0.15$ in phytochrome) |
| Chemical stability | Poor; ready formation of metal complexes, facile nucleophilic addition or reduction at C-10, sensitive towards photooxidation | Good; little to no reaction with these reagents |

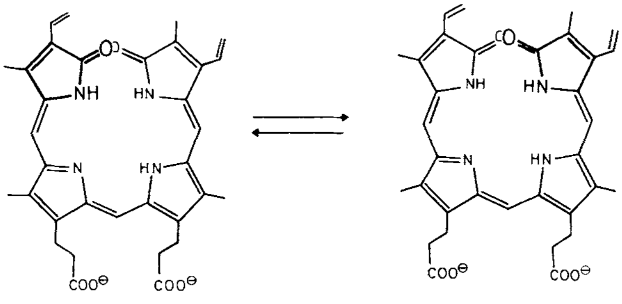
[a] All extinction coefficients are given with respect to one chromophore. They have to be multiplied by the number of chromophores (Table 3) to obtain the extinction coefficients of the respective biliprotein. Somewhat varying $\varepsilon$-values are cited in the literature, due to different methods of determination.

### 3.2. Geometry of Chromophores

The first detailed analysis of the geometry of free bile pigments stems from *Moscowitz et al.*[114], postulating a cyclohelical porphyrin-like structure in solution for urobilins [*(28)*; for sake of clarity, the substituents have been omitted], with the sign of the twist determined by the absolute configuration of the α-pyrrolic centers C-4 and C-16. Cyclohelical structures have also been established for bilindiones, like *(19)*, both by X-ray analysis[115,116] as well as by $^1$H-NMR[117,118] measurements and measurements of solvent-induced circular dichroism (SICD)[117,119] in solution. In the formally achiral bilindiones of the biliverdin type, this results in a uniform population of two enantiomeric conformations *(29a)* and *(29b)* which differ in their sign of rotation and are in equilibrium with each other ($\Delta H_0^{\ddagger} = 42$ kJ/mol for a derivative of *(19)*[120]). The equilibrium may be shifted sufficiently by dissolution in chiral solvents[117] or by adsorption to the chiral biopolymer serum-albumin[121] to allow the observation of typical Cotton effects of inherently dissymmetric chromophores. In support of this, purpurins like *(25)* containing planar chromophores[122] give no SICD-effect[123].



*(28)*

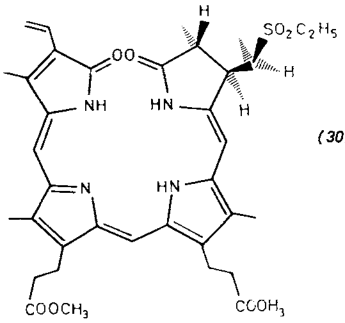


*(29a)* *(29b)*

The *E,Z,Z*-isomeric bilindiones are SICD-negative[90], too, thus supporting the suggested *anti-,syn-,syn*-conformation [Formula *(20)*][91].

The state of equilibrium between the two helical forms may also be shifted by asymmetric centers within the molecule. The high rotational values of optically active urobilins are due to the asymmetric centers C-4 and C-16 having the same absolute configuration by which one form is preferentially populated for steric reasons[114]. Since the absolute configuration of the helix can be derived from the sign of rotation of helical chromophores, the absolute configuration of the assymmetric centers is thus also indirectly accessible[46,57,94b,114].

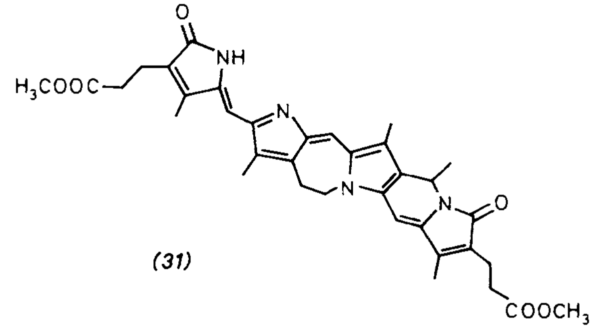
In the biliprotein-chromophores *(1)—(3)*, ring A has at least three asymmetric centers. The different steric hindrance of the two forms has been estimated by Ramachandran calculations on *(30)* as a model of denaturated PC and $P_r$ to result in an energy difference of $\Delta G^0 = 4$—8 kJ/mol[94]. Accordingly, denaturated PC exhibits a rather strong optical activity ($\Theta_{605} = 133000$[124]). In the chromophore *(2)* of PE, the influence of the asymmetric centers of ring A is opposite to the influence of the asymmetric C-16; accordingly the optical activity of denaturated PE is much lower[144].



*(30)*

The hitherto described effects can only be rationalized in terms of a preferential cyclohelical conformation of free bile pigments of the biliverdin type. This conformation is, however, not rigid but rather flexible, and it also exists in equilibrium with more extended conformations. The broad absorption bands, which are unstructured even at low temperatures[19,125], refer to this situation, as well as the exceptions in planar pigments like *(25)*[66]. Recently, the problem was investigated in detail by the Mülheim group. It was possible, by fluorescence spectroscopy, to differentiate at least two conformer populations in biliverdin[119]. The form fluorescing at longer wavelengths was identified as a cyclic conformation, since only this one showed an SICD effect; the form emitting at shorter wavelengths was associated with a more extended conformation because of its higher ratio of absorption of the visible and near UV-band, $Q_{uv}^{vis}$ *(vide infra)*. The equilibrium between both forms is dependent on temperature and solvent; the open form is preferred in viscous H-donor solvents[126], especially in lipid-vesicles[127]. Strong intramolecular H-bridges similar to those of bilirubin[128] were also implicated as the origin of the formation of isomers in biliprotein cleavage products. These H-bridges were only observed in the case of the free acids[43].

The denaturated biliproteins are so similar in their properties to free bile pigments of corresponding structure [*(18)* for PE, *(23)* for $P_r$ and PC], that they also are expected to assume preferentially cyclohelical conformations. The modified spectroscopic properties of native biliproteins (*e.g.* PC, Fig. 1) originate mainly from their chromophores being rigidly fixed by the protein in an extended conformation[19,125]. The intensity ratio $Q_{uv}^{vis}$ of the visible with respect to the near UV-band is mainly determined by the geometry of the chromophore. In the case of cyclohelical conformations $Q_{uv}^{vis}$ is small and thus similar to that for a porphyrin, whereas in extended conformations it is large and thus similar to that for a polyene. This is one essentially consistent result obtained from MO-calculations by several groups[80,91,121,131,134] and is confirmed by the spectral data of free bilins of known conformation. $Q_{uv}^{vis} = 0.25$ in cyclohelical *(19) (vide supra)*, but is increased to 6.4 in isophorcabilin *(31)*, which by reason of its additional intramolecular bridges can only assume extended conformations[27b].



*(31)*

A value of $Q_{uv}^{vis} = 0.15$ was measured recently for a 21,24-methanobilindione, which necessarily possesses the *all-syn,Z*-conformation[321]. The variation in the $Q_{uv}^{vis}$ of bilindiones due to formation of cations, anions and Zn-complexes is comparatively small, and the absorption in the near UV, in particular, remains essentially unchanged[36].

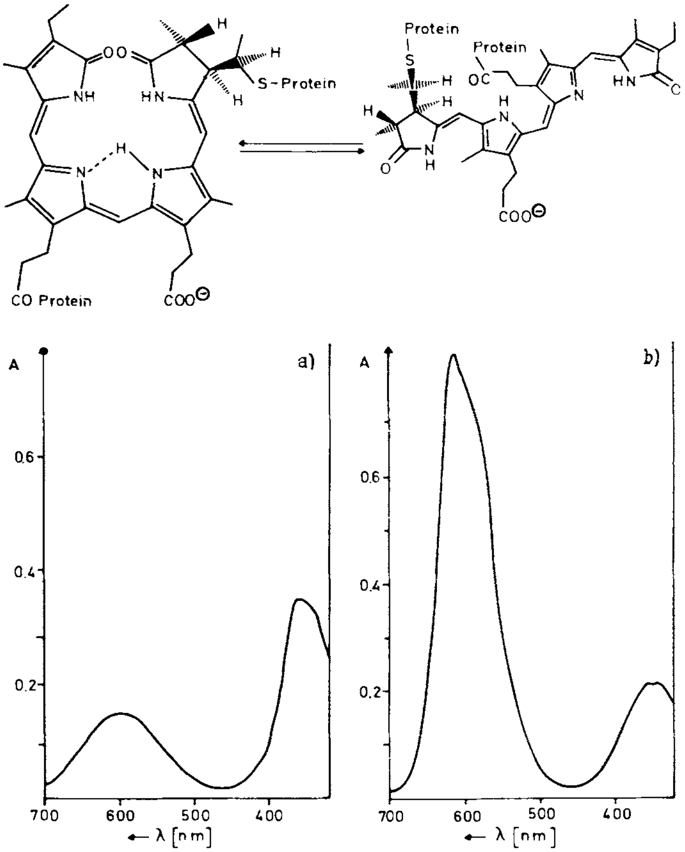


Fig. 1. Spectrum of denatured (a) and native phycocyanin (b) from *Spirulina platensis* (same concentrations in (a) and (b)). The denaturation by urea (8 M) is reversible; similar changes are observed upon thermal denaturation. The formulas depict the type of conformation for the two forms: cyclohelical for (a) and extended (in a sterically unhindered conformation) for (b).

In denaturated PC at pH 7.5, $Q_{uv}^{vis}=0.43$; it is increased to 4.1 in native PC, with both bands changing their intensity in opposite directions (see Fig. 1)[125]. Similar effects are observed with $P_r$[55]. Thus, the chromophores of both native pigments are present in an extended conformation. There is an interesting aspect of these findings: the extended conformations of bilindiones are higher in energy than the cyclic ones[92,94] and the necessary energy has to be provided by the protein. The energies of folding of several phycocyanins are indeed much lower than in other proteins of comparable size[135], *i.e.* the difference is possibly due to the strained chromophores[129]. In native PE, $Q_{uv}^{vis}$ increases to a comparable extent as found in PC, as compared with the denaturated pigment[139,144]. To our knowledge, the relation between the absorption and geometry of chromophores of PE has only once been studied theoretically[144a], and extended pigments corresponding to bilindione *(31)* possessing the tetrahydro-conjugation system of rhodin *(18)* have so far not been reported. On the basis of calculations, however, it is likely that $Q_{uv}^{vis}$ is also a certain indicator of the geometry of molecules, which would suggest extended chromophores for native PE, too.

The high ellipticities of the long-wavelength CD-bands of native PC as well as of PE would indicate an inherently dissymmetric chromophore, and therefore a more or less uniform twist of the extended chromophore. Generally, the bands have a positive sign. $P_r$ is a remarkable exception in having a negative CD-band despite it presumably[37] having the same absolute configuration of the asymmetric centers as $P_{fr}$ at ring A[135a]. At least in this case, an exciton-coupling would seem to be unlikely since phytochrome carries only one chromophore.

The picture is more complex with $P_{fr}$, the active form of phytochrome. On the one hand, $Q_{uv}^{vis}$ of native $P_{fr}$ is only half that in native $P_r$ (see *e.g.* [18]) and, on the other, the absorption maximum of the native pigment is extremely red-shifted. Denaturated $P_{fr}$ absorbs in its protonated form (pH = 2) at 610 nm[35], corresponding to a maximum for the free base at about 570 nm[35,71]. The absorption maximum of native $P_{fr}$ ($\lambda_{max}=730$ nm) is shifted to the red by more than 160 nm ($\hat{=}3850\ cm^{-1}$). While the lower value of $Q_{uv}^{vis}$ is still compatible with a rather extended conformation, the pronounced red-shift cannot be explained by a conformational change alone. Since the deprotonation of bilindiones leads to red-shifts of the same magnitude [*e.g.* 3800 cm$^{-1}$ in *(23)*][36] this effect was rationalized as a deprotonation of the $P_{fr}$-chromophore[35] in the native pigment. Recent MO-calculations on chromophores with the conjugation system of *(3)* support this interpretation[133].

### 3.3. Charge and Chromophore-Chromophore Interactions

In addition to geometrical transformations, electric charges in the vicinity of the chromophore are possibly important factors for the functionally important fine-tuning (see Section 5.1) of the absorption maxima of phycobiliproteins. Phycobiliproteins contain up to four chromophores on one subunit and up to six within the (αβ)-monomer (Table 3). Although they frequently have the same molecular structure [*e.g.* *(2)* in C-PE] and by and large the same geometries,

Table 3. Classification and properties of biliproteins.

| Type [a] | $\lambda_{max}$ [nm] (VIS) | Chromophore α- | β- chain | γ- | Protein structure Monomer | Aggregation | Mol.wt. [k] α- | β- chain | γ- | Occurrence | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| APC I | 656 | 1 × *(1a)* | 1 × *(1a)* | ? | $\alpha_3\beta_3\gamma$ | 1 | 18 | 18 | 30 | Cyanobacteria, Red algae | [152, 181, 182] |
| II, III | 650 | 1 × *(1a)* | 1 × *(1a)* | — | αβ | (1), 3, 6 | 16 | 18 | — | Cyanobacteria, Red algae | [1, 147, 149, 153, 154, 181–183] |
| B | 670 | 1 × *(1a)* | 1 × *(1a)* | — | αβ | (1), 3, 6 | 16 | 20 | — | Cyanobacteria, Red algae | [148b, 184] |
| C-PC | 635 [e], 620, (590) [f] | 1 × *(1a)* | 2 × *(1a)* | — | αβ | 1, 3, 6 | 16 | 20 | — | Cyanobacteria | [1, 13, 15, 20, 22–25, 147, 185–187] |
| PEC [b] | 590, 568 | 1 × PXB [h] | 2 × *(1a)* | — | αβ | 3 | 17 | 20 | — | Cyanobacteria | [32] |
| R-PC | 620, 555 | 1 × *(1a)* | 1 × *(1a)*, 1 × *(2)* | — | αβ | 3, 6 | 18 | 20 | — | Red algae | [72, 153, 188] |
| K-PC [b] | 645, 610, 580 *etc.* | 1 × *(1a)* *etc.* [33] [i] | 1 × *(1a)*, 1 × *(2)* (?) | — | $\alpha\alpha'\beta_2$ | 1 | 9, 10 | 16 | — | Cryptophytes | [33, 34, 189] |
| C-PE | 575 [e], 560, 540 | 2 × *(2)* | 3–4 × *(2)* | — | αβ | 1, 3, 6 | 17 | 21 | — | Cyanobacteria | [1, 13, 15, 20, 22–25, 154] |
| R-PE [c] | 568, 540, 498 [g] | 2 × *(2)* | 4 × *(2)* | 2 × PUB [j], 2 × *(2)* | $\alpha_6\beta_6\gamma$ | 1 | 19 | 19 | 35 | Red algae | [22, 190] |
| b-PE | 575 [e], 565, 540 | 2 × *(2)* | 4 × *(2)* | — | αβ | 3 | 19 | 19 | — | Red algae | [153, 190] |
| B-PE | 565, 545, 498 [g] | 2 × *(2)* | 4 × *(2)* | 2 × PUB [j], 2 × *(2)* | $\alpha_6\beta_6\gamma$ | 1 | 19 | 19 | 35 | Red algae [h] | [31, 153, 192–194] |
| K-PE | 545–565 | ? × *(2)* | ? × *(2)* | — | αβ | 2 | 10 | 17 | — | Cryptophytes | [1, 195–198] |
| Phytochrome $P_r$ [d] | 660 | 1 × *(1b)* | — | — | α | (1) 2 | 120 | — | — | Green plants and others | [9, 13, 14, 18, 21, 191, 199–203] |
| $P_{fr}$ | 730 | 1 × *(3)* | — | — | α | (1) 2 | 120 | — | — | Green plants and others | |

[a] The prefixes are derived from the parent organisms: C = Cyanobacteria, R = red algae, B = *Bangiales* (on order of red algae), K = cryptophytes, b and B refer to different quaternary structure. [b] Phycoerythrocyanin. [c] R-PE is possibly a glycochromoprotein [25, 226]. [d] Phytochrome is probably a glycochromophosphoprotein [111, 201]. [e] Special form, possibly aggregate [147, 182]. [f] Shoulder, resolved below 77 K [125, 137, 138, 151a]. [g] Shoulder due to phycourobilin chromophores [i]. [h] Chromophore of unknown structure $\lambda_{max,\ pH=3.0}^{denatured}=600$ nm. [i] Additional chromophors of unknown structure: $\lambda_{max,\ pH=2.0}^{denatured}=690$ nm [33, 34, 189]. [j] Phycourobilin chromophore, detailed structure unknown: $\lambda_{max,\ 0.1\ M\ HCl}^{denatured}=498$ nm [22]. [k] Approximate value $10^{-3}$. [l] A pigment similar to B-PE has also been reported for a marine cyanobacterium [204].

too, they differ spectroscopically, chemically and functionally, due to the different environments of their chromophores (see Section 3.4) and their correspondingly different chromophore-protein interactions. For example, APC-B absorbs at 670 nm[148b], the s-chromophore of C-PC at 590 nm[36,140–142]; in spite of their absorption difference of 80 nm ($\hat{=}$2020 $cm^{-1}$), however, they possess the identical chromophore *(1a)*. Chemical differences are evidenced, *e.g.*, by a different stability towards reduction[129] or unfolding[125], spectroscopically several absorption bands can be resolved, especially at low temperatures[125,136–139], in the fluorescence[139–143] and CD-spectra[144–147]. These differential effects are physiologically essential (see Section 5.1) for an optimal energy-transfer and they were investigated for the first time in some detail by fluorescence-measurements[140]. The site-specific chromophore interactions are obviously already fixed in the sub-units, since the CD- and absorption spectra are unchanged during aggregation to the (αβ)-monomers. In a C-PE the spectrum was identical with the sum of the subunit spectra[144]. In contrast, further aggregation of the monomers causes shifts to longer wavelengths of the visible bands. An additional long-wavelength band appears in the difference[148–154], low-temperature[136,137] and CD-spectra[145–147,152]. Its displacement is small in PC and PE (10—15 nm $\hat{=}$ 250—450 $cm^{-1}$), but rather pronounced in APC. Monomeric APC absorbs at 620 nm, the trimer at 650—670 nm, at the same time the absorption is almost doubled[149].

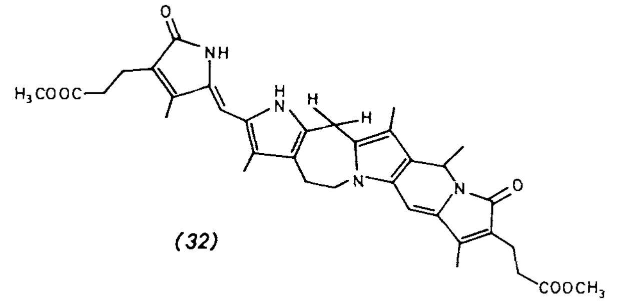
Recently, evidence has also accumulated for chromophore-chromophore interactions which have been related to displacements of absorption maxima. S-shaped CD-bands were observed in C-PE[144], B-PE[31], K-PC[34] and an allophycocyanin[152]. This type of band may be caused by exciton splitting, but a decision is difficult if several chromophores are present. The long-wavelength shift of the absorption-band[147] of the trimeric APC $(\alpha\beta)_3$[149] was recently interpreted as a chromophore-chromophore interaction of "intermediate strength" (= CD-inactive) between different monomers in the aggregate[150].

### 3.4. Increased Fluorescence and Chemical Stability

The second conspicuous feature of native biliproteins is their photochemical behavior. Phycobiliproteins fluoresce with quantum yields near to one (see [142]), phytochrome has quantum yields of 0.13 and 0.17 for the photoreversible transformation between the two forms[17]. Free bilindiones and denaturated biliproteins show only a very low fluorescence[96,119,130,132,155–157] and phosphorescence[156,158]; the "natural" *all-syn,Z*-bilindiones[66,105,159–162] and even the distinctly more reactive A-dihydrobilindiones[66,105] are also photochemically rather inert. The major pathway of deexcitation of free bile pigments or denaturated biliproteins is therefore radiationless deactivation. Two mechanisms are plausible: vibration-induced deactivation[163] and proton-transfer or even only perturbations of hydrogen-bond potential-curves[164]. Both are able to cooperate in a complex manner, since, *e.g.*, an intramolecular hydrogen bond is able to hinder torsional movements, but at the same time can open a new channel of radiationless deactivation (see [163,164]).

Both mechanisms have been investigated on partial-structures[159] and—hitherto less systematically—on integral bile pigments[96,155–157]. Both were recognized as essential, but a quantitative estimation is difficult, since chemical manipulations will generally influence both factors. Thus, *e.g.*, the *N*-methylation of a dipyrromethenone will inhibit intermolecular proton transfer by suppression of dimerization in unpolar solvents[156], but will at the same time restrict the conformative mobility. Similar reasoning applies to *N*-protonation[96,155]. The influence of viscosity which essentially decreases vibrational relaxations has hitherto mainly[158] been investigated at lower temperatures[96,132,155]. Bilindiones[96,132,155] and especially conformatively more rigid pigments like isophorcabilin *(31)* show a moderate fluorescence at 77 K[155c].

In this respect, the rather strong fluorescence of isophorcarubin *(32)* is noteworthy[165]. The ring-A,B fragment of *(32)* is identical to that of a common 10,23-dihydrobilindione ("bilirubin"), and its fluorescence should therefore only be weak[86,166]. The C,D-fragment is rather rigid, however, and is incapable of allowing intramolecular H-transfer, so the fluorescence has thus been related to the latter[165]. Hitherto, no direct approach has been tested to quantitatively separate the contributions of proton-transfer processes; one possibility would be a systematic investigation of $^2H$-isotope effects[167].



*(32)*

In biliproteins the radiationless deactivation is strongly decreased. The vibrational relaxation can be effectively decreased by a rigid fixation of the chromophores. Indications of this are the decreased bandwidths of the absorption spectra[66,125] which is also evident in the fluorescence-excitation-spectra[139–143], the large negative temperature coefficient of the fluorescence[17,139], and the small phonon-coupling to the protein[138].

An effective instrument for repressing proton-transfer-reactions would be the transfer of chromophores into a hydrophobic environment, *e.g.* into the interior of proteins. An extended conformation of the molecule would further inhibit intramolecular transfer. The lack of typical reactions of bilindiones, *e.g.* the formation of Zn-complexes[168] in biliproteins, could be evidence of this[22,169] as well as the quenching of fluorescence with benzoquinone[170,322].

On the other hand, there are several recent results which put the chromophores into a hydrophilic or at least water accessible position near the surface of the biliproteins: Thus there are reports of redox-reactions of chromophores at electrode-surfaces[171], in solution[99,100,129,172] and at membranes[173], of the reversible addition of thioles and dithionite (or rather sulfoxylate[174]) to the central methine bridge[129,172], of chromophore-chromophore interactions during the aggregation of APC[151], of low-temperature photochemistry related to proton transfer[138] and of an $H_2{}^{18}O$-exchange of *both* lactam oxygens at C-1 and C-19[175]. In the case of the reaction of PC, APC and PE with dithionite, it could be demonstrated that this reagent is in thermodynamic equilibrium with the chromophores. At least in this case, the decreased reactivity of the chromophores in the native pigment is thus determined thermodynamically and not kinetically[129]. Possibly, the conformational changes are one direct cause of the increased stability.

Perhaps the quantum yield of fluorescence is the most sensitive parameter of the state of phycobiliproteins. During controlled protein unfolding it already clearly decreases before the absorption- or CD-spectra noticeably change[144,176]. Under partial denaturating conditions, the photochemical behavior of phycobiliproteins changes in a complementary fashion. In presence of allylthiourea[178], the photochemical stability of PC is decreased[177]. In presence of 0.5 M guanidinium chloride[179] or on diminution of the pH-value to 3.8[180], solutions of PC and APC become photoreversibly-photochromic. The latter result is especially of interest with regard to the phycochromes[10-12] and possibly to phytochrome, too, because they show similar difference-spectra.

## 4. Proteins

Phycobiliproteins represent a period of evolution of about 3.5 billion years and they exist in procaryotes as well as in eucaryotes, in very different biotopes. They are thus of interest for comparative investigations which currently culminate in a complete sequencing of two PC-molecules[62,63]. The most important data of biliproteins that have been characterized spectroscopically and by their origin, are summarized in Table 3. The phycobiliproteins are globular and soluble in water, those isolated from red algae and cyanobacteria show pronounced aggregation. Analysis of the N-terminal sequences, immunochemical investigations and hybridization experiments indicate a common phylogenetic tree for these pigments (Fig. 2). The closest relationship exists between corresponding subunits of one type of protein from different organisms; a more distant relationship exists between corresponding subunits of different types of pigments and between the different subunits of the same pigment. Also the pigments of red algae and cyanobacteria seem to be more closely related with each other than than with the pigments of cryptophytes.

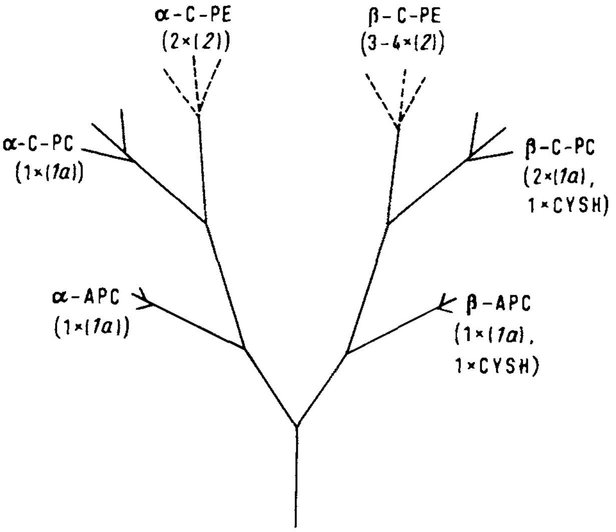


Fig. 2. Phylogenetic tree of biliproteins and their α- and β-subunits from cyanobacteria. C-PC = Phycocyanin, C-PE = phycoerythrin, APC = allophycocyanin (after [205]).

The protein moiety of phytochrome is distinctly different from that of the phycobiliproteins. It is considerably larger, it probably possesses a dumbbell-shaped structure, and $P_{fr}$ in particular has a tendency to associate with membranes. Immunochemical and spectroscopical investigations demonstrate the distinct similarity of phytochrome(s) from different organisms. So far there is no direct indication of a phylogenetic relationship with the phycobiliproteins. The similar structure of the chromophores, their similar binding to the apoprotein, comparable non-covalent interactions, and finally the occurrence of phycochromes are indirect indications thereof, but they don't exclude a converging development.

### 4.1. Phycobiliproteins: Monomers

The most data available on primary structures are those for phycocyanins. Aside from the determination of N-terminal sequences (see[15,205,206]) and of chromophore binding regions[62-65,207-211] of several organisms, the sequences of PC isolated from *Mastigocladus laminosus*[62], a thermophilic cyanobacterium, and from *Cyanidium caldarium*[63], a monocellular thermoacidophilic red alga, have recently been established. The complete analyses of the β-chain of PC isolated from *Synechococcus spec.* 6301 (formerly called *Anacystis nidulans*)[64], a monocellular mesophilic cyanobacterium, and of the β-chain of APC from *M. laminosus* have also been carried out[205]. The homologies of the respective α- or β-chains of the two complete structures are remarkable (80 or 78%) considering the different taxonomic positions and biotopes of the organisms.

However both are thermophilic organisms and the sequence, known up to 80%, of the marine cyanobacterium *Agmenellum quadruplicatum* shows only a homology of about 30% (*L. Fox,* private communication). A high homology is also found on comparing the PC β-chains with that of *S. spec.* The α- and β-chains of PC from each of the two organisms show much lower homologies (25% in PC from *M. laminosus*)[205]. The relationship between the same subunits of pigments of a different spectral-type is also obvious in the primary structures. Thus, the β-chains of PC and APC of *M. laminosus* are homologous to 25%, and the relationship becomes even more distinct on comparing the secondary structures (as calculated by the method of *Chou* and *Fassman*)[205].

The homology is not uniform, but particularly high in the chromophore regions. An earlier survey indicated a very high homology of the N-terminal regions within the corresponding subunits of pigments of different origin and of different spectral-type[15]. The low homology of these regions of PC and APC of *M. laminosus* found by the "Zürich-group", is, however, the first example of an exception to this rule, or it indicates an exceptional position of APC. The homology of the chromophore binding regions is supported by comparison of sequences of chromopeptides isolated from different phycoerythrins[209] and cyanins[62-65,207,210,211]. Thus, five different amino acid sequences have been identified in the region of the binding cysteins in PE from *Pseudanabaena* W1173, containing five chromophores. PE from *Phormidium persicum,* containing six chromophores, possesses six different binding regions, five of which correspond unequivocally to the five regions of the first named pigment[209]. The sequences of peptides characteristic of the individual chromophores can be correlated with the spectra of the chromophores in these pigments[139]. Hitherto, little was known about the phylogenetic origin of the increasing number of chromophores on the individual peptide chains on going from APC to PC to PE. Interestingly, however, a comparison of PC and APC from *M. laminosus* shows that the additional chromophore binding site on the $\beta$-chain of PC is formed by insertion of a short peptide in the APC sequence[205].

Studies on the protein moieties of the biliproteins complement the data on the chromophore binding mode as derived from investigations of chromophores (see Section 2). With only one exception[213] all of the known "chromopeptides" contain cysteine[35,62–65,205–216]. The early proposition[212], that this amino acid takes part in chromophore binding was first verified for a B-PE peptide from *Porphyridium cruentum*[208], and it was later recognized that cysteine functions as the binding amino acid for *all* chromophores in several C-phycocyanins and phycoerythrins[62–63,209,211,216]. These results are supported by a comparison of the number of bonded cysteines and the number of chromophores in pigments of several red algae and cyanobacteria[217]. It follows, together with the proof of the thioether bond to ring A of the chromophores [Section 2.2, formulas *(1), (2)*], that the blue *(1a)* and red *(2)* chromophores are bound to the protein *via* cysteine residues. The yellow urobilinoid chromophores of B-PE and R-PE are supposed to have even a second cysteine-chromophore bond to ring D[22,217].

Pigments of cryptophytes have hitherto been the subject of fewer investigations; the finding of a single, free cysteine-SH in one chromopeptide is indicative of a special binding position[215].

There is less agreement on other and possibly additional chromophore protein bonds. In particular, the linking of serine with one of the propionic acid side chains is plausible[22,209,213,215]. There are no such indications from the sequenced phycocyanins and allophycocyanins, but such a connection is discussed as being the only binding site of a K-PC[215] and of a R-PE[22], and it was identified in addition to the cysteine bond in one C-PE chromophore[209]. The problem is complicated by the possibility of both artifactual hydrolysis of esters and the formation of new bonds during protein degradation (see [22]). *Crespi* and *Smith*[214] postulated a lactim-ester binding to aspartate to account for the easy splitting of the thioether bond, but investigations of models show that this activation is not necessary[54c,58,218]. Also, a binding to glutamate is reported for a cryptophytan chromopeptide[215].

Only little is known so far about the secondary- and tertiary structures. Although PC and PE in particular can be readily isolated and crystallize well, there exists as yet no high-resolution X-ray analyses[32,193,194,219,220]. This may be explained by an unfavorable packing, leading to partial obliteration of reflexes due to interference from neighboring molecules[221]. The amino acid sequences and the solubilities are typical for globular proteins, with APC containing a higher proportion of hydrophobic amino acids than PC and PE. The crystal packing[32,193,194] and the investigations in solution[222] show an oblong shape (2.5—3.5 nm diameter, 5—6 nm in length) of the ($\alpha\beta$)-monomer of PC; a size which has also been deduced for other biliproteins[223–225] from electron-microscopical measurements. According to circular dichroism measurements on several pigments, the $\alpha$-helix content is about 60% in the $\alpha$- and 40% in the $\beta$-chain[144,147]. The secondary structure of PC and APC of *M. laminosus* has been estimated from the sequence. Here, too, the $\alpha$- and $\beta$-chains show differences, and there are indications of a different flexibility of the peptide backbone in the environment of the different chromophores[205].

As the second essential method, the immunochemistry confirms the relationships between the phycobiliproteins. The pigments of the same spectroscopic type, APC[148b,149,187,227–229] or PC[32,72,148b,149,187,227–229] or PE[198,227,228,230,231] are closely related immunochemically irrespective of their origin from the procaryotic cyanobacteria and the eucaryotic red algae. In contrast, the pigments of the different spectroscopic types do not undergo cross reactions, even if they are produced from the same organism. On this basis, R-PC[72] and phycoerythrocyanin[32,230], which contain blue chromophores *(1a)* as well as red chromophores *(2)*, were classified as phycocyanins, and APC-B as a true allophycocyanin[148b]. The subunits of individual C-PE[231] and also those of APC[149]—which are difficult to differentiate by other methods—are immunochemically not related, in contrast to the close relationship of corresponding subunits of pigments from other different organisms.

The cryptophytan-pigments, too, assume an immunochemically special position. First investigations[227] revealed no relationship with pigments from cyanobacteria and red algae; this has been supported for PC[228], whereas PC as well as PE from two different cryptophytes cross-react with PE from the red alga *Prophyridium cruentum,* but not with C-PE[198]. Accordingly, both pigments of cryptophytes seem to be related to PE from red algae.

Until now no defined immunological determinants are known. The missing cross-reaction of APC and PC has been taken as an indication of the chromophore not being a determinant, since both contain *(1a)*[231]. The different spectra of PC and APC, however, point to different states of this chromophore in the native pigments which may lead to significant differences in immunochemically relevant criteria, *e.g.* conformation and charge. There are also indications of the chromophore being accessible from the outside (Section 3.4). Immunochemical methods are principally suitable for a numeric taxonomy. With C-PE, isolated from seven different types of cyanobacteria, it could be demonstrated by a quantitative study that there are determinants specific of the species, as well as determinants specific of the spectral type, and that the results depend upon the method used (phage test or precipitation test)[230].

### 4.2. Phycobiliproteins: Quaternary Structure

The quaternary structure and higher aggregates have been investigated more thoroughly than the secondary and tertiary structures. They are decisive for the biological function of the phycobiliproteins. Most of the pigments possess an

$(\alpha,\beta)_n$-structure, with $n$-varying between one and higher than 12 depending on their state of aggregation and their origin *(vide infra)* (Table 3). In some pigments, yet a third subunit has been found, as in B-PE and R-PE ($\alpha_6\beta_6\gamma$)[153,193,194], in APC I ($\alpha_3\beta_3\gamma$)[182] and in PC from *Chroomonas spec.* with an $\alpha\alpha'\beta_2$ structure[189].

The molecular weights vary between 9200[189] and 20500[232] for the $\alpha$-subunits and between 16000 and 23500 for the $\beta$-chain, with the $\alpha$-subunits of the cryptophytan biliproteins at the lower limits. The $\gamma$-chains are considerably heavier. The subunits are classified by definition according to their molecular weights ($\alpha < \beta$). In the case of a different number of chromophores, the $\beta$-subunit always contains more than the $\alpha$-subunit. An alternative classification is possible immunochemically. It has been proven especially useful with APC[149], which has subunits carrying one chromophore each and which may have very similar molecular weights[1].

The subunits can be separated preparatively by ion-exchange chromatography, after being partially[139,196] or completely[62-64,147,149,223,234] unfolded. The separately renaturated subunits preferentially aggregate to dimers. In a mixture, the native pigments $(\alpha\beta)_n$ can be reconstituted in good yields. Smooth hybridization in 40—60% yield has been found[233] with complementary C-PC subunits isolated from monocellular and filamentous cyanobacteria, respectively; and there are even APC hybrids from the subunits of cyanobacteria and the red alga, *Cyanidium caldarium*[149]. A limiting factor for the yields is certainly the sensitivity of the chromophore in the denaturated pigments.

The controlled denaturation of monomer pigments has been investigated in the case of PC[125] and PE[144]. In each case sequential effects could be observed. The fluorescence decreases first[144,176], followed by absorption changes of the chromophores (in C-PC in a stepwise fashion[125]), and finally the protein structure (observed by CD) melts[144].

Corresponding to the strong coupling between chromophore and protein the quantum yield of fluorescence and the absorption spectra are the most sensitive indicators of the state of the protein (see Sections 3.3 and 3.4), *e.g.* partial proteolysis or denaturation.

The thermodynamics of the unfolding of proteins has been investigated on phycocyanins from several biotopes. Starting with undefined aggregates, $\Delta G^{0'}$ for pigments from meso-, psychro- and halophilic organisms is in the range of 10—22 kJ/mol[135] for complete unfolding by 8 M urea. These values are considerably lower than for globular proteins of similar size and free of disulfide bonds[235,236]. Comparable values have been found only for pigments of thermophilic organisms[135]. A possible factor is the energy necessary for "stretching" the chromophores of the native pigments[129] (see Section 3.2). The refolding kinetics of PC from *Spirulina platensis* is multiphasic, with a rapid first phase ($\tau_{1/2} = 110$ msec) accessible by fluorescence as well as by absorption measurements[237].

Phycobiliproteins from cyanobacteria and red algae show (with exception of the already complex-monomers APC-I, B-PE and R-PE (Table 3)) a distinct aggregation, which was mainly investigated systematically by *Berns et al.*[23] on C-PC. Starting from monomers, preferentially tri- and hexamers are formed[238]. These are the basic building blocks both for the crystalline pigments[32,194,219] as well as for phycobilisomes[223-225], as the light harvesting superstructures of these organisms[5]. Dependent on the conditions of isolation, higher aggregates[23,239] and hetero aggregates[223,224,240] have also been found, which represent more or less intact fragments of phycobilisomes[5] and even aggregates thereof[225]. Electron microscopic investigations by *Mörschel et al.*[248] revealed that the hexamers of PC are made up of two torus-shaped $(\alpha,\beta)_3$-trimers, one on top of the other, and that in B-PE the $\gamma$-chain occupies the central cavity of the cylinder that is formed.

In the pH range close to the isoelectric point ($\approx 5.3$) the equilibrium is mainly shifted in favor of the hexamer. In dilute solutions at $pH = 6$ to $pH = 5.4$, an equilibrium between monomer and hexamer has been established for several phycocyanins with an equilibrium constant of about $10^{30}$, in favor of the hexamer[239,241].

Also, trimer-hexamer equilibria[242] and—at higher pH values—monomer-tetramer[243] and monomer-dimer[244] equilibria have been studied by ultracentrifugation. At low concentrations, C-PE exists in a monomer-dimer equilibrium[139]. The aggregation is favored at elevated temperatures[238], at higher ionic strengths[245], by arenes[246], and by low concentrations of guanidinium chloride[247]; it is decreased by chaotropic salts[245] and H/D exchange[239,249]. These results, which indicate a high degree of hydrophobic interactions in aggregate formation, have been compared with the formation of detergent micelles[238]. The role of ordered water structures was recently studied in association experiments with tetraalkylammonium salts[250]. Since cyanobacteria also occur in extreme biotopes, the phycobiliproteins are suitable objects for the study of such adaptations. C-PC from a psychrophilic organism[251] possesses similar aggregation properties as the pigments from mesophilic organisms, whereas phycocyanins from halophilic[252] and thermophilic[253] organisms are clearly different. The molecular causes of these adaptions have also been investigated by calorimetric measurements of the protein folding[135] and sequencing studies[62].

In contrast to the pigments of the red algae and of the cyanobacteria, cryptophytan biliproteins show no significant aggregation. This is reflected in the absence of phycobilisomes in cryptophytes.

### 4.3. Phytochrome

Although ubiquitous in green plants, phytochrome has been purified from only a few species sufficiently enough to allow the chemical characterization of the protein.

Monomeric phytochrome from oats and rye has a molecular weight of about 120000[200,201] and it probably has a dumbbell shape[203,204] (for reviews see [1,14,18,21]). The hitherto best characterized pigment from oats is readily cleaved by endogenous proteases (at the incision?), to yield a still photochemically active fragment with a molecular weight of 60000[255-257]. This fragment is generally referred to as "small" phytochrome; for some time it was regarded as the native monomer. This partial degradation changes the absorption spectra, the photochemical quantum yield[262], the energy transfer from tryptophan to the chromophore[263], and the immunological properties[264]. "Large" phytochrome forms aggregates, whose dimeric structure is confirmed by gel-filtration[203,256,258], sedimentation[201,254,255], and electron microscopy[254]. Additional forms of $P_{fr}$ of even higher molecular weight have been reported, whose nature is still unknown[256]. Phytochrome contains about 35% hydrophobic amino acids and about 27 cysteines[201,203] including the chromophore-binding one. In addition, 4% sugar has been found in "small" phytochrome[111]; the "large" pigment contains one phosphate group[201,202].

There are conflicting results regarding the symmetry of the "large" phytochrome. Dimeric "large" phytochrome appears in the electron microscope as "tetramer" (9 × 9 nm)[254]. The molecular weight[255–257] of "small" phytochrome would also indicate two domains of roughly the same size to be present in "large" phytochrome. Two research groups have compared the peptides of the trypsin digests of "large" and "small" pytochrome from oats. *Stoker et al.*[259,260] have concluded a high degree of symmetry from the similar peptide maps, whereas *Kidd et al.*[261] arrived at the opposite conclusion on the basis of significant differences when using a different labeling technique. The available data also point to an asymmetric chromophore distribution, *i. e.* only one half contains a chromophore (see [14,18,21]). Antiserum against "large" phytochrome produces spurs with "small" phytochrome but not *vice versa,* which also indicates an asymmetry of the determinant regions[264].

The phytochromes from different sources are spectroscopically indistiguishable. Immunochemical experiments, too, reveal a close relationship between the hitherto investigated phytochromes from oat, rye, corn, barley, pea[203,258,264]. The amino acid analyses as well as the N-terminal sequences are different for "large" phytochrome from rye and oats, but this is possibly due to the purification procedures used[201,203].

For a better understanding of the function (see Section 5.3), protein-chemical differences between the two forms are essential. Following the works of *Tobin* and *Briggs*[191], who in 1973 questioned a greater part of the formerly reported differences, greatly improved isolation methods[200,265–267] and new analytical techniques led to more promising results. Thus, indications of a preferential interaction between $P_{fr}$ and cholesterol[268] were obtained, and *Smith* discovered a preferential assoziation of $P_{fr}$ with dextran blue[269] which may also be useful for the purification of phytochrome by sorption in the $P_{fr}$-form on dextran blue-agarose and subsequent desorption after irradiation with far-red light[269a]. $P_{fr}$ isolated after *in vivo* transformation, contains a larger fraction of high molecular weight components ($\geq$400000)[256]. In presence of bivalent ions, it binds relatively unspecifically to particulate fractions ("pelletability", see [270,271]). $P_r$ and $P_{fr}$ are immunochemically indistinguishable[272], and isoelectric focussing also gives identical results[113]. Significant differences were found, however, on titration of readily accessible amino acids[113]. $P_{fr}$ contains one accessible cysteine and one histidine more than $P_r$, and the modification of two tyrosines inhibits the photochemical reactions.

### 4.4. Phycochromes

Originally, the term phycochromes was coined—in analogy to phytochrome—for the light sensory pigments in cyanobacteria (for a recent survey see [10]). Today, however, all potentially photoreversibly-photochromic pigments of these organisms are called phycochromes, irrespective of any known function (see [10]). To characterize the function of these photoreceptors, which in no case is as yet certain, *Bogorad*[1] proposed the term adaptochromes, in accord with the most important and obvious effect of light-regulation, the chromatic adaption (see Section 5.3). Already at an early stage, phycochromes were related to phycobiliproteins. *Scheibe*[273] succeeded for the first time in the enrichment of a fraction having photoreversibly-photochromic properties. Subsequently, the *Björns* characterized four such pigments as fractions of phycobiliproteins from different algae[274,275] which were called phycochromes a, b, c and d. Of these, phycochrome c is of particular interest, as its light-induced difference spectrum is similar to the action spectra of chromatic adaption of several cyanobacteria and to the photomorphogenesis of *Nostoc.* The phycochromes have been enriched by isoelectric focussing; in the case of phycochrome b an almost complete separation was possible from the photochemically inactive light-harvesting phycobiliproteins present in large excess. So far, only one of the proteins has been characterized in detail. It is suggested to be identical with the α-subunit of phycoerythrocyanin[275a].

A fascinating aspect was revealed by two research groups during recent investigations on partially denaturated "common" biliproteins. Treatment of PC and APC from *Tolipothrix tenuis* with 0.5 M guanidinium chloride[179] gave them photoreversibly-photochromic properties characteristic of phycochrome a or c[174], and likewise APC from *Fremyella diplosiphon* obtained the photochromic properties of phycochrome c, on lowering the pH to 3.8[180]. By this treatment the chromophores seem to be sufficiently decoupled from the protein such that the fluorescence is already decreased, but the radiationless deactivation is not yet prominent. The quantum yields of the photoreactions (about 10%) are comparable to those of phytochrome. Independent of the proof of the biological relevance of phycochromes these results throw new light on the physicochemical interactions between chromophore and protein, and on the possible phylogenetic relations between phycobiliproteins and phytochrome.

## 5. Biological Functions

### 5.1. Phycobiliproteins

Phycobiliproteins are antenna or light-harvesting pigments of cyanobacteria, red algae, and cryptophytes. The absorption bands of the most abundant pigments of this group, the phycoerythrins (PE) and phycocyanins (PC), are found in the green to orange spectral range. The light-harvesting pigments of green plants, chlorophyll a and b, absorb only slightly in this range, thus guaranteeing biliprotein producing organisms an ecological advantage in deep water and under a canopy of green plant.

The organization of biliproteins and the mechanism of energy transfer is very similar in cyanobacteria and red algae, but the cryptophytes differ considerably. In the former, the phycobiliproteins are localized in particles visible by electron microscopy, called phycobilisomes, which are located at the outer surface of the thylacoid membranes[5,224,276]. The phycobilisomes of different species have distinctly different sizes and fine-structures, the ones most thoroughly investigated to date being those from the two red algae, *Porphyridium cruentum*[5,279] and *Rhodella violacea*[223,224] (see Fig. 3), and from the cyanobacterium *Synechococcus sp.* 6301 *(Anacystis nidulans)*[278]. Besides the light-harvesting pigments proper, *e.g.* PC and PE, they contain small amounts of several different allophycocyanins[148b,182], which are essential for the transfer of energy to chlorophyll. In addition, small amounts of colorless proteins have been described which are possibly important for the organization of phycobilisomes[223,278,280].

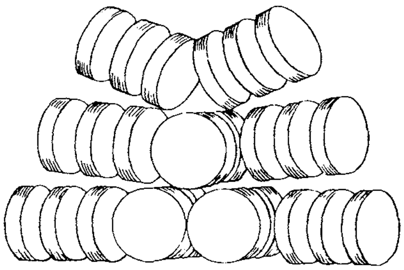


Fig. 3. Model of a phycobilisome of the monocellular red algae, *Rhodella violacea.* The "core" is made up from three APC hexamers, the rods fixed to it ("tripartite units") consist of one PC hexamer and two B-PE monomers, in this order when looking from the core (after *E. Mörschel, W. Wehrmeyer,* Ber. Dtsch. Bot. Ges. *92,* 393 (1979)).

Within the phycobilisomes the different pigments are densely packed in such order, that the absorption maximum increases from the "outside" to the "interior" of the phycobilisome. *Gantt et al.*[5] developed a model for phycobilisomes from *Porphyridium cruentum,* which reminds one of an onion cut in half: layers composed of PE surround inner layers of PC, which surrounds an APC-core. This arrangement was derived from dissociation experiments in buffers of low ionic strength, whereby the pigments were released sequentially[5]. It was convincingly proved by fluorescence spectroscopy[281] and immuno-electron-microscopy[281,282]. Using the latter method, APC could be shown to be localized on that side of the phycobilisome facing towards the membrane[282].

The architecture of phycobilisomes of the monocellular red alga *Rhodella violacea* (see Fig. 3) is basically similar but perhaps even more impressive, due to their flatness[223,224]. Six conspicuous rod-shaped stacks are attached to the APC-core[224]. These rods can be isolated by careful dissociation[223]. By electron-microscopic inspection, they appear as stacks of three small double-disks ("tripartite units"). The double-disks have the dimensions and fine structure of hexameric C-PC $(\alpha\beta)_6$ or of the fundamentally similar B-PE $(\alpha_6\beta_6\gamma)$. The former are supposed to be identical with the C-PC-hexamers which have been observed during the *in-vitro* association or during the crystallization (homoaggregates, see Section 4.3). A further dissociation of the rods and an analysis of the fragments revealed that two adjacent double-disks consist of PE, the final one of PC, *i.e.* they form a heteroaggregate of two different biliproteins[223]. Such heteroaggregates of PC and PE were recently also isolated from *P. cruentum*-phycobilisomes and from cyanobacteria[240,283a,284]. They show an excellent energy-transfer from PE to PC (reversible dissociation, see [283a]). A reconstitution of phycobilisomes starting with the isolated biliproteins is not (yet) possible. Perhaps the aforementioned colorless proteins are necessary as structural elements[280]. In support of this, phycobilisomes partially dissociated into a crude APC fraction and a PC-PE-complex can be reconstituted[283b]. Since the tripartite units of *R. violacea* contain no colorless proteins, these rather seem to take part in the APC-PC-coupling or in the membrane-binding[223]. A first experimental indication of this is the recent identification of a heavy, colorless protein (molecular weight about 80000), in both isolated phycobilisomes and thylacoid membranes freed of biliproteins[283b].

Comparatively less is known about phycobilisomes of cyanobacteria, but the results indicate similar structural principles as in those of *R. violacea.* By electron microscopy, *Wildman* and *Bowen*[277] have identified phycobilisomes in all of the 27 tested cyanobacteria, in some of them with excellent resolution, but until recently the isolation was more difficult than in red algae. A complete separation from other pigments was achieved by immunochromatography, but the elution of the phycobilisomes purified in this manner was only possible under dissociating conditions[280]. Phycobilisomes have been isolated from *Nostoc* species[151a,284] from *Synechococcus spec.* 6031 *("Anacystis nidulans")*[278] and from other species[285,286]. The phycobilisomes of *S. spec.* 6301 appear in the electron microscope as aggregates of rods similar to those of *R. violacea* (Fig. 3). Here, too, APC seems to be located at the coupling position, since the energy transfer from PC to APC is interrupted by the dissociation[278]. Recently, the electron-microscopic characterization of phycobilisomes of two other cyanobacteria was achieved by using zwitterionic detergents which are reported to inhibit the aggregation during purification[225]. These investigations confirm the general structural principle of Figure 3, with variations in the number of the central APC-disks, the number and the length of the "branches"[278], and also by their arrangement in two (Fig. 3) or three dimensions (*P. cruentum*[279,282]). The phycobilisomes of chromatically adapting cyanobacteria show small but distinct differences in size and arrangement[287], as well as in the pattern of the colorless proteins[280]. The "branches" of *Tolypothrix tenuis* increase in length in green light[288]. In this process, not only additional PE-units seem to be added, but also part of the PC is removed.

Phycobilisomes are extraordinary efficient antennas which absorb light by a high effective cross-section, and transfer the excitation energy to the reaction-centers. This energy transfer has quantum yields up to 100%[142,143,289,290] and is only decoupled under starving conditions (light[201], N[292]). The transfer mainly occurs to photosystem II (PS II), as was originally concluded from the bichromatic action-spectra[3,4]. Heterocysts contain no PS II and have been regarded as being free of phycobilisomes[293] (see, however, [323]). Recently, *Katoh* and *Gantt*[294] isolated photosynthetic vesicles with the phycobilisomes still bound, showing PS II activity. This activity decreases in parallel with the dissociation of the phycobilisomes (induced by a decrease in ionic strength). The coupling between the phycobilisomes and the reaction centers is variable and depends on the physiological conditions[295]. For *Anabaena variabilis,* grown heterotrophically in darkness, however, an energy transfer to PS I was reported, and recently in PS I samples from *Chlorogloea fritschii*[296], fluorescence-spectroscopic evidence was obtained for the occurrence of APC. APC fluoresces similarly to certain chlorophylls[294], but direct support comes from the results cited in ref. [323].

One reason for the efficient energy transfer is the organization of the phycobilisomes. This ensures that the energetically favored "downhill" transport of excitation-energy from the "high-energy PE" to the "low-energy APC" is directed at the same time from the PE periphery to the APC-core of the phycobilisome. Possibly, a recently described "foot structure"[279] serves for further transfer into the membrane and for the fixation of the phycobilisomes[279]. A second factor is the intense absorptions of the biliproteins ($\approx 10^5$ $cm^2 \times mol^{-1}$) which cover almost the entire spectral region from about 500 to 670 nm (cf. [5]), combined with a high degree of fluorescence (= low radiationless deactivation) of the chromophores[142] and distances of 3.5—6 nm between the chromophores[139,142,297]. These distances are optimal in a disordered structure for the energy transfer between suitable chromophores by the Förster-mechanism, because they are below the critical radius. As has recently been described for C-PE, the quantum yield of fluorescence increases by aggregation of isolated subunits to the monomer[139]. It increases even more during aggregation of the monomers to tri- and hexamers[141], or to the quasi-hexamer B-PE[142]. At the same time the fluorescence-polarization[139,142,297] and the time constant of the energy transfer decreases[297].

Due to the rapid migration of energy and the greater probability of a "downhill"-transport of energy, the fluorescence in each aggregate[139] is emitted almost exclusively from the chromophores, absorbing at the longest wavelengths, which were thus classified as "f"-chromophores[140]. The "s"-chromophores absorbing at shorter wavelengths act as sensitizers, and only exceptionally show a detectable fluorescence[139]. During the gradual association of phycobilisomes, this transfer chain is extended successively to yield "Förster-cascades". Due to their architecture, each pair of neighboring pigments provides for an optimal overlap of the emission band of the donor and the absorption band of the acceptor (Table 4). This process was demonstrated for biliproteins with different chromophores[140,142,297], of heteroaggregates[223,253], and of whole phycobilisomes[143,289,290]. In the intact phycobilisome, the result of this process is such, that the chromophores of APC, the biliprotein present in least amount, are the only ones to fluoresce, and all the remaining chromophores serve as sensitizers, with a transfer-probability of "at least 99%" in phycobilisomes of *P. cruentum*[290].

Table 4. Schematic representation of energy transfer within a phycobilisome like the one shown in Fig. 3 (only one tripartite unit and one APC are considered), and of the absorption and emission spectra of the phycobiliproteins (averaged absorption maxima, the emission maxima of "s"-chromophores have been estimated from the absorption maxima by assuming a Stokes-shift of 15 nm).

| Pigment | Chromophore | Absorption [nm] | Fluorescence [nm] |
|---|---|---|---|
| P-BE | PUB [a] | 500 | 515 |
| | "s" *(2)* | 545 | 560 |
| | "f" *(2)* | 570 | 585 |
| C-PC | "s" *(1a)* | 590 | 605 |
| | "f" *(1a)* | 620 | 635 |
| APC | *(1a)* | 650 | 665 |
| Chl $a_{II}$ | | 686<br>↓<br>photochemistry | |

[a] PUB = phycourobilin chromophore.

Cryptophytes possess biliproteins as antenna-pigments, too, but they are distinct from those of cyanobacteria and red algae (for a recent review, see [298]). Cryptophytan biliproteins are localized on the inner side of the thylacoid membrane[299]. Hitherto, the search for phycobilisomes has met without success, although *Wehrmeyer et al.*[300] recently obtained electron-microscopic evidence of particulate structures which may contain biliproteins. The energy transfer in cryptophytes must also be different, since no APC has so far been detected, and generally they only contain either PC *or* PE. As in the biliproteins of cyanobacteria and of red algae[34,297,300], only the chromophore lowest in energy fluoresces. In accord with the exciton-coupling between the chromophores postulated by *Jung et al.*[34], *Kobayashi et al.*[297] reported an extremely fast transient (energy-transfer) ($\leq 8$ ps) in PC of *Chroomonas*. The transfer from K-PC to chlorophyll a by the Förster-mechanism appears unproblematical, especially in pigments like PC-645 from *Chroomonas*[34,189,300] and PC-641 from *Hemiselmis virescens*[33], absorbing and emitting at rather long wave-lengths. In contrast, the emission-band of PE is located in a region of minimal absorption of chlorophyll a, so that either only incomplete energy-transfer is possible, or another pigment has to be positioned between them[301]. Indeed, cryptophytes contain possible candidates, *e.g.* chlorophyll *c*.

According to the data summarized above, the morphology of the antennas and the structure of the biliproteins would seem to be closely related. Each biliprotein of the cyanobacteria covers only a comparably small portion of the spectrum. Only APC has properties favorable for energy transfer to chlorophyll; an energy transfer of PE to chlorophyll requires the aggregation of several pigments. This disadvantage is compensated for by the flawless architecture of the phycobilisomes, which enables a vectorial energy flux direct to the reaction-center of PS II. In the cryptophytan phycocyanins, such energy transfer-chains are already realized within the individual biliproteins. *Chroomonas*-PC, for example, contains chromophores absorbing in the region from 573 to 652 nm[32,189], so a higher degree of organization would seem unnecessary. Finally, in the red algae both strategies are combined. They contain phycobilisomes, as well as the pigments R-PC, R-PE and B-PE, each of which contain different chromophores already joined to an energy transfer-chain of moderate length.

In addition to the well documented light-harvesting functions, other functions of phycobiliproteins are discussed. Under conditions of deficient N[1] and S[302], phycobiliproteins are degraded as protein-reserves (?). In cyanobacteria in particular they constitute a considerable fraction of the total protein, and basically they are of less importance for photosynthesis than the reaction centers. They also may have functions in light protection, since mutants free of biliproteins are more sensitive to light than the wild-types.

Finally, there is substantial evidence for phycobiliproteins, also having or having had functions in the electron transfer[303,304]. A corresponding function *in vivo* has as yet not been detected, and may have been lost during evolution.

Electrodes covered with biliproteins show photopotentials[171,305]; moreover, PC catalyzes electron-transfer through synthetic lipid-membranes[173,304]. In both cases the action spectra and absorption spectra are similar. PC undergoes specific interactions with $Fe^{3+}$, but not with $Fe^{2+}$, and it shows an asymmetric effect on the electron transfer of charged synthetic membranes loaded asymmetrically with that pigment[306]. The redox potentials of free bile pigments have been calculated theoretically[95,307], and the chromophores of native biliproteins have been shown to be much more stable towards redox reagents than those of the denaturated pigments[35,129].

### 5.2. Phytochrome

The function of phytochrome is that of a light-sensory pigment of green plants. In the transformation from heterotrophic etiolated growth in higher plants, *e.g.* in seedlings below the surface, to autotrophic, photosynthetic growth, phytochrome mainly functions as a sensor of light as such, in the "high-energy reactions" phytochrome functions as a sensor of light-intensity, and finally due to the $P_r$ and $P_{fr}$ equilibrium being dependent on the spectral distribution of the light especially within the photosynthetically important red spectral region, it renders possible a "color-vision" in green plants. Whereas a large variety of physiological and some structural aspects of phytochrome have been investigated in considerable detail[9,14,16 18], knowledge of the mechanism of information-transfer and -transduction is as yet only fragmentary. The models are difficult to evaluate in this context and shall only be outlined here. For further information, the reader is referred to recent reviews[9,14,16b,17,18,21,303,309].

Phytochrome is synthesized in its physiologically inactive form, $P_r$; the beginning of each physiological reaction sequence is the photochemical transformation into $P_{fr}$. The formation of $P_{fr}$ is fundamentally and nearly completely reversible by light ≥740 nm; this is not true, however, for all steps of the subsequent reaction-sequence. The *in vivo* decomposition of $P_{fr}$ or $P_r$-receptor complexes is a simple example (cf. *e.g.* [14,18]). Depending on the duration of the reaction ($\tau_{rev}$) until an irreversible step is reached, the physiological answer is reversible (or annulled) only for a certain time. Since the time ($\tau_{rev}$) of escape from reversibility varies among the diverse physiological answers by several orders of magnitude, the phytochrome answers have been classified into modulation (large $\tau_{rev}$-value = "reversible") and differentiation processes (small $\tau_{rev}$-value = "irreversible") (for recent discussions, see [18,308]). A variety of biochemical and physiological results critically summarized by *Marmé*[309] have indicated, at least for the modulation reactions, reversible changes of membrane properties to be operative.

Based on the hitherto known differences between $P_r$ and $P_{fr}$ (see Section 4.4) and on the photochemistry of model-systems (see Section 3.3), several hypotheses have been proposed for the primary reactions. *Song et al.*[263] postulated a light-induced photoisomerization[40] by proton-transfer, by which a receptor site formerly covered by the chromophore becomes accessible. *Hunt* and *Pratt*[113] argue, that chemical modifications of amino acids newly accessible by this transformation should interfere with the photoreversibility. As this is not the case[113], they regard this result as support of the conformational change of the protein, discussed by *Smith*[9a] as a primary signal. Finally, a third hypothesis postulates a reversible redox-reaction between protein and chromophore with the formation of a new chromophore-protein bond[106]. Each of these hypotheses is able to explain modification of membrane-properties, directly by redox and/or protonation-deprotonation processes, and indirectly by conformational changes by uncovering receptor binding sites, but a differentiation is not yet possible.

### 5.3. Phycochromes and Phycobiliprotein Biosynthesis

The biosynthesis of the phycobiliprotein-chromophores follows fundamentally similar pathways as does the formation of the more thoroughly investigated mammalian bile pigments. δ-Aminolevulinic acid is condensed to a cyclic tetrapyrrole, most probably protoporphyrin, which is subsequently opened oxidatively resulting in formation of a bile pigment with loss of the former C-5 as carbon monoxide[311 313]. The ring-opening process is formally and mechanistically similar[314] to the heme-oxygenation[315], but chemical evidence would indicate that the ring-opening of a Mg-porphyrin *via* 7,8-dihydroporphinatomagnesium may also be possible[161]. It is also not clear, whether the apoprotein is bound to the chromophore after (and not before) the ring-opening, and whether it adds to the 3-ethylidene group of bilindione *(4)* (and not to the vinyl-groups of a precursor). A hint as to the alternatives, not put in brackets here, is the finding[312] that *Cyanidium caldarium* excretes *(4)* as well as addition-product(s) of *(4)* in the dark[54c,316]. Another indirect indication is the facile and reversible addition of nucleophiles to *(4)* and *(6)*[54c,58,59], and very recently *Troxler et al.* (private communication, 1980) have demonstrated the uptake of heme and its conversion into phycocyanin in cyanobacterial protoplasts.

The biliprotein-synthesis in most of the cyanobacteria and at least in some red algae is regulated by light. It is of special interest that the antenna-pigments adjust to the quality of light available ("chromatic adaption"). In prevailing red light, especially the blue phycocyanins are formed, whereas in green light, *e.g.* under a canopy of leaves or in deeper waters, the red phycoerythrins are preferentially formed[1,11,287,317]. This effect has been investigated mainly with *Tolypothrix tenuis*[12,318] and with *Freymella displosiphon*[319,320]. Based on the action spectra, the chromatic adaption has been explained in terms of photochromic receptor pigment-systems, functionally termed adaptochromes, or chromes. There are also photomorphogenetic effects in cyanobacteria and red algae which are connected with such receptors. Little is known about receptor pigments (see Section 4.4), and virtually nothing about their mechanism of action.

## 6. Concluding Remarks

For a long time phycobiliproteins have been the victims of "mammalian chauvism" and, owing to their covalent protein bonds, have been much less investigated than the other tetrapyrrolic pigments of photosynthesis, the chlorophylls. In contrast to the latter, however, the phycobiliproteins have the great advantage of not being integrated into membranes. This property and the discovery of the central function of another biliprotein, phytochrome, during the development of plants, recently led to a boom in biliprotein research. No other photosynthetic light-harvesting system is as well investigated as the phycobilisomes, and—with the exception of rhodopsin—no light-sensory pigment is as well characterized as phytochrome.

In this report an attempt has been made to correlate the properties of the isolated chromophores with the function of the pigments *in vivo*. The correlation is somewhat subjective and partly fragmentary, but has been borne out for the most part in recent years. Some of the obvious gaps in the case of phytochrome are the structure of $P_{fr}$ and the closely related questions regarding the nature of the primary signal and the role of specific interactions between phytochrome and certain receptor membranes and organelles. An advancement in this area should certainly stimulate further investigation of the related phycochromes as well.

Many of the numerous questions arising from the functionally and morphologically impressive model of the phycobilisomes will only be possible to answer by the collaboration of biophysicists and biochemists. Details on the chromophore-protein interactions and the interrelationships between the biliprotein-chromophores and the chlorophylls within the photosynthetic membrane are essential for an understanding of the energy transfer on a molecular basis. The increasing complexity of the phycobilisome structures raises questions as to their elements of organization, their biogenesis and its regulation. The answers will not only be of interest to the inquisitive, but may perhaps also contribute to our understanding of light-harvesting and information-transduction in general.

*The author's work cited in this report was supported by the Deutsche Forschungsgemeinschaft and by the Münchner Universitätsgesellschaft.*

Received: May 29, 1980 [A 355 IE]
German version: Angew. Chem. 93, 230 (1981)

---

[1] *L. Bogorad*, Annu. Rev. Plant Physiol. *26*, 369 (1975).

[2] *Th. W. Engelmann*, Bot. Z. *42*, 81 (1884).

[3] *F. T. Haxo* in *M. B. Allen:* Comparative Biochemistry of Photoreactive Systems. Academic Press, New York 1960, p. 339.

[4] *R. Emerson*, Annu. Rev. Plant Physiol. *9*, 1 (1958).

[5] *E. Gantt*, BioScience *25*, 781 (1975); Photochem. Photobiol. *26*, 685 (1977).

[6] *R. Lemberg*, Justus Liebigs Ann. Chem. *461*, 46 (1928).

[7] *M. W. Parker, S. B. Hendricks, H. A. Borthwick, N. J. Scully*, Science *102*, 152 (1945).

[8] *W. L. Butler, K. H. Norris, H. W. Siegelman, S. B. Hendricks*, Proc. Natl. Acad. Sci. USA *45*, 1703 (1959).

[9] a) *H. Smith:* Phytochrome and Photomorphogenesis. McGraw-Hill, London 1975; b) *K. Mitrakos, W. Shropshire, Jr.:* Phytochrome. Academic Press, New York 1972; c) *H. Mohr:* Lectures on Photomorphogenesis. Springer, Berlin 1972.

[10] *L. O. Björn*, Q. Rev. Biophys. *12*, 1 (1979).

[11] a) *N. G. Carr, B. A. Whitton:* The Biology of Blue-Green Algae. Blackwell, Oxford 1973; b) *N. Lazaroff* in [11a], p. 279.

[12] *S. Diakoff, I. Scheibe*, Plant Physiol. *51*, 382 (1973).

[13] a) *W. Rüdiger*, Fortschr. Chem. Org. Naturst. *29*, 60 (1971); b) Ber. Dtsch. Bot. Ges. *88*, 125 (1975); c) *ibid. 92*, 413 (1979); d) *B. Deutch, B. I. Deutch, A. O. Gyldenholm:* Plant Growth and Light Perception. University of Aarhus, 1978; e) *W. Rüdiger* in [13d], p. 53.

[14] *L. H. Pratt*, Photochem. Photobiol. *27*, 81 (1978).

[15] *A. N. Glazer*, Mol. Cell. Biochem. *18*, 125 (1977).

[16] a) *T. W. Goodwin:* Chemistry and Biochemistry of Plant Pigments. 2nd Edit. Academic Press, New York 1976; b) *H. Smith, R. E. Kendrick* in [16a], p. 378.

[17] *K. M. Hartmann, W. Haupt* in *W. Hoppe, W. Lohmann, H. Mark, H. Ziegler:* Biophysik. Springer, Berlin 1978, p. 449.

[18] a) *W. Rüdiger*, Struct. Bonding (Berlin) *40*, 101 (1980); b) *W. Rüdiger, H. Scheer* in *W. Shropshire, Jr., H. Mohr:* Encyclopedia of Plant Physiology. New Series. Springer, Berlin, in press.

[19] *H. Scheer* in [13d], p. 25.

[20] *R. T. Troxler* in *P. D. Berk, N. I. Berlin:* Chemistry and Physiology of Bile Pigments. U. S. Dept. of Health, DHEW Publ. No. (NIH) 77-1100, Washington, D. C. 1977, p. 431.

[21] *W. R. Briggs, H. V. Rice*, Annu. Rev. Plant Physiol. *23*, 293 (1972).

[22] *P. O'Carra, C. O'hEocha* in [16a], p. 328.

[23] a) *D. S. Berns* in *S. N. Timasheff, G. D. Fasman:* Subunits in Biological Systems. Dekker, New York 1971, Part A, p. 105; b) *R. McColl, D. S. Berns*, Trends Biochem. Sci. *4*, 44 (1979).

[24] a) *D. Dolphin:* The Porphyrins. Academic Press, New York; b) *A. Bennett, H. W. Siegelman* in [24a], Vol. VI, 1979, p. 493.

[25] *B. J. Chapman* in [11a], p. 162.

[26] *G. Blauer*, Struct. Bonding (Berlin) *18*, 69 (1974).

[27] a) *M. Choussy, M. Barbier*, Helv. Chim. Acta *58*, 2651 (1975); b) *M. Bois-Choussy, M. Barbier*, Heterocycles 9, 677 (1978).

[28] *W. H. Bannister, J. V. Bannister, H. Micaleff*, Comp. Biochem. Physiol. *35*, 237 (1970).

[29] a) *W. Rüdiger*, Naturwissenschaften *57*, 331 (1970); b) Hoppe-Seylers Z. Physiol. Chem. *348*, 129 (1967).

[30] *T. Ogata, N. Fusetani, K. Yamaguchi*, Comp. Biochem. Physiol. *B 63*, 239 (1979).

[31] *A. N. Glazer, C. S. Hixson*, J. Biol. Chem. *252*, 32 (1977).

[32] *D. A. Bryant, A. N. Glazer, F. A. Eiserling*, Arch. Microbiol. *110*, 61 (1976).

[33] *A. N. Glazer, G. Cohen-Bazire*, Arch. Microbiol. *104*, 29 (1975).

[34] *J. Jung, P.-S. Song, R. J. Paxton, M. S. Edelstein, R. Swanson, E. E. Hazen, Jr.*, Biochemistry *19*, 24 (1980).

[35] *S. Grombein, W. Rüdiger, H. Zimmermann*, Hoppe-Seylers Z. Physiol. Chem. *356*, 1709 (1975).

[36] *H. Scheer*, Z. Naturforsch. *C 31*, 413 (1976).

[37] a) *G. Klein, S. Grombein, W. Rüdiger*, Hoppe-Seylers Z. Physiol. Chem. *358*, 1077 (1977); b) *J.-P. Weller, A. Gossauer*, Chem. Ber. *113*, 1603 (1980); c) *W. Rüdiger, T. Brandlmeier, I. Blos, A. Gossauer, J. P. Weller*, Z. Naturforsch. *C 35*, 763 (1980).

[38] *J. C. Lagarias, H. Rapport*, J. Am. Chem. Soc. *102*, 4821 (1980).

[39] *H. Lehner, T. Brandlmeier, W. Rüdiger*, private communication (1980).

[40] *H. Falk, K. Grubmayr, E. Haslinger, T. Schlederer, K. Thirring*, Monatsh. Chem. *109*, 1451 (1978).

[41] *C. Krauss, C. Bubenzer, H. Scheer*, Photochem. Photobiol. *30*, 473 (1979).

[42] *P. O'Carra, C. O'hEocha*, Phytochemistry *5*, 993 (1966).

[43] *E. Fu, L. Friedman, H. W. Siegelman*, Biochem. J. *179*, 1 (1979).

[44] *B. L. Schram, H. H. Kroes*, Eur. J. Biochem. *19*, 581 (1971).

[45] *G. Klein, W. Rüdiger*, Justus Liebigs Ann. Chem. *1978*, 267.

[46] *A. Gossauer, J.-P. Weller*, J. Am. Chem. Soc. *100*, 5928 (1978).

[47] *H. Scheer, C. Bubenzer*, unpublished.

[48] *H. L. Crespi, U. Smith, J. J. Katz*, Biochemistry *7*, 2232 (1968).

[49] *H. L. Crespi, L. J. Boucher, G. D. Norman, J. J. Katz, R. C. Dougherty*, J. Am. Chem. Soc. *89*, 3642 (1967).

[50] *W. J. Cole, D. J. Chapman, H. W. Siegelman*, Biochemistry *7*, 2929 (1968).

[51] *D. J. Chapman, W. J. Cole, H. W. Siegelman*, J. Am. Chem. Soc. *89*, 5976 (1967).

[52] a) *W. Rüdiger, P. O'Carra, C. O'hEocha*, Nature *215*, 5109 (1967); b) *W. Rüdiger, P. O'Carra*, Eur. J. Biochem. *7*, 509 (1969).

[53] *W. Rüdiger*, Hoppe-Seylers Z. Physiol. Chem. *350*, 1291 (1969).

[54] a) *A. Gossauer, W. Hirsch*, Justus Liebigs Ann. Chem. *1974*, 1496; b) *A. Gossauer, R.-P. Hinze*, J. Org. Chem. *43*, 283 (1978); c) *A. Gossauer, R.-P. Hinze, R. Kutschan*, Chem. Ber. *114*, 132 (1981).

[55] *T. Brandlmeier, I. Blos, W. Rüdiger*, in *J. A. de Greef:* Photoreceptors and Plant Development. Antwerpen University Press, Antwerpen 1979, p. 47 ff.

[56] *H. Brockmann Jr., G. Knobloch*, Chem. Ber. *106*, 803 (1973).

[57] *W. J. Cole, C. O'hEocha, A. Moscowitz, W. R. Krueger*, Eur. J. Biochem. *3*, 202 (1967).

[58] *S. Schoch, G. Klein, U. Linsenmeier, W. Rüdiger*, Justus Liebigs Ann. Chem. *1976*, 549.

[59] *H. Lotter, G. Klein, W. Rüdiger, H. Scheer*, Tetrahedron Lett. *1977*, 2317.

[60] *R. F. Troxler, A. S. Brown, H. P. Köst*, Eur. J. Biochem. *87*, 181 (1978).

[61] *G. Muckle, W. Rüdiger*, Z. Naturforsch. *C 32*, 957 (1977).

[62] *F. Frank, W. Sidler, H. Widmer, H. Zuber*, Hoppe-Seylers Z. Physiol. Chem. *359*, 1491 (1978).

[63] *R. Troxler*, unpublished.

[64] *P. Freidenreich, G. S. Apell, A. N. Glazer*, J. Biol. Chem. *253*, 212 (1978).

[65] *J. C. Lagarias, A. N. Glazer, H. Rapoport*, J. Am. Chem. Soc. *101*, 5030 (1979).

[66] *H. Scheer, U. Linsenmeier, C. Krauss,* Hoppe-Seylers Z. Physiol. Chem. *358,* 185 (1977).

[67] *C. Krauss, H. Scheer,* part of a lecture at the Chemiedozententagung, Erlangen 1980.

[68] *P. Ehrlich,* Zentralbl. Klin. Med. *45,* 721 (1883).

[69] *K. P. M. Heirwegh, J. Fevery, J. A. T. P. Neuwissen, F. Compernolle, V. Desmet, F. P. van Roy,* Methods Biochem. Anal. *22,* 205 (1974).

[70] *W. Kufer, H. Scheer,* part of a lecture at the Chemiedozententagung, Erlangen 1980.

[71] *H. P. Köst, W. Rüdiger, D. J. Chapman,* Justus Liebigs Ann. Chem. *1975,* 1582.

[72] *A. N. Glazer, C. S. Hixson,* J. Biol. Chem. *250,* 5487 (1975).

[73] *G. Struckmeier, U. Thewaldt, J.-H. Fuhrhop,* J. Am. Chem. Soc. *98,* 278 (1976).

[74] *G. R. Anderson, E. L. Jenner, F. E. Mumford,* Biochemistry *8,* 1182 (1969).

[75] *R. E. Kendrick, C. J. P. Spruit,* Photochem. Photobiol. *26,* 201 (1977).

[76] *H. Linschitz, V. Kasche,* Proc. Natl. Acad. Sci. USA *58,* 1059 (1967).

[77] *W. L. Butler, L. H. Pratt,* Photochem. Photobiol. *11,* 361 (1970).

[78] *S. E. Braslavsky, J. J. Matthews, H. J. Herbert, J. de Kok, C. J. P. Spruit, K. Schaffner,* Photochem. Photobiol. *31,* 417 (1980).

[79] *C. J. P. Spruit, R. E. Kendrick,* Photochem. Photobiol. *26,* 133 (1977).

[80] *M. J. Burke, D. C. Pratt, A. Moscowitz,* Biochemistry *11,* 4025 (1972).

[81] a) *D. R. Cross, H. Linschitz, V. Kasche, J. Tenenbaum,* Proc. Natl. Acad. Sci. USA *61,* 1095 (1968); b) *A. P. Balangé,* Dissertation, Université Rouen 1973.

[82] *H. H. Kroes,* Meded. Landbouwhogesch. Wageningen 70–181 (1970).

[83] *E. Tobin, W. R. Briggs, P. K. Brown,* Photochem. Photobiol. *18,* 497 (1973).

[84] *C. J. P. Spruit, R. E. Kendrick, R. J. Cooke,* Planta *127,* 121 (1975).

[85] *S. E. Ostroy,* Biochim. Biophys. Acta *463,* 91 (1977).

[86] *D. A. Lightner,* Photochem. Photobiol. *26,* 427 (1977).

[87] a) *A. Gossauer, H. H. Inhoffen,* Justus Liebigs Ann. Chem. *1970,* 18; b) *A. Gossauer, M. Blacha, W. S. Sheldrick,* J. Chem. Soc. Chem. Commun. *1976,* 764.

[88] *H. Falk, K. Grubmayr, G. Höllbacher, O. Hofer, A. Leodolter, N. Neufingerl,* J. M. Ribo, Monatsh. Chem. *108,* 1113 (1977).

[89] a) *H. Falk, K. Grubmayr,* Angew. Chem. *89,* 487 (1977); Angew. Chem. Int. Ed. Engl. *16,* 470 (1977); b) *H. Falk, N. Müller, T. Schlederer,* Monatsh. Chem. *111,* 159 (1980).

[90] a) *A. Gossauer, M. Blacha-Puller, R. Zeisberg, V. Wray,* unpublished; b) *M. Blacha-Puller,* Dissertation, Technische Universität Braunschweig 1979.

[91] *H. Falk, G. Höllbacher,* Monatsh. Chem. *109,* 1429 (1978).

[92] *H. Falk, K. Grubmayr,* Monatsh. Chem. *110,* 1237 (1979).

[93] *H. Falk, K. Thirring,* Z. Naturforsch. *B 34,* 1448 (1979); *B 35,* 376 (1980).

[94] *H. Scheer, H. Formanek, W. Rüdiger,* Z. Naturforsch. *C 34,* 1085 (1979).

[95] *B. Pullman, A.-M. Perault,* Proc. Natl. Acad. Sci. USA *45,* 1476 (1959).

[96] *A. R. Holzwarth, H. Lehner, S. E. Braslavsky, K. Schaffner,* Justus Liebigs Ann. Chem. *1978,* 2002.

[97] *W. Kufer, H. Scheer,* Z. Naturforsch. *C 34,* 776 (1979).

[98] *H. Falk, T. Schlederer,* Monatsh. Chem. *109,* 1013 (1978).

[99] *P. Manitto, D. Monti,* Experientia *35,* 1418 (1979).

[100] *F. E. Mumford, E. L. Jenner,* Biochemistry *10,* 98 (1971).

[101] *R. M. Klein, P. C. Edsall,* Plant Physiol. *41,* 949 (1966).

[102] *L. H. Pratt, S. C. Cundiff,* Photochem. Photobiol. *21,* 91 (1975).

[103] *H. Scheer* in [24a], Vol. II, 1978, p. 45.

[104] *I. B. C. Matheson, M. M. Toledo,* Photochem. Photobiol. *25,* 243 (1977).

[105] *H. Scheer, C. Krauss,* Photochem. Photobiol. *25,* 311 (1977).

[106] *C. Krauss,* Dissertation, Universität München 1980.

[107] a) *G. Löber, L. Kittler,* Photochem. Photobiol. *25,* 215 (1977); b) *E. R. Lochmann, A. Michler* in *J. Duchesnel:* Physico Chemical Properties of Nucleic Acids. Academic Press, New York 1973.

[108] *F. Eivazi, W. M. Lewis, K. M. Smith,* Tetrahedron Lett. *1977,* 3083; *F. Eivazi, K. M. Smith,* J. Chem. Soc. Perkin Trans. I, *544* (1979).

[109] *C. Krauss, H. Scheer,* Tetrahedron Lett. *1979,* 3553.

[110] *J. V. Bonfiglio, R. Bonnett, M. B. Hursthouse, K. M. A. Malik, S. C. Naithani,* J. Chem. Soc. Chem. Commun. *1977,* 829.

[111] *S. J. Roux, S. G. Lisansky, B. M. Stoker,* Physiol. Plant *35,* 85 (1975).

[112] *G. Gardner, W. F. Thompson, W. R. Briggs,* Planta *117,* 367 (1974).

[113] *R. E. Hunt, L. H. Pratt,* Biochemistry, in press; part of a lecture at the Eur. Symp. Photomorphogenesis, Antwerpen 1979.

[114] *A. Moscowitz, W. C. Krueger, I. T. Kay, G. Skews, S. Bruckenstein,* Proc. Natl. Acad. Sci. USA *52,* 1190 (1964).

[115] *W. S. Sheldrick,* J. Chem. Soc. Perkin Trans. II *1976,* 1457.

[116] *H. Lehner, S. E. Braslavsky, K. Schaffner,* Angew. Chem. *90,* 1012 (1978); Angew. Chem. Int. Ed. Engl. *17,* 948 (1978).

[117] *H. Lehner, S. E. Braslavsky, K. Schaffner,* Justus Liebigs Ann. Chem. *1978,* 1990.

[118] *H. Falk, K. Grubmayr, K. Thirring,* Z. Naturforsch. *B 33,* 924 (1978).

[119] *S. E. Braslavsky, A. R. Holzwarth, E. Langer, H. Lehner, J. J. Matthews, K. Schaffner,* Isr. J. Chem. *20,* 196 (1980).

[120] *H. Lehner, W. Riemer, K. Schaffner,* Justus Liebigs Ann. Chem. *1979,* 1798.

[121] *G. Wagnière, G. Blauer,* J. Am. Chem. Soc. *98,* 7806 (1976).

[122] *D. L. Cullen, F. E. Meyer, Jr., F. Eivazi, K. M. Smith,* J. Chem. Soc. Perkin Trans. II *1978,* 259.

[123] *H. Lehner, H. Scheer,* Z. Naturforsch. *B,* in press.

[124] *H. Scheer, P. Bartholmes, H. Lehner,* unpublished.

[125] *H. Scheer, W. Kufer,* Z. Naturforsch. *C 32,* 513 (1977).

[126] *I. M. Tegmo-Larsson, S. E. Braslavsky, K. Schaffner,* private communication (März 1980).

[127] *I. M. Tegmo-Larsson, S. E. Braslavsky, C. Nicolau, K. Schaffner,* unpublished.

[128] *R. Bonnett, J. E. Davies, M. B. Hursthouse, G. M. Sheldrick,* Proc. R. Soc. Ser. *B 202,* 249 (1978).

[129] *W. Kufer, H. Scheer,* Hoppe-Seylers Z. Physiol. Chem. *360,* 935 (1979).

[130] *W. Kufer, A. R. Holzwarth, H. Scheer,* unpublished.

[131] *T. Sugimoto, K. Ishikawa, H. Suzuki,* J. Phys. Soc. Jpn. *40,* 258 (1976).

[132] *Q. Chae, P. S. Song,* J. Am. Chem. Soc. *97,* 4176 (1975).

[133] *R. Pasternak, G. Wagnière,* J. Am. Chem. Soc. *101,* 1662 (1979).

[134] *J.-H. Fuhrhop, P. K. W. Wasser, J. Subramanian, U. Schrader,* Justus Liebigs Ann. Chem. *1974,* 1450.

[135] *C. H. Chen, D. S. Berns,* Biophys. Chem. *8,* 191 (1978).

[135a] *T. Brandlmeier, H. Lehner, W. Rüdiger,* Photochem. Photobiol., in press; see also [18b].

[136] *D. Frackowiak, J. Grabowski,* Photosynthetica *5,* 146 (1971).

[137] *D. Frackowiak, K. Fiksinski, J. Grabowski,* Photosynthetica *9,* 185 (1975).

[138] *J. Friedrich, H. Scheer, B. Zickendraht-Wendelstadt, D. Haarer,* J. Chem. Phys. *74,* 2260 (1981); J. Am. Chem. Soc. *103* (1981), in press.

[139] *B. Zickendraht-Wendelstadt, J. Friedrich, W. Rüdiger,* Photochem. Photobiol. *31,* 367 (1980).

[140] a) *F. W. J. Teale, R. E. Dale,* Biochem. J. *116,* 161 (1970); b) *R. E. Dale, F. W. J. Teale,* Photochem. Photobiol. *12,* 99 (1970).

[141] *C. Vernotte,* Photochem. Photobiol. *14,* 163 (1971).

[142] *J. Grabowski, E. Gantt,* Photochem. Photobiol. *28,* 39 (1978).

[143] *J. Grabowski, E. Gantt,* Photochem. Photobiol. *28,* 47 (1978).

[144] *E. Langer, H. Lehner, W. Rüdiger, B. Zickendraht-Wendelstadt,* Z. Naturforsch. *C 35,* 367 (1980).

[144a] *P. S. Song,* private communication.

[145] *L. J. Boucher, H. L. Crespi, J. J. Katz,* Biochemistry *5,* 3796 (1966).

[146] *D. Frackowiak, J. Grabowski, H. Manikowski,* Photosynthetica *10,* 204 (1976).

[147] *A. S. Brown, J. A. Foster, P. V. Voynow, C. Franzblau, R. F. Troxler,* Biochemistry *14,* 3581 (1975).

[148] a) *E. Fujimori, J. Pecci,* Biochim. Biophys. Acta *221,* 132 (1970); b) *A. C. Ley, W. L. Butler, D. A. Bryant, A. N. Glazer,* Plant. Physiol. *59,* 974 (1977).

[149] *G. Cohen-Bazire, S. Beguin, S. Rimon, A. N. Glazer, D. M. Brown,* Arch. Microbiol. *111,* 225 (1977).

[150] *R. McColl, K. Csatorday, D. S. Berns, E. Traeger,* Biochemistry, *19,* 2817 (1980).

[151] a) *B. H. Gray, E. Gantt,* Photochem. Photobiol. *21,* 121 (1975); b) *B. H. Gray, J. Cosner, E. Gantt,* ibid. *24,* 299 (1976).

[152] *E. Gantt, O. Canaani,* Biochemistry *19,* 2950 (1980).

[153] *E. Gantt, C. A. Lipschultz,* Biochemistry *13,* 2960 (1974).

[154] *A. Bennett, L. Bogorad,* Biochemistry *10,* 3625 (1971).

[155] a) *C. Petrier, P. Jardon, C. Dupuy, R. Gautron,* J. Chim. Phys. *76,* 97 (1979); b) *C. Petrier, C. Dupuy, P. Jardon, R. Gautron,* private communication; c) *R. Gautron, P. Jardon, C. Petrier, M. Choussy, M. Barbier, M. Vuillaume,* Experientia *32,* 1100 (1976).

[156] *H. Falk, K. Grubmayr, F. Neufingerl,* Monatsh. Chem. *110,* 1127 (1979).

[157] *P. S. Song, Q. Chae, D. A. Lightner, W. R. Briggs, D. Hopkins,* J. Am. Chem. Soc. *95,* 7892 (1973).

[158] *E. J. Land,* Photochem. Photobiol. *29,* 483 (1979).

[159] *H. Falk, F. Neufingerl,* Monatsh. Chem. *110,* 987 (1979).

[160] *A. F. McDonagh* in [24a], Vol. VI, 1979, p. 294.

[161] *M. F. Hudson, K. M. Smith,* Chem. Soc. Rev. *4,* 363 (1975).

[162] *P. Manitto, D. Monti,* Experientia *28,* 379 (1972).

[163] *G. Calzaferri, H. Gugger, S. Leutwyler,* Helv. Chim. Acta *59,* 1969 (1976).

[164] *W. Windhager, S. Schneider, F. Dörr,* Z. Naturforsch. A 32, 876 (1977).

[165] *C. Petrier, W. Kufer, H. Scheer, R. Gautron,* unpublished.

[166] *A. R. Holzwarth, E. Langer, H. Lehner, K. Schaffner,* Photochem. Photobiol. *32,* 17 (1980).

[167] pronounced isotope effects on the lifetime of excited states have been observed in poryphyrins: *A. T. Gradyushko, M. P. Tsvirko,* Opt. Spektrosk. *31,* 291 (1971); *R. P. Burgner, A. M. Ponte-Goncalves,* J. Chem. Phys. *60,* 2942 (1974).

[168] *C. O'hEocha, P. O'Carra,* J. Am. Chem. Soc. *83,* 1091 (1961).

[169] *C. O'hEocha,* Biochemistry *2,* 375 (1963).

[170] *B. Zickendraht-Wendelstadt,* Dissertation, Universität München 1980.

[171] *D. Frackowiak, A. Skowron,* Photosynthetica *12,* 76 (1978).

[172] *W. Kufer, H. Scheer,* Z. Naturforsch. *C 34,* 776 (1979).

[173] *S. S. Chen, D. S. Berns,* J. Membrane Biol. *47,* 113 (1979).

[174] *G. Blankenhorn, E. G. Moore,* J. Am. Chem. Soc. *102,* 1092 (1980).

[175] *R. Troxler,* private communication (1980).

[176] *W. Kufer,* Diplomarbeit, Universität München 1977.

[177] *A. Abeliovich, M. Shilo,* Biochim. Biophys. Acta *283,* 483 (1972).

[178] *J. S. Bellin, C. A. Gergel,* Photochem. Photobiol. *13,* 399 (1971).

[179] *K. Ohki, Y. Fujita,* Plant Cell Physiol. *20,* 483 (1979).

[180] *I. Ohad, R. K. Clayton, L. Bogorad,* Proc. Natl. Acad. Sci. USA *76,* 5655 (1979).

[181] *J. Gysi, H. Zuber,* FEBS Lett. *68,* 49 (1976).

[182] *B. A. Zilinskas, B. K. Zimmermann, E. Gantt,* Photochem. Photobiol. *27,* 587 (1978).

[183] *J. Gysi, H. Zuber,* FEBS Lett. *48,* 209 (1974).

[184] *A. N. Glazer, D. A. Bryant,* Arch. Microbiol. *104,* 15 (1975).

[185] *B. T. Cope, U. Smith, H. L. Crespi, J. J. Katz,* Biochim. Biophys. Acta *133,* 446 (1967).

[186] *P. A. Torjesen, K. Sletten,* Biochim. Biophys. Acta *263,* 258 (1972).

[187] *A. N. Glazer, G. Cohen-Bazire,* Proc. Natl. Acad. Sci. USA *68,* 1398 (1971).

[188] *D. J. Chapman, W. J. Cole, H. W. Siegelman,* Biochem. J. *105,* 903 (1967).

[189] *E. Mörschel, W. Wehrmeyer,* Arch. Microbiol. *105,* 153 (1975).

[190] *P. O'Carra,* Biochem. J. *119,* 2P (1970).

[191] *E. Tobin, W. R. Briggs,* Photoechem. Photobiol. *18,* 487 (1973).

[192] *H. H. van de Velde,* Biochim. Biophys. Acta *303,* 246 (1973).

[193] *C. Abad-Zapatero, J. L. Fox, M. L. Hackert,* Biochem. Biophys. Res. Commun. *78,* 266 (1977).

[194] *R. M. Sweet, H. E. Fuchs, R. G. Fisher, A. N. Glazer,* J. Biol. Chem. *252,* 8258 (1977).

[195] *A. N. Glazer, G. Cohen-Bazire, R. Y. Stanier,* Arch. Microbiol. *80,* 1 (1971).

[196] *R. McColl, D. S. Berns,* Biochem. Biophys. Res. Commun. *90,* 849 (1979).

[197] *E. Mörschel, W. Wehrmeyer,* Arch. Microbiol. *113,* 83 (1977).

[198] *R. McColl, D. S. Berns, O. Gibbons,* Arch. Biochem. Biophys. *177,* 265 (1976).

[199] *K. T. Fry, F. E. Mumford,* Biochem. Biophys. Res. Commun. *45,* 1466 (1971).

[200] *H. V. Rice, W. R. Briggs, C. J. Jackson-White,* Plant Physiol. *51,* 917 (1973).

[201] *R. E. Hunt, L. H. Pratt,* Biochemistry, *19,* 390 (1980).

[202] *P. H. Quail, W. R. Briggs, L. H. Pratt,* Carnegie Inst. Yearbook *77,* 252 (1978).

[203] *H. V. Rice, W. R. Briggs,* Plant Physiol. *51,* 927 (1973).

[204] *S. Shimura, Y. Fujita,* Mar. Biol. *31,* 121 (1975).

[205] *H. Zuber,* Ber. Dtsch. Bot. Ges. *91,* 459 (1978).

[206] *J. U. Harris, D. S. Berns,* J. Mol. Evol. *5,* 153 (1975).

[207] *P. G. H. Byfield, H. Zuber,* FEBS Lett. *28,* 36 (1972).

[208] *E. Köst-Reyes, H. P. Köst, W. Rüdiger,* Justus Liebigs Ann. Chem. *1975,* 1594.

[209] *G. Muckle, J. Otto, W. Rüdiger,* Hoppe-Seylers Z. Physiol. Chem. *359,* 345 (1978).

[210] *D. A. Bryant, C. S. Hixson, A. N. Glazer,* J. Biol. Chem. *253,* 220 (1978).

[211] *V. P. Williams, A. N. Glazer,* J. Biol. Chem. *253,* 202 (1978).

[212] *T. Fujiwara,* J. Biochem. (Tokyo) *43,* 195 (1956).

[213] *S. D. Kililea, P. O'Carra,* Biochem. J. *110,* 14P (1968).

[214] *H. L. Crespi, U. H. Smith,* Phytochemistry *9,* 205 (1970).

[215] *C. Brooks, D. J. Chapman,* Phytochemistry *11,* 2663 (1972).

[216] *E. Köst-Reyes, H. P. Köst,* Eur. J. Biochem. *102,* 83 (1979).

[217] *A. N. Glazer, C. S. Hixson, R. J. DeLange,* Anal. Biochem. *92,* 489 (1979).

[218] *G. Klein, W. Rüdiger,* Z. Naturforsch. *C 34,* 192 (1979).

[219] *S. D. Dobler, K. Dover, K. Laves, A. Binder, H. Zuber,* J. Mol. Biol. *71,* 785 (1972).

[220] *M. L. Hackert, C. Abad-Zapatero, S. E. Stevens, Jr., J. L. Fox,* J. Mol. Biol. *111,* 365 (1977).

[221] *J. L. Fox,* private communication (1979).

[222] *A. Kotera, T. Saito, N. Iso, H. Mizuno, N. Taki,* Bull. Chem. Soc. Jpn. *48,* 1176 (1975).

[223] *K. P. Koller, W. Wehrmeyer, E. Moerschel,* Eur. J. Biochem. *91,* 57 (1978).

[224] *E. Moerschel, K. P. Koller, W. Wehrmeyer, H. Schneider,* Cytobiology *16,* 118 (1977).

[225] *A. N. Glazer, R. C. Williams, G. Yamanaka, H. K. Schachman,* Proc. Natl. Acad. Sci. USA *76,* 6162 (1979).

[226] *M. A. Raftery, C. O'hEocha,* Biochem. J. *94,* 166 (1965).

[227] *D. S. Berns,* Plant Physiol. *42,* 1569 (1967).

[228] *A. N. Glazer, G. Cohen-Bazire, R. Y. Stanier,* Proc. Natl. Acad. Sci. USA *68,* 3005 (1971).

[229] *L. Bogorad,* Rec. Chem. Prog. *26,* 1 (1965).

[230] *J. Eder, R. Wagenmann, W. Rüdiger,* Immunochemistry *15,* 315 (1978).

[231] *J. Takemoto, L. Bogorad,* Biochemistry *14,* 1211 (1975).

[232] *S. Boussiba, A. E. Richmond,* Arch. Microbiol. *120,* 155 (1979).

[233] *A. N. Glazer, S. Fang,* J. Biol. Chem. *248,* 663 (1973).

[234] *G. Frank, H. Zuber, W. Lergier,* Experientia *31,* 23 (1975).

[235] *A. Salahuddin, C. Tanford,* Biochemistry *9,* 1342 (1970).

[236] *J. A. Knapp, C. N. Pace,* Biochemistry *13,* 1289 (1974).

[237] *P. Bartholmes, H. Scheer,* unpublished.

[238] *R. McColl, J. J. Lee, D. S. Berns,* Biochem. J. *122,* 421 (1971).

[239] *J. J. Lee, D. S. Berns,* Biochem. J. *110,* 465 (1968).

[240] *J. Grabowski, C. A. Lipschultz, E. Gantt,* Plant Physiol., in press.

[241] *T. Saito, N. Iso, H. Mizuno, I. Kitamura,* Bull. Chem. Soc. Jpn. *51,* 3471 (1976).

[242] *R. McColl, M. R. Edwards, M. H. Mulks, D. S. Berns,* Biochem. J. *141,* 419 (1974).

[243] *N. Iso, H. Mizuno, T. Saito, N. Nitta, K. Yoshizaki,* Bull. Chem. Soc. Jpn. *56,* 2892 (1977).

[244] *G. J. Neufeld, A. F. Riggs,* Biochim. Biophys. Acta *181,* 234 (1969).

[245] *R. McColl, D. S. Berns, N. L. Koven,* Arch. Biochem. Biophys. *146,* 477 (1971).

[246] *R. McColl, D. S. Berns,* Arch. Biochem. Biophys. *156,* 161 (1973).

[247] *D. S. Berns, A. Morgenstern,* Arch. Biochem. Biophys. *123,* 640 (1968).

[248] a) *E. Mörschel, W. Wehrmeyer, K.-P. Koller,* Eur. J. Cell. Biol. *21,* 319 (1980); b) *E. Mörschel, K.-P. Koller, W. Wehrmeyer,* Arch. Microbiol. *125,* 43 (1980).

[249] *A. Hattori, H. L. Crespi, J. J. Katz,* Biochemistry *4,* 1225 (1965).

[250] *C. H. Chen, D. S. Berns,* J. Phys. Chem. *82,* 2781 (1978).

[251] *S. M. Adams, O. H. W. Kao, D. S. Berns,* Plant Physiol. *64,* 525 (1979).

[252] *O. H. W. Kao, D. S. Berns, W. R. Town,* Biochem. J. *131,* 39 (1973).

[253] *O. H. W. Kao, M. R. Edwards, D. S. Berns,* Biochem. J. *147,* 63 (1975).

[254] *D. L. Correll, E. Steers, Jr., K. M. Towe, W. Shropshire, Jr.,* Biochim. Biophys. Acta *168,* 46 (1968).

[255] *G. Gardner, C. S. Pike, H. V. Rice, W. R. Briggs,* Plant Physiol. *48,* 686 (1971).

[256] *S. Grombein, W. Rüdiger,* Hoppe-Seylers Z. Physiol. Chem. *357,* 1015 (1976).

[257] *C. S. Pike, W. R. Briggs,* Plant Physiol. *49,* 521 (1972).

[258] *L. H. Pratt,* Plant Physiol. *51,* 503 (1973).

[259] *B. M. Stoker, K. McEntire, S. J. Roux,* Photochem. Photobiol. *27,* 597 (1978).

[260] *B. M. Stoker, S. J. Roux, W. E. Brown,* Nature *271,* 180 (1978).

[261] *G. H. Kidd, R. E. Hunt, M. L. Boeshore, L. H. Pratt,* Nature *276,* 733 (1978).

[262] *L. H. Pratt,* Photochem. Photobiol. *22,* 33 (1975).

[263] *P. S. Song, Q. Chae, J. D. Gardner,* Biochim. Biophys. Acta *576,* 479 (1979).

[264] *S. C. Cundiff, L. H. Pratt,* Plant Physiol. *55,* 212 (1975).

[265] *R. E. Hunt, L. H. Pratt,* Plant Physiol., in press.

[266] *A. P. Balangé, P. Rollin,* Plant. Sci. Lett. *1,* 59 (1973).

[267] *D. Marmé, J. Boisard, W. R. Briggs,* Proc. Natl. Acad. Sci. USA *70,* 3861 (1973).

[268] *N. Roth-Bejerano, R. E. Kendrick,* Proc. Eur. Symp. Photomorphogenesis, Aarhus (1978).

[269] *W. O. Smith,* Eur. Symp. Photoreceptors and Plant Development, Antwerpen (1979).

[269a] *S. Daniels, W. O. Smith,* private communication.

[270] *P. H. Quail,* Photochem. Photobiol. *27,* 147 (1978).

[271] *L. H. Pratt, D. Marmé,* Plant Physiol. *58,* 686 (1976).

[272] *L. H. Pratt,* private communication (1979).

[273] *J. Scheibe,* Science *176,* 1037 (1972).

[274] *G. S. Björn, L. O. Björn,* Physiol. Plant. *26,* 297 (1976).

[275] *G. S. Björn,* Physiol. Plant. *42,* 321 (1978).

[275a] *G. S. Björn,* private communication.

[276] *E. Gantt, S. F. Conti,* J. Cell Biol. *29,* 423 (1966).

[277] *R. B. Wildman, C. C. Bowen,* J. Bacteriol. *117,* 866 (1974).

[278] *G. Yamanaka, A. N. Glazer, R. C. Williams,* J. Biol. Chem. *253,* 8303 (1978).

[279] *G. Wanner, H.-P. Köst,* Protoplasma *102,* 97 (1980).

[280] *N. Tandeau de Marsac, G. Cohen-Bazire,* Proc. Natl. Acad. Sci. USA *74,* 1635 (1977).

[281] *E. Gantt, B. A. Zilinskas,* Biochim. Biophys. Acta *430,* 375 (1976).

[282] *E. Gantt, C. A. Lipschultz,* J. Phycol. *13,* 185 (1977).

[283] a) *O. Canaani, C. A. Lipschultz, E. Gantt,* FEBS Lett. *115,* 225 (1980); b) *T. Redlinger, E. Gantt,* 5th Int. Congr. Photosynthesis, Halkidiki 1980.

[284] *M. Rigbi, J. Rosinski, H. W. Siegelman, J. C. Sutherland,* Proc. Natl. Acad. Sci, USA, in press.

[285] *B. H. Gray, C. A. Lipschultz, E. Gantt,* J. Bacteriol. *116,* 471 (1973).

[286] *E. Gantt, C. A. Lipschultz, J. Grabowski, K. Zimmerman,* Plant Physiol. *63,* 615 (1979).

[287] *R. Wagenmann,* Dissertation, Universität München 1977.

[288] *H. W. Siegelman,* private communication (1980).

[289] *G. Porter, C. J. Tredwell, G. F. W. Searle, J. Barber,* Biochim. Biophys. Acta *501,* 232 (1978).

[290] *G. F. W. Searle, J. Barber, G. Porter, C. J. Tredwell,* Biochim. Biophys. Acta *501,* 246 (1978).

[291] *K. Ohki, Y. Fujita,* Plant Cell Physiol. *20,* 1341 (1979).

[292] *K. Csatorday,* Biochim. Biophys. Acta *504,* 341 (1978).

[293] *P. Fay* in [11a], p. 238.

[294] *T. Katoh, E. Gantt,* Biochim. Biophys. Acta *546,* 383 (1979).

[295] *G. Harnischfeger, G. A. Codd,* Biochim. Biophys. Acta *502,* 507 (1978).

[296] *C. A. Pullin, R. G. Brown, E. H. Evans,* FEBS Lett. *101,* 110 (1979).

[297] *T. Kobayashi, E. O. Degenkolb, R. Behrson, P. M. Rentzepis, R. McColl, D. S. Berns,* Biochemistry *18,* 5073 (1979).

[298] *E. Gantt* in *M. Levandovski, S. H. Hufner:* Biochemistry and Physiology of Protozoa. 2. Aufl. Academic Press, New York 1979, p. 12.
[299] a) *W. Wehrmeyer*, Arch. Microbiol. *71*, 367 (1979); b) *E. Gantt, M. R. Edwards, L. Provasoli*, J. Cell. Biol. *48*, 280 (1971).
[300] *W. Wehrmeyer*, private communication (1979).
[301] *R. McColl, D. S. Berns*, Photochem. Photobiol. *27*, 343 (1978).
[302] *A. Schmidt*, unpublished.
[303] *V. B. Evstigneev* in *K. Dose, S. W. Fox, G. A. Deborin, T. E. Pavlovskaya:* The Origin of Life and Evolutionary Biochemistry. Plenum, New York 1974, S. 97.
[304] *D. S. Berns*, Photochem. Photobiol. *24*, 117 (1976).
[305] *V. B. Evstigneev, O. D. Bekasova*, Biofizika *17*, 997 (1972).
[306] *A. Ilani, D. S. Berns*, Biochem. Biophys. Res. Commun. *45*, 1423 (1971).
[307] *M. Kumbar, R. McColl*, Res. Commun. Chem. Pathol. Pharmacol. *11*, 627 (1975).
[308] *H. Mohr, P. Schopfer:* Lehrbuch der Pflanzenphysiologie. 3rd Edit. Springer, Berlin 1978.
[309] *D. Marmé*, Annu. Rev. Plant Physiol. *28*, 173 (1977).
[310] *H. W. Siegelman, D. J. Chapman, W. J. Cole* in [16a], p. 107.
[311] *R. F. Troxler, A. Brown*, Biochim. Biophys. Acta *215*, 503 (1970).
[312] *R. F. Troxler*, Biochemistry *11*, 4235 (1972).
[313] *R. F. Troxler, J. M. Dokos*, Plant Physiol. *51*, 72 (1973).
[314] *R. F. Troxler, A. S. Brown, S. B. Brown*, J. Biol. Chem. *254*, 3411 (1979).
[315] *S. B. Brown, R. F. G. J. King*, Biochem. J. *170*, 297 (1978).
[316] *R. J. Beuhler, R. C. Pierce, L. Friedman, H. W. Siegelman*, J. Biol. Chem. *251*, 2405 (1976).
[317] *N. Tandeau de Marsac*, J. Bacteriol. *130*, 82 (1977).
[318] *K. Ohki, Y. Fujita*, Plant Cell Physiol. *19*, 7 (1978).
[319] *S. Gendel, I. Ohad, L. Bogorad*, Plant Physiol. *64*, 786 (1979).
[320] *J. F. Haury, L. Bogorad*, Plant Physiol. *60*, 835 (1977).
[321] *H. Falk, K. Thirring*, Tetrahedron, *37*, 761 (1981).
[322] *H.-P. Köst, G. Wanner, H. Scheer*, Photochem. Photobiol., in press.
[323] The occurrence of biliproteins and an energy transfer to PSI in heterocysts has recently been reported: *R. B. Petterson, E. Dolan, H. E. Calvert, B. Ke*, Biochim. Biophys. Acta *634*, 237 (1981).

# COMMUNICATIONS

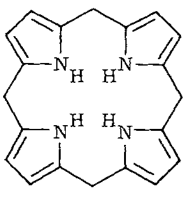
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

## Interconversion of the Chromophore Systems of Porphyrinogen and 2,3,7,8,12,13-Hexahydroporphyrin[**]

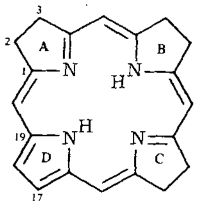
By *Jon Eigill Johansen, Virginia Piermattie, Christof Angst, Eva Diener, Christoph Kratky*, and *Albert Eschenmoser*[*]

*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

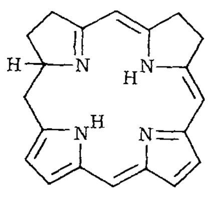
Our search for a non-oxidative isomerization of porphyrinogens *(1)* to the corphinoid ligand system of 2,3,7,8,12,13-hexahydroporphyrin *(2)* led at first to structures of type *(3)*[1a,b], in which the cyclic conjugation of the chromophore double bonds is broken, and not to *(2)*. We have now been able to convert a porphyrinogen into the ligand system *(2)*, about which only little is known so far[2]. This structure is of interest in relation to the problem of the origin of the corrin structure[1b], and also to problems of contemporary corrin biosynthesis[3].



*(1)*



*(2)*



*(3)*

The tautomerization of octaethylporphyrinogen *(4)* under strict exclusion of oxygen produces nickel complexes of type *(3)*, as described earlier[1a]. This transformation proceeds faster, and gives different products, if instead of triethylamine the guanidine derivative 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD)[4] is used as the base for tautomerization. Under the conditions shown in Scheme 1, *(4)* forms a mixture of nickel complexes, which apart from didehydrogenated components[5a] consists mainly of the diastereomers *(5)* (see Table 1). After anaerobic column chromatography on silica gel, a total of seven diastereomers were discernible by high pressure liquid chromatography (HPLC); three of them could be separated preparatively by HPLC on silica gel and crystallized, the major components being *tctcc-(5)*[5b] and *tctct-(5)*[5c]. The assignment of configuration for *tctct-(5)* followed from the molecular symmetry evident in the $^1$H-NMR spectrum, as well as from the spontaneous didehydrogenation in air to the known[1a,d] Ni$^{2+}$-isobacteriochlorinate *tct-(6)* and a Ni$^{2+}$-bacteriochlorinate (*ttc-(7)*, Table 1). The corresponding didehydrogenation of *tctcc-(5)* gives as the main product *tct-(6)*[6] and a new (therefore not the *ttt*-configuration[1a,d]) isobacteriochlorinate, which must have the configuration *tcc-(6)*. X-ray structure analysis of *tctcc-(5)* (Fig. 1) again reveals the specific macro-ring deformation, which was previously

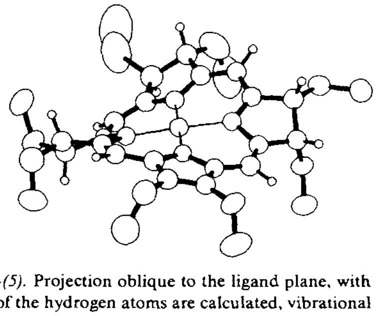
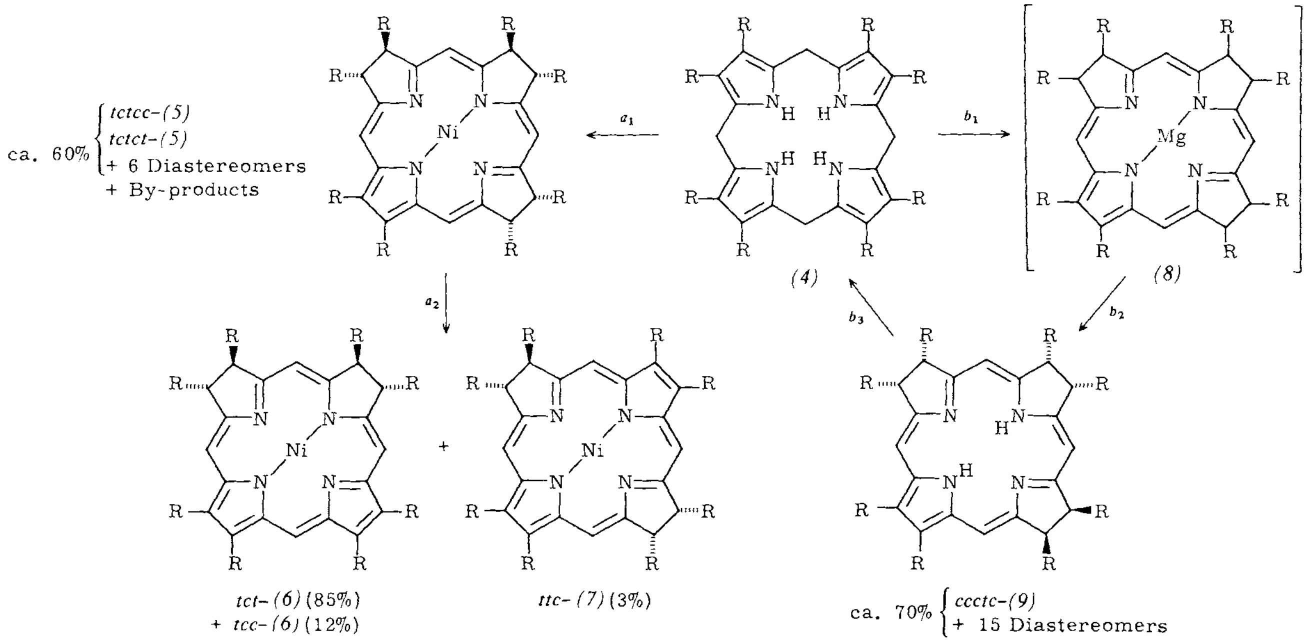


Fig. 1. Crystal structure of *tctcc-(5)*. Projection oblique to the ligand plane, with ring D in foreground. Positions of the hydrogen atoms are calculated, vibrational ellipsoids of non-hydrogen atoms with 50% probability (cf. also Table 1 and [1c], Fig. 3).

---

[*] Prof. Dr. A. Eschenmoser, Dr. J. E. Johansen, Dr. V. Piermattie, Dipl. Naturwiss. ETH Ch. Angst, Dipl. Naturwiss. ETH E. Diener
Laboratorium für Organische Chemie
Eidgenössische Technische Hochschule
ETH-Zentrum
Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Dr. Ch. Kratky
Institut für Physikalische Chemie der Universität
Heinrichstrasse 28, A-8010 Graz (Austria)

[**] This work was supported by the Swiss National Science Foundation, the Austrian National Science Foundation and the Austrian Academy of Sciences. We thank Professor *H. H. Inhoffen* for the donation of octaethylporphyrin, Dr. *E. Zass* for assistance in completing the manuscript, and Dr. *J. Schreiber* for his advice on the use of HPLC.



Scheme 1. Anaerobic tautomerization of octaethylporphyrinogen *(4)*, $R=C_2H_5$, in the presence of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) and $Ni^{2+}$ or $Mg^{2+}$ ions respectively. $a_1$: 20 TBD/AcOH (4:1), 1.2 $Ni(OAc)_2 \cdot 4H_2O$; *p*-xylene, 140 °C, 15 min. $a_2$: air, $CH_2Cl_2$, room temperature. $b_1$: 4.7 BrMg-TBD/TBD (2:3); *p*-xylene, 80 °C, 2.5 h. $b_2$: AcOH, room temperature. $b_3$: pyridine/AcOH (1:1.4), 80 °C, 4 d. Starting material molarities: $4.4 \times 10^{-3}$ and $1.6 \times 10^{-2}$ M for *(4)*→*(5)* and *(4)*→*(8)* respectively. Configurations: *t* = *trans*, *c* = *cis*: relative configurations of successive centres beginning with C-1 (or C-2 resp.) in Ring A.

Table 1. Spectroscopic and crystallographic data ($\lambda_{max}$ [nm], $\delta$ values, $\delta(TMS)=0$) [12].

*tctcc-(5)*: dark green crystals from ether/methanol. UV/VIS (hexane, green): $\lambda_{max}=335$ (lg $\varepsilon=4.18$), 342 sh (4.17), 404 (4.13), 500 (3.36), 531 (3.57), 613 (3.77), 669 (4.29).—MS: $m/e=596$ (100%, $M^+$, $^{58}Ni$) + isotope peaks.—$^1$H-NMR (360 MHz, $C_6D_6$): $\delta=0.61/0.76/0.83/0.84/0.85/0.99$ (6t/6$CH_3$), 1.23—1.53 (many peaks/6$CH_2$), 1.55/1.57 (2t/each $J=7$ Hz/2$CH_3$), 1.87/1.98 (2m/2CH), 2.90—3.10 (many peaks/2$CH_2$), 3.16—3.40 (many peaks/4CH), 6.23—6.29 (2s/H-5, 10), 7.29 (s/H-20), 7.43 (s/H-15).—Structure determination: triclinic $P\bar{1}$, $a=11.442(6)$, $b=12.014(4)$, $c=13.430(13)$ Å, $\alpha=102.03(3)$, $\beta=98.92(2)$, $\gamma=112.55(2)°$, $Z=2$, $\rho_x=1.237$ g cm$^{-3}$. 5684 refined reflections, $R=0.097$ (245 parameters) (cf. Fig. 1)

*ttc-(7)*: brown-green crystals from ether/hexane. UV/VIS (hexane): $\lambda_{max}=331$ (4.54), 388 (4.75), 469 (3.40), 508 (3.51), 689 (3.64), 715 (3.97), 751 (4.84).—MS: $m/e=594$ (100%, $M^+$, $^{58}Ni$) + isotope peaks, 592 (70%, $M^+ - H_2$). *(8)* (Reaction mixture for the transformation *(4)*→*(8)*; mainly containing *(8)*: UV/VIS (hexane + traces of xylene, blue): $\lambda_{max}=343$ sh ($\varepsilon_{rel}=0.75$), 354 (0.88), 373 (0.56), 392 (0.87), 407 (1.00), 450—570 ($\leqslant 0.10$), 599 (0.28) [a], 651 (0.37), 740 (0.02) (traces of $Mg^{2+}$ isobacteriochlorinate)

*ccctc-(9)*: red prisms from ether/methanol. M.p. = 167 °C.—UV/VIS (benzene, rose): $\lambda_{max}=330$ sh (4.62), 348 (4.71), 356 sh (4.64), 380 (4.54), 450 sh (3.64), 477 sh (3.88), 504 (4.03), 548 (4.04), 593 (4.08) (cf. Fig. 3).—MS: $m/e=540$ (100%, $M^+$).—$^1$H-NMR (360 MHz, $C_6D_6$): $\delta=0.77/0.79/0.84/0.85$ (4t/each $J=7$ Hz/4$CH_3$), 1.02 (t/$J=7$ Hz/2$CH_3$), 1.3—2.0 (many peaks/6$CH_2$) superimposed at 1.54 (t/$J=7$ Hz/2$CH_3$), 2.85—3.05 (many peaks/2$CH_2$), 3.1—3.4 (many peaks/6CH), 5.99/6.05 (2s/2H/H-5, 10), 6.47/6.86 (2s, br/2NH), 7.11 (s/2H/H-15, 20).—$^{13}$C-NMR ($C_6D_6$): $\delta=11.86/11.99$ (2q/2$CH_3$), 12.43/13.05/18.11 (3q/each 2$CH_3$), 18.77 (t/2$CH_2$), 21.34 (t/4$CH_2$), 20.25/20.45 (2t/2$CH_2$), 47.23/47.51/52.30 (3d/each 2CH), 91.00/91.60 (2d/2CH), 99.70 (d/C-15, 20), 125.29/127.87 (2s/each 2C), 151.17/151.56 (2s/2C), 153.45/171.90 (2s/each 2C).—Structure determination at −170 °C: monoclinic $P2_1/c$, $a=15.086(4)$, $b=12.419(3)$, $c=20.086(5)$ Å, $\beta=123.23(3)°$, $Z=4$, $\rho_x=1.146$ g cm$^{-3}$. 5252 refined reflections, $R=0.076$ (362 parameters) (cf. Fig. 2)

[a] Presumably also containing absorption from isobacteriochlorinate components.

found in isomers of type *(3)* in the hexaporphyrinate series[1a], as well as in the series of $Ni^{2+}$-isobacteriochlorinates[1d]. This deformation[7] indicates that the inner coordination cavity of the hexa- and tetrahydroporphinoid ligand systems tends to be too large for ions such as $Ni^{2+}$.

Using the reaction conditions which resulted in high yields of nickel complexes of type *(3)*[1a] from *(4)* (triethylamine/acetic acid (4:1), 140 °C in xylene), the mixture of diastereomers *(5)* did not isomerize to complexes of type *(3)*.

The porphyrinogen → corphin tautomerization is not only—as was originally assumed—mediated by transition metal ions such as $Ni^{2+}$, but by $Mg^{2+}$ as well. This allows the preparation of metal-free hexahydroporphyrins of type *(2)* [≙ *(9)*]. In this way, the transformation of *(4)* in the presence of bromomagnesium-TBD/TBD under rigorous exclusion of oxygen, leads to the almost exclusive formation (UV/VIS!) of compounds of type *(8)* which, however, could not be isolated because of their extremely high air-sensitivity (didehydrogenation within seconds to $Mg^{II}$-isobacterio- and bacteriochlorinates; UV/VIS). By decomplexation of the reaction mixture with acetic acid and separation by anaerobic column chromatography, a fraction consisting of 16 diastereomers of type *(9)* (identified by HPLC and UV/VIS) was obtained in over 70% yield. These metal-free ligands are distinctly less air-sensitive than the corresponding magnesium complexes and three individual diastereomers could be isolated by preparative HPLC and crystallization. X-ray structure analysis (Fig. 2) revealed the major component[8] to be the diastereomer *ccctc-(9)* (which probably is not the thermodynamically most stable isomer). Figure 3 shows the UV/VIS spectrum (see Table 1).

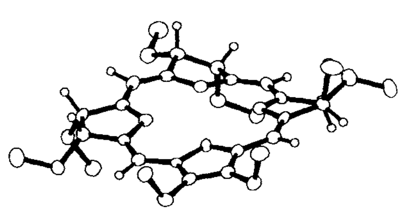


Fig. 2. Crystal structure of *ccctc-(9)* (cf. legend to Fig. 1).

Equilibration of *ccctc-(9)* [or the total fraction of diastereomers *(9)*] by tautomerization in pyridine-acetic acid under rigorous exclusion of oxygen (cf. Scheme 1) led to re-formation of octaethylporphyrinogen *(4)* as the major product (74% in crystalline form[9]); by-products were small amounts of isobacterio- and bacteriochlorins (UV/VIS) formed by dehydrogenation. Pure *(4)* remained unaffected by similar reaction conditions. This result answers one of the questions which had led to the present investigation[1a,b]: *Hexahydroporphinoid ligand systems prefer corrin-like arrangements of the chromophore double bonds in the presence of suitable metal ions; in their metal-free and neutral forms, however, these systems exist preferentially as tetrapyrrolic porphyrinogens*[10]. What should be remembered in this context is the coronoid array of peripheral methyl groups in the structure of natural corrinoids.

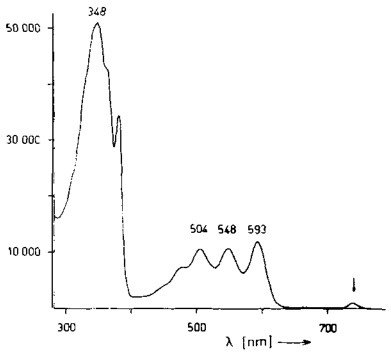


Fig. 3. UV/VIS spectrum of *ccctc-(9)* in benzene, $c = 17.3 \times 10^{-6}$ mol/dm$^3$ (cf. also Table 1). The absorption in the vicinity of 720 nm (arrow) originates from a trace (< 1%) of didehydrogenation product (bacteriochlorin).

Within the family of hydroporphyrins, the corphinoid[11a] ligand system *(2)* [$\triangleq$ *(9)*] occupies a central position; it presents itself as a direct preparative link between porphyrinogens and the chromophore systems of sirohydrochlorin and bacteriochlorophyll[11b]. We suspect that reaction conditions exist that will allow a transition of *(2)* to the corrin structure.

Received: January 14, 1981 [Z 707a IE]
German version: Angew. Chem. 93, 273 (1981)

CAS Registry numbers:
*(4)*, 24477-51-8; *tctcc-(5)*, 76945-57-8; *tctct-(5)*, 76880-07-4; *tct-(6)*, 72881-00-6; *tcc-(6)*, 76945-56-7; *ttc-(7)*, 76880-06-3; *(8)*, 76880-05-2; *ccctc-(9)*, 76879-11-3

---

[1] a) *Ch. Angst, M. Kajiwara, E. Zass, A. Eschenmoser,* Angew. Chem. *92*, 139 (1980); Angew. Chem. Int. Ed. Engl. *19*, 140 (1980); *J. E. Johansen, Ch. Angst, Ch. Kratky, A. Eschenmoser, ibid. 92*, 141 (1980) and *19*, 141 (1980) resp.; b) *A. Eschenmoser* in *B. J. Zagalak, W. Friedrich:* Vitamin $B_{12}$ and Intrinsic Factor (Proc. 3rd Eur. Symp., Zürich). de Gruyter, Berlin 1979, pp. 89—117; c) *Ch. Angst, Ch. Kratky, A. Eschenmoser,* Angew. Chem. *93*, 275 (1981); Angew. Chem. Int. Ed. Engl. *20*, 263 (1981); d) *Ch. Kratky, J. E. Johansen, Ch. Angst, ibid. 93*, 204 (1981) and *20*, 211 (1981) resp.

[2] The hexahydroporphyrin fraction prepared by *U. Eisner* (J. Chem. Soc. 1957, 3460) by reduction of iron(III)octaethylchlorinate with sodium and isoamyl alcohol, previously considered to be a derivative of the chromophore type *(2)*, is according to [1a] (cf. [12a]) a mixture of diastereomers of chromophore type *(3)*. The hexahydro reduction product of zinc(II) tetraphenylporphyrinate, assumed to be a derivative of *(2)* by *G. R. Seely, M. Calvin* (J. Chem. Phys. *23*, 1068 (1955)), was insufficiently characterized. "Octaethyl-geminiporphin triketones" which are 3,8,13- or 3,8,12-trioxo derivatives of *(2)*, were described by *H. H. Inhoffen* and *W. Nolte* (Justus Liebigs Ann. Chem. *725*, 167 (1969)). An unpublished palladium(II) 2,2,7,7,12,12,17,18-octaethyl-2,3,7,8,12,13-hexahydroporphyrinate was obtained by reduction of the corresponding 3,8,13-trioxo complex with $LiAlH_4/ZnCl_2$ and characterized spectroscopically by *N. Müller* and *H. H. Inhoffen* (cf. *N. Müller*, Dissertation, Universität Braunschweig 1969; pp. 12—16).

[3] *V. Rasetti, A. Pfaltz, Ch. Kratky, A. Eschenmoser,* Proc. Natl. Acad. Sci. USA *78*, 16 (1981).

[4] The use of TBD was prompted by results described in [1c]. We thank Dr. *R. Schwesinger* for a sample of TBD. For its synthesis, cf. *A. F. McKay, M. E. Kreling,* Can. J. Chem. *35*, 1438 (1957); *F. P. Schmidtchen*, Chem. Ber. *113*, 2175 (1980).

[5] a) By-product mixtures: *ca.* 30% isobacteriochlorinates *(6)* (UV/VIS), *ca.* 1% bacteriochlorinates *ttc-(7)* and *ttt-(7)* (crystalline, UV/VIS, MS), as well as a few percent of nickel complexes of ligand type *(3)* (cf. [1a]). HPLC: Si 60; pentane-triethylamine 500:3; b) *ca.* 30% of the mixture of diastereomers *(5)*; c) *ca.* 15% is present in the mixture of diastereomers *(5)*, contamined to about 1/3 with the *ttct*-diastereomer of ligand type *(3)* ($^1$H-NMR [1a]).

[6] Ring C of *tctcc-(5)* has a *cis*-arrangement of the ethyl groups and is more easily dehydrogenated than ring A, which has a *trans*-arrangement. The didehydrogenation of rings A, B and C of *tctct-(5)* (all neighboring ethyl groups *trans*) proceeds more or less statistically.

[7] In *tctcc-(5)*, the four nitrogen atoms and the nickel ion are essentially in the same plane (cf. also [1c], Fig. 3).

[8] Seventeen percent of the mixture of diastereomers *(9)*. HPLC: Partisil 5; pentane-dimethoxyethane-triethylamine 1000:10:6.

[9] The mother liquor of the reaction product from *ccctc-(9)* (HPLC, UV/VIS) contained *ca.* 1% *(9)* (not initial diastereomer), *ca.* 2% bacteriochlorins, and a few percent isobacteriochlorins. Starting from the total mixture of diastereomers *(9)*, 71% of crystalline *(4)* was isolated. A fraction of 17% contained starting material, mainly the two diastereomers *tctct-(9)* and *tttct-(9)* (inferred from HPLC, $^1$H-NMR and dehydrogenation to isobacteriochlorins). A few percent of the reaction product mixture were dehydrogenation products.

[10] Cf. also the quantitative isomerization [1a, b] of two (diastereomeric) dipyrrolic octaethyl-2,3,7,8,15,23-hexahydroporphyrins to *(4)*, as well as the deuteration of the *meso*-positions of *(4)* with $CH_3COOD$; *H. W. Whitlock, D. A. Buchanan*, Tetrahedron Lett. *1969*, 3711.

[11] a) Constitutionally, the chromophore *(9)* is a monopyrrolic tautomer of the corphin chromophore; *A. P. Johnson, P. Wehrli, R. Fletscher, A. Eschenmoser,* Angew. Chem. *80*, 622 (1968); Angew. Chem. Int. Ed. Engl. *8*, 623 (1968); *P. Müller, S. Farooq, B. Hardegger, W. S. Salmond, A. Eschenmoser, ibid. 85*, 954 (1973) and *12*, 914 (1973) resp.; b) cf. also the formation of bacterio- and isobacteriochlorin by tetramerization of 2-(dimethylamino)pyrrole by reaction with Grignard reagents; *G. D. Egorova, K. N. Solov'ev, A. M. Shul'ga,* J. Gen. Chem. USSR *37*, 333 (1967); cf. also *U. Eisner, R. P. Linstead,* J. Chem. Soc. *1955*, 3742, 3749.

[12] For experimental details see a) *Ch. Angst*, dissertation ETH Zürich, Prom. No. 6783, 1981 (in press); b) *E. Diener*, dissertation, ETH Zürich (in preparation).

---

# Cyclization of a Seco-porphyrinogen to Nickel(II) C,D-Tetradehydrocorrinates[**]

By *Christof Angst, Christoph Kratky,* and *Albert Eschenmoser*[*]

*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

Among the hexahydroporphinoid ligand systems isomeric to porphyrinogen, structures of type *(1)* are formed with conspicuous ease[1a-c]. The interrupted conjugation of the double bond system at position C-1 is reminiscent of the corrin ligand. In the corrin series, the exact analogue of *(1)* is the ligand system of C,D-tetradehydrocorrin *(2)*. We report here experiments in which we obtained members of this previously unknown class of compounds[2].

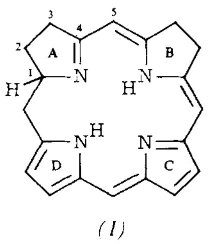
We had attempted to apply the process of tautomerization/complexation found for (octaethyl-)porphyrino-

---

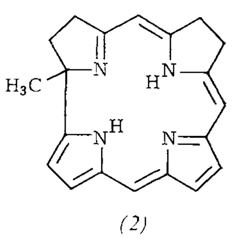
[*] Prof. Dr. A. Eschenmoser, dipl. Naturwiss. ETH Ch. Angst
Laboratorium für Organische Chemie
Eidgenössische Technische Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Dr. Ch. Kratky
Institut für Physikalische Chemie der Universität
Heinrichstrasse 28, A-8010 Graz (Austria)

[**] This work was supported by the Swiss National Science Foundation, the Austrian National Science Foundation and the Austrian Academy of Sciences. We thank Dr. *E. Zass* for assistance in completing the manuscript, and Dr. *J. Schreiber* for his advice on the use of HPLC.

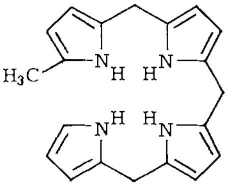
gens[1a,b,d] to the non-macrocyclic analogues, *i. e.* to seco-porphyrinogens of type *(3)* (1-methylbilinogens), aiming at a direct formation of complexes of the isomeric D-didehydrocorrin *(4)*. At the same time, this implied the question as to whether the oxidative dihydrobilin → octadehydrocorrinate (A→D) ring closure of *A. W. Johnson et al.*[3] would also operate non-oxidatively at the lower oxidation level of hexahydrobilins or didehydrocorrins[4].



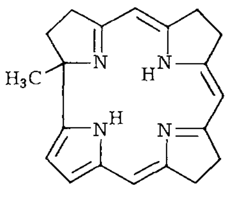
*(1)*



*(2)*

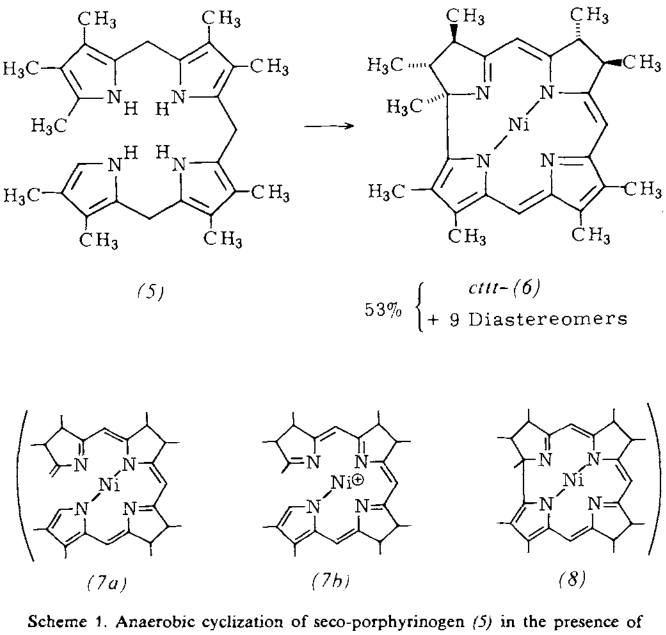


*(3)*



*(4)*

Under the conditions shown in Scheme 1, a mixture of diastereomeric *rac*-$Ni^{2+}$-1,2,3,7,8,12,13,17,18-nonamethyl-12,13,18,19-tetradehydro-[24H]corrinates *(6)* was formed in respectable yield from nonamethylbilinogen *(5)*[5] by tautomerization, complexation, cyclization and, unexpectedly, didehydrogenation. After anaerobic column chromatography of the deep-green reaction product on silica gel (hexane/ether (5:1)), ten from a total of 16 detected components of the product fraction were identified as diastereomeric C,D-tetradehydrocorrinates *(6)* by HPLC and UV/VIS spectroscopy (yield 53%). Eight of the ten diastereomers were isolated by chromatography[6a] and crystallized. X-ray analysis (cf. Fig. 1) showed the major component[6b] to possess, probably the thermodynamically most stable, *cttt (6)*-configuration (see Table 1). The constitution of five of the six by-product fractions from HPLC (cf. above) was assigned by UV/VIS spectroscopy as follows: $Ni^{II}$-A,B,C,D-octadehydrocorrinate *(9)* (*ca.* 2% of the product mixture, one fraction)[7], B,C,D-hexahydro type *(10)* (*ca.* 4%, two fractions)[8a], and A,C,D-hexadehydrocorrinate *(11)* (*ca.* 12%, two fractions)[8b]. The D-didehydro chromophore *(8)*[1e] was not found.



Scheme 1. Anaerobic cyclization of seco-porphyrinogen *(5)* in the presence of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) and $Ni^{2+}$ ions. 12 TBD/AcOH (4:1), 0.9 $Ni(OAc)_2 \cdot 4H_2O$, *p*-xylene, 140 °C, 16 h, starting material molarity $1.2 \times 10^{-2}$ M.

Table 1. Spectroscopic and crystallographic data ($\lambda_{max}$ [nm]; $\delta$-value, $\delta$ (TMS) = 0; experimental details cf. [1c]).

*cttt-(6)*: dark green needles from ether/hexane. UV/VIS ($CH_2Cl_2$): $\lambda_{max} = 379$ (lg $\varepsilon = 4.40$), 423 (3.94), 489 (3.79), 600 sh (3.93), 641 (4.19).—MS: $m/e = 484$ (89%, $M^+$, $^{58}Ni$) + isotope peaks, 469 (100%, $M^+ - CH_3$, $^{58}Ni$), *etc.*—$^1$H-NMR ($CDCl_3$): $\delta = 1.19$ (s/$CH_3$), 1.21/1.38/1.40/1.47 (4d/each $J = 7$ Hz/4$CH_3$), 2.03 (m/CH), 2.17/2.23/2.26/2.31 (4s/4$CH_3$), 2.69 (m/CH), 2.85 (m/2CH), 5.28 (s/H-5), 5.99 (s/H-10), 7.04 (s/H-15).—$^{13}$C-NMR ($CDCl_3$): $\delta = 9.7$ (2q/2$CH_3$), 10.1/11.3/13.6/15.8/17.3/17.5/21.8 (7q/7$CH_3$), 45.3/46.8/49.3/50.1 (4d/4CH), 79.5 (s/C-1), 86.7 (d/C-5), 91.2 (d/C-10), 113.2 (d/C-15), 114.8/126.0/127.3/127.5/136.5/137.0/152.1/155.6/158.1/167.7/168.7 (11s/11C).—Structure determinations: triclinic $P\bar{1}$, $a = 8.248(3)$, $b = -1.855(3)$, $c = 14.700(8)$ Å, $\alpha = 90.42(1)$, $\beta = 103.77(1)$, $\gamma = 93.60(1)^\circ$, $Z = 2$, $\rho_x = 1.159$ g cm$^{-3}$. 4906 refined reflections, $R = 0.097$ (298 parameters) (cf. Fig. 1 and 2)

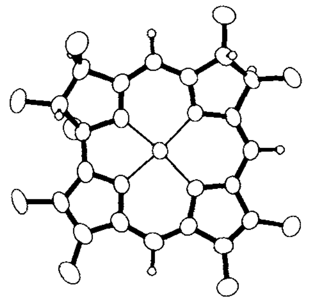
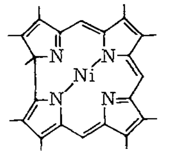
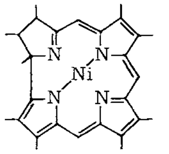


Fig. 1. Crystal structure of *cttt-(6)*. Projection in the plane of atoms N-21, N-22 and N-23; vibrational ellipsoids of the non-hydrogen atoms with 50% probability; hydrogen atom positions calculated (cf. also Table 1).

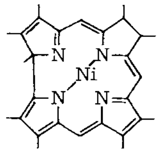
The use of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD)[9a] as buffer-partner was imperative for the transformation *(5)*→*(6)*; other organic bases led to mixtures which either did not contain *(6)* at all (triethylamine, cf. [1a,b]) or only in small and non-reproducible amounts (diazabicycloundecene). Substitution of TBD by *N*-methyl-TBD[9b] led—*ceteris paribus*—to lower yields of *(6)*. Therefore, it is not the high basicity alone which makes TBD so suitable for the reaction. A series of over thirty experiments[1c] revealed that the nature of the product depends to an unusually high degree on details of the reaction conditions[10].



*(9)*



*(10)*



*(11)*

In all probability, there is more than one reaction path from *(5)* to *(6)*. A probable route is a tautomerization/complexation of the seco-porphyrinogen *(5)* to seco-corphinoid intermediates of type *(7)*; from there, various pathways to D-didehydrocorrinates *(8)* exist (cf. [1d] as well as the facile (A→D) cyclization of an nickel-seco-corrinate analogous to

*(7a)*[1e]). The conjugative stabilization accompanying the formation of the pyrromethenic partial structure in the C,D-ring region presumably promotes an eventual didehydrogenation step[11] to *(6)*. The same partial structure also occurs in the hexahydroporphinoid ligand system *(1)*.

The transformation *(5)*→*(6)* is another experimental variant of *Johnson*'s synthesis of corrinoid structures from tetrapyrrolic precursors[3].

Fig. 2. Crystal structure of *cttt-(6)*. Projection at right angles to the plane of atoms N-21, N-22 and N-23; ring-D in foreground (ligand system without substituents).

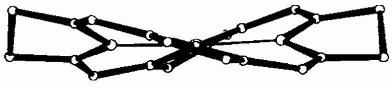


Fig. 3. Crystal structure of *tctcc*-Ni$^{II}$-2,3,7,8,12,13,17,18-octaethyl-2,3,7,8,12,13-hexahydroporphyrinate (cf. *tctcc-(5)* in [1d]). Same projection and scale as Fig. 2.

Figure 2 shows the molecule *cttt-(6)* (cf. Fig. 1) in side view. The four coordination centres and the metal ion have essentially a coplanar arrangement; the characteristic macroring deformation observed in the nickel(II) complexes of the tetrahydro-[12] and hexahydroporphyrin[1a,d] series is absent (for comparison see Fig. 3). This observation corroborates our contention that the coordination cavity of corrinoid ligand systems is closer to the spatial coordination optimum of transition metal ions such as $Ni^{2+}$ than the cavity of hydroporphinoid ligand systems.

Received: January 14, 1981 [Z 707 b IE]
German version: Angew. Chem. *93*, 275 (1981)

CAS Registry Numbers:
*(5)*, 76879-12-4; *cttt-(6)*, 76880-04-1; *(9)*, 76880-03-0; *(10)*, 76880-02-9; *(11)*, 76880-01-8

---

[1] a) *J. E. Johansen, Ch. Angst, Ch. Kratky, A. Eschenmoser*, Angew. Chem. *92*, 141 (1980); Angew. Chem. Int. Ed. Engl. *19*, 141 (1980); b) *A. Eschenmoser* in *B. J. Zagalak, W. Friedrich:* Vitamin $B_{12}$ and Intrinsic Factor (Proc. 3rd Eur. Symp., Zürich), de Gruyter, Berlin 1979, p. 89; c) *Ch. Angst*, Dissertation, ETH Zürich (Prom. No. 6783) 1981 (in press); d) *J. E. Johansen, V. Piermattie, Ch. Angst, E. Diener, Ch. Kratky, A. Eschenmoser*, Angew. Chem. *93*, 273 (1981); Angew. Chem. Int. Ed. Engl. *20*, 261 (1981); e) *V. Rasetti, B. Kräutler, A. Pfaltz, A. Eschenmoser, ibid. 89*, 475 (1977) and *16*, 459 (1977) resp.: cf. also *A. I. Scott*, Tetrahedron *31*, 2639 (1975).

[2] This type of ligand was first observed in our laboratory by *S. Ofner* during work on a synthesis of isobacteriochlorins. A *de novo* synthesis of metal-free C,D-tetradehydrocorrins will be published later (cf. *S. Ofner*, Dissertation, ETH Zürich 1981).

[3] a) *A. W. Johnson*, Chem. Soc. Rev. *9*, 125 (1980), and literature cited therein; *D. Dolphin, R. L. N. Harris, J. L. Huppatz, A. W. Johnson, I. T. Kay*, J. Chem. Soc. *C 1966*, 30; b) *D. Dicker, R. Grigg, A. W. Johnson, H. Pinnock, K. Richardson, P. van den Brock, ibid. C 1971*, 536.

[4] For nomenclature, see *R. Bonnett* in *D. Dolphin:* The Porphyrins. Academic Press, New York 1978, Vol. 1, pp. 1—27; *J. E. Merritt, K. L. Loening*, Pure Appl. Chem. *51*, 2251 (1979).

[5] Colorless needles, m.p. = 166 °C (under $N_2$ in evacuated capillary) characterized by MS, $^{1}H$- and $^{13}C$-NMR; prepared by reduction of 1,2,3,7,8,12,13,17,18-nonamethyl-10,23-dihydrobilin dihydrobromide with $NaBH_4$ in 80% methanol (yield 51%). For the synthesis of the starting material, a modified procedure of that described by *A. F. Mironov, O. D. Popova, Kh. Kh. Alarkon, V. M. Bairamov, R. P. Evstigneeva*, Zh. Org. Khim. *15*, 1086 (1979); J. Org. Chem. USSR *15*, 970 (1979) was used. For details, cf. [1c].

[6] a) HPLC: Partisil 5; pentane-dimethoxyethane-triethylamine 200:2:1; b) present to 21% in the mixture of diastereomers *(6)*.

[7] a) Identified by comparison of UV/VIS and mass spectra with those of *(9)* [7b]; this compound was prepared [1c] from nonamethyl-10,23-dihydrobilin dihydrobromide by *Johnson*-cyclization [3b]; b) *D. A. Clarke, R. Grigg, R. L. N. Harris, A. W. Johnson, I. T. Kay, K. W. Shelton*, J. Chem. Soc. C *1967*, 1648.

[8] UV/VIS spectrum ($CH_2Cl_2$) of a crystalline precipitate characterized by MS and $^{1}H$-NMR spectroscopy; for isolation and constitutional assignment cf. [1c]; a) binary mixture of diastereomers *(10)*: $\lambda_{max} = 295$ nm (lg $\varepsilon = 4.20$), 330 sh (4.11), 360 sh (4.23), 408 (4.57), 476 sh (3.72), 545 (3.52), 625 sh (3.60), 657 sh (3.72), 695 (3.86), 758 (4.23); b) diastereomer *(11)* (from nonamethyl-5,15,21,24-tetrahydrobilin; (cf. [11]): $\lambda_{max} = 303$ nm (lg $\varepsilon = 4.25$), 399 (4.33), 455 (4.03), 508 (3.87), 675 (3.90).

[9] a) We thank Dr. *R. Schwesinger* for a sample of TBD; cf. also [1d], reference [4]; b) *R. Schwesinger*, unpublished results.

[10] *E.g.* using $1.5 \cdot 10^{-2}$ M *(5)* in *p*-xylene, 1.5 mole equivalents DBU/HOAc (2:1), 5 mole equivalents $Ni(OAc)_2 \cdot 4H_2O$, anaerobic conditions, 16 h, 140 °C, produced *inter alia*, a mixture of diastereomeric Ni$^{II}$-octamethylisobacteriochlorinates (!) in 45% yield; using the same conditions, but with four times as much buffer, led [apart from *ca.* 20% isobacteriochlorinate, *ca.* 10% chlorinate and traces of *(6)*] to 16% of a product fraction, which according to UV/VIS, MS and $^{1}H$-NMR data surprisingly must be a Ni$^{II}$-1,2,3,7,8,12,13,17,18-nonamethyl (!)-1,7,8,20-tetrahydroporphyrinate; for details cf. [1c].

[11] The nature of the hydrogen acceptor remains unknown. The reaction sequence does not proceed *via* the didehydrogenated nonamethyl-5,15,21,24-tetrahydrobilin, because this gives practically no *(6)* under the reaction conditions of Scheme 2; under milder conditions (11 mole equivalents TBD, 1 mole equivalent $Ni(OAc)_2 \cdot 4H_2O$, benzene, anaerobic, 2.5 h, 60 °C), diastereomers of types *(11)* and *(6)* are formed, yields *ca.* 15 and 12%, respectively (cf. [1c]).

[12] *Ch. Kratky, Ch. Angst, J. E. Johansen*, Angew. Chem. *93*, 204 (1981); Angew. Chem. Int. Ed. Engl. *20*, 211 (1981).

## Electrophilic Reactions of Aryl- and Heteroaryl(trimethyl)silanes with a Remarkable Nucleophilic Catalysis[**]

By *Franz Effenberger* and *Wolfgang Spiegler*[*]

*Dedicated to Professor Gerhard Pfleiderer on the occasion of his 60th birthday*

*Eaborn et al.*[1] have shown that the facile displacement of the trimethylsilyl moiety by electrophiles is a decisive factor in the protodesilylation of aryl(trimethyl)silanes; on the basis of kinetic data, they have proposed a mechanism for this reaction analogous to that for electrophilic aromatic substitution. The very high *ipso* rate factors for a series of electrophilic desilylation processes[2] gave rise to the expectation that aryl(trimethyl)silanes[3] might also be successfully employed for synthetic purposes; this was confirmed by a regiospecific route to polysubstituted benzenes *via* aryl(trimethyl)silanes reported recently[4].

Our own investigations of the acylation of aryl(trimethyl)silanes[5], and reports in the literature on reactions of aldehydes with trimethylsilyl(pentahalo)benzenes[6a] and heteroaryl(trimethyl)silanes[6b], have led us to the assumption that a mechanism different from that formulated by *Eaborn*[1] might be operative in these cases. For this pathway, the breaking of the aryl-silyl bond—with at least partial evolution of aryl anions—would be rate-limiting; substituents which stabilize negative charges should therefore enhance the reactivity of aryl(trimethyl)silanes towards electrophiles.

But 2-nitrophenyl(trimethyl)silane *(1a)* does not react with benzaldehyde even upon heating to 100 °C in dimethylformamide (DMF) for three days. If, however, potassium *tert*-butanolate is added in catalytic amounts, electrophilic

---

[*] Prof. Dr. F. Effenberger, Dipl.-Chem. W. Spiegler
Institut für Organische Chemie der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie. We wish to thank *H. Kottmann* for experimental assistance. Electrophilic Aromatic Substitution, Part 20.—Part 19: *F. Effenberger, G. König, K. Klenk*, Chem. Ber., *114*, 926 (1981).

substitution proceeds smoothly even at $-60\,^\circ C$, *(2a)* being formed within 1 h in 92% yield. Analogously, from a series of substituted phenyl(trimethyl)silanes *(1a)*—*(1h)* and benzaldehyde, the benzhydrylsilyl ethers *(2a)*—*(2h)* or, after hydrolysis, the benzhydrols *(3)* were obtained (Table 1).

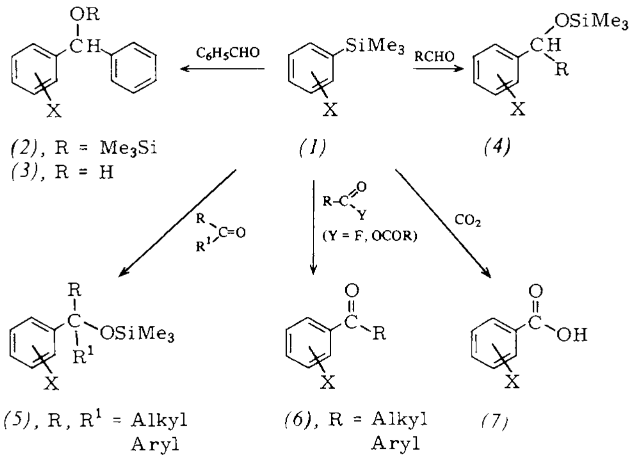


Table 1. Benzhydrylsilyl ethers *(2)* and benzhydrols *(3)* from mono-substituted phenyl(trimethyl)silanes *(1)* and benzaldehyde.

| Educt | *(1)* X | $KOC(CH_3)_3$ [mol-%] | Conditions Solvent | [h] | [°C] | Product | Yield [%] |
|---|---|---|---|---|---|---|---|
| *(1a)* | *o*-$NO_2$ | 10 | DMF | 1 | − 60 | *(2a)* | 92 [a] |
| *(1b)* | *o*-Cl | 20 | DMF | 1 | − 30 | *(2b)* | 80 [a] |
| *(1c)* | *o*-F | 5 | DMF | 1 | + 20 | *(2c)* | 76 [b] |
| *(1d)* | *o*-$C_6H_5O$ | 14 | DMF | 2 | + 20 | *(2d)* | 68 [b] |
| *(1e)* | *o*-$C_6H_5SO_2$ | 7 | DMF | 1 | + 20 | *(2e)* | 97 [b] |
| *(1f)* | *o*-$CH_3O$ | 25 | HMPT [c] | 0.3 | + 20 | *(2f)* | trace [a] |
| *(1g)* | *m*-Cl | 30 | HMPT [c] | 4 | + 100 | *(3g)* | 78 [d] |
| *(1h)* | *p*-Cl | 30 | HMPT [c] | 3 | + 100 | *(3h)* | 42 [d] |

[a] Determined by gas chromatography. [b] Isolated. [c] Hexamethylphosphoric triamide. [d] Determined by gas chromatography after acid hydrolysis.

For the nitro- and chlorophenyl(trimethyl)silanes, the relative reactivity correlates well with the $\sigma^I$-substituent constants[7a], but diverges significantly from the order of stabilization of the phenyl anions which would be essential intermediates for a nucleophilic desilylation[7b]. The $\sigma^I$ correlation holds also for the other arylsilyl substrates *(1c)*—*(1f)* in Table 1; the remarkable increase in reactivity from *(1d)* to *(1f)* is similarly mirrored in the substituent constants. This clearly indicates that the electrophile participates significantly in the rate-limiting step of the reactions reported here—in contrast to normal nucleophilic desilylation[7b]. Since "hard" bases have proven especially effective nucleophilic catalysts ($KOC(CH_3)_3$, KF, CsF, tetraalkylammonium fluoride, KOAc)[8], one must assume that interaction of the catalyst with the silicon is the decisive factor for the reaction.

We have also extended the reaction to substituted benzaldehydes and aliphatic aldehydes, to ketones, acyl fluorides and carboxylic acid anhydrides as well as to carbon dioxide; the respective products, secondary *(4)* and tertiary benzyl alcohols *(5)*, aryl ketones *(6)* and substituted benzoic acids *(7)*, are obtained, at least in part, in excellent yields.

The scope of the procedure can be further widened by variation of the arylsilyl substrate. From 2-trimethylsilylbenzthiazole and benzaldehyde, for instance, the substitution product is formed in 78% yield, only after heating to $160\,^\circ C$ for 40 h[6b]; in the presence of 1 mol-% of potassium *tert*-butanolate, 91% of the product is obtained after 15 min at $-60\,^\circ C$. Since the heteroaryl(trimethyl)silanes are readily accessible *via* cycloaddition reactions[3], this method allows the introduction of substituents into heterocyclic substrates with high regioselectivity[9].

The reaction will be of special preparative advantage in those cases where organometallic derivatives cannot be employed because of the presence of reactive functional groups in the molecule (nitro or carbonyl compounds) or because of secondary reactions, *e.g.* formation of dehydroarenes from halogen compounds or isomerization to more stable anions.

### *Experimental:*

*(2a)*: Potassium *tert*-butanolate (83 mg, 0.74 mmol) is added to a constantly stirred mixture of *(1a)*[10] (3.91 g, 20 mmol) and benzaldehyde (2.12 g, 20 mmol) in 25 $cm^3$ DMF at room temperature. The solutions warms slightly and turns red; as indicated by GLC, the reaction is complete after 1 h. The catalyst is filtered off, and the DMF distilled off. Upon fractional distillation, the oily residue yields 4.81 g (80%) *(2a)*, b.p. 136—138 °C/0.1 torr. $^1H$-NMR ($CDCl_3$): $\delta = 0.07$ (s, 9H), 6.57 (s, H), 7.20—8.00 (m, 9H).

Received: September 8th, 1980 [Z 706a IE]
German version: Angew. Chem. *93*, 287 (1981)

---

[1] *C. Eaborn*, J. Organomet. Chem. *100*, 43 (1975).

[2] a) *C. L. Perrin*, J. Org. Chem. *36*, 420 (1971); b) *S. R. Hartshorn*, Chem. Soc. Rev. *3*, 167 (1974).

[3] *D. Häbich, F. Effenberger*, Synthesis *1979*, 841.

[4] *G. Félix, J. Dunoguès, R. Calas*, Angew. Chem. *91*, 430 (1979); Angew. Chem. Int. Ed. Engl. *18*, 402 (1979).

[5] *D. Häbich*, Dissertation, Universität Stuttgart 1977.

[6] a) *A. F. Webb, D. S. Sethi, H. Gilman*, J. Organomet. Chem. *21*, P61 (1970). b) *F. H. Pinkerton, S. F. Thames*, J. Heterocycl. Chem. *6*, 433 (1969); *ibid. 8*, 257 (1971); *ibid. 9*, 67 (1972); *T. Ogawa, M. Yasui, M. Matsui*, Agr. Biol. Chem. *34*, 970 (1970).

[7] a) *G. B. Barlin, D. D. Perrin*, Q. Rev. Chem. Soc. *20*, 75 (1966). b) *C. Eaborn, G. Seconi*, J. Chem. Soc. Perkin Trans. II *1976*, 925; *C. Eaborn, J. G. Stamper, G. Seconi*, J. Organomet. Chem. *150*, C23 (1978).

[8] *Tse-Lok Ho*: Hard and Soft Acids and Bases Principle in Organic Chemistry. Academic Press, New York 1977.

[9] *A. Krebs*, intended Dissertation, Universität Stuttgart 1981.

[10] *C. Eaborn, D. R. M. Walton, D. J. Young*, J. Chem. Soc. *B 1969*, 15.

## Nucleophilic Catalysis of Reactions of Tricarbonyl(trimethylsilylarene)chromium Complexes with Electrophiles[**]

By *Franz Effenberger* and *Klaus Schöllkopf*[*]

*Dedicated to Professor Gerhard Pfleiderer on the occasion of his 60th birthday*

Electrophilic substitution of aryl(trimethyl)silanes having electron-donating substituents, *e.g.* alkyl- or aminophenyl(trimethyl)silanes, is not amenable to nucleophilic catalysis[1]; Friedel-Crafts catalysts, on the other hand, specially facilitate reactions of such substrates with electrophiles. In this case, however, the directing influence of the substituents often overrides the tendency of the trimethylsilyl moiety to *ipso*-substitution, and regular H-substitution results[2]. Recent investigations have established the electron-withdrawing effect

---

[*] Prof. Dr. F. Effenberger, Dipl.-Chem. K. Schöllkopf
Institut für Organische Chemie der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie. We thank Herr *Steegmüller* for experimental assistance; NATO research grant No. 1602 is gratefully acknowledged. Electrophilic aromatic substitution, Part 21.—Part 20: [1].

of the tricarbonylchromium group in arene(tricarbonyl)-chromium complexes and given many examples for their preparative application[3a]. Both the facile metalation of these complexes[3b] and the dissociation constants of the respective complexed benzoic acids[3c] clearly demonstrate the high inductive aryl anion stabilization potential of the $Cr(CO)_3$ group; thus, an electrophilic desilylation under nucleophilic catalysis[1] seems feasible.

Tricarbonylchromium complexes of mono- and bis(trimethylsilyl)benzenes [*(2)*, R = H, $Me_3Si$], which are readily obtainable in good yield from the respective benzene derivatives *(1)* by heating with hexacarbonylchromium[4], do not react with aldehydes and ketones even at elevated temperatures. Upon addition of nucleophilic catalysts such as potassium *tert*-butanolate or cesium fluoride, however, formation of *(3)* takes place, even at room temperature (Table 1).

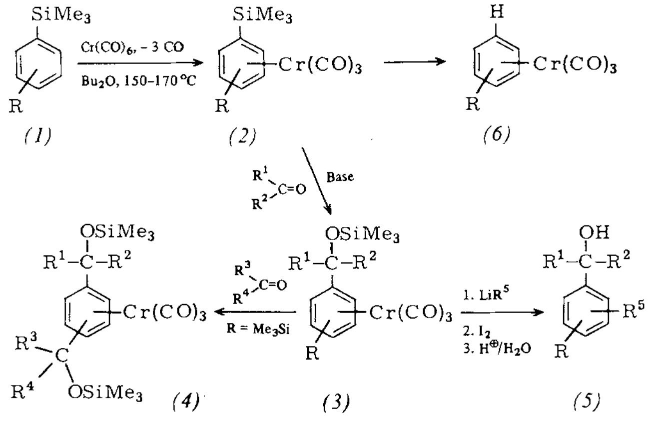


Table 1. Reaction of tricarbonyl(trimethylsilylarene)chromium complexes *(2)* with electrophiles in dimethylformamide (DMF) with addition of 10 mol-% CsF.

| Educt | R | R¹ | R² | *t* [h] | Product | Yield [%] |
|---|---|---|---|---|---|---|
| *(2a)* | *o*-$CH_3$ | H | $C_6H_5$ | 0.25 | *(3a)* | 81 |
| *(2b)* | *m*-$CH_3$ | H | $C_6H_5$ | 0.5 | *(3b)* | 83 |
| *(2c)* | *p*-$CH_3$ | H | $C_6H_5$ | 2.5 | *(3c)* | 81 |
| *(2d)* | *o*-Cl | H | $C_6H_5$ | 0.75 | *(3d)* | 83 |
| *(2e)* | *m*-Cl | H | $C_6H_5$ | 0.3 | *(3e)* | 70 |
| *(2f)* | *p*-Cl | H | $C_6H_5$ | 2.0 | *(3f)* | 57 |
| *(2g)* | H | H | $C_6H_5$ | 5.0 | *(3g)* | 88 |
| *(2g)* | H | H | $CH_3$ | 5.0 | *(3h)* | 30 [a] |
| *(2g)* | H | H | $C_3H_7$ | 6.0 | *(3i)* | 43 [b] |
| *(2g)* | H | $CH_3$ | $CH_3$ | 10.0 | *(3k)* | 50 [c] |
| *(2g)* | H | $CH_3$ | $C_6H_5$ | 7.0 | *(3l)* | 29 [d] |
| *(2g)* | H | $C_6H_5$ | $C_6H_5$ | 40.0 | *(3m)* | 75 |

[a] 32% *(6g)*. [b] 38% *(6g)*. [c] 28% *(6g)*. [d] 55% *(6g)*.

The position of R relative to the trimethylsilyl group does not greatly influence the rate of formation of *(3)* from *(2)*, as is to be expected from the dissociation constants of the substituted (tricarbonylchromium)benzoic acid complexes[3c]. This is in sharp contrast, though, to the nucleophilic catalysis of electrophilic substitutions where the rate is enhanced by electron-withdrawing groups in the substrate[1]. With enolizable carbonyl reagents, partial protodesilylation of the complexes *(2)* to *(6)* is unavoidable.

Products which still bear a trimethylsilyl group are susceptible to secondary reactions with another carbonyl compound to give *(4)*. Since the activating $Cr(CO)_3$ group is retained in formation of *(3)* or *(4)*, the respective benzene derivatives *(5)* can be obtained by subsequent addition of nucleophiles[3a] and oxidative work-up.

The introduction of many different types of substituents into easily accessible benzene derivatives *(1)*, can therefore be carried out using this method. Compared to the transformations *(2)*→*(3)* or *(3)*→*(4)* *via* organometallic derivatives, the procedure offers a much wider range of substituent variation[1]; at the same time, undesirable metalation processes, *e.g.* benzyl anion formation from alkylbenzenes[3b], are avoided.

*Experimental:*

*(3g)*: Benzaldehyde (2.13 g, 20 mmol) is added dropwise to a stirred solution of *(2g)*[5] (5.73 g, 20 mmol) and CsF (0.30 g, 2 mmol) in 15 $cm^3$ DMF under an inert gas atmosphere. The completion of the reaction is monitored by GC. The reaction mixture is diluted with 150 $cm^3$ ether, the precipitated salt filtered off, and the ethereal phase washed with water and dried over sodium sulfate. The solvent is stripped off, and the residue recrystallized from *n*-hexane. Yield: 6.9 g (88%) *(3g)*, m.p. 90—91 °C.

Received: September 8th, 1980 [Z 706 b IE]
German version: Angew. Chem. *93*, 288 (1981)

---

[1] *F. Effenberger, W. Spiegler*, Angew. Chem. *93*, 287 (1981); Angew. Chem. Int. Ed. Engl. *20*, 265 (1981).

[2] *D. Häbich, F. Effenberger*, Synthesis *1979*, 841 and references cited therein.

[3] a) *M. F. Semmelhack*, Ann. N. Y. Acad. Sci. *295*, 36 (1977); *M. F. Semmelhack, H. T. Hall, Jr., R. Farina, M. Yoshifuji, G. Clark, T. Barger, K. Hirotsu, J. Clardy*, J. Am. Chem. Soc. *101*, 3535 (1979). b) *M. F. Semmelhack, J. Bisaha, M. Czarny, ibid. 101*, 768 (1979); *M. D. Rausch, G. A. Moser, W. A. Lee*, Synth. React. Inorg. Met. Org. Chem. *1979*, 357; c) *F. van Meurs, A. J. Hoefnagel, B. M. Wepster, H. van Bekkum*, J. Organomet. Chem. *142*, 299 (1977).

[4] a) *P. J. Dossor, C. Eaborn, D. R. M. Walton*, J. Organomet. Chem. *71*, 207 (1974); b) *K. Schöllkopf*, intended Dissertation, Universität Stuttgart 1981.

[5] *(2g)* was first characterized by *D. Seyferth* and *D. L. Alleston* [Inorg. Chem. *2*, 417 (1963)]; we have prepared *(2g)* in 95% yield, following a procedure described by *C. A. L. Mahaffy* and *P. L. Pauson* [Inorg. Synth. *19*, 154 (1979)].

---

## Synthesis and ESR Characterization of the Triplet Species $\mu$-($\eta^6$:$\eta^6$-Biphenyl)-bis[($\eta^6$-benzene)vanadium][**]

By *Christoph Elschenbroich* and *Jürgen Heck*[*]

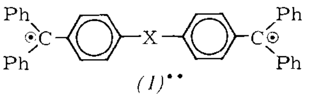
While the individual electrons of the two radical centers in a real diradical are neither paired nor unpaired, but independent of each other so that no distinction can be made between a mono- and a diradical by ESR spectroscopy, a triplet radical can be recognized by its zero field splitting and by a characteristic hyperfine structure[1]. The transition between diradical and triplet radical is, however, gradual and it is therefore important to study the extent of spin-spin interaction as a function of the nature, separation, and charge of the radical centers. Such investigations have been carried out on coupled pairs of triphenylmethyl radicals *(1)*[2] and, *inter alia*, on bisnitroxides *(2)*[3].

Our interest focusses on paramagnetic intersandwich compounds of the type *(3)*[4]. We report here on the preparation and properties of the neutral complex $\mu$-($\eta^6$:$\eta^6$-biphenyl)-bis[($\eta^6$-benzene)vanadium(0)] *(5)*$^{\cdot\cdot}$, which is isoelectronic with the dication {$\mu$-($\eta^6$:$\eta^6$-biphenyl)-bis[($\eta^6$-benbenzene)chromium(I)]}$^{+\,+}$ *(4)*$^{+\,+}$[4b]. We obtained the novel in-

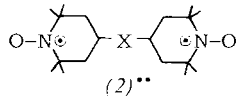
---

[*] Prof. Dr. Ch. Elschenbroich, Dipl.-Chem. J. Heck
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)

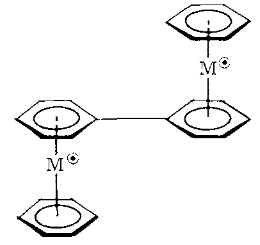
[**] Metal π-Complexes of Benzene Derivatives, Part 14. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 13: *Ch. Elschenbroich, H. Burdorf*, Z. Naturforsch. *B 36*, 94 (1981).



*(1)*$^{\bullet\bullet}$

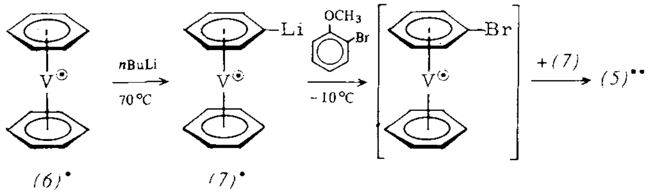


*(2)*$^{\bullet\bullet}$



*(3)*
*(4)*$^{\dot{+}\dot{+}}$, M = Cr$^{\oplus}$
*(5)*$^{\bullet\bullet}$, M = V

tersandwich compounds *(5)*$^{\bullet\bullet}$ by metalation of *(6)*$^{\bullet}$ with *n*-butyllithium (during which not only *(7)*$^{\bullet}$ but also higher metalated products are formed), and subsequent coupling as shiny black, very air-sensitive crystals. They are moderately soluble in toluene and almost insoluble in ethers. *(5)*$^{\bullet\bullet}$ can be sublimed ($>180\,^{\circ}C/<10^{-4}$ torr; decomp. 285 °C). The composition of *(5)*$^{\bullet\bullet}$ follows from elemental analysis and from the high-resolution mass spectrum[5].



*(6)*$^{\bullet}$ *(7)*$^{\bullet}$

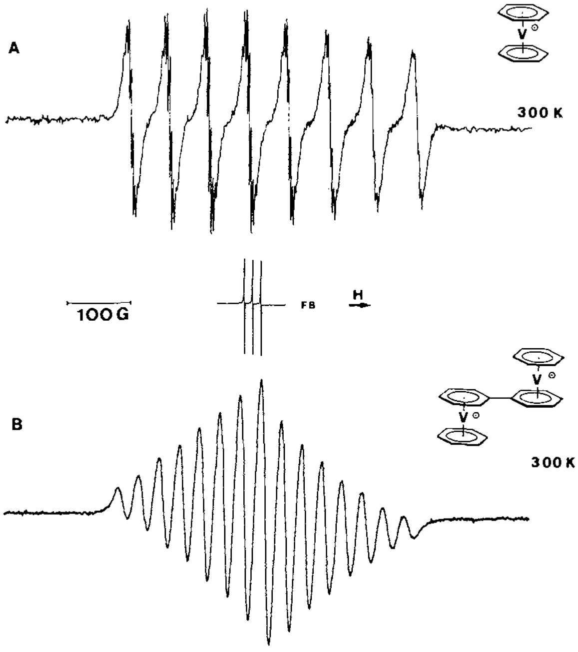


Fig. 1. X-band ESR spectra of the mononuclear complex *(6)*$^{\bullet}$ (A) and of the dinuclear complex *(5)*$^{\bullet\bullet}$ (B) at room temperature in liquid solution (toluene). FS = Fremy's salt, $g = 2.0056$.

In contrast to *(4)*$^{\dot{+}\dot{+}}$, *(5)*$^{\bullet\bullet}$ displays a well resolved ESR spectrum ($g = 1.988 \pm 0.001$) in liquid solution at room temperature; this is shown in Figure 1 together with the spectrum of the mononuclear complex *(6)*$^{\bullet}$. The hyperfine structure of *(6)*$^{\bullet}$ is governed by the vanadium coupling $a(1\ ^{51}V) = 63.8 \pm 0.3$ G[6] ($I\ ^{51}V = 7/2$) and by the small proton coupling $a(12\ ^{1}H) = 4.0 \pm 0.10$ G[6], whereas the spectrum of the dinuclear complex *(5)*$^{\bullet\bullet}$ comprises 15 lines in the intensity ratio 1:2:3:4:5:6:7:8:7.... with a separation of $31.0 \pm 0.5$ G between adjacent lines. Hence, the unpaired electrons in *(5)*$^{\bullet\bullet}$ couple with *both* $^{51}V$ nuclei, and there is rapid exchange, *i.e.* the exchange interaction $J$ is substantially greater than the hyperfine interaction $a(^{51}V)$.

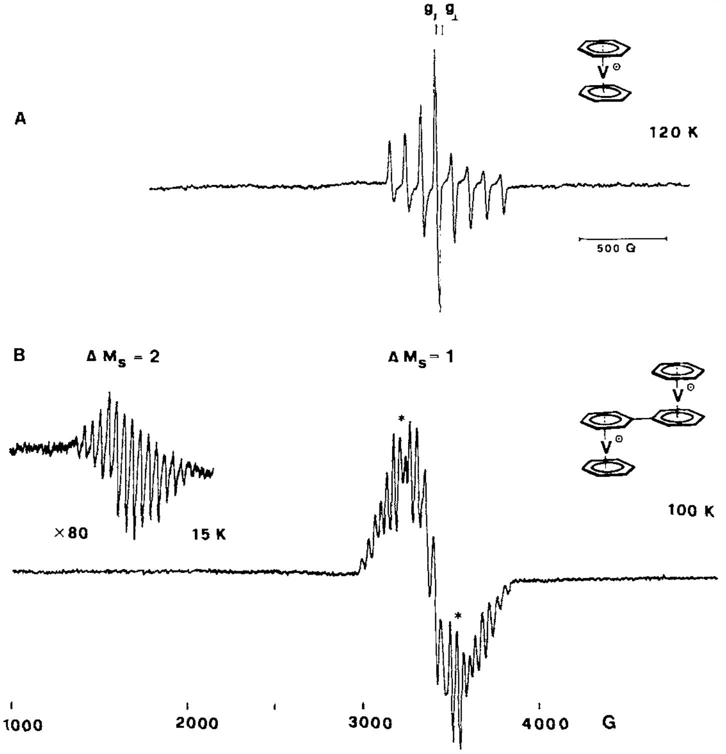


Fig. 2. X-band ESR spectra of the complexes *(6)*$^{\bullet}$ (A) and *(5)*$^{\bullet\bullet}$ (B) in rigid glassy solution (toluene). The $g \approx 4$ region was recorded with 80-fold amplification. Lines marked with asterisks: centers of the two outer $^{51}V$ multiplets at separation $2D$.

The triplet character of the intersandwich complex *(5)*$^{\bullet\bullet}$ is supported by its ESR spectrum in rigid glassy solution (Fig. 2), which shows a structure with more lines than the mononuclear complex *(6)*$^{\bullet}$ in the region $g \approx 2$ and a half-field signal ($\Delta M_S = 2$) in the region $g \approx 4$. From the overall extension of the spectrum of *(5)*$^{\bullet\bullet}$, and taking into account the $^{51}V$-hyperfine structure, a zero field parameter $D = 0.0154$ cm$^{-1}$ can be deduced[8] which in the point-dipole approximation corresponds to an average distance of the two unpaired electrons[7] of $R_{ESR} \approx 540$ pm and thus a *trans*-conformation of the two sandwich complex moieties ($R_{model} = 550$ pm). Other than in the case of the isoelectronic complex *(4)*$^{\dot{+}\dot{+}}$ the half-field signal for *(5)*$^{\bullet\bullet}$ is only observable at high amplification. This is consistent with the fact that the zero field splitting for *(5)*$^{\bullet\bullet}$[9] is smaller than for *(4)*$^{\dot{+}\dot{+}}$ ($D = 0.0257$ cm$^{-1}$[4b]). Further, the total intensity of the $\Delta M_S = 2$ signal in the case of *(5)*$^{\bullet\bullet}$ is spread over 15 hyperfine components [$a(2\ ^{51}V) = 43 \pm 1$ G], whereas only one component appears for *(4)*$^{\dot{+}\dot{+}}$ owing to the preponderance of the non-magnetic nuclei $^{52}Cr$ (90.5%).

The smaller magnitude of the parameter $D$ for *(5)*$^{\bullet\bullet}$, as compared to *(4)*$^{\dot{+}\dot{+}}$, might contribute to the fact that *(5)*$^{\bullet\bullet}$, in contrast to *(4)*$^{\dot{+}\dot{+}}$, affords a well resolved ESR spectrum in liquid solution. Furthermore, an averaging of the zero field splitting in the case of *(5)*$^{\bullet\bullet}$ is promoted by a shorter correlation time of the molecular motion, since *(5)*$^{\bullet\bullet}$ should have a smaller effective radius than the solvated dication *(4)*$^{\dot{+}\dot{+}}$.

*Procedure*

All operations were carried out under $N_2$ with anhydrous and $O_2$-free solvents.—*(6)* (5.4 g, 26 mmol) is metalated in methylcyclohexane (300 $cm^3$) for 4 h at +90 °C with *n*-butyllithium (27.3 ml, 54.6 mmol) (5% excess) and tetramethylethylenediamine (8.4 ml, 54.6 mmol). The mixture is then cooled to −10 °C, treated dropwise with a solution of *o*-bromoanisole (1.6 ml, 13 mmol) in methylcyclohexane (50 $cm^3$), stirred for 7 h at −10 °C and 9 h at room temperature, hydrolyzed with 1 $cm^3$ $H_2O$, stirred for a further 1 h, and evaporated to dryness. The blackish brown residue is taken up in 200 $cm^3$ toluene and filtered through a column (silanated silica gel, length 25 cm, ∅ 2 cm). After extraction with toluene (3 × 200 $cm^3$) the combined filtrates are evaporated to dryness. On sublimation ($<10^{-4}$ torr) of the black-brown residue, two fractions were obtained: 1) $T = 120$ °C: 4.14 g *(6)*; 2) $180 \leq T \leq 210$ °C: 150 mg $(5)^{\cdot-}$, yield 13%, based on the amount of $(6)^{\cdot}$ used. $(5)^{\cdot-}$ crystallizes from toluene/petroleum ether (40:60) as black, shiny platelets.

Received: August 28, 1980 [Z 705 IE]
German version: Angew. Chem. 93, 278 (1981)

Registry numbers:
$(5)^{\cdot-}$, 76847-28-4; $(6)^{\cdot}$, 12129-72-5

---

[1] a) *S. P. McGlynn, T. Azumi, M. Kinoshita:* Molecular Spectroscopy of the Triplet State. Prentice Hall, Englewood Cliffs, 1969; b) *L. Salem, C. Rowland,* Angew. Chem. *84*, 86 (1972); Angew. Chem. Int. Ed. Engl. *11*, 92 (1972).

[2] a) *D. C. Reitz, S. I. Weissman,* J. Chem. Phys. *27*, 968 (1957); *33*, 700 (1960); b) *R. K. Waring, G. J. Sloan, ibid. 40*, 772 (1964).

[3] a) *R. M. Dupeyre, H. Lemaire, A. Rassat,* J. Am. Chem. Soc. *87*, 3771 (1965); b) *R. Brière, R. M. Dupeyre, H. Lemaire, C. Morat, A. Rassat, P. Rey,* Bull. Soc. Chim. Fr. *1965*, 3290; c) *B. Nickel, A. Rassat,* Tetrahedron Lett. *1978*, 633; d) *S. H. Glarum, J. H. Marshall,* J. Chem. Phys. *47*, 1374 (1967).

[4] a) *Ch. Elschenbroich, J. Heck,* Angew. Chem. *89*, 497 (1977); Angew. Chem. Int. Ed. Engl. *16*, 479 (1977); b) *Ch. Elschenbroich, J. Heck,* J. Am. Chem. Soc. *101*, 6773 (1979).

[5] EI/MS (70 eV): $m/e = 412$ (53.4%, $M^+$, $C_{24}H_{22}V_2^+$), 332 (100, $C_{18}H_{14}V_2^+$), 283 (20.8, $C_{18}H_{16}V^+$), 254 (41, $C_{12}H_8V_2^+$), 228 (12.3, $C_{18}H_{12}^+$), 205 (16.9, $C_{12}H_{10}V^+$), 203 (7.9, $C_{12}H_8V^+$), 154 (10.3, $C_{12}H_{10}^+$), 152 (7.1, $C_{12}H_8^+$), 129 (8.4, $C_6H_6V^+$), 78 (30, $C_6H_6^+$), 51 (40.5, $V^+$). High resolution: $m/e = 412.0591$. Contrary to the analogous Cr compound *(4)* [4a], the intensity of $M^+$ is high in the case of $(5)^{\cdot-}$. Furthermore, a peak $m/e = 332$ (elimination of $C_6H_6 + 2H$) occurs as base peak for *(5)*. In contrast the corresponding peak $m/e = 334$ is not observed in the mass spectrum of *(4)*.

[6] *Ch. Elschenbroich, F. Stohler,* Chimia *28*, 730 (1974).

[7] *N. D. Chasteen, R. L. Belford,* Inorg. Chem. *9*, 169 (1970).

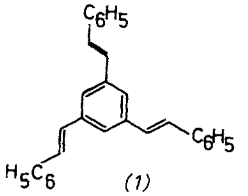
[8] In our analysis we have assumed, that the distance between the two lines marked with asterisks in Fig. 2 corresponds to the parameter $2D$. These positions were obtained by counting eight lines from the low field and high field ends of the spectrum towards its center. The analysis of the spectrum was affirmed by computer simulation.

[9] The intensity of the formally forbidden ($\Delta M_S = 2$)-transitions increases with decreasing distance between the unpaired electrons, *i.e.* with increasing dipole-dipole interaction *D*.

## A Simple Route to a New Type of Cyclophane[**]

By *Juri Juriew, Tatjana Skorochodowa, Jewgeni Merkuschew, Werner Winter,* and *Herbert Meier*[*]

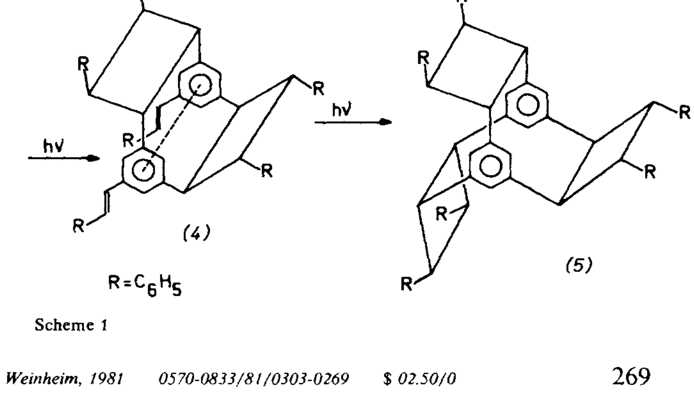
Although the first synthesis of a cyclophane was reported as long ago as 1899[1], this class of compounds has only relatively recently become the subject of extensive studies[2]. The stepwise synthesis of several bridges between two aromatic ring systems is preparatively laborious. Consequently, methods in which several bridges are formed in a single step have proven particularly attractive[2]. In order to check whether this is possible by photochemical cycloaddition we have investigated the *(E,E,E)*-1,3,5-tristyrylbenzene *(1)*, which is directly accessible by various methods[3,4] from 1,3,5-trimethylbenzene.



*(1)*

The UV spectrum of *(1)* [$\lambda_{max} = 317$ nm ($\log\varepsilon = 4.96$)] shows the characteristic $\pi,\pi^*$-transition of the *trans*-stilbene; there is only slight interaction between the three styryl groups[5]. On irradiation at this wavelength one can observe, as well as the fluorescence ($\lambda_{max} = 410$ nm), a photoreaction. The olefinic double bonds disappear and the $^1H$-NMR spectrum shows groups of signals of saturated aliphatic protons. It may be assumed that dimers with one, two, and finally three four-membered rings are formed by $[2\pi + 2\pi]$-cycloaddition with preservation of the *E*-configurations (Scheme 1). The formation of head-to-head and head-to-tail adducts is possible. The fact that *e.g.* two head-substituents can be arranged *cis* or *trans* to each other results in a number of stereochemical possibilities. However, the successive formation of four-membered rings considerably limits these possibilities.

The reaction, involving the loose singlet excimers *(2)*, which guarantee an efficient stereochemically controlled photoreaction, proceeds *via (3)* and *(4)* to *(5)*. After irradiation of *(1)* in *ca.* 0.02 M benzene solution a compound of m.p. 280 °C can be isolated as main product in 25—30% yield. The FD-MS spectrum indicates formation of a dimer, and according to the UV spectrum the product does not contain any stilbene groups. The $^1H$-NMR spectrum reveals the presence of three four-membered rings with 12 protons (sharp signal at $\delta = 4.45$). Only two signals ($\delta = 56.2$ and 43.0)



Scheme 1

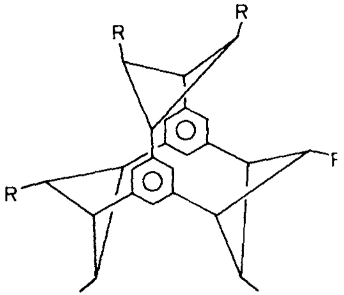
---

[*] Prof. Dr. H. Meier [+], Doz. Dr. W. Winter
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)
Doz. Dr. J. Juriew, Doz. Dr. J. Merkuschew, Z. Skorochodowa
Polytechnisches Institut der Chemisch-technologischen Fakultät
634004 Tomsk (USSR)

[**] This work was supported by the Fonds der Chemischen Industrie. *J. J.* thanks the Deutsche Akademische Auslandsdienst for a stipendium.

[+] Author to whom correspondence should be addressed.

appear in the upfield part of the $^{13}$C-NMR spectrum ($CD_2Cl_2$); under "off-resonance conditions" each of them splits into a doublet. Both *(5)* ($C_{3h}$ symmetry) and *(5a)* ($D_{3h}$ symmetry) are compatable with these results; *(5a)* would be formed on threefold stereospecific head-to-tail cycloaddition. Both *(5)* and *(5a)* represent a new type of cyclophane in which both benzene nuclei are bridged by rings.



*(5a)*

All attempts to reach a decision between *(5)* and *(5a)* by spectroscopic methods failed. An X-ray structure analysis[6] (Fig. 1) finally confirmed the "lateral" coupling of the cyclobutane rings, *i.e.* the structure *(5)*.

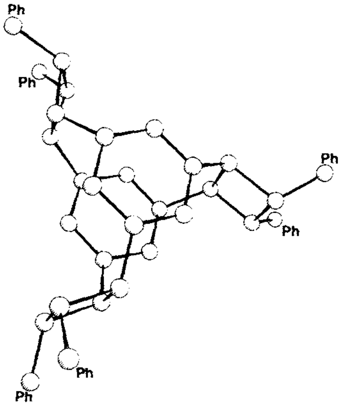
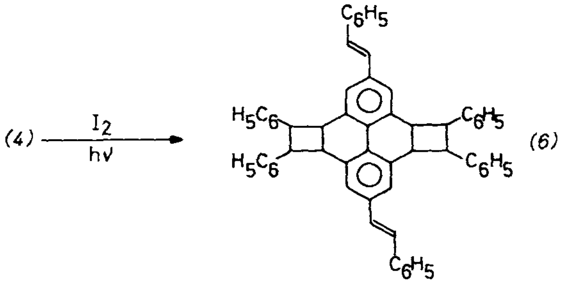


Fig. 1. Structure of the cyclophane *(5)* in the crystal. For sake of clarity only the central cyclophane moiety is shown.

The packing in the crystal in this "paddle wheel" molecule leads to a symmetry distortion[7]. "Levorotatory" and "dextrorotatory" systems are formed which effect a complicated disorder within the unit cell[8]. The average distance between the two central benzene rings in *(5)* is 2.85 ± 0.06 Å. Due to strain the cyclobutane bonds in the three bridges of the [$2_3$]cyclophane are stretched to 1.64(2) Å. The [$3_3$]cyclophane *(5a)* ought to exhibit considerably less strain. We ascribe the regio- and stereoselective formation of *(5)* to the above-mentioned excimer formation.

The photoreaction is blocked by iodine at *(4)*, since dehydration at this stage gives the pyrene derivative *(6)* (m.p. 312—314 °C).



Thus the dimerization of di- and tristyrylbenzenes[9] in preference to dehydrogenating cyclization to polycyclic arenes takes place in $10^{-2}$ M solutions, even in the presence of iodine. Only the third ring-closure, which leads to the strained cyclophane *(5)*, is hindered by iodine.

Received: August 1, 1980 [Z 704a IE]
German version: Angew. Chem. *93*, 285 (1981)

CAS Registry numbers:
*(1)*, 34631-15-7; *(3)*, 76900-46-4; *(4)*, 76900-47-5; *(5)*, 76900-48-6; *(5a)*, 76900-49-7; *(6)*, 76915-16-7

---

[1] *M. Pellegrin*, Recl. Trav. Chim. Pays-Bas *18*, 458 (1899).

[2] Neuere Übersichten: *F. Vögtle, G. Hohner*, Top. Curr. Chem. *74*, 1 (1978); *S. Misumi, T. Otsubo*, Acc. Chem. Res. *11*, 251 (1978); *H. Hopf*, Nachr. Chem. Tech. Lab. *28*, 311 (1980); *V. Boekelheide*, Acc. Chem. Res. *13*, 65 (1980).

[3] *L. Y. Malkes, N. P. Kovalenko*, Zh. Org. Khim. *2*, 297 (1966); cf. also *L. Y. Malkes, N. P. Kovalenko, ibid. 7*, 2149 (1971); *L. Y. Malkes, V. N. Dmitrieva, L. I. Dmitrievskaya, T. P. Boronenko*, Zh. Obshch. Khim. *45*, 1481 (1975).

[4] *A. E. Siegrist, P. Liechti, H. R. Meyer, K. Weber*, Helv. Chim. Acta *52*, 2521 (1969).

[5] *A. E. Lutskii, L. A. Antropova, L. Y. Malkes, N. P. Kovalenko, Z. A. Shevchenko*, Vestn. Khar'k Politekh. Inst. *76*, 3 (1973).

[6] Orthorhombic, space group Pccn, $Z=4$; $a=9.663(1)$, $b=18.320(2)$, $c=24.170(3)$ Å. Solution of the phase problems with MULTAN 80; refinement: $R=0.137$, and $R_w=0.117$ for 1905 reflections with $F \geq 3\sigma(F)$ (isotropic temperature factors and phenyl moiety as "rigid group", SHELX).

[7] The cyclobutane ring on te left in Figure 1 is slightly folded, the other two are planar within the limits of error.

[8] *H. Meier, W. Winter, et. al.*, unpublished results.

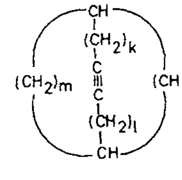
[9] For the complex photochemistry of these systems cf. *F. Dietz, M. Scholz*, Tetrahedron *24*, 6845 (1968); *E. Müller, H. Meier, M. Sauerbier*, Chem. Ber. *103*, 1356 (1970); *D. D. Morgan, S. W. Morgan, M. Orchin*, Tetrahedron Lett. *1970*, 4347; *Th. E. M. Van den Hark, P. I. Beurskens, W. H. Laarhoven*, J. Cryst. Mol. Struct. *4*, 227 (1974); *T. S. Skorochodowa, G. N. Iwanov, V. I. Luk'yanov, J. Juriew, V. F. Kam'yanov, E. B. Merkushev*, Neftekhimiya *19*, 839 (1979).

---

# Isolation of a Highly Strained Bicyclic Alkyne[**]

By *Herbert Meier, Cornelius Schulz-Popitz*,
and *Hermann Petersen*[*]

With the exception of norbornyne ($k=l=0$, $m=1$, $n=2$)[1], strained bicyclic hydrocarbons *(1)* containing a triple bond, have so far not been reported in the literature. Higher bicycloalkynes[2] without geometrical ring strain[3], however, have already been described on a number of occasions. For the preparation of highly strained and reactive cycloalkynes, the fragmentation of 1,2,3-selenadiazolene has proved especially useful[4].



*(1)* (k, l, m, n = 0,1,2...)

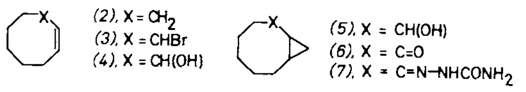
We report here on the synthesis of bicyclo[6.1.0]non-2-yne *(1a)* ($k=0$, $l=4$, $m=0$, $n=1$) and bicyclo[5.1.0]oct-2-yne *(1b)* ($k=0$, $l=3$, $m=0$, $n=1$). Starting from cyclooctene *(2)* the bicyclic ketone *(6)*[7] was obtained *via (3)*[5], *(4)*[6], and *(5)*. The ketone *(6)* can be transformed *via* the semicarbazone *(7)* into the selenadiazole *(8)*, thermolysis of which affords *(1a)*, which is distilled directly into a cold trap. The *in-situ* prepa-

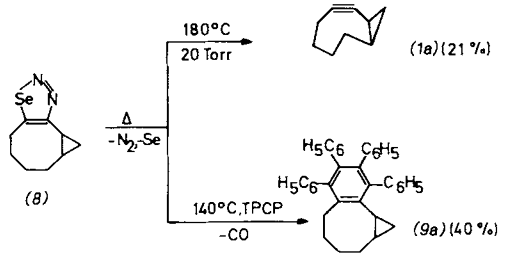
---

[*] Prof. Dr. H. Meier, Dipl.-Chem. C. Schulz-Popitz, Dr. H. Petersen
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

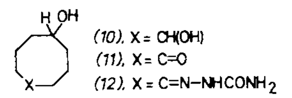
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

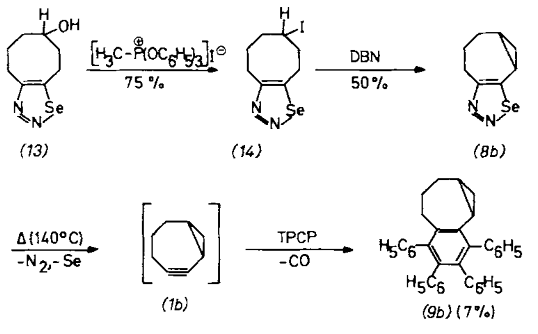
ration in boiling xylene proceeds in high yields, as shown by the trapping reaction with tetraphenylcyclopentadienone (TPCP), which yields *(9a)* (m.p. 231 °C) in 40% yield.





Pure *(1a)* is moderately stable at room temperature and is characterized by its Raman spectrum ($CDCl_3$, $\nu_{C\equiv C}=2204$, 2220 $cm^{-1}$) and especially by its $^{13}C$-NMR spectrum. The acetylenic C-atoms C-2 and C-3 absorb at $\delta=98.4$ and 89.0 respectively, the three-membered ring C-atoms at 5.8 (C-1), 14.1 (C-9) and 22.5 (C-8). C-4 gives a signal at $\delta=19.9$. The signals for C-5, C-6 and C-7 ($\delta=36.5$, 31.6 and 22.7) were not assigned. The ring strain in cycloalkynes leads—most markedly in the case of the acetylenic C-atoms—to a downfield shift of the $^{13}C$-absorptions[4a]; the δ-values found for *(1a)* indicate a high degree of geometrical ring strain.





The next lower homologue *(1b)* is prepared from 1,5-cyclooctadiene *via (10), (11), (12)* and the selenadiazole *(13)*. Conversion into the iodide *(14)* and 1,3-elimination of HI[8], during which regioselective deprotonation takes place with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), leads to *(8b)*. Thermolysis of *(8b)* affords *(1b)*, which however cannot be isolated. The enormous strain, and thus short lifetime, manifest themselves in the trapping reaction with TPCP, in which *(9b)* (m.p. 217 °C) is formed in only 7% yield. (Cycloheptyne can be trapped in 29% yield by this method, cyclohexyne in 6% yield[9]). *(1a)* is thus the first bicyclic alkyne to be isolated, despite high geometric ring strain.

Received: August 20, 1980 [Z 704b IE]
German version: Angew. Chem. 93, 286 (1981)

CAS Registry numbers:
*(1a)*, 76832-30-9; *(1b)*, 76832-31-0; *(2)*, 931-88-4; *(3)*, 7422-06-2; *(4)*, 3212-75-7; *(5)*, 38433-06-6; *(6)*, 29800-55-3; *(7)*, 76832-32-1; *(8a)*, 76832-33-2; *(8b)*, 76832-34-3; *(9a)*, 76847-15-9; *(9b)*, 76832-35-4; *(10)*, 55343-44-7; *(11)*, 61755-97-3; *(12)*, 67959-46-0; *(13)*, 67959-47-1; *(14)*, 76832-36-5; 1,5-Cyclooctadiene, 111-78-4; TPCP, 479-33-4

---

[1] a) *P. G. Gassman, T. J. Atkins*, Tetrahedron Lett. *1975*, 3035; b) *P. G. Gassman, J. J. Valcho*, J. Am. Chem. Soc. *97*, 4768 (1975); c) on the basic skeleton with $k=0$, $l=m=n=2$ cf. *H. D. Carnadi, P. Hildenbrand, J. Richter, G. Schröder*, Justus Liebigs Ann. Chem. *1978*, 2074, and on the basic framework with $k=0$, $l=2$, $m=4$, $n=1$ cf. *W. A. Böll*, Angew. Chem. *78*, 755 (1966); Angew. Chem. Int. Ed. Engl. *5*, 733 (1966).

[2] Cf. *D. J. Cram, M. F. Antar*, J. Am. Chem. Soc. *80*, 3109 (1958).

[3] For a description of geometric ring strain cf. [4a].

[4] a) *H. Meier, H. Petersen, H. Kolshorn*, Chem. Ber. *113*, 2398 (1980); b) cf. also *H. Petersen, H. Meier, ibid. 113*, 2383 (1980), and references cited therein.

[5] *A. C. Cope, L. L. Estes*, J. Am. Chem. Soc. *72*, 1129 (1950).

[6] *N. Heap, G. H. Whitham*, J. Chem. Soc. *B 1966*, 164.

[7] Cf. *C. D. Poulter, E. C. Friedrich, S. Winstein*, J. Am. Chem. Soc. *92*, 4274 (1970).

[8] On the subject of 1,2-elimination and incorporation of a double bond cf. [4b].

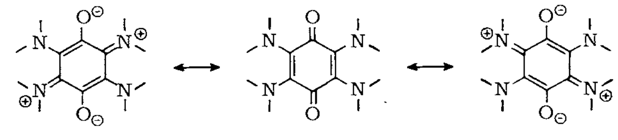
[9] *H. Meier, E. Voigt*, Tetrahedron *28*, 187 (1972).

---

## Polymethinic Ring Compounds and the Polymethinic Carbonyl Group

By *Siegfried Kulpe*[*]

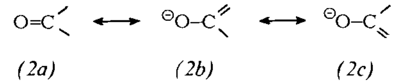
The name "stellaquinones" had been proposed by *Wallenfels* and *Draber*[1] for the deep-colored and stable tetraaminoquinones. In these compounds a bonding system with hexagonal symmetry and capable of resonance was concluded from the mesomerism of the resonance structures *(1a)*—*(1c)*.



*(1a)* *(1b)* *(1c)*

The same authors, however, later tried to explain the physicochemical properties of the di- and triaminobenzoquinones in terms of steric effects in pure quininoid (polyenic) electronic structures. The sole reason for revocation of their original hypothesis was the unexpectedly small red shift of such important C=O stretching vibrations shown by all investigated diaminoquinones ($\nu_{C=O}$ between 1653 and 1667 $cm^{-1}$) and tetraaminoquinones ($\nu_{C=O}$ between 1620 and 1639 $cm^{-1}$) in comparison to the carbonyl frequency in *p*-benzoquinone ($\nu_{C=O}=1681$ $cm^{-1}$). The C=O bond length in *p*-benzoquinone (1.222(24) Å[3]) is ideal for an unsaturated six-membered carbon ring. This particular type of symmetric oxygen substitution at the benzene ring permits conversion from the aromatic into the quininoid (polyenic) electronic structure. According to the mesomeric resonance structures *(1a)*—*(1c)* the carbonyl bond must be drastically extended. This should lead to a large red shift of its valence vibration frequencies, which however is not observed.

Essential for this hypothesis for the di- and tetraaminoquinones, which is contrary to experimental findings, was that only mesomerism between the three structural units *(2a)*—*(2c)*[10] was assumed[1,2].



*(2a)* *(2b)* *(2c)*

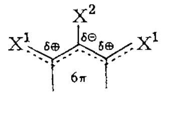
---

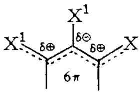
[*] Prof. Dr. S. Kulpe
Akademie der Wissenschaften der DDR, Zentralinstitut für physikalische Chemie
Rudower Chaussee 5, DDR-1199 Berlin-Adlershof (Germany)

In spite of this, *Wallenfels* and *Draber* were working in the right direction: The tetra- and diaminoquinones are a *non-quininoid* class of compounds. Their properties are understandable if one regards them as *coupled polymethinic* electron systems[4].

If tetraaminoquinones are likewise assumed to have a *polymethinic* electron structure, then apart from their general properties the behavior of their carbonyl group is also plausible. Tetraaminoquinones can be regarded a cross-conjugated, non-alternating polymethines. Formally, the two non-alternating substituted trimethine structural units *(3a)* and *(3b)* (Scheme 1) can be regarded as polymethine units which superpose and ramify in the six-membered ring.

*(3a)*





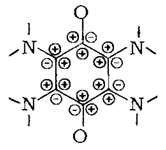
*(3b)*

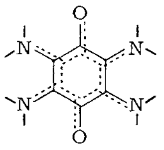
Scheme 1. $X^1 = N$, $X^2 = O$, small π-electron density at the methine C-atom corresponding to a partial positive charge δ⊕, and large π-electron density to a partial negative charge δ⊖.

The superposition of the structural units *(3a)* and *(3b)* follows the rules given in Ref. [5]. According to the sign of the π-electron charge they give *(4a)*, according to the π-electron distribution *(4b)*; that is, there is a high π-electron delocalization over all non-hydrogen atoms of polymethine character, which is responsible for the deep color of the compounds.

Without accurate X-ray structure analyses it is difficult to quote more accurate charge distributions in such cross-decoupled, non-alternating systems such as *(4)*. It is suggested that the C-atoms in the six-membered ring are partially positively charged, the O-atoms partially negatively charged. It is more difficult to comment on the N-atoms[6].

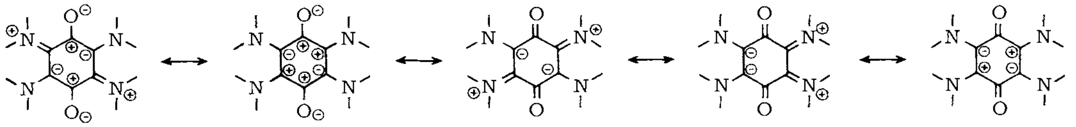
*(4a)*





*(4b)*

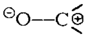
For an explanation of these polymethinic electron structures in terms of resonance theory many polar resonance structures must be taken into consideration, *e.g.* *(5a)*—*(5e)*. As a rule, polymethinic atoms are not electrically neutral (π-charge alternation!).

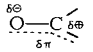


*(5a)* *(5b)* *(5c)* *(5d)* *(5e)*

Carbonyl groups in polymethinic structures with mesomeric participation of resonance structures such as *(5a)* and *(5b)* contain the well known dipolar structural unit *(6)*.

*(6)*





*(7)*

The heteropolarity of this bond effects elongation as would have to exist according to *(2b)* and *(2c)*. We refer to such a C=O group as a *polymethinic carbonyl group*[7] and exemplify it by *(7)*.

This description expresses the MO concept far better and corresponds to a mesomerism of the four resonance structures *(2a)*—*(2c)* and *(6)* in the VB concept.

The *polymethinic carbonyl group* has the following properties: 1) its C=O bond is not drastically stretched; 2) its valence vibration frequency is not drastically shifted bathochromically; 3) nevertheless, it acts as an electron acceptor, is resonance stabilizing, and acts as member of a polymethinic base chromophore, which results in longwave and especially intense light-absorption, as is observed for the di- and tetraaminoquinones.

In the case of highly symmetric polymethines (*e.g.* open-chain, unsubstituted "oxonoles"[*]) there can be a significant widening of the carbonyl bond, which however is not so drastic as would be the case on neglection of its ionic character according to *(6)* and *(7)*.

An inappropriate assignment of the C=O valence vibration always arises when the *polymethinic* character of the carbonyl group is overlooked[8]. Such *polymethinic carbonyl groups* can occur on any desirable ring as well as open-chain systems. In our opinion they can be distinguished from *polyenic carbonyl groups,* which are essentially described by *(2a)*, are not ionic, not conjugated with stretched electron systems, and consequently have other properties. Both kinds of carbonyl groups are not easy to differentiate in their bond lengths and IR spectra. However, they are distinguishable by an accurate X-ray structure analysis.

Drastic expansion of bonding due to homopolarity of polymethinic bond partners has already been described[4b,9]. This phenomenon is closely connected with the problem discussed above.

Received: August 1, 1980 [Z 703 IE]
German version: Angew. Chem. *93*, 283 (1981)
Revised: January 8, 1981

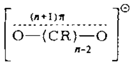
CAS Registry numbers:
Tetraaminobenzoquinone, 1128-13-8; diaminobenzoquinone, 76915-97-4

---

[1] *K. Wallenfels, W. Draber,* Angew. Chem. *70*, 313 (1958).
[2] *K. Wallenfels, W. Draber,* Tetrahedron *20*, 1889 (1964).
[3] *J. Trotter,* Acta Crystallogr. *13*, 86 (1960).
[4] a) *S. Dähne, S. Kulpe,* Abh. Akad. Wiss. DDR *N8*, 1 (1977); b) *S. Kulpe, S. Dähne,* Acta Crystallogr. B *34*, 3616 (1978); c) *J. Fabian, G. Tröger-Naake,* J. Prakt. Chem. *318*, 801 (1976).
[5] *S. Dähne, S. Kulpe,* J. Prakt. Chem. *320*, 395 (1978).
[6] *K.-D. Nolte,* Dissertation, Humboldt-Universität Berlin 1972.
[7] *S. Kulpe,* Z. Chem. *20*, 377 (1980).
[8] a) *S. Dähne, D. Leupold,* Angew. Chem. *78*, 1029 (1960); b) *H. Dorn, A. Otto,* Chem. Ber. *101*, 3287 (1968).
[9] *S. Dähne,* Z. Chem., *21*, 58 (1981).

[10] The two additional electrons in *(2b)* and *(2c)* stem from the adjacent chromophore reagion.

[*] Oxonoles are polymethines with the arrangement *(8)*, which are singly negatively charged.



$$\left[\overset{(n+1)\pi}{\overline{O-(CR)_{n-2}-O}}\right]^{\ominus}$$

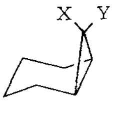
*(8)*, $n = 3, 5, 7 \ldots$

# Stereochemistry of Substitution at the Cyclopropane Ring in 7-Aminonorcaranes[**]

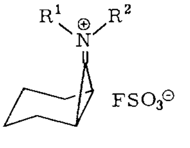
By *Elmar Vilsmaier, Wolfgang Tröger,*
and *Michael Gewehr*[*]

In nucleophilic substitutions on norcarane derivatives *(1)*, X, Y$\neq$NR$_2$, a substituent in the *endo* position is a better leaving group than in the *exo* position[1a–d]. In these cases a *cis*-cycloheptenyl-[1a,c] or a partially opened cyclopropyl-cation[1b,e] is formed as an intermediate. The different rates of formation of these cations cause the discrimination between *endo* and *exo* leaving groups.

On the other hand, 7-aminobicyclo[4.1.0]heptane derivatives, are capable of forming a cation with an unopened three-membered ring, *e.g.* *(2a)*[2]. We report here on differences in the reactivity of *exo* and *endo* leaving groups in norcarane derivatives from which a cation of type *(2)* can be formed.



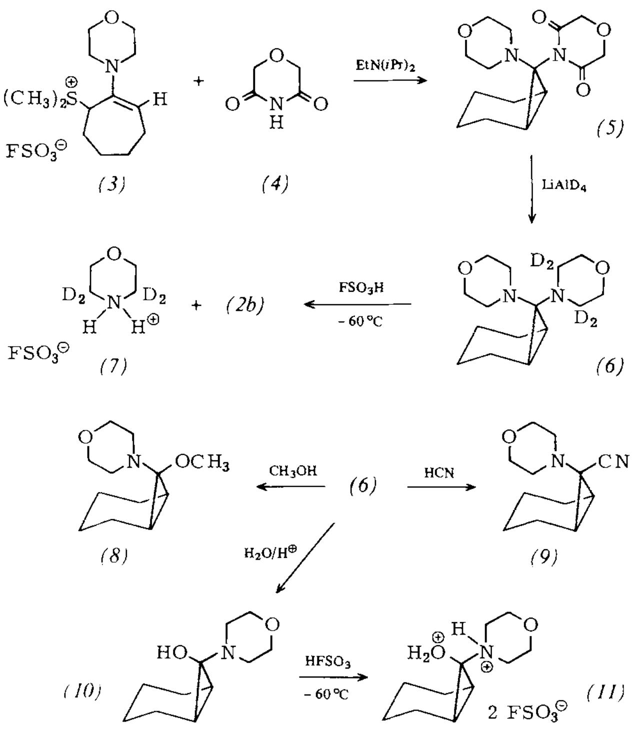
*(1)*



*(2a)*, R$^1$ = R$^2$ = CH$_3$
*(2b)*, R$^1$, R$^2$ = –(CH$_2$)$_2$–O–(CH$_2$)$_2$–

Since the morpholino moiety in the bicyclo[4.1.0]heptane system is a simple "stereoindicator"[3], we have chosen the dimorpholine derivative *(6)* for our investigations; deuterium-labeling enables the differentiation between *exo*- and *endo*-substituents.

For the synthesis of *(6)*, the enaminosulfonium salt *(3)* was reacted with the imide *(4)* to give the bicycle *(5)*, whose $^1$H-NMR spectrum shows the typical ABXY system of an *endo*-morpholino moiety. Reduction of *(5)* with LiAlD$_4$ affords the tetradeuterioaminal *(6)* in 48% yield.



An ABXY system for the eight morpholino H-atoms[3] shows that the *endo*-morpholino moiety is undeuterated. The *exo*-morpholino H-atoms appear as a singlet at $\delta = 3.62$ (C$_6$D$_6$); *exo*-NC*H*$_2$-signals (cf. [3]) are absent. The $^{13}$C-NMR spectrum in each case shows exclusively a triplet ($\delta = 50.2$), $^1J_{^1H^{13}C} = 133$ Hz) for the NCH$_2$-atoms and a quintet $\delta = 51.0$, $^1J_{^2H\text{-}^{13}C} = 20$ Hz) for the NCD$_2$ atoms.

Reaction of *(6)* with HFSO$_3$ at $-60\,^\circ$C leads to formation of an iminium ion, which can be characterized by $^{13}$C-NMR spectroscopy. A singlet shifted to very low field ($\delta = 204$) and a doublet in the alkane region ($\delta = 21$) (Table 1) establish the cyclopropylideneammonium structure of *(2b)*[4]. In the case of a partially[1e] or completely[5] opened cyclopropyl cation, the doublet would appear at $\delta = 150$—180. The cyclopropylidenemorpholinium salt *(2b)* differs markedly from the morpholinium salt *(7)*, which gives only a broad signal for NCD$_2$. No triplet splitting and hence no NCH$_2$ group can be detected for *(7)* ($^1J_{^1H\text{-}^{13}C} = 140$ Hz) within a limit of error of 5%. It thus follows that the *exo*-substituent is cleaved with a selectivity of $\geq 95\%$ on generation of *(2b)* from *(6)*.

The different substitutability of the two morpholino moieties in *(6)* can also be established by solvolysis. Methanolysis[3] of *(6)* leads to formation of *(8)*, acid hydrolysis[3] to *(10)*, and reaction with HCN (cf. [6]) to *(9)*, in each case with the given configurations. The $^2$H$_4$-morpholine content can be determined by mass spectroscopy; in the case of *(8)* it is 0.1%, in *(10)* 1%, and in *(9)* 8%[7]. The same result is also obtained, though less accurately, from the $^1$H-NMR spectra by integration of the OC*H*$_2$- and NC*H*$_2$-signals. This means that at least 99% of the *exo*-morpholino moiety is replaced on reaction of *(6)* with methanol or H$_2$O/H$^\oplus$.

The lower selectivity in the reaction of *(6)* with HCN is ascribed to an isomerization of the educt (longer reaction time). In CH$_3$CN the acidity of *(7)* is sufficient for this. Owing to concomitant formation of *(7)*, attempts to prepare *(6)* from *(3)* and 3,3,5,5-tetradeuteriomorpholine[8] (analogously to [3]) led only to a mixture of isomers of *(6)*. According to the mass spectrum (molecular peaks for $^2$H$_0$, $^2$H$_4$ and $^2$H$_8$-aminal), the *exo-endo* isomerization also takes place intermolecularly.

Table 1. $^{13}$C-NMR signals of the cations studied; $\delta$ values, HFSO$_3$ solvent, $-60\,^\circ$C, TMS as external standard.

| | Morpholine | | Bicyclic system | | |
|---|---|---|---|---|---|
| | OCH$_2$ (t) | NCH$_2$ (t) | C-7 (s) | C-1,6 (d) ($^1J_{^1H\text{-}^{13}C}$ [Hz]) | C-2,5, C-3,4 (t) |
| *(2b)* | 71.1 | 54.3 | 204 | 21.0 (173) | 19.8, 18.4 |
| *(11)* | 67.8 | 47.4 | 81.1 | 19.3 (163) | 19.6, 16.0 |
| *(13)* | 66.6 | 48.8 | 81.5 | 21.9, 19.2 [a], | 15.8 |
| *(7)* | 69.3 | 43.8 [b] | | | |

[a] Unequivocal assignment not possible owing to the low intensity. [b] Unresolved signal (halfwidth 50 Hz).

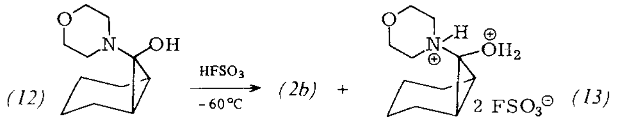
In HFSO$_3$ at $-60\,^\circ$C the hemiaminal *(10)* is not converted into the expected compound *(2b)*, but into an ammonium salt *(11)*, which is presumably diprotonated. In contrast to *(2b)*, which undergoes ring-opening even at $-20\,^\circ$C in HFSO$_3$, *(11)* is stable for several hours, even at $+20\,^\circ$C. However, addition of *(12)*[3], an isomer of *(10)*, to HFSO$_3$ at $-60\,^\circ$C leads to formation of the iminium salt *(2b)*. Low-intensity $^{13}$C-NMR signals [corresponding to *ca.* 20% of *(2b)*] are observed (Table 1) which, on comparison with the spectrum of *(11)*, can be assigned to the salt *(13)*[10].

Both the reactions of *(6)*, *(10)* and *(12)* in HFSO$_3$, as well as the solvolyses, clearly show that the *exo*-substituent is the preferred leaving group in a 7-aminonorcarane derivative. Other than in the case of the solvolyses, equilibrium reactions can be ignored with HFSO$_3$ as solvent. Hence, the find-

---

[*] Prof. Dr. E. Vilsmaier, Dipl.-Chem. W. Tröger, M. Gewehr
Fachbereich Chemie der Universität
Paul-Ehrlich-Strasse, D-6750 Kaiserslautern (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.



ings in HFSO$_3$ can be interpreted in terms of a sterically determined, more rapid protonation of the *exo*-substituents. Since a non-protonated amino group is necessary for the generation of *(2b)* only *exo*-protonated *(6)* and *(12)*, but not *(10)*, lead to *(2b)*.

### *Procedure*

*(5)*: A mixture of *(3)* (6.8 g), *(4)* (2.3 g) and ethyldiisopropylamine (2.6 g) (20 mmol of each) in anhydrous acetonitrile (20 cm$^3$) is heated to 70 °C for 1.5 h and worked up as described in Ref. [10]. Yield of *(5)*: 5.2 g (88%); m.p. 160 °C.

*(6)*: A mixture of *(5)* (4.4 g, 15 mmol) and LiAlD$_4$ (1.3 g, 30 mmol) in anhydrous tetrahydrofuran (THF) is heated under reflux for 70 h. After removal of THF by distillation, the residue is extracted five times with 50 cm$^3$ of pentane. Removal of the pentane affords 1.9 g (48%) of pure *(6)*; m.p. 75 °C.

Received: September 4, 1980 [Z 702 IE]
German version: Angew. Chem. *93*, 277 (1981)

CAS Registry numbers:
*(2a)*, 52999-11-8; *(2b)*, 76879-17-9; *(3)*, 71482-07-0; *(4)*, 4430-05-1; *(5)*, 76879-18-0; *(6)*, 76879-19-1; *(7)*, 76879-20-4; *(8)*, 71672-42-9; *(9)*, 76900-16-8; *(10)*, 71672-43-0; *(11)*, 76879-21-5; *(12)*, 71699-80-4; *(13)*, 76819-22-6

---

[1] a) *S. J. Cristol, R. M. Sequeira, C. H. De Puy*, J. Am. Chem. Soc. *87*, 4007 (1965); b) *U. Schöllkopf, K. Fellenberger, M. Patsch, P. von R. Schleyer, T. Su, G. W. van Dine*, Tetrahedron Lett. *1967*, 3639; c) *U. Schöllkopf*, Angew. Chem. *80*, 603 (1968); Angew. Chem. Int. Ed. Engl. *7*, 588 (1968), and references cited therein; d) Exception: Diazonium-Gruppe, vgl. *W. Kirmse, H. Jendralla*, Chem. Ber. *111*, 1857 (1978); e) *G. A. Olah, G. Liang, D. B. Ledlie, M. G. Costopoulos*, J. Am. Chem. Soc. *99*, 4196 (1977); *X. Creary*, J. Org. Chem. *41*, 3734 (1976).

[2] *E. Jongejan, H. Steinberg, Th. J. de Boer*, Synth. Commun. *4*, 11 (1974).

[3] *E. Vilsmaier, W. Tröger*, Angew. Chem. *91*, 860 (1979); Angew. Chem. Int. Ed. Engl. *18*, 798 (1979); *E. Vilsmaier, W. Tröger, G. Haag*, Chem. Ber. *114*, 67 (1981).

[4] Similar $^{13}$C-NMR values are quoted for *(2a)*; a proton-coupled spectrum could not be obtained. *E. Jongejan*, Thesis, University of Amsterdam 1976.

[5] *G. A. Olah, G. Liang*, J. Am. Chem. Soc. *94*, 6434 (1972).

[6] a) *H. Böhme, H. Ellenberg, O. E. Herboth, W. Lehners*, Chem. Ber. *92*, 1608 (1959); b) *W. J. M. van Tilborg, H. Steinberg, Th. J. de Boer*, Recl. Trav. Chim. Pays-Bas *93*, 290 (1974); c) *E. Vilsmaier, L. Scheiber*, Synthesis *1980*, 465.

[7] Determined from the ratio of the $M^+$ and $(M+4)^+$ peaks.

[8] *P. le Cam, J. Sandström*, Chem. Scr. *1*, 65 (1971).

[9] Addition of *(10)* shows that this signal does not arise from *(11)*.

[10] *E. Vilsmaier, C. M. Klein*, Angew. Chem. *91*, 861 (1979); Angew. Chem. Int. Ed. Engl. *18*, 800 (1979).

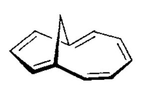
---

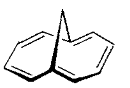
## A Convenient Synthesis of “Homoazulene” (1,5-Methano[10]annulene)[**]

By *Lawrence T. Scott, William R. Brunsvold, Mark A. Kirms* and *Ihsan Erden*[*]

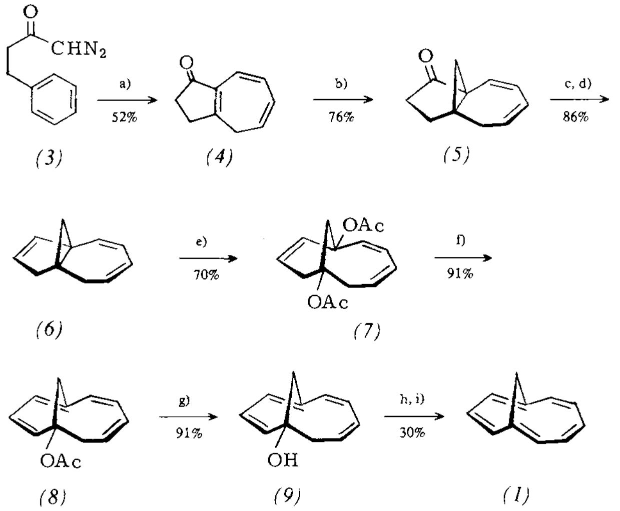
The beautiful annulene chemistry developed by *Vogel et al.* during the past two decades has contributed enormously to current thinking about cyclic conjugation in nonbenzenoid systems[1]. Throughout this work, formidable challenges in organic synthesis have time and again been masterfully met in a fashion rarely rivaled outside natural product chemistry. Exciting new advances continue to be made as the family of bridged annulenes and related ions grows ever larger. In this regard, the elegant synthesis of 1,5-methano[10]annulene *(1)* by *Masamune* and *Brooks* in 1977 must be recognized as a major step forward[2]. A long-missing member of the bridged annulene family, this pivotal compound bears an isomeric relationship to the parent hydrocarbon of *Vogel et al. (2)*. Herein we wish to describe an alternative synthesis of *(1)* which is suitable for the preparation of material in sufficient quantity to permit extensive physical and chemical studies[3] (Scheme 1).

*(1)*





*(2)*



Scheme 1. Synthesis of *(1)*. a) CuCl, C$_6$H$_5$Br, 80 °C; b) CH$_2$SO(CH$_3$)$_2$, CH$_3$SOCH$_3$, 75 °C; c) TsNHNH$_2$, CH$_3$OH, 25 °C; d) CH$_3$Li, Et$_2$O, 25 °C; e) Pb(OAc)$_4$, C$_6$H$_6$/HOAc (4:1), 0 °C; f) catalytic amounts of Pd(OAc)$_2$, (C$_6$H$_5$)$_3$P, Na$_2$CO$_3$, *n*C$_7$H$_{16}$, 85 °C; g) CH$_3$Li, Et$_2$O, 0 °C; h) CH$_3$SO$_2$Cl, Et$_3$N, CH$_2$Cl$_2$, 0 °C; i) *t*BuOK, *t*BuOH/25 °C.

Diazoketone *(3)*, available in essentially quantitative yield from hydrocinnamic acid, has previously been shown to give the excellently functionalized bicyclic trienone *(4)* by way of an intramolecular carbene addition[4]. Nucleophilic cyclopropanation[5] then completes the carbon framework of *(1)*. Conversion of dienone *(5)* to triene *(6)*, *via* the tosylhydrazone[6], followed by cleavage of the undesired propellane bond with lead tetraacetate[7] in benzene produces the nicely crystalline diacetate *(7)* (m.p. 90—92 °C) in good yield. Subsequent elimination of one acetoxy group, *via* a transient $\pi$-allyl palladium intermediate[8], affords the tetraene acetate *(8)* which can be carried through to 1,5-methano[10]annulene *(1)* by classical methods. Spectral properties of the orange hydrocarbon thus obtained agree with those in the literature[2].

Although still in the early stages, our program to thoroughly explore the physical and chemical properties of *(1)* and its derivatives has already yielded evidence that the $10\pi$-system of this novel hydrocarbon bears a conspicuous resemblance to that of azulene[9]. Accordingly, we advocate the trivial name “homoazulene” for *(1)* rather than the alternative “1,5-methano[10]annulene” which suggests only perimeter conjugation.

Received: August 18, 1980 [Z 700 IE]
German version: Angew. Chem. *93*, 282 (1981)

CAS Registry numbers:
*(1)*, 65754-71-4; *(3)*, 10290-42-3; *(4)*, 52487-41-9; *(5)*, 67313-65-9; *(6)*, 67313-66-0; *(7)*, 67313-67-1; *(8)*, 76833-20-0; *(9)*, 76833-21-1

---

[*] Prof. Dr. L. T. Scott, Dr. W. R. Brunsvold, M. A. Kirms, Dr. I. Erden
Department of Chemistry, University of Nevada
Reno, Nevada 89557 (USA)

[**] Financial support from the National Science Foundation, the National Institutes of Health (Grant NCI-CA-23488) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

Table 1. Spectroscopic data of new compounds *(5)*—*(9)* [a].

| Compound | $^1$H-NMR ($CDCl_3$, TMS, δ-values) | IR [$cm^{-1}$] | UV $\lambda_{max}$ [nm] [b] |
|---|---|---|---|
| *(5)* | 1.15 (d, $J$=4 Hz, 1 H), 2.0 (s, 4 H), 2.50 (d, $J$=4 Hz, 1 H), 2.62 (d, $J$=6 Hz, 2 H), 5.3—6.0 (m, 3 H), 6.35 (d, $J$=11 Hz, 1 H) | 3010, 2915, 1710, 1595, 1420, 1285, 1250, 1080, 1048, 1012, 920, 848, 775, 702 | 245 |
| *(6)* | 0.30 (d, $J$=3 Hz, 1 H), 2.26 (d, $J$=3 Hz, 1 H), 2.4—2.8 (m, 4 H), 5.1—5.9 (m, 5 H), 6.0 (d, $J$=12 Hz, 1 H) | 3050, 2940, 2860, 1600, 1425, 948, 937, 900, 848, 738, 705, 682 | 275 |
| *(7)* | 1.93 (s, 6 H), 2.0—3.0 (m, 5 H), 3.36 (d, $J$=13 Hz, 1 H), 5.3—5.9 (m, 5 H), 6.10 (dd, $J$=4 Hz, 10 HZ, 1 H) | 2950, 1730, 1365, 1255, 1225, 1190, 1020, 1005, 957, 940, 880, 791, 742 | 247 |
| *(8)* | 2.00 (s, 3 H), 2.34 (dd, $J$=8 Hz, 14 Hz, 1 H), 3.50 (br. s., 2 H), 3.99 (dd, $J$=8 Hz, 14 Hz, 1 H), 5.1—5.9 (m, 6 H), 6.01 (d, $J$=10 Hz, | 3015, 1735, 1450, 1370, 1238, 1050, 1017, 736, 708 | 244, 276, 355 |
| *(9)* | 1.80 (dd, $J$=7 Hz, 13 Hz, 1 H + −OH), 2.95 (dt, $J$=12 Hz, 2 Hz, 1 H), 3.52 (dd, $J$=1 Hz, 12 Hz, 1 H), 3.91 (dd, $J$=7 Hz, 13 Hz, 1 H), 5.2—5.8 (m, 6 H), 5.95 (d, $J$=12 Hz, 1 H) | 3500, 3030, 1380, 1282, 1088, 1061, 930, 742, 709 | 246, 282, 356 |

[a] All the new compounds gave satisfactory elemental analyses and/or mass spectrometrically determined molecular weights.

[b] In ethanol.

---

[1] a) *E. Vogel*, Chem. Soc. Spec. Publ. (London) *21*, pp. 113 (1967); b) Proc. Robert A. Welch Found. Conf. Chem. Res. *12*, 214 (1969); c) Pure Appl. Chem. *28*, 355 (1971); d) Rheinisch-Westfäl. Akad. Wiss., Nat. Ing.-Wirtschaftswiss., Vortr. *288* (1973).

[2] *S. Masamune, D. W. Brooks*, Tetrahedron Lett. *1977*, 3239.

[3] Substituted homoazulenes have previously been prepared by two routes: a) *S. Masamune, D. W. Brooks, K. Morio, R. L. Sobczak*, J. Am. Chem. Soc. *98*, 8277 (1976); b) *L. T. Scott, W. R. Brunsvold, ibid. 100, 4320 (1978).*

*[4] a) L. T. Scott*, J. Chem. Soc. Chem. Commun. *1973*, 882; b) *L. T. Scott, M. A. Minton, M. A. Kirms*, J. Am. Chem. Soc. *102*, 6311 (1980).

[5] *E. J. Corey, M. Chaykovsky*, J. Am. Chem. Soc. *87*, 1353 (1965).

[6] *R. H. Shapiro*, Org. React. *23*, 405 (1976).

[7] See, for example, a) *S. Moon*, J. Org. Chem. *29*, 3456 (1964); b) *R. J. Ouellette, D. Miller, A. South, Jr., R. D. Robins*, J. Am. Chem. Soc. *91*, 971 (1969).

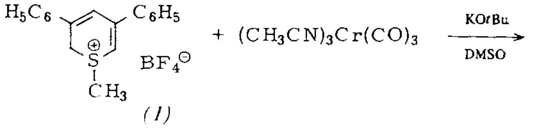
[8] *J. Tsuji, T. Yamakawa, M. Kaito, T. Maudai*, Tetrahedron Lett. *1978*, 2075.

[9] *L. T. Scott et al.*, unpublished results.

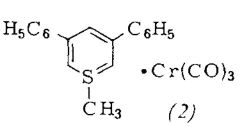
## Tricarbonyl(1-methyl-3,5-diphenyl-$\lambda^4$-thiabenzene)chromium(0)[**]

By *Lothar Weber*[*]

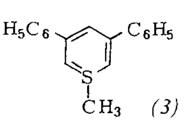
$\lambda^4$-Thiabenzenes merit interest in being examples of six-membered ring systems with 6π-electrons. Some derivatives, *e.g.* *(3)*, have been previously generated and studied in solution by means of $^1$H-NMR spectroscopy, but their inherent thermolability precluded their isolation and complete characterization[1]. We have, for the first time, been successful in stabilizing a thiabenzene derivative as a ligand in a transition metal complex: the title compound *(2)*.



*(1)*



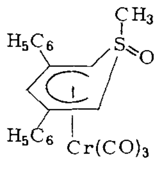
*(2)*



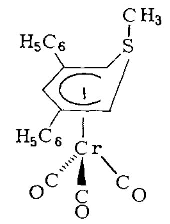
*(3)*

Complex *(2)* is formed by reaction of the thiinium salt *(1)*[1] with potassium *tert*-butanolate and triacetonitrile(tricarbonyl)chromium(0) in dimethylsulfoxide (DMSO) as a dark red crystalline, air stable solid; yield 75%[2].

In addition to the molecular ion, the mass spectrum of *(2)* contains readily characterizable fragments formed by ligand cleavage. IR- and NMR-spectroscopic data of *(2)* are consistent with coordination of the heterocycle to the metal (Table 1). The highest wave number CO band of *(2)* is shifted to lower wave numbers by 18 $cm^{-1}$, relative to the analogous thiabenzene oxide complex *(4)*[3].



*(4)*



*(2)*

Table 1. Selected data of complex *(2)* and its analogous 1-ethyl-complex.

*(2)*, MS: $m/e$=400 ($M^+$), 372 $(M-CO)^+$, 344 $(M-2CO)^+$, 316 $(M-3CO)^+$, 300 $(M-3CO, -CH_3, -H)^+$, 269 $(C_5H_3(C_6H_5)_2Cr)^+$, 217 $(C_5H_3(C_6H_5)_2)^+$; IR ($CH_2Cl_2$): 1952 vs, 1888 s, 1851 s $cm^{-1}$ (ν(CO); $^1$H-NMR ([$D_6$]acetone, TMS): δ=2.21 (s, $CH_3$), 3.39 (d, 2-, 6-H, $J$=1.5 Hz), 6.74 (t, 4-H, $J$=1.5 Hz), 7.33—7.89 (m, $C_6H_5$); $^{13}$C-NMR ([$D_6$]acetone, δ(CO)=206.0): δ=27.88 (C-2, -6), 41.48 ($CH_3$), 90.54 (C-4), 106.28 (C-3, -5), 128.89, 129.32, 129.59 and 141.64 ($C_6H_5$), 237.60 (CO).

Analogue: IR ($CH_2Cl_2$): 1951 vs, 1886 s, 1850 s $cm^{-1}$ (ν(CO)); $^1$H-NMR ([$D_6$]acetone, TMS): δ=1.06 (t, $CH_3$, $J$=8 Hz), 2.49 (q, $CH_2$, $J$=8 Hz), 3.39 (d, 2-, 6-H, $J$=1 Hz), 6.72 (t, 4-H, $J$=1 Hz), 7.36—7.78 (m, $C_6H_5$)

The enhanced donor capacity of the ligand *(3)* in complex *(2)* relative to the thiabenzene oxide ligand in complex *(4)* is revealed by a downfield shift of the $^{13}$CO resonance of 2.12 ppm.

The X-ray structure analysis of *(2)* clearly establishes that the chromium atom is $\eta^5$-bonded to the five carbon atoms of the heterocycle, which lie in a planar arrangement. The sulfur atom is located 0.76 Å above this plane and does not interact with the metal: $d$(Cr—S)=2.88 Å[4]. Thus the properties of thiabenzene *(3)* as a ligand can best be described in terms of an ylide and not as an arene.

The reaction of *(1)* with tricarbonyl(cycloheptatriene)molybdenum(0) or with tricarbonyl(cycloheptatriene)tungsten(0) affords a molybdenum (42% yield, m.p.=169 °C, decomp.) or tungsten analogue (47% yield, m.p.=132 °C, de-

---

[*] Dr. L. Weber
Fachbereich Chemie der Universität Essen-GHS
Universitätsstr. 5-7, D-4300 Essen 1 (Germany)

[**] Transition Metal Sulfur Ylide Complexes, Part 10. This work was supported by the Deutsche Forschungsgemeinschaft. The X-ray structure analysis of *(2)* was carried out by Dr. *R. Boese*. I am grateful to Prof. Dr. *G. Schmid* for helpful discussions. Part 9: *L. Weber*, Chem. Ber. *114*, 1 (1981).

comp.) respectively. The spectroscopic properties of these purple air stable, diamagnetic solids correspond to those of *(2)*, indicating analogous structures.

Preliminary studies have shown, that the novel complexes of type *(2)* undergo alkylation at the methyl group. Thus, the lithiation of *(2)* in tetrahydrofuran at −70 °C with the equivalent amount of *tert*-butyllithium and subsequent addition of excess methyl iodide produces reddish-brown tricarbonyl(1-ethyl-3,5-diphenyl-$\lambda^4$-thiabenzene)chromium(0) in 63% yield (m.p. = 156—158 °C, decomp., see Table 1).

### *Procedure*

30 cm$^3$ of anhydrous DMSO is added to a mixture of $(CH_3CN)_3Cr(CO)_3$ (1.011 g, 3.9 mmol), *(1)* (1.057 g, 3.0 mmol)[1], and potassium *tert*-butanolate (0.337 g, 3.0 mmol) under nitrogen at room temperature. The resulting dark red solution is stirred for 1.5 h at room temperature. After evaporation of the solvent and volatile components *in vacuo*, the residual red oil is taken up in $CH_2Cl_2$ (20 cm$^3$). The solution is filtered through a G4-frit, and 5 cm$^3$ of methylcyclohexane added to the filtrate, which is then slowly evaporated *in vacuo* until a dark red oil separates. The supernatant liquid is decanted, and the oil washed with light petroleum (4 × 10 cm$^3$). The residue is recrystallized twice from $CH_2Cl_2$/light petroleum and after drying *in vacuo* yields dark red *(2)*; yield 0.897 g (75%), m.p. = 152—154 °C.

Received: June 6, 1980, supplemented: December 19, 1980 [Z 723 IE]
German version: Angew. Chem. 93, 304 (1981)

CAS Registry numbers:
*(1)*, 28275-94-7; *(2)*, 76900-60-2; tricarbonyl(1-ethyl-3,5-diphenyl-$\lambda^4$-thiabenzene)chromium, 76900-61-3; tricarbonyl(1-methyl-3,5-diphenyl-$\lambda^4$-thiabenzene)molybdenum, 76900-62-4; tricarbonyl(1-methyl-3,5-diphenyl-$\lambda^4$-thiabenzene)tungsten, 76900-63-5; tricarbonyl(cycloheptatriene)molybdenum, 12125-77-8; tricarbonyl(cycloheptatriene)tungsten, 12128-81-3; $(CH_3CN)_3Cr(CO)_3$, 16800-46-7

---

[1] *A. G. Hortmann, R. L. Harris, J. A. Miles*, J. Am. Chem. Soc. 96, 6119 (1974); *B. E. Maryanoff, J. Stackhouse, G. H. Senkler, Jr., K. Mislow, ibid. 97*, 2718 (1975).

[2] Here only one isomerically pure compound is obtained. In the reaction of 1-methyl-3,5-diphenylthiabenzene 1-oxide with $(CH_3CN)_3Cr(CO)_3$ two isomers are generated which differ in the orientation of the $S(O)CH_3$-group to the chromium atom [3].

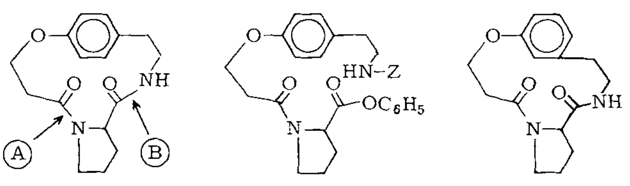
[3] *L. Weber, C. Krüger, Y.-H. Tsay*, Chem. Ber. *111*, 1709 (1978).

[4] Space group $P2_1/n$, monoclinic, cell constants: $a = 10.004(3)$, $b = 13.073(6)$, $c = 14.840(8)$ Å; $\beta = 101.75(3)°$, $Z = 4$, $V = 1900$ Å$^3$.

## A Novel Method for Preparation of Ansapeptides; Synthesis of Model Peptide Alkaloids

By *Ulrich Schmidt, Helmut Griesser,*
*Albrecht Lieberknecht,* and *Jörg Talbiersky*[*]

In the course of experiments directed towards the synthesis of peptide alkaloids[1] we have developed a novel ring closure method for formation of these 13- and 14-membered ansa peptides. We investigated the cyclization using the model compound *(1)*, which differs principally from the natural product by substitution of a β-phenoxyamino acid by β-phenoxypropionic acid. *Rapoport et al.*[2] had previously prepared *(1)* by ring closure at Ⓐ using the nitrophenyl ester method[3a]. For synthesis of the natural product[3b], however, it appeared to us that ring closure at the unhindered primary amino group, positionⒷ, would be more favorable.



*(1)* *(2)* *(3)*

$Z = C_6H_5CH_2OCO$

For the ring closure, a dioxane solution of the pentafluorophenyl ester *(2)*[4] was added dropwise to a rapidly stirred suspension of Pd/charcoal in dioxane at 95 °C into which hydrogen was passed. The solution contained 1 mol 4-pyrrolidinopyridine[5] per mol *(2)* as catalyst and 2% alcohol (with respect to the solvent). The benzyloxycarbonyl group is first removed by hydrogenolysis, and ring closure apparently occurs on the ω-amino ester which is still adsorbed on the catalyst[9].

Using conditions of dilution, 50% of *(1)* was formed (determined gas chromatographically). The yields drop dramatically if alcohol is not added or its concentration exceeds 5%, if the reaction temperature is lower than 70 °C and if other, or no bases are used as catalysts (*e.g.* pyridine, *N*-methylimidazole). Under these conditions dimeric cyclopeptide is only obtained in small amounts, whereas it becomes the major product (yield 45%) if the reaction is carried out in ethyl acetate at 75 °C.

The smallest bridge in *para*-ansa compounds, which can be formed by ring closure of a *para*-substituted aromatic compound in satisfactory yields, contains ten members. In the model compound *(1)*, which has a ten-membered bridge, the formation of the bridge is made all the more difficult by the *s-trans*-conformation of both amide groups.

We obtained the 13-membered ring compound *(3)*, which has a 10-membered *meta*-bridge, in 80% yield[6]; *(3)* is therefore considerably more easily formed than *(1)*. Up till now, the shortest *meta*-bridge to a benzene ring, formed by ring closure in satisfactory yield, is nine-membered (resorcinol heptamethylene ether)[7].

The method described here leads to formation of difficultly accessible compounds of this type in up to three or four times better yield than the nitrophenyl ester route[2]. A further advantage is the considerably easier work-up, since the reaction solution does not contain any trifluoroacetic acid (for deblocking the Boc-group) or high boiling solvent (dimethylacetamide).

### *Procedure*

A solution of *(2)*[4] (165 mg) in 20 cm$^3$ dioxane is uniformly injected over 18 h[9] to a rapidly stirred suspension of Pd/activated charcoal (600 mg, 5%) in 350 cm$^3$ pure dioxane at 90 °C (temp. in flask), which contains 7 cm$^3$ ethanol and 40 mg 4-pyrrolidinopyridine. At the same time, hydrogen is passed through the solution. The solution is filtered, concentrated, and the product isolated using medium pressure chromatography on silica gel (dichloromethane/methanol 98:2); (yield 39 mg, 50%) of *(1)*. The chromatographically pure product ($[\alpha]_{546}^{20} = -27.3$ ($c = 1.15$, ethanol)) is dissolved in 20 cm$^3$ water-free ether and after a few hours *ca.* 2 mg racemate[8] precipitates (M.p. = 202—205 °C). Concentrating the mother liquor yields the *S*-enantiomer as an oil ($[\alpha]_{546}^{20} = -28.1$ ($c = 0.56$, ethanol)). The racemate and *S*-en-

---

[*] Prof. Dr. U. Schmidt, Ing. H. Griesser, Dr. A. Lieberknecht, Dr. J. Talbiersky
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] Synthesis of Peptide Alkaloids, Part 1. Part 30 of Amino Acids and Peptides. This work was supported by the Fonds der Chemischen Industrie and by BASF AG—Part 29: *U. Schmidt, E. Öhler, J. Häusler, H. Poisel*, Chem. Org. Naturst. *37*, 251 (1979); Part 28: *E. Öhler, U. Schmidt*, Chem. Ber. *112*, 107 (1979).

antiomer have the same spectra and retention times as determined by GC-MS.

Received: February 4, supplemented February 27, 1980,
publication delayed at authors' request [Z 699a IE]
German version: Angew. Chem. 93, 271 (1981)

*(1)*, 69100-22-7; *(2)*, 76847-29-5; *(3)*, 69100-22-7; *p*-hydroxyphenylacetonitrile, 14191-95-8; methyl acrylate, 96-33-3; L-prolinebenzyl ester, 41324-66-7

---

[1] For a review see: *R. Tschesche, E. U. Kaußmann* in *R. H. F. Manske:* The Alkaloids, Vol. 15. Academic Press, New York 1975.

[2] *J. Clark Lagarias, R. A. Houghten, H. Rapport*, J. Am. Chem. Soc. *100*, 8202 (1978).

[3] a) After cleavage of the Boc-group, a solution of the trifluoroacetate salt of the ω-amino carboxylic acid nitrophenyl ester in dimethylacetamide is added over 50 h to a solution of pyridine at 90 °C. The yield of *(1)* as an oil amounts to 24% according to [2]; the rotational value is not specified. Upon repetition, we determined the yield to be 12% by gas chromatography. b) See *U. Schmidt, A. Lieberknecht, H. Griesser, J. Häusler*, Angew. Chem. *93*, 272 (1981); Angew. Chem. Int. Ed. Engl. *20*, 281 (1981).

[4] Synthesis of *(2)*: Addition of *p*-hydroxyphenylacetonitrile to methyl acrylate, saponification of the ester group, coupling with L-prolinebenzyl ester (DCCD process), catalytic hydrogenation of the nitrile group, cleavage of the benzyl ester group by hydrogenolysis, acylation of the primary amino group by benzyl chloroformate (Z—Cl) and formation of the pentafluorophenyl ester (DCCD process).

[5] The catalytic effect is absent if the amide is formed *via* the nitrophenyl ester (*D. Hollitzer, W. Steglich*, unpublished results; cited in *G. Höfle, W. Steglich, H. Vorbrücken*, Angew. Chem. *90*, 602 (1978); Angew. Chem. Int. Ed. Engl. *17*, 569 (1978)).

[6] The starting material was prepared analogously to *(2)* [4]. After crystallization, the product was separated by medium pressure chromatography. M.p. = 165—168 °C (partial decomp.); $[\alpha]_{546}^{20} = -5.5$ ($c = 0.42$, ethanol); $[\alpha]_{364}^{20} = -50.7$ ($c = 0.42$, ethanol).

[7] *A. Lüttringhaus*, Justus Liebigs Ann. Chem. *528*, 181 (1936).

[8] *(1)* Crystallized in space group $P2_1/C$; from its centre of symmetry this must be the racemate ($a = 11.28$, $b = 14.70$, $c = 12.60$ Å; $\beta = 134.1°$, $Z = 4$) (determined by Dr. *J. J. Stezowski*).

[9] Note added in proof (1. 3. 81): We assume that ring closure is accomplished on the surface of the catalyst; consequently the reaction time (and with that the dilution) can be diminished drastically: the ring closure giving rise to *(1)* and *(3)* was accomplished in 5 h and 0.5 h respectively.

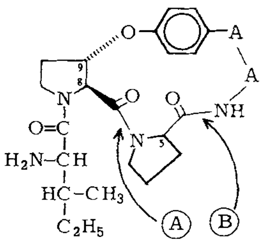
## Synthesis of Dihydrozizyphin G[**]

By *Ulrich Schmidt, Albrecht Lieberknecht, Helmut Griesser*, and *Johannes Häusler*[*]

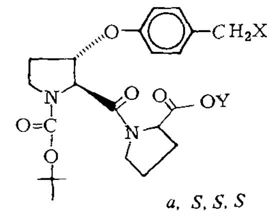
*Dedicated to Professor Gerhard Pfleiderer on the occasion of his 60th birthday*

Peptide alkaloids typically have a 13-, 14- or 15-membered ansa structure, the bridge of which contains a dipeptide unit. Approximately 80 alkaloids having this structural element have been isolated over the past 15 years, principally from *Rhamnaceae*, and their structures determined. Many of these alkaloids have antibiotic activity against lower funghi and gram positive bacteria[1]. Until now, no synthetic route to these species was known: we describe here, however, the synthesis of dihydrozizyphin G *(1)* (zizyphin G: *(2)*[2]).

Racemic *trans*-3-(*p*-cyanomethylphenoxy)proline was obtained using a method previously described for the preparation of *trans*-3-phenoxyproline[3]: The ester of 3-bromodehydroproline was treated with sodium *p*-cyanomethylphenolate, the product saponified and reduced with dimethylaminoborane/acetic acid. (Yield 25% relative to bromodehydroproline ester). The corresponding Boc-compound (yield 95%) couples with *S*-prolinebenzyl ester. Both diastereomers, *(3a)* and *(3b)* were easy to isolate using medium pressure chromatography on silica gel (petroleum ether/ethyl acetate 1:1). Hydrogenolysis of the ester group (Pd/carbon in dioxane), catalytic hydrogenation of the nitrile group ($Rh/Al_2O_3$, 10% $NH_3$ in ethanol, 3 bar $H_2$), and acylation with benzyl chloroformate (Z—Cl) leads to *(4a)* and *(4b)* respectively [yields 88 and 84% relative to *(3a)* and *(3b)* respectively], which were converted into the active esters *(5a)* and *(5b)* (yields 88 and 83% respectively) using pentafluorophenol and DCCD (dicyclohexylcarbodiimide). The diastereomeric series designated *a* and *b* could not be assigned until dihydrozizyphin G had been synthesized.

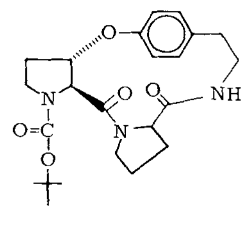


*(1a)*, 5*S*, 8*S*, 9*S*;
–A–A– = $-CH_2-CH_2-$
*(1b)*, 5*S*, 8*R*, 9*R*;
–A–A– = $-CH_2-CH_2-$
*(2)*, 5*S*, 8*S*, 9*S*;
–A–A– = $-CH{=}C-$

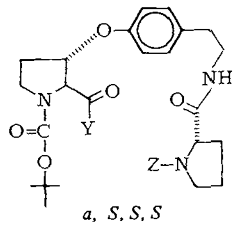


*a*, *S*, *S*, *S*
*b*, *R*, *R*, *S*

*(3)*, X = –CN, Y = $-CH_2C_6H_5$
*(4)*, X = $-CH_2NHCOOCH_2C_6H_5$, Y = –H
*(5)*, X = $-CH_2NHCOOCH_2C_6H_5$, Y = $-C_6F_5$



*(6a)*, 5*S*, 8*S*, 9*S*
*(6b)*, 5*S*, 8*R*, 9*R*



*a*, *S*, *S*, *S*
*b*, *R*, *R*, *S*
*(7)*, Y = –OH; *(8)*, Y = $-OC_6F_5$
Z = $COOCH_2C_6H_5$

Using a method which we had developed[4], and reaction conditions of 50 h at 95 °C, the cyclopeptide *(6a)* was obtained from the "correct" diastereoisomer *(5a)*, by ring closure at position Ⓑ, in 35% yield. Although "tight" cyclopeptides are frequently more easily prepared if one of the amino acids of the ring belongs to the *R*-series, the "incorrect" diastereoisomer *(6b)* was formed from *(5b)* in lower yield (10%). Apart from the monomeric cycles *(6a)* and *(6b)*, the corresponding dimers were formed in approximately equal amounts. The monomers and dimers could be separated chromatographically on silica gel using ethyl acetate as eluent. *(6a)* and *(6b)*—in contrast to the dimeric compounds—could be sublimed without decomposition at 120 °C in high vacuum. Ring closure at position Ⓐ was more favorable, and resulted in the formation of *(6a)* from *(8)* in 67% yield. For this purpose, Boc-*trans*-3-(*p*-cyanomethylphenoxy)proline was hydrogenated to the *p*-aminomethyl compound and acylated with the benzyloxycarbonyl protected *S*-prolinehydroxysuccinimide ester to the diastereomeric dipeptides *(7a)* and *(7b)* (yield 100%, relative to the Boc-compound). The diastereomers could not be separated

---

[*] Prof. Dr. U. Schmidt, Dr. A. Lieberknecht, H. Griesser
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)
Dr. J. Häusler
Organisch-chemisches Institut der Universität
Währinger Strasse 38, A-1090 Wien (Austria)

[**] Synthesis of Peptide Alkaloids, Part 2: Part 31 of Amino Acids and Peptides. This work was supported by the Fonds der Chemischen Industrie, by BASF AG and by the Deutsche Forschungsgemeinschaft.—Parts 1 and 30 respectively: [4].

by chromatography, either at this stage or as the pentafluorophenyl esters *(8a)* and *(8b)*. We therefore used the diastereomeric mixture, *(8a)* + *(8b)*, [yield 80% relative to *(7a)* + *(7b)*] for the ring closure reaction. The "correct" cyclopeptide *(6a)* was also formed more easily here (yield 67%) than its diastereomer *(6b)* (yield 30%). The diastereomers *(1c)* and *(1d)*, which are easily separable by chromatography were coupled with Boc-isoleucine using the DCCD-procedure after removal of the Boc-group. Cleavage of the Boc-group (trifluoroacetic acid, resorcinol dimethyl ether, 3 h, 20 °C) resulted in formation of dihydrozizyphin G *(1a)*, for the *a*-series, and isomer *(1b)* for the *b*-series.

Table 1. Selected physical data of the compounds synthesized.

| Compd. | Yield [%] | Educt | $R_f$ [c] | $[\alpha]_D^{20}$ (Methanol) | MS (20 eV), *m/e* [d] |
|---|---|---|---|---|---|
| *(6a)* | 35<br>67 | *(5a)*<br>*(8a)* + *(8b)* | 0.29 | −95.5 ($c=0.78$) | 429 ($M^+$, 100%), 329 ($M^+$ − Boc, 83) |
| *(6b)* | 10<br>30 | *(5b)*<br>*(8a)* + *(8b)* | 0.12 | +43.0 ($c=1.14$) | 429 ($M^+$, 57%), 329 ($M^+$ − Boc, 90), 310 (100) |
| *(1c)* [a] | 60 | *(6a)* | 0.39 | −113.7 ($c=0.38$) | 542 ($M^+$, 100%), 442 ($M^+$ − Boc, 18), 329 ($M^+$ − Boc-Ile, 10) |
| *(1d)* [b] | 60 | *(6b)* | 0.17 | 12.3 ($c=0.72$) | 542 ($M^+$, 100%), 442 ($M^+$ − Boc, 23), 329 ($M^+$ − Boc-Ile, 20) |
| *(1a)* [5] | 95 | *(1c)* [a] | 0.52 | −62 ($c=0.23$) | 442 ($M^+$, 22%), 329 ($M^+$ − Ile, 5), 238 (100); highest mass resolved: 442.2580 |
| *(1b)* | 95 | *(1d)* [b] | 0.5 | 34 ($c=0.23$) | 442 ($M^+$, 38%), 329 ($M^+$ − Ile, 5), 238 (100) |

[a] *(1c)* = *(1a)*, Boc-isoleucyl instead of isoleucyl. [b] *(1d)* = *(1b)*, Boc-isoleucyl instead of isoleucyl. [c] On silica gel; eluent ethyl acetate, with *(1a)* and *(1b)* dichloromethane/methanol 8:2. [d] We thank Dr. *W. Rozdzinski* for recording the measurements.

Since acylation with Boc-isoleucine proceeded very slowly, an amino acid analysis was carried out after hydrolysis of *(1a)*, which apart from proline and isoleucine showed no trace of alloisoleucine.

Received: May 29, 1980
supplemented: June 9, 1980,
publication delayed at authors' request [Z 699b IE]
German version: Angew. Chem. *93*, 272 (1981)

CAS Registry numbers:
*(1a)*, 76899-36-0; *(1b)*, 76847-39-7; *(3a)*, 76847-30-8; *(3b)*, 76847-31-9; *(4a)*, 76847-32-0; *(4b)*, 76847-33-1; *(5a)*, 76861-90-0; *(5b)*, 76847-34-2; *(6a)*, 76847-35-3; *(6b)*, 76899-37-1; *(7a)*, 76847-36-4; *(7b)*, 76898-66-3; *(8a)*, 76847-37-5; *(8b)*, 76898-67-4; 3-bromodehydroprolinebenzyl ester, 76847-38-6; sodium-*p*-cyanmethylphenolate, 73756-90-8; BOC (+-)-*trans*-3-(*p*-cyanmethylphenoxy)prolinebenzyl ester, 76847-40-8; (*S*)-prolinebenzylester, 41324-66-7; benzyl chloroformate, 501-53-1; pentafluorphenol, 771-61-9

---

[1] Review: *R. Tschesche, E. K. Kaussmann* in *R. H. F. Manske:* The Alkaloids, Vol. 15. Academic Press, New York 1975.

[2] *R. Tschesche, I. Khokhar, Ch. Spilles, G. Eckhardt, B. K. Cassels*, Tetrahedron Lett. *1974*, 2944.

[3] *J. Häusler, U. Schmidt*, Justus Liebigs Ann. Chem. *1979*, 1881.

[4] *U. Schmidt, H. Griesser, A. Lieberknecht, J. Talbiersky*, Angew. Chem. *93*, 271 (1981); Angew. Chem. Int. Ed. Engl. *20*, 280 (1981).

[5] Dihydrozizyphin G prepared from zizyphin has a value of $[\alpha]_D^{20} = -67°$ (*J. Khokhar*, dissertation, Universität Bonn 1974). We thank Dr. *Eckhardt* for this communication. Zizyphin G and dihydrozizyphin G were not available for direct comparison with the synthetic products.

## Configurational Isomerization of *N,N*-Disubstituted Hydroxylamido(1-)-*O,N*-Molybdenum(VI) Complexes[**]

By *Edgar Hofer, Wolfgang Holzbach*, and *Karl Wieghardt*[*]

$Mo^{VI}$ oxoanions react with *N,N*-disubstituted hydroxylamines in aqueous solution (pH = 6) to give the colorless neutral complexes *(1a)* and *(1b)*[1,2]. Solutions of *(1a)* and *(1b)* in benzene at 20 °C react with gaseous $H_2S$ to give the yellow complexes *(2a)* and *(2b)* respectively, as well as the violet-red compounds *(3a)* and *(3b)* respectively[3].

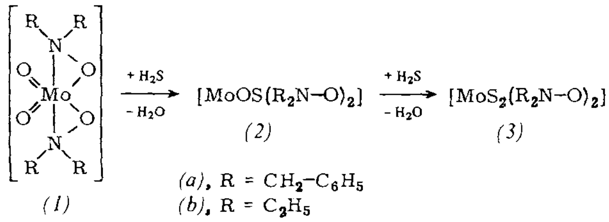


Table 1. Physical data of complexes *(1)*—*(3)*.

| |
|---|
| $^1$H-NMR (90 MHz, 300 K, $CDCl_3$, TMS int.), *(1a)*: $\delta = 4.11$ (d/$J$ = 14.0 Hz/4 H, 4.23 (d/$J$ = 14.0 Hz/4 H), 7.43 (m/20 H); *(2a)*: $\delta = 4.09$ (s/4 H), 4.23 (d/$J$ = 14.7 Hz/2 H), 4.51 (d/$J$ = 14.7 Hz/2 H), 7.42 (m/20 H); *(3a)*: $\delta = 4.33$ (s/8 H), 7.38 (m/20 H); *(1b)*: $\delta = 1.24$ (t/$J$ = 7.3 Hz/12 H), 3.07 (dq/$J$ = 14.0 Hz and $J$ = 7.3 Hz/4 H), 3.29 (dq/$J$ = 14.0 Hz and $J$ = 7.3 Hz/4 H); *(2b)*: $\delta = 1.22$ (t/$J$ = 7.3 Hz/6 H), 1.23 (t/$J$ = 7.3 Hz/6 H), 2.97 (dq/$J$ = 13.8 Hz and $J$ = 7.3 Hz/2 H), 3.29 (dq/$J$ = 13.8 Hz and $J$ = 7.3 Hz/2 H), 3.25 (dq/$J$ = 13.5 Hz and $J$ = 7.3 Hz/2 H), 3.54 (dq/$J$ = 13.5 Hz and $J$ = 7.3 Hz/2 H); *(3b)*: $\delta = 1.22$ (t/$J$ = 7.3 Hz/12 H); 3.14 (dq/$J$ = 13.5 and $J$ = 7.3 Hz/4 H), 3.46 (dq/$J$ = 13.5 Hz and $J$ = 7.3 Hz/4 H)<br>Coalescence temperatures [a, b] ([$D_7$]-DMF), *(1a)*: $T_c = 385$ K; *(1b)*: $T_c = 409$ K, $\Delta G^{\neq} = 86$ kJ/mol; *(3b)*: $T_c = 370$ K, $\Delta G^{\neq} = 77$ kJ/mol; *(2a)* and *(2b)* decompose before the onset of coalescence. |

[a] $\Delta G^{\neq}$ was not calculated for *(1a)*, since the method of approximation is not applicable; *D. Kost, E. H. Raban, E. H. Carlson*, Chem. Commun. *1971*, 656; *D. Kost, A. Zeichner*, Tetrahedron Lett. *1974*, 4533. [b] Above the coalescence temperature, the diastereotopic protons from *(1a)* gave a singlet, and those from *(1b)* and *(3b)* resp. a quartet.

The configurational stability of complexes *(1)*—*(3)* at 27 °C is indicated by their $^1$H-NMR spectra in solution (Fig. 1, Table 1): while only an AB- and $ABX_3$-system is found for the eight equivalent diastereotopic methylene protons in *(1a)* and *(1b)* respectively, an AB-system and in addition a somewhat broad singlet, which can be interpreted as an AB-system with small $\Delta\nu/J$ ratio, is found for *(2a)*. Two $ABX_3$-systems are obtained for *(2b)*. In *(3a)* and *(3b)* all diastereotopic methylene protons are again equivalent: a broad singlet is observed for *(3a)* and an $ABX_3$-system for *(3b)*.

At higher temperatures, coalescence of the methylene proton signals of *(1a)*, *(1b)* and *(3b)* is observed. Since the "free" lone-pair of electrons on the hydroxylamine N-atom form a bond to molybdenum, and are therefore sterically fixed, simple nitrogen inversion[4] as in the free ligands cannot occur[5,6]. We therefore suggest that the configurational isomerization stem from a rapid rotation-inversion at nitrogen[5,6] with concomitant reformation of the Mo—N bond, the rate

---

[*] Prof. Dr. K. Wieghardt, Dipl.-Chem. W. Holzbach
Anorganische Chemie I der Universität
Postfach 102148, D-4630 Bochum (Germany)
Dr. E. Hofer
Institut für Organische Chemie der Universität
Schneiderberg 1 B, D-3000 Hannover 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.

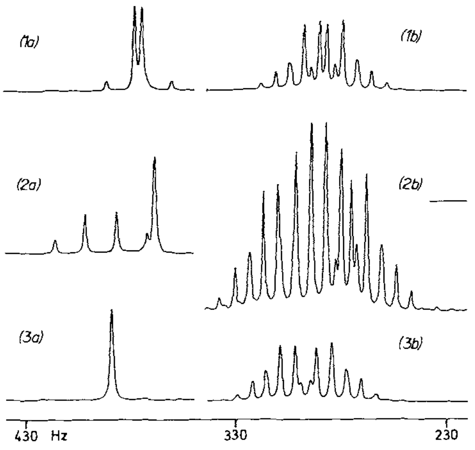


Fig. 1. $^1H$-NMR spectra of the diastereotopic protons of complexes *(1)*—*(3)* at 27 °C.

determining step being the dissociation of the Mo—N bonds at a rate which is rapid on the NMR time scale. The values of $\Delta G^{\neq}$ for *(1b)* and *(3b)* could be determined from the coalescence temperatures by simultaneous decoupling of the methyl protons (Table 1). The values obtained support the suggested mechanism; they are clearly higher than those of the noncomplex bonded ligands[7].

Finally, it is interesting that substitution of both oxo-oxygen atoms in *(1b)* by two sulfur atoms in *(3b)* lowers the dissociation barrier of the Mo—N bond. An increase in the electron density at the molybdenum(VI)-centre weakens the Mo—N bond.

### *Procedure*

$H_2S$ is passed for 30 mins into a stirred solution of *(1a)*[2] (3 g, 5.4 mmol) and *(1b)*[8] (3 g, 10 mmol) respectively, in 150 cm³ benzene over 10 g dry $Na_2SO_4$. The mixture is stirred for 12 h in a closed flask, the deep red solution filtered off and the solvent removed. One half of the residue is dissolved in 20 cm³ benzene and chromatographed at 20 °C on 150 g aluminum oxide 90 (activity grade II—III); the other half is dissolved in 20 cm³ $CHCl_3$ and chromatographed on 100 g silica gel 60. The red-violet *cis*-dithio compounds *(3a)*$\cdot C_6H_6$ (yield 15%) and *(3b)*$\cdot 0.33\ C_6H_6$ (13%) are obtained from the first half. The faster eluting violet fraction from the chromatographed chloroform solution is rejected: solvent is removed from the succeeding yellow fraction until crystallization just begins. Yellow crystals of *(2a)* (yield 10%) and *(2b)* (8%) respectively are filtered off and air-dried.

Received: March 24, 1980,
supplemented: August 29, 1980 [Z 722 IE]
German version: Angew. Chem. 93, 303 (1981)

CAS Registry Numbers:
*(1a)*, 74081-87-1; *(1b)*, 74081-86-0; *(2a)*, 76900-50-0; *(2b)*, 76900-51-1; *(3a)*, 76900-52-2; *(3b)*, 76900-53-3

---

[1] *K. Wieghardt, W. Holzbach, J. Weiss, B. Nuber, B. Prikner,* Angew. Chem. *91*, 582 (1979); Angew. Chem. Int. Ed. Engl. *18*, 548 (1979).

[2] *K. Wieghardt, E. Hofer, W. Holzbach, B. Nuber, J. Weiss,* Inorg. Chem. *19*, 2927 (1980).

[3] The diamagnetic compounds *(2a)*, *(2b)*, *(3a)* and *(3b)* were obtained in pure crystalline form and identified by C, H, N, S, Mo elemental analyses, cryoscopic molecular weight determinations (in benzene) and IR spectra.

[4] *H. Kessler,* Angew. Chem. *82*, 237 (1970); Angew. Chem. Int. Ed. Engl. *9*, 219 (1970).

[5] *M. Raban, G. W. J. Kenney, Jr.,* Tetrahedron Lett. *1969*, 1295; *M. Raban, D. Kost,* J. Org. Chem. *37*, 499 (1972); *D. Kost, M. Raban, ibid. 41*, 1748 (1976); *T. B. Posner, D. A. Couch, C. D. Hall,* J. Chem. Soc. Perkin Trans. II, 450 (1978).

[6] *J. R. Fletcher, J. O. Sutherland,* Chem. Commun. *1970*, 687.

[7] $\Delta G^{\neq}$ for nitrogen inversion in *N,N*-dibenzylhydroxylamine amounts to 54 kJ/mol [6].

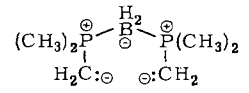
[8] Compound *(1b)* has, in the meantime, been independently described. *L. Saussine, H. Mimoun, J. Fischer,* Nouveau J. Chim. *4*, 235 (1980). The X-ray structural analysis confirms the suggested structure.

---

# Synthesis of a Borato(phosphoniomethanide)(phosphoniooxide)-Ligand and Its Organoberyllium Complex[**]

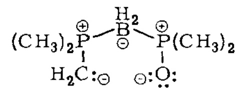
By *Hubert Schmidbaur* and *Erwin Weiss*[*]

Incorporation of onium centers into organoelement ligands effects a drastic change in the complexation properties, as occurs, *e.g.*, in numerous coordination compounds of the phosphorus ylides[1]. The strong σ-donor effect, in the absence of effective back-bonding, leads to particularly high electron densities at the central atom. These effects are also discernable in the boratobis(phosphoniomethanide) ligand *(A)* with its continuously alternating charges[2,3]. Interest therefore attaches to a related chelate system in which one of the two $CH_2$-functions is replaced by a strongly electronegative donor atom. We now report on the synthesis of the bidenate ligand *(B)*, its precursors, and a typical complex.



$$\begin{array}{c}(CH_3)_2\overset{\oplus}{P}-\underset{\ominus}{\overset{H_2}{B}}-\overset{\oplus}{P}(CH_3)_2\\ H_2C{:}^{\ominus}\qquad {}^{\ominus}{:}CH_2\end{array}$$

*(A)*

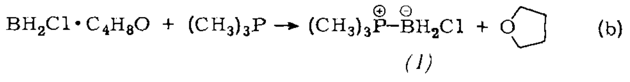


$$\begin{array}{c}(CH_3)_2\overset{\oplus}{P}-\underset{\ominus}{\overset{H_2}{B}}-\overset{\oplus}{P}(CH_3)_2\\ H_2C{:}^{\ominus}\qquad {}^{\ominus}{:}\ddot{\underset{..}{O}}{:}\end{array}$$

*(B)*

Trimethylphosphanechloroborane *(1)*[4] is readily accessible *via* the route outlined by steps (a) and (b) (cf. Procedure); yield 96%; m.p. 73 °C; $\nu(BH_2) = 2395$ and $2420\ cm^{-1}$; $\delta(P) = -11.1$, q, $J(PB) = 81$ Hz.

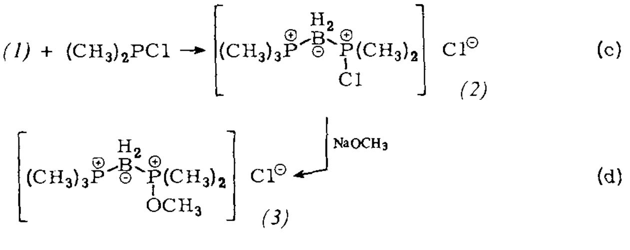
$$BH_3\cdot C_4H_8O + HCl \rightarrow BH_2Cl\cdot C_4H_8O + H_2 \qquad (a)$$



$$BH_2Cl\cdot C_4H_8O + (CH_3)_3P \rightarrow (CH_3)_3\overset{\oplus}{P}-\overset{\ominus}{B}H_2Cl + \qquad (b)$$

*(1)*

Reaction of *(1)* and chlorodimethylphosphane at 70 °C, in the absence of solvent, affords the boratobis(phosphonium) salt *(2)*; yield 71%; m.p. 84 °C; $\nu(BH_2) = 2400$ and $2440\ cm^{-1}$; $\delta(PC_3) = -9.05$, $^1J(PB) = 89$ Hz, $\delta(PC_2Cl) = 90.0$, $^1J(PB) = 98$ Hz. The P—Cl function of *(2)* reacts with sodium methoxide [step (d)] to give the derivative *(3)*; yield 90%; m.p. 130 °C (dec.); $\nu(BH_2) = 2380$ and $2420\ cm^{-1}$; $\delta(PC_3) = -7.96$, $^1J(PB) = 79$ Hz; $\delta(PC_2O) = 104.17$, $^1J(PB) = 101$ Hz.



$$(1) + (CH_3)_2PCl \rightarrow \left[(CH_3)_3\overset{\oplus}{P}-\underset{\ominus}{\overset{H_2}{B}}-\underset{Cl}{\overset{\oplus}{P}}(CH_3)_2\right]Cl^{\ominus} \qquad (c)$$

*(2)*

$$\left[(CH_3)_3\overset{\oplus}{P}-\underset{\ominus}{\overset{H_2}{B}}-\underset{OCH_3}{\overset{\oplus}{P}}(CH_3)_2\right]Cl^{\ominus} \xleftarrow{NaOCH_3} \qquad (d)$$

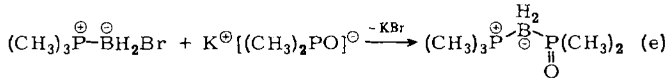
*(3)*

---

[*] Prof. Dr. H. Schmidbaur, Dr. E. Weiss
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and by Hoechst AG.

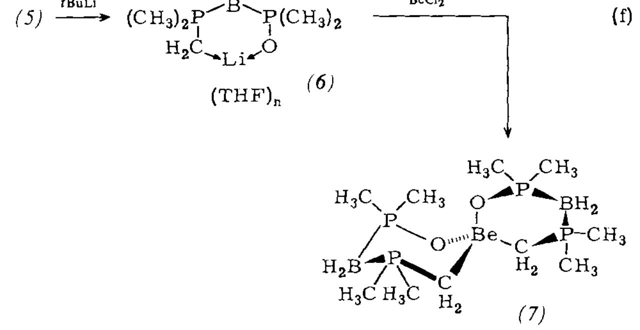
Hydrolysis of *(2)* or *(3)* with water or alkali hydroxide affords only small amounts of an oxide *(5)*, whereas reaction (e) of the readily accessible[5] bromine analog of *(1)* with the potassium salt of dimethylphosphinous acid leads directly to the neutral oxide *(5)*; yield 82%; m.p. 79 °C; $\nu(BH_2) = 2360$—2395, $\nu(P{=}O) = 1120\ cm^{-1}$; $\delta(PC_3) = -5.45$, $^1J(PB) = 79$ Hz, $\delta(PC_2O) = 50.22$, $^1J(PB) = 123$ Hz; $m/e = 166$ ($M^+$).



$$(CH_3)_3\overset{\oplus}{P}-\overset{\ominus}{B}H_2Br + K^{\oplus}[(CH_3)_2PO]^{\ominus} \xrightarrow{-KBr} (CH_3)_3\overset{\oplus}{P}-\overset{H_2}{\underset{\ominus}{B}}-\underset{O}{\underset{\|}{P}}(CH_3)_2 \quad (e)$$

*(4)* *(5)*

*(5)* can be metalated with *tert*-butyllithium at −78 °C in tetrahydrofuran (THF)/pentane; loss of alkane takes place with formation of the lithium complex *(6)*, which does not have to be isolated free of solvent but can be reacted further, *in situ*, with metal halides. Thus, *e.g.* with $BeCl_2$ the spirocyclic beryllium complex *(7)*, m.p. 59 °C, subl. at 60—100 °C/$10^{-4}$ torr, is obtained. The colorless, slightly air- and moisture-sensitive crystals are soluble in polar aprotic solvents.



In the mass spectrum the molecular ion appears as base peak ($m/e = 339$, $2\times{}^{11}B$). In the IR spectrum $\nu(P{=}O)$ is reduced to 1065 cm$^{-1}$ owing to metal coordination. As expected the phosphorus atoms are pairwise non-equivalent: $\delta(PC_3) = -5.07$, qd, $^1J(PB) = 95$, $^2J(PP) = 15$ Hz; $\delta(PC_2O) = 63.62$, qd, $^1J(PB) = 107$, $^2J(PP) = 15$ Hz. The $^1H$- and $^{13}C$-NMR spectra show the sets of doublet signals derivable from the symmetry. The $^{13}C$-NMR spectrum, in particular, demonstrates the non-equivalence of the two $CH_3$ groups on each P-atom, also recognizable on models. In the solid state *(7)* undergoes oligomerization on storage at room temperature, so that aged samples are no longer volatile.

The ligands (B) of complex *(7)* thus correspond to the isoelectronic[2,3,7] chelate type *(A)*, but they favor complexation with highly charged, small, and difficultly polarizable ("hard") metal centers. Beryllium is one of the most favorable candidates for this purpose.

### *Procedure*

Combination of equimolar amounts of $BH_3\cdot THF$ in excess THF and ethereal HCl at −20 °C leads, with evolution of $H_2$, to a clear solution of $H_2BCl\cdot THF$, which is allowed to react at 0 °C with one equivalent $(CH_3)_3P$ to give *(1)* quantitatively. The product crystallizes from ether/pentane. Addition of $(CH_3)_2PCl$ (6.32 g) to *(1)* (8.2 g) (66 mmol of each) and heating to 70 °C (without solvent) leads to formation of the salt *(2)*, which for purification is taken up in $CH_2Cl_2$, filtered, and crystallized at −30 °C by addition of ether (yield 11.2 g; 71%). Reaction of *(2)* (1.97 g) with $NaOCH_3$ (0.48 g) (8.92 mmol of each) in THF at 0—20 °C yields the methoxy derivative *(3)*, which after 16 h is crystallizeable by removal of solvent, dissolution in $CH_2Cl_2$, filtration and addition of ether to the filtrate at −30 °C (1.74 g; 90%).

$(CH_3)_3P$—$BH_3$ is transformed into $(CH_3)_3P$—$BH_2Br$ in the usual way[5], and 10.3 g (61.2 mmol) of the product *(4)* allowed to react at 0 °C in THF with K $[(CH_3)_2PO]$—freshly prepared from $(CH_3)_2POH$[6] (4.78 g) and KH (2.46 g) (61.24 mmol of each) in 100 ml of THF at 0 °C, but not isolated. After filtration from KBr, *(5)* can be crystallized at −30 °C from ether/pentane (8.3 g; 82%).

A solution of *(5)* (0.96 g, 5.78 mmol) in THF (10 ml) is treated at −78 °C with an equivalent of *t*BuLi (in pentane) and, after 1 hours' stirring, $BeCl_2$ (0.23 g), 2.89 mmol) is added to the mixture. Stirring is continued for 16 h, the mixture allowed to warm to room temperature, the solvent removed and replaced by toluene, the resulting solution filtered, and the residue finally obtained from the filtrate is sublimed (0.11 g; 11%).

All the compounds gave correct elemental analyses and characteristic $^1H$-, $^{13}C$-, $^{31}P$-NMR and mass spectra.

Received: October 22, 1980 [Z 720 IE]
German version: Angew. Chem. *93*, 300 (1981)

CAS Registry numbers:
*(1)*, 64160-46-9; *(2)*, 76880-09-6; *(3)*, 76880-08-5; *(4)*, 60228-69-5; *(5)*, 76879-14-6; *(6)*, 76880-11-0; *(7)*, 76880-10-9; $(CH_3)_2PCl$, 811-62-1; $K^+[(CH_3)_2PO]^-$, 76819-15-7

---

[1] *H. Schmidbaur*, Pure Appl. Chem. *50*, 19 (1978); *52*, 1057 (1980).

[2] *H. Schmidbaur*, J. Organomet. Chem. *200*, 287 (1980).

[3] *H. Schmidbaur, G. Müller, U. Schubert, O. Orama*, Angew. Chem. *90*, 126 (1978); Angew. Chem. Int. Ed. Engl. *17*, 126 (1978); *G. Müller, U. Schubert, O. Orama, H. Schmidbaur*, Chem. Ber. *112*, 3302 (1979); *H. Schmidbaur, G. Müller, K. C. Dash, B. Milewski-Mahrla, ibid. 114*, 441 (1981).

[4] Attempts to prepare this compound from $(CH_3)_3PBH_3$ and HCl or $Cl_2$ gave only impure products: *H. H. Sisler, M. A. Mathur*, J. Inorg. Nucl. Chem. *39*, 1745 (1977).

[5] *G. Müller*, Diplomarbeit, Technische Universität München 1977; cf. also [3, 4].

[6] Preparation of $(CH_3)_2POH$ according to the method described by *H.-J. Kleiner*, Justus Liebigs Ann. Chem. *1974*, 751. Conversion into the potassium salt with KH in tetrahydrofuran.

[7] *H. Schmidbaur, G. Müller*, Monatsh. Chem. *111*, 1233 (1980).

## Synthesis and Crystal Structure of a ($\eta^5$-$C_5H_5$)$(CO)_2$-Molybdenum Bicyclophosphoranide: The first Transition Metal Complex with a "$R_4P^{\ominus}$"-Ligand[**]

By *Joachim Wachter, Bernard F. Mentzen* and
*Jean G. Riess*[*]

Phosphoranides, $R_4P^-$, were postulated as reaction intermediates in nucleophilic substitutions at tricoordinated phosphorus by *Wittig* in 1967[1], but remained elusive until *Granoth* and *Martin* succeeded in producing direct evidence for the existence of a lithium phosphoranide salt in 1978[2]. Fur-

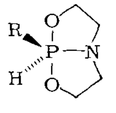
---

[*] Prof. Dr. J. G. Riess
Laboratoire de Chimie Minérale Moléculaire
Equipe de Recherche Associée au C.N.R.S.
Université de Nice, Parc Valrose, F-06034 Nice Cedex (France)
Dr. B. F. Mentzen
Institut de Recherches sur la Catalyse, C.N.R.S.
F-69626 Villeurbanne (France)
Dr. J. Wachter
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg (Germany)

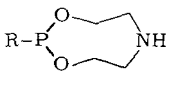
[**] The Centre National de la Recherche Scientifique is thanked for the Associate Research position of J. W. in Nice (1978—79).

thermore, evidence for the presence of a sodium phosphoranide in an equilibrium mixture in solution has recently been obtained[3]. We report here the isolation and crystal structure of a molybdenum adduct, which is the first transition metal complex with a phosphoranide ion as ligand.

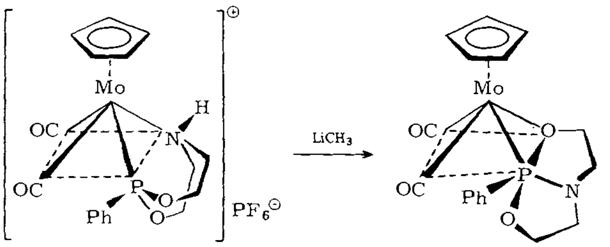
Bicyclic phosphoranes of type *(1a)* react with a variety of transition metal carbonyl complexes to give coordination adducts of their normally undetected tautomeric form *(1b)*. Coordination occurs either *via* P alone or *via* P and N[4]. The reaction of *(1a)* with $C_5H_5(CO)_3MoCl$ can be directed towards substitution of either two carbonyl groups or of one carbonyl and the chloride. In the latter case it yields the cationic species *(2)*[4b]. We selected *(2)* as a substrate on which to attempt the abstraction of the nitrogen bonded proton.



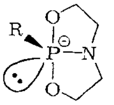
*(1a)*



*(1b)*



*(2)* *(3)*



*(4)*, R = $C_6H_5$

The action of methyllithium on *(2)* in THF at 60 °C yielded the neutral complex *(3)*, in which the pentacoordinated bipyramidal phosphorus atom is bonded to molybdenum and acts as an anionic phosphoranide ligand *(4)*. The two additional electrons needed by the metal to achieve an 18-electron configuration are provided by one of the oxygen atoms, giving the hitherto unknown MoPO three-membered ring. It is noteworthy that this structural arrangement, rather than one in which the nitrogen acts as the additional donor, avoids the unfavorable location of the oxygen atoms in equatorial positions and the phenyl group in an apical position, which would have resulted had this structural alternative been adopted.

All spectroscopic and analytical data of the red-orange crystalline material, isolated in 21% yield, are in accord with structure *(3)*. It exhibits two $\nu$(CO) vibrations at 1925 and 1835 cm$^{-1}$; the $\nu$(N—H) vibration of the educt *(2)* has disappeared. The $^1$H-NMR spectral data exclude the possibility of addition of $CH_3^\ominus$. The only sharp signal observed is that of the $\delta(C_5H_5) = 5.32$ (in $CDCl_3$); the signal integrations are also consistent with the abstraction of a proton. $^{31}P\{^1H\}$-NMR spectra of *(3)* show a singlet at an unusual location ($\delta = +23.8$) relative to the free phosphorane *(1a)*: $-44.3$ and to the metal complexes of the tautomer *(1b)*: $+185$ to $+200$[4b].

The structure of *(3)* was further established by X-ray crystal structure analysis[5] and is shown in Fig. 1.

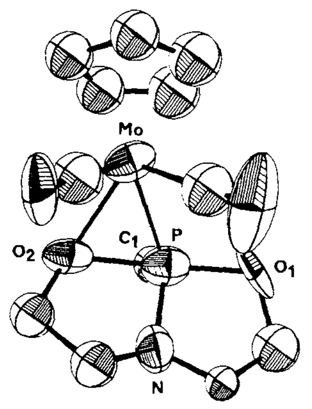


Fig. 1. Molecular structure of complex *(3)* in the crystal; of the phenyl group bonded to phosphorus only C-1 is reproduced (ellipsoids with 50% probability).

The bicyclic phosphoranide ligand whose N-bridgehead is close to planar (sum of angles 345 ± 5°), is almost perpendicularly orientated with respect to the $C_5H_5$ ring. The P—N bond length (1.69(5) Å) is in the range expected when N is equatorially bound to a bipyramidal pentacoordinated P atom[6]. The P—O2 distance in the coordinated five-membered ring (1.893(4) Å) is 0.24 Å longer than P—O1 in the uncoordinated ring. The P—Mo distance 2.375(2) Å) is 0.07—0.14 Å shorter than in complexes having the $C_5H_5MoPR_3$ pattern ($R = OCH_3, C_6H_5$)[7]; this may simply result from the contraction of the radii normally observed when going from a tri- to a pentacoordinated phosphorus atom.

### *Procedure*

An equimolar mixture of the $PF_6$ salt *(2)* (630 mg, 1.1 mmol) and $CH_3Li$ (0.7 cm$^3$ of 1.6 M solution in diethyl ether) in THF (50 cm$^3$) is stirred for 60 min at 60 °C. After evaporation of THF the oily residue is dissolved in ether (20 cm$^3$) and filtered. The concentrated filtrate is chromatographed on $SiO_2$ (column 20 × 2 cm), the product eluted with ether as an orange band (yield 100 mg, 21%), and recrystallized from ether/pentane (2:1) to give *(3)* as red-orange crystals (decomp. 86 °C)[8].

Received: April 24, 1980 [Z 719 IE]
German version: Angew. Chem. *93*, 299 (1981)

CAS Registry Numbers:
*(2)*, 73456-62-9; *(3)*, 76915-17-8

---

[1] *G. Wittig, A. Maercker*, J. Organomet. Chem. *8*, 491 (1967).

[2] *I. Granoth, J. C. Martin*, J. Am. Chem. Soc. *100*, 7434 (1978); *101*, 4623 (1979).

[3] *B. Garrigues, M. Koenig, A. Munoz*, Tetrahedron Lett. *1979*, 4205.

[4] a) *D. Bondoux, I. Tkatchenko, D. Houalla, R. Wolf, C. Pradat, J. G. Riess, B. F. Mentzen*, J. Chem. Soc. Chem. Commun. *1978*, 1022; *C. Pradat, J. G. Riess, D. Bondoux, B. F. Mentzen, I. Tkatchenko, D. Houalla*, J. Am. Chem. Soc. *101*, 2234 (1979); b) *J. Wachter, F. Jeanneaux, J. G. Riess*, Inorg. Chem. *19*, 2169 (1980).

[5] Monoclinic crystals (space group $P2_1/c$) with unit cell parameters $a = 12.280(3)$, $b = 8.185(2)$, $c = 18.263(7)$ Å, $\beta = 108.07(2)°$; $V = 1745.2$ Å$^3$, $\varrho_{calc} = 1.63$ g · cm$^{-3}$, $Z = 4$. From 3689 measured reflections ($Mo_{K\alpha}$ radiation), 516 were used for a preliminary refinement of the structure ($R = 5.7\%$).

[6] *R. A. Shaw*, Phosphorus Sulfur *4*, 701 (1978).

[7] *M. G. Reisner, I. Bernal, H. Brunner, J. Doppelberger*, J. Chem. Soc. Dalton Trans. *1979*, 1664.

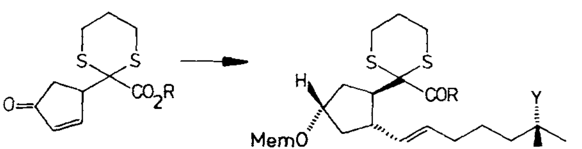
[8] The 70 eV mass spectra contain $[M-CO]^+$, $[M-CO-C_6H_6]^+$, and $[M-2CO]^+$ as fragments of highest mass numbers. The parent ion can be observed in the FD spectrum (Varian 311 A). We thank Dr. *K. K. Mayer* and *E. Fischer* for recording the spectra.

# The Stereospecificity of Brefeldin A Cyclization[**]

By *Peter Raddatz* and *Ekkehard Winterfeldt*[*]

*Dedicated to Professor Hans Herloff Inhoffen*
*on the occasion of his 75th birthday*

In our total synthesis of brefeldin A[1], the epimeric alcohols *(3)* and *(4)* as well as their silyl ethers *(3a)* and *(4a)* are important intermediates.



*(1), (2)* *(3), (4)*

*(1)*, $R = C_2H_5$
*(2)*, R = Mem

Mem = $CH_2O(CH_2)_2OCH_3$

*(3)*, $R = OC_2H_5$, X = OH, Y = H
*(4)*, $R = OC_2H_5$, X = H, Y = OH
*(3a)*, $R = OC_2H_5$, $X = OSi(CH_3)_2C(CH_3)_3$, Y = H
*(4a)*, $R = OC_2H_5$, X = H, $Y = OSi(CH_3)_2C(CH_3)_3$
*(3b)*, R = O-Mem, $X = OSi(CH_3)_2C(CH_3)_3$, Y = H
*(4b)*, R = O-Mem, X = H, $Y = OSi(CH_3)_2C(CH_3)_3$
*(3c)*, R = H, $X = OSi(CH_3)_2C(CH_3)_3$, Y = H
*(4c)*, R = H, X = H, $Y = OSi(CH_3)_2C(CH_3)_3$
*(3d)*, R = H, X and Y = H and OH

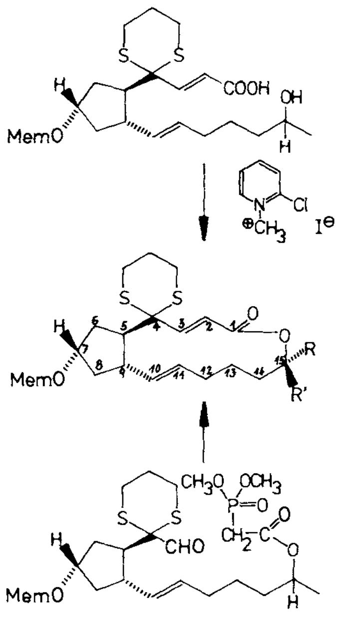
They can be obtained most easily, and with excellent stereoselectivity, from the readily preparable cyclopentenone derivative *(1)*[2] by vinyl cuprate addition of the intact silyl-protected side chains to C-9 and a subsequent reduction-inversion sequence[1].

If this sequence is carried out with the corresponding Mem esters *(4)* the ability of this special ester group[3] in *(3b)* and *(4b)* to form complexes enables direct reduction to the mixture of aldehydes *(3c)/(4c)*. Wittig chain-expansion, hydrolysis, and cleavage of silyl ether afford the seco-acids *(5)* as a mixture of epimers (C-15).

Although the lactonization reaction of the corresponding 4-Mem ethers is said to be highly stereospecific, with distinct preference for the natural configuration at C-15[4], *(5)* shows no stereospecificity whatsoever on lactone formation according to the method of *Mukaiyama, i. e.* the two C-15 epimeric lactones *(6a)* and *(6b)* are formed in exactly equal amounts.

Since many Wittig or Wittig-Horner cyclizations have recently been successfully employed for the synthesis of medium-sized and large rings[5] we have examined the possible use of these cyclizations for the synthesis of the 13-membered ring system brefeldin A.

The silyl ether in *(3c)/(4c)* was cleaved off and the phosphonate *(7)* generated by the DCCD technique; *(7)* was then deprotonated as the C-15 epimeric mixture with sodium hydride, resulting in cyclization (Table 1). After 8 h at room temperature a lactone is isolated which, according to the NMR data, corresponds with high selectivity (10:1) to the epimer *(6b)* (Table 1). The sequence already described by us: thioketal cleavage, reduction, Mem-ether cleavage, leads indeed to 4-epi-15-epi-brefeldin A. Owing to the higher polarity of the phosphonate, the non-cyclized portion can be separated, hydrolyzed and protected at the hydroxyl group as the silyl ether. The enriched aldehyde *(3c)* thus obtained can be subjected to chain-expansion in the above-mentioned way, and on lactonization affords brefeldin A.



*(5)*

*(6a)*, R = H; R' = $CH_3$

*(6b)*, R = $CH_3$; R' = H

*(7)*

Table 1. Some physical data of the compounds *(6)* and *(5b)*.

*(6)*, IR ($CCl_4$): 1735, 1720, 1200, 910 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 90 MHz): $\delta = 1.23$ (3H, d, $J = 6.5$ Hz), 1.31 (6H, t, $J = 7$ Hz), 1.45—2.75 (18H, m), 2.95 (2H, d, $J = 21$ Hz), 3.41 (3H, s), 3.62 (4H, m), 4.18 (4H, q), 4.18 (1H, m), 4.71 (2H, s), 4.9 (1H, m), 5.3 (2H, m), 8.87 (1H, s); MS (250 °C): $M^{\oplus}$ absent, 582 ($M^{\oplus} - 28$, 5%), 505 (15.5), 492 (14), 473 (19.5), 434 (15), 309 (17.5), 279 (12.5), 198 (54.5), 187 (64.5), 179 (39), 151 (26.5), 123 (31), 89 (25), 59 (100); high resolution calc. 582.2449, obs. 582.2449 ($M^{\oplus} - 28$)

*(5b)*, IR ($CCl_4$): 1715, 1630 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 90 MHz): $\delta = 1.24$ (3H, d, $J = 6.5$ Hz), H-15, 1.25—2.5 (14H, m), 2.5—3.25 (4H, m, thioketal), 3.34 (3H, s, Mem ether, O—$CH_3$), 3.65 (4H, m, Mem ether, O—$CH_2$—$CH_2$—O), 4.13 (1H, m, H-7), 4.71 (2H, s, Mem ether, O—$CH_2$—O), 4.95 (1H, m), 5.2 (2H, m, inactive olefin), 6.13 (1H, d, $J = 15.5$ Hz), 6.70 (1H, d, $J = 15.5$ Hz, active olefin); MS (70 °C): 455 ($M^{\oplus} - 1$, 9.5%), 427 (2), 380 (5), 350 (195), 274 (12), 149 (45.5), 89 (100), 59 (86); high resolution calc. 455.1926, obs. 455.1924 ($M^{+} - 1$)

This constitutes a case of a kinetic separation of the epimers of the stereoisomeric C-15 alcohols, and it is noteworthy that the phosphonate with natural configuration at C-15 leads to cyclization products only after several days at room temperature. Attempts to accelerate this process by increasing the temperature lead to considerable resinification. Hence, in the phosphonate cyclization there is a dependence on the configuration at C-15—interestingly, however, in the reverse sense to that in the Corey cyclization.

## *Procedure*

*(7)*: A solution of *(3d)* (740 mg, 1.72 mmol) in anhydrous dichloromethane (20 $cm^3$) is treated with dimethoxyphosphorylacetic acid (320 mg, 1.9 mmol), dicyclohexylcarbodiimide (395 mg, 1.9 mmol) and 4-(dimethylamino)pyridine (40 mg) and the mixture stirred for 3 h at room temperature. The urea is filtered off. The filtrate is taken up in $CH_2Cl_2$, washed with water, dried, and evaporated down. The residue is chromatographed on silica gel (eluent: ether + 5% $CH_3OH$); yield 905 mg (86%).

*(6b)*: Under an $N_2$ atmosphere a solution of *(7)* (100 mg, 0.16 mmol) in anhydrous dimethoxyethane (5 $cm^3$) is added dropwise within 8 h to a suspension of NaH (30 mg) in anhydrous dimethoxyethane (25 $cm^3$). After one hours' stirring at

---

[*] Prof. Dr. E. Winterfeldt, Dipl.-Chem. P. Raddatz
Institut für Organische Chemie der Universität
Schneiderberg 1 B, D-3000 Hannover (Germany)

[**] Cyclopentenones, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 3: [1].

0570-0833/81/0303-0286 $ 02.50/0

room temperature the reaction solution is treated with glacial acetic acid (0.3 cm$^3$) and evaporated down. The residue is taken up in ether, washed with a saturated $NaHCO_3$ solution and water, dried with $MgSO_4$, and evaporated down. The residue is chromatographed on silica gel (eluent: ether); yield 21—26 mg (28—36%).

Received: December 19, 1980 [Z 716 IE]
German version: Angew. Chem. *93*, 281 (1981)

---

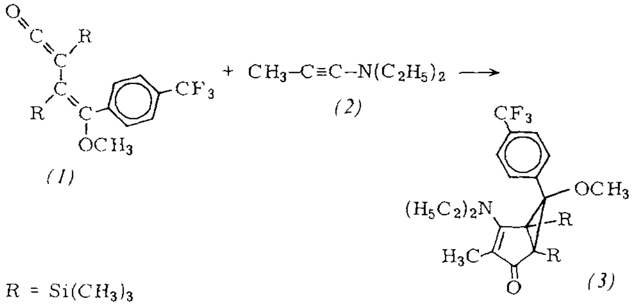
[1] *Y. Köksal, P. Raddatz, E. Winterfeldt,* Angew. Chem. *92*, 486 (1980); Angew. Chem. Int. Ed. Engl. *19*, 472 (1980).
[2] *Y. Köksal, V. Osterthun, E. Winterfeldt,* Justus Liebigs Ann. Chem. *1979*, 1300.
[3] *R. E. Ireland, W. J. Thompson,* Tetrahedron Lett. *1979*, 4705.
[4] *E. J. Corey, R. H. Wollenberg,* Tetrahedron Lett. *1976*, 4701.
[5] *K. B. Becker,* Tetrahedron Rep. *86*, 1717 (1980); *G. Stork, E. Nakamura,* J. Org. Chem. *44*, 4011 (1979).

## Addition of Ynamines to Vinylketenes[**]

By *Karl Heinz Dötz, Barbara Trenkle,*
and *Ulrich Schubert*[*]

Ketenes can add ynamines at the C=C- or at the C=O-bond[1]. The recently discovered entry to stable vinylketenes[2] also provides the possibility of investigating the virtually unresearched cycloaddition behavior[3] of this class of compounds.

On reaction of 4-methoxy-4-(4-trifluoromethylphenyl)-2,3-bis(trimethylsilyl)-1,3-butadien-1-one *(1)* with 1-diethylamino-1-propyne *(2)* in hexane at room temperature the bicyclo[3.1.0]hex-3-en-2-one derivative *(3)* is obtained instead of the expected four-membered ring derivative. Of the possible *endo-exo* isomers only the *endo*-aryl form is obtained. Such bicycles are already accessible by photolysis of cyclohexadienones: for example, *o*-quinol acetates give exclusively the *endo*-aryl compounds, while *p*-quinol derivatives afford predominantly *exo*-isomers[4].



*(1)*

*(2)*

*(3)*

R = $Si(CH_3)_3$

The IR spectrum[5] of *(3)* shows a $\nu$(C=C) absorption shifted to extremely long wavelength at 1585 cm$^{-1}$, indicating a considerable charge transfer from the amino group to the carbonyl group. This is confirmed by the X-ray structure analysis[6] (Fig. 1), which shows a shortening of the C4—N (137.9 pm) and C2—C3 (141.5 pm) bond lengths and a lengthening of the C2—O2 (125.2 pm) bond in the aminoenone grouping of the five-membered ring compared to those in analogous bicycles not containing an amino function. The two *cis* trimethylsilyl substituents may be responsible for the lenthening of the C1—C5 bond (156.6 pm) and widening of the C5(C6)—C1—Si1 (136.7°, 124.1°) and C1(C6)—C5—Si2 (124.8°, 129.2°) angles.

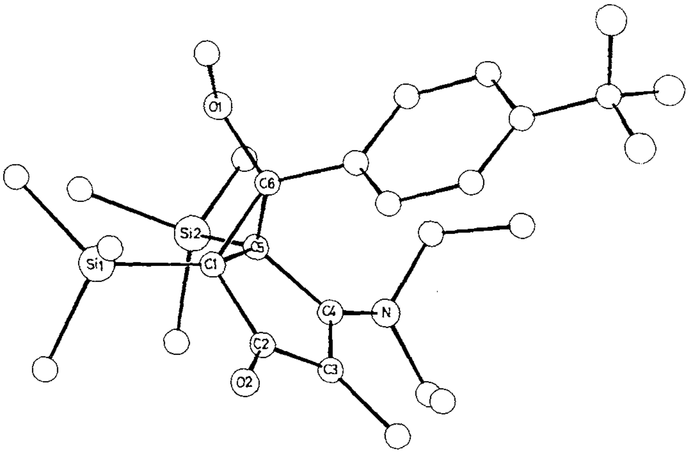


Fig. 1. Molecular structure of *(3)* [6].

The formation of the bicycle *(3)* can be explained in terms of an initial [2+2]-cycloaddition of the ynamine to the vinylketene to give cyclobutenone, followed by ring opening to an homologized dienylketene. Such compounds have already been detected as precursors of bicyclohexenones in the photoisomerization of cyclohexadienones[7].

*Procedure*

A mixture of *(1)* (1.08 g, 2.7 mmol) in hexane (15 cm$^3$) and *(2)* (0.84 cm$^3$, 6.0 mmol) is stirred for 3 h at room temperature. After removal of solvent the residue is chromatographed on silica gel (Merck, Act. 2—3). Elution of the yellow main zone with dichloromethane/pentane (1:1) and subsequent recrystallization from pentane affords *(3)* as colorless crystals; m.p. 122 °C, yield 0.51 g (38%).

Received: July 23, 1980 [Z 715 IE]
German version: Angew. Chem. *93*, 296 (1981)

CAS Registry numbers:
*(1)*, 76833-11-9; *(2)*, 4231-35-0; *(3)*, 76833-12-0

---

[*] Dr. K. H. Dötz [+], B. Trenkle, Dr. U. Schubert
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[+] Author to whom correspondence should be addressed.

[**] Vinylketenes, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 2: [2b].

[1] *H. G. Viehe:* The Chemistry of Acetylenes. Marcel Dekker, New York 1969.
[2] a) *K. H. Dötz,* Angew. Chem. *91*, 1021 (1979); Angew. Chem. Int. Ed. Engl. *18*, 954 (1979); b) *K. H. Dötz, B. Fügen-Köster,* Chem. Ber. *113*, 1449 (1980).
[3] *G. B. Payne,* J. Org. Chem. *31*, 718 (1966).
[4] *W. J. Seifert, H. Perst, W. Dannenberg,* Tetrahedron Lett. *1973*, 4999; *W. Dannenberg, H. Perst,* Justus Liebigs Ann. Chem. *1975*, 1873.
[5] KBr disk.
[6] 2421 structural factors ($F_0 \geq 4.3\sigma$, Syntex $P2_1$/XTL, $2° \leq 2\theta \leq 46°$, $\lambda = 71.069$ pm, $R_1 = 0.081$; triclinic, space group $P\bar{1}$, $Z = 2$; $a = 1035(3)$, $b = 1039(2)$, $c = 1341(3)$ pm; $\alpha = 98.2(2)$, $\beta = 96.2(2)$, $\gamma = 100.3(2)°$, $V = 1391 \times 10^6$ pm$^3$.
[7] Review: *G. Quinkert,* Angew. Chem. *84*, 1157 (1972); Angew. Chem. Int. Ed. Engl. *11*, 1072 (1972).

## Intramolecular Nucleophilic Addition in a Thiolato-bridged "Crown-like" Iridium Complex

By *Jean Devillers, Dominique de Montauzon,*
and *René Poilblanc*

The oxidative addition of alkynes to Ir(I) atoms of binuclear complexes has recently been described[1]. Starting from

---

[*] Prof. Dr. R. Poilblanc, J. Devillers, D. de Montauzon
Laboratoire de Chimie de Coordination du CNRS
associé à l'Université Paul Sabatier
205 route de Narbonne, F-31400 Toulouse (France)

$[Ir(\mu\text{-}S\text{—}tBu)(CO)_2]_2$, a trinuclear complex with Ir(II)—Ir(II) bonding was obtained.

$Ir_3(\mu\text{-}S\text{—}tBu)_3(\mu\text{-}C_4F_6)(CO)_6$ *(1)*

We now report on the reaction of *(1)* with excess hexafluoro-2-butyne, which leads to formation of a complex whose chemical and spectroscopic data[2] are consistent with formula *(2)*

$Ir_3(S\text{—}tBu)_3(CO)_5(C_4F_6)_2$ *(2)*

The infrared spectra[2] show five CO bands, and two groups of C=C bands. The band at 1621 $cm^{-1}$ can be assigned to a σ-bonded alkyne, as in complex *(1)*[3]. The two other bands at 1830 and 1802 $cm^{-1}$ are attributed to a π-bonded alkyne[4]. The $^{19}F$-NMR spectrum[2] confirms the existence of these two modes of coordination of the alkyne ligands. Furthermore the $^1H$-NMR spectrum[2] shows that the three *tert*-butylthiolato groups are nonequivalent.

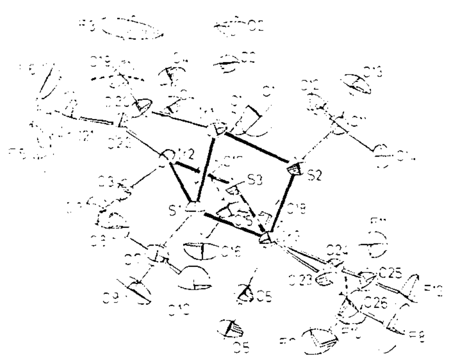


Fig. 1. ORTEP-drawing of complex *(2)* in the crystal [5]; atoms F1, F2 and F9 are not shown. Most important bond lengths and angles: Ir1—Ir2 = 2.707(1), Ir1—Ir3 = 3.730(1), Ir2—Ir3 = 3.717(1), Ir1—S1 = 2.342(2), Ir2—S1 = 2.339(3), Ir3—S1 = 2.467(2), Ir3—S2 = 2.453(2), Ir3—S3 = 2.431(3), Ir1—C1 = 1.940(13), C1—O1 = 1.115(13), Ir1—C20 = 2.085(10), Ir3—C24 = 2.036(10), S1—C7 = 1.889(10), C20—C22 = 1.291(15), C23—C24 = 1.244(14) Å; Ir1—S1—Ir2 = 70.7, Ir2—S3—Ir3 = 99.7, S1—Ir1—S2 = 78.7, S1—Ir2—S3 = 80.7, S1—Ir3—C5 = 97.2, C24—Ir3—S2 = 93.3, S2—Ir3—C5 = 170.8, Ir1—S1—C7 = 124.3, C1—Ir1—C2 = 98.2°.

Figure 1 shows the results of the X-ray structure analysis. The geometry around the $Ir^{II}$ atoms (Ir1 and Ir2) is almost the same as in *(1)*. The similarity of the Ir1—Ir2 distances in *(1)* and *(2)* (2.71 and 2.69 Å respectively), strongly suggests the existence of a metal-metal bond in *(2)*. Substitution of a CO group by a π-bonded $C_4F_6$ group at $Ir^I$-atom (Ir 3) leads to significant changes in the geometry of the remaining part of the complex. The chair conformation of the ring formed by Ir1—S1—Ir2—S3—Ir3—S2 in *(1)* is transformed into a "boat" conformation in *(2)*. The rotation of Ir3 around the S3—S2 axis is probably correlated with inversion of configuration at the S3 atom as well as with the formation of the S1—Ir3 bond. The Ir3—S1, Ir3—S3 and Ir3—S2 bond lengths are similar (Fig. 1). As a consequence, the S1 atom is linked to all three Ir atoms and is thus tetracoordinated. For the same reason, the coordination number of the Ir3 atom, which was four in *(1)*, increases to five in *(2)*. The geometry around Ir3 can be described as a distorted trigonal bipyramid with S1, S3 and the center of C23—C24 bond in the equatorial plane. The formation of the S1—Ir3 bond and the related modifications of the structure are attributed to the electron-withdrawing effect of the fluoroalkyne group bonded to Ir3.

*Procedure*

*(1)* (0.587 g, *ca.* 0.5 mmol) was transferred to a thick-walled glass reaction vessel fitted with a Teflon stopcock. After evacuation and cooling to −196 °C, pentane (*ca.* 30 $cm^3$) and 1.0 g hexafluorobut-2-yne (excess) were condensed into the flask. The reaction mixture was then allowed to warm-up slowly to room temperature and stirred for three days. The solution was then evaporated under reduced pressure, and lemon yellow crystals obtained at −20 °C from 3 $cm^3$ pentane. These were vacuum dried: yield 72%.

Received: July 23, 1980 [Z 714 IE]
German Version: Angew. Chem. *93*, 296 (1981)

---

[1] *J. Devillers, J. J. Bonnet, D. de Montauzon, J. Galy, R. Poilblanc*, Inorg. Chem. *19*, 154 (1980).

[2] IR (Hexadecane): $\nu_{CO} = 2096$ s, 2080 vs, 2051 vs, 2036 m, 2020 s; (CsBr): $\nu_{C=C} = 1621$ s, 1830 vs, 1802 vs; $^1H$-NMR ($C_6H_6$, TMS int.): $\delta = 1.28$, 1.19, 1.01; $^{19}F$-NMR ($C_6H_6$, $CF_3COOH$ int.): $\delta = 19.9$, 18.9; m.p. = 119 °C.

[3] *J. L. Davidson, W. Harrison, D. W. A. Sharp, G. A. Sim*, J. Organomet. Chem. *46*, C47 (1972); *R. Mathieu, R. Poilblanc, ibid. 142*, 351 (1977).

[4] *D. R. Russel, A. Tucker*, J. Organomet. Chem. *125*, 303 (1977); *D. A. Clarke, R. D. Kemmitt, D. R. Russel, P. Tucker, ibid. 93*, C37 (1975).

[5] Space group: $P\bar{1}$, $Z = 2$; $a = 11.4892(17)$, $b = 16.0528(25)$, $c = 10.2673(22)$ Å, $\alpha = 95.764(17)$, $\beta = 101.740(17)$, $\gamma = 90.781(12)°$; $V = 1843.4$ $Å^3$; $\rho_{calc.} = 2.41$ g $cm^{-3}$, $\rho_{exp} = 2.40$ g $cm^{-3}$; 6657 Reflections ($Mo_{K\alpha}$-radiation), from which 4672 have $I > 3\sigma(I)$, refined to $R = 3.49\%$.

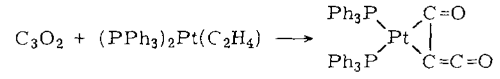
---

## Reactions of Carbon Suboxide with Platinum(0) Complexes[**]

By *Gastone Paiaro* and *Luciano Pandolfo*[*]

Until now, no systematic study of the properties of carbon suboxide *(1)*[1] as a ligand in transition metal complexes has been reported. *(1)* has been regarded as an activated olefin in reactions with transition metals. On the one hand, by analogy with $C_3S_2$[2], it reacts with C=O and C=C groups, but on the other it can for example form diphenylketene-carbene complexes by dissociating into CO and $C_2O$ moieties[4].

We report here on the reactions of *(1)* with the complexes $(PPh_3)_2Pt(C_2H_4)$ *(2)* and $(PPh_3)_2Pt(O_2)$ *(4)*. Reaction of *(2)*



$$C_3O_2 + (PPh_3)_2Pt(C_2H_4) \longrightarrow (Ph_3P)_2Pt\begin{matrix} C{=}O \\ | \\ C{=}C{=}O \end{matrix}$$

*(1)* *(2)* *(3)*

with *(1)* affords the complex *(3)*, whose IR spectrum exhibits a strong ketene band ($\nu = 2080$ $cm^{-1}$) and a carbonyl band ($\nu = 1765$ $cm^{-1}$). Cyclic voltammetric measurements performed in DMSO using a mercury-covered spherical gold electrode indicate that *(3)* undergoes irreversible reduction at a potential of −1.8 V (*vs.* SCE). Furthermore, potentiostatic coulometry carried out at a mercury electrode indicate that two electrons are involved in the overall cathodic process. These results suggest that a metallocyclopropane structure[5] is probable for *(3)*, formed by formal oxidative addition of *(1)* to *(2)*.

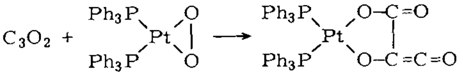
Reaction of *(1)* with *(4)* *via* 1,2-addition of the dioxygen moiety across the C=C bond results in formation of a product whose elemental analysis and spectroscopic parameters

---

[*] Prof. Dr. G. Paiaro, Dr. L. Pandolfo
Istituto di Chimica Analitica, Università di Padova
Via F. Marzolo 1, I-35100 Padova (Italy)

[**] This work was supported by C.N.R. (Roma).

are consistent with the structure *(5)*[6]. The IR spectrum of *(5)* exhibits strong ketene and carbonyl bands ($\nu = 2080$ and $1625\ cm^{-1}$ resp.): a peroxide O—O bond could not be observed either by IR-spectroscopy (no band at $825\ cm^{-1}$) or by an iodine test[7]. *(5)* isomerizes in solution giving a known compound $[(PPh_3)_2Pt(O)_2]C_3O_2$ having an intense band at $\nu = 1685\ cm^{-1}$[8].



*(1)* *(4)* *(5)*

These types of reactions of carbon suboxide *(1)* with compounds *(2)* and *(4)* are of interest because they lead to complexes in which there is a "free" ketene group and indicate that the dioxygen ligand in *(4)* attacks $C_3O_2$ directly.

*Procedure*

All solvents were degassed and manipulations carried out under an argon atmosphere. *(1)* was prepared by dehydration of malonic acid with $P_4H_{10}$.

*(3)*: *(1)* (0.25 mmol) is passed into a solution of *(2)* (0.19 mmol) in 10 cm$^3$ ether at $-20\,^\circ C$; white microcrystalline *(3)* is filtered off. Yield 37%, m.p. = 128—129 °C (decomp.).

*(5)*: *(1)* (2.8 mmol) is passed into a solution of *(4)* (2.1 g, 2.8 mmol) in 30 cm$^3$ $CH_2Cl_2$; white microcrystalline *(5)* is filtered off and washed with cold $CH_2Cl_2$. Yield 41%, m.p. = 130—132 °C (decomp.). Elemental analysis corresponded to *(5)*·$CH_2Cl_2$.

Received: June 9, 1980 [Z 713a IE]
German version: Angew. Chem. 93, 294 (1981)

CAS Registry Numbers:
*(1)*, 504-64-3; *(2)*, 12120-15-9; *(3)*, 76900-29-3; *(4)*, 29894-57-3; *(5)*, 76879-99-7

---

[1] See *e.g.*: *T. Kappe, E. Ziegler*, Angew. Chem. 85, 529 (1974); Angew. Chem. Int. Ed. Engl. 13, 491 (1974); *L. D. Brown, W. N. Lipscomb*, J. Am. Chem. Soc. 99, 3968 (1977).

[2] *A. P. Ginsberg, W. E. Silverthorn*, Chem. Commun. 1969, 823.

[3] *P. Hong, N. Nishii, K. Sonogashira, N. Hagihara*, J. Chem. Soc. Chem. Commun. 1972, 993; *H. Ueda, Y. Kai, N. Yasuoka, N. Kasai*, Bull. Chem. Soc. Jpn. 50, 2250 (1977).

[4] Rhodium(I) and Nickel(0) complexes react in this manner: *G. Paiaro, L. Pandolfo, P. Segala*, XII Natl. Congr. of Inorg. Chem., Trieste, 11—15th Sept. 1979.

[5] *K. Schorpp, W. Beck*, Z. Naturforsch. B 28, 738 (1973).

[6] A similar reaction has been reported recently for activated acetylenes, *H. C. Clark, A. B. Goel, C. S. Wong*, J. Am. Chem. Soc. 100, 6241 (1978).

[7] $(Ph_2Et)_2PtO_2$ and $(Cy_3P)PtO_2$ oxidize coordinated phosphane derivatives; see also *A. Sen, J. Halpern*, J. Am. Chem. Soc. 99, 8337 (1977).

[8] This compound can be obtained directly from solutions of $(PPh_3)_2Pt(O_2)$ and $C_3O_2$; *K. S. Kolomnikov, Y. D. Koreshkov, T. S. Lobeeva, M. E. Volpin*, Izv. Akad. Nauk. SSSR, Ser. Khim. 1972, 1181.

## Reactions of Carbon Suboxide with Rhodium(I) Complexes[**]

By *Gastone Paiaro* and *Luciano Pandolfo*[*]

As part of our studies on the coordinating properties of carbon suboxide *(1)* with transition metals[1], we examined the reaction of rhodium(I) complexes with *(1)*.

Reaction of $(PPh_3)_3RhCl$ *(2)* with *(1)* in benzene gives *trans*-$(PPh_3)_2(CO)RhCl$ *(3)* in addition to polymers derived from $C_2O$[2].

$$\underset{(1)}{C_3O_2} + \underset{(2)}{(PPh_3)_3RhCl} \rightarrow \underset{(3)}{(PPh_3)_2(CO)RhCl} + PPh_3 + 1/n\,(C_2O)_n$$

The course of the reaction in $CH_2Cl_2$ has been followed by IR spectroscopy: an intense band at $2080\ cm^{-1}$ ($\nu_{ketene}$) soon appears but decreases in intensity and eventually disappears while a band at $1970\ cm^{-1}$ ($\nu_{CO}$) increases. Another band at $2210\ cm^{-1}$ reaches its maximum intensity after 1 h and completely disappears after 24 h. These results suggest that the reaction proceeds *via* nucleophilic attack of a tricoordinated rhodium species on the electrophilic C-1 of *(1)*. In this way *(1)* is cleaved into CO and $C_2O$, producing the thermodynamically stable carbonyl rhodium complex *(3)*[3].

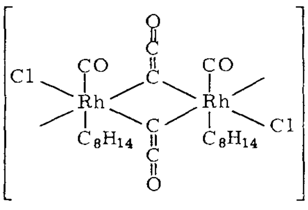
The binuclear $[(C_8H_{14})_2RhCl]_2$ *(4)* reacts with *(1)* in toluene to give the brick-red complex *(5)*.

$$\underset{(1)}{C_3O_2} + \underset{(4)}{[(C_8H_{14})_2RhCl]_2} \rightarrow \underset{(5)}{1/n\,[C_8H_{14})(CO)Rh(C_2O)Cl]_n} + C_8H_{14}$$

Compound *(5)* is stable and insoluble in most organic solvents; only chloro-bridge splitting reagents such as pyridine "dissolve" it.

$$(5) + n\text{py} \rightarrow \frac{n}{2}\,[(C_8H_{14})(CO)(py)Rh(C_2O)Cl]_2 \quad (6)$$

The IR spectrum of *(5)* contains bands which can be assigned to a terminal carbonyl group ($\nu = 2010\ cm^{-1}$), an Rh—Cl bridge ($\nu = 303\ cm^{-1}$), a ketene ($\nu = 2080\ cm^{-1}$) and cyclooctene ligand ($\nu = 2935$, $2800\ cm^{-1}$); these assignments were confirmed by $^1H$-NMR spectroscopy ($[D_6]$-dimethylsulfoxide; $\delta = 5.51$ (2H), 2.51 (4H), 1.43 (8H)). Potentiostatic coulometry ($-1.75$ V *vs.* SCE) carried out at a platinum electrode, indicates that three electrons are involved in the overall cathodic reaction of *(5)*. On the basis of these results the structure of *(5)* must consist of a polymeric rhodium(III) complex having chlorine and carbene bridges as shown in *(5a)*[4].



*(5a)*

Carbon suboxide *(1)* does not react with $[(C_8H_{12})RhCl]_2$ or $[(C_2H_4)_2Rh(C_5H_5)]$ in $CH_2Cl_2$ solution. The type of reaction described here is of particular interest in relation to catalytic decarbonylation[5].

*Procedure*

All reactions were carried out under an atmosphere of argon. *(1)* was prepared by dehydration of malonic acid with $P_4O_{10}$.

*(3)*: *(1)* (2.3 mmol) is passed into a solution of *(2)* (2.27 mmol) in 100 cm$^3$ benzene at room temperature. A red solid precipitates and is filtered off and crystallized from acetone. Yellow crystals[3], m.p. = 195 °C.

*(5)*: *(1)* (1.45 mmol) is passed into a solution of *(4)* (1.28 mmol) in 50 cm$^3$ toluene at 0 °C; the solution becomes red. After 24 h the solution is colorless and a red solid is formed. After elemental analysis this corresponds to *(5)*·$C_7H_8$; yield 77%.

Received: June 30, 1980 [Z 713b IE]
German version: Angew. Chem. 93, 295 (1981)

---

[*] Prof. Dr. G. Paiaro, Dr. L. Pandolfo
Istituto di Chimica Analitica, Università di Padova
Via F. Marzolo 1, I-35100 Padova (Italy)

[**] This work was supported by C.N.R. (Roma).

CAS Registry Numbers:
*(1)*, 507-64-3; *(2)*, 14694-95-2; *(3)*, 15318-33-9; *(4)*, 12279-09-3; *(5)*, 76879-83-9; *(6)*, 76900-30-6

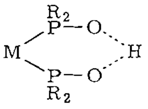
---

[1] *G. Paiaro, L. Pandolfo*, Angew. Chem. *93*, 294 (1981); Angew. Chem. Int. Ed. Engl. *20*, 288 (1981).
[2] *D. G. Williamson, K. D. Bayes*, J. Am. Chem. Soc. *90*, 1957 (1968).
[3] X-ray crystal structure of *(3)*: *A. Del Pra, G. Zanotti, P. Segala*, Cryst. Struct. Comm. *8*, 959 (1979).
[4] *P. Hong, N. Nishii, K. Sonogashira, N. Hagihara*, J. Chem. Soc. Chem. Commun. *1972*, 993; *H. Veda, Y. Kai, N. Yasuoka, N. Kasai*, Bull. Chem. Soc. Jpn. *50*, 2250 (1977).
[5] *M. C. Baird, C. J. Nyman, G. Wilkinson*, J. Chem. Soc. *1968*, 348.

## Reaction of Platinum(II) *N*,*N*-Dialkyldithiocarbamates with Diphenylphosphane Sulfide[**]

By *David M. Anderson, E. A. V. Ebsworth, T. Anthony Stephenson*, and *Malcolm D. Walkinshaw*[*]

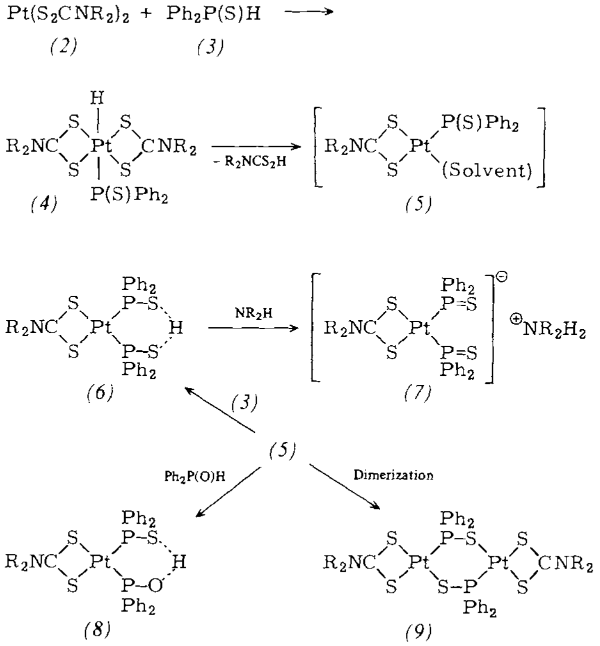
A variety of transition metal complexes containing the six membered ring *(1)* has been isolated in recent years. They were produced either by addition of phosphinous acids or their salts to suitable metal complexes or by solvolysis of coordinated P—X bonds (X = halogen, OR *etc.*)[1]. Replacement of the proton in *(1)* by Lewis acids or transition metal ions is also well established[1].



*(1)*, R = Ph, OMe, OEt

In contrast, no evidence has been found for the thio-analogues of *(1)*. In an attempt to remedy this deficiency, we reacted [Pt($S_2CNR_2$)$_2$] *(2)* with diphenylphosphane sulfide *(3)* in alcohols and found a variety of products (Scheme 1), depending both on the amount of sulfide and water present in the reaction mixture (cf. related studies on the reaction of *(2)* with $Ph_2P(O)H$ in which the well-known [Pt($S_2CNR_2$)($Ph_2PO$)$_2$H][2] is the only product isolated).

Thus, refluxing a mixture of *(2)* with an excess of *(3)* in *dry* ethanol for 24 h gives, as the major product, the novel anions [Pt($S_2CNR_2$)($Ph_2PS$)$_2$]$^-$ *(7)*, isolated as their dialkylammonium salts. Evidence for this formulation is based on elemental analyses, conductivity measurements in methanol, $^1$H- and $^{31}$P{$^1$H}-NMR studies[3] and verification of the structure of *(7a)* by X-ray structural analysis (Fig. 1). This shows the platinum atom to be coordinated in square planar fashion by two sulfur and two phosphorus atoms. Each $NEt_2H_2^{\oplus}$ ions lies close to one [Pt($S_2CNEt_2$)($Ph_2PS$)$_2$]$^{\ominus}$ ion, making contacts N2...Pt 3.65 Å, N2...S4 3.18 Å and N2...S3 3.27 Å. All atoms on other neighbouring anions are more than 4 Å from N2. The P1, P2, S3, S4 plane is tilted 70° from the coordination plane and the sulfur atoms are 4.7 Å apart (cf. [Pd($S_2PMe_2$)($Ph_2PO$)$_2$H] where the PPOO-plane is tilted 26.1° from the metal coordination plane and the O—H—O distance is 2.41 Å[2]).



Scheme 1. Possible mode of formation of compounds *(7)*, *(8)* and *(9)* from *(2)* and *(3)*. *(a)*, R = $C_2H_5$, *(b)*, R = $iC_3H_7$.

However, if the reactions are carried out in *wet* solvents, the major products are the unique, neutral, mixed chalcogenide complexes *(8)*[3].

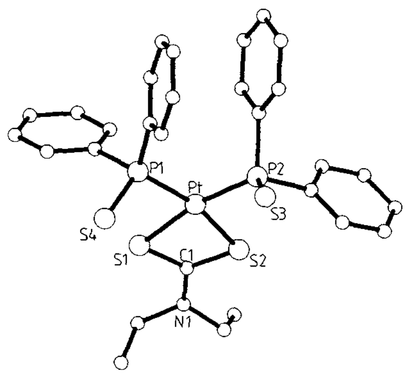


Fig. 1. Molecular structure of diethylammonium salt *(7a)* [4].

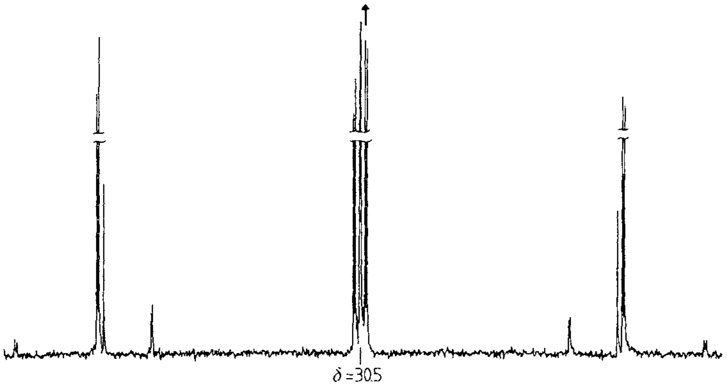


Fig. 2. $^{31}$P-{$^1$H}-NMR spectrum of *(9a)* in $CDCl_3$ at 301 K. $^1J_{PtP}$ = 3656.4, $^2J_{PtP}$ = 80.5, $^3J_{PP}$ = 13.6, $^3J_{PtPt}$ = 940 Hz.

---

[*] Professor Dr. E. A. V. Ebsworth, Dr. T. A. Stephenson, Dr. M. D. Walkinshaw, D. M. Anderson
Department of Chemistry, University of Edinburgh
Edinburgh EH9 3JJ, Scotland

[**] We thank the Science Research Council for a research studentship (to *D. M. A.* and Johnson Matthey Ltd. for loans of potassium tetrachloroplatinate(II).

In contrast, refluxing *(2)* and *(3)* (1:1 molar ratio) in dry ethanol gives the *binuclear* complex $[\{Pt(S_2CNEt_2)(Ph_2PS)\}_2]$ which on the basis of detailed $^{31}P\{^1H\}$-NMR studies (Fig. 2) is assigned structure *(9)*. Related complexes of platinum(I) of type $[Pt(PR_3)R_2PS]_2$ have recently been synthesized from $[Pt(PPh_3)_4]$ either by reaction with *(3)*[5] or $[R_2PS]_2$[6].

A possible rationalization of the mode of formation of compounds *(7)*, *(8)* and *(9)*, involving oxidative addition of *(3)* to *(2)* and subsequent reductive elimination of $R_2NCS_2H$ (which readily decomposes to $R_2NH$ and $CS_2$[7]), is outlined in Scheme 1.

Finally, preliminary studies show that analogous complexes can be formed starting from *(2)* and $PF_2(S)H$ and also, as for compounds of type *(1)*, their thio-analogues *(7)* and *(8)* will react with both Lewis acids and transition metal ions.

Received: July 23rd 1980 [Z 712 IE]
German version: Angew. Chem. *93*, 289, 1981

---

[1] See *D. M. Roundhill, R. P. Sperline, W. B. Beaulieu*, Coordination Chem. Rev. *26*, 263 (1978) and references cited therein.

[2] *M. C. Cornock, R. O. Gould, C. L. Jones, T. A. Stephenson*, J. Chem. Soc. Dalton Trans., 1307 (1977).

[3] Spectroscopic data of some of the novel compounds *(7a)*: $^{31}P\{^1H\}$-NMR: $\delta=27.3$ (t, $^1J_{PtP}=3427.3$ Hz); $^1H$-NMR: $\delta=1.05$ (t), 1.52 (t), 3.43 (q), 7.0—8.0 (m), $^3J_{HH}=7.0$ Hz. *(8a)*, $^{31}P\{^1H\}$-NMR: $\delta=65.4$ (td, $^1J_{PtP}=3774.0$ Hz, $^2J_{PP}=28.0$ Hz), 31.2 (td, $^1J_{PtP}=3172.0$ Hz, $^2J_{PP}=28.0$ Hz).

[4] Space group $P2_12_12_1$; $a=21.098$ (18), $b=11.679$ (8), $c=14.816$ (18) Å, $Z=4$, $\varrho=1.546$ g cm$^{-3}$. The structure was refined to $R=0.064$ for 1480 independent reflections ($MoK_\alpha$) with $I>3\sigma(I)$. Pt, S and P atoms with anisotropic temperature factors. The phenyl rings were constrained to be planar with all C—C distances 1.395 Å.

[5] *B. Walther, B. Messbauer, H. Meyer*, Inorg. Chim. Acta *37*, L525 (1979).

[6] *K. P. Wagner, R. W. Hess, P. M. Treichel, J. C. Calabrese*, Inorg. Chem. *14*, 1121 (1975).

[7] *E. E. Reid:* Organic Chemistry of Bivalent Sulfur. Vol. IV. Chemical Publishing, New York, 1962, p. 209.

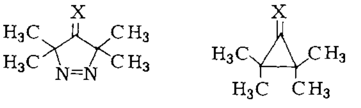
---

# Tetramethylcyclopropanone and Isopropylidene(dimethyl)thiirane *via* Photolysis of Reluctant 3,3,5,5-Tetramethyl-1-pyrazolines; Influence of Solvent and Temperature on the Competition between [3+2]- and [4+1]-Photocycloelimination[**]

By *Helmut Quast* and *Andreas Fuss*[*]

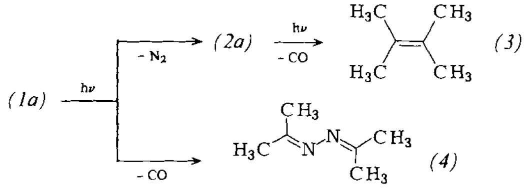
*Dedicated to Professor Alfred Roedig on the occasion of his 70th birthday*

Photolysis of 1-pyrazolines of type *(1)* having an exocyclic double bond at C-4, still holds many surprises[1]. For example, on photolysis of the pyrazolinimine *(1b)* we recently obtained cyclopropanimine *(2b)*, but only at 90 °C[2]. This unexpected temperature dependence of the $N_2$ photoextrusion from *(1b)* encouraged reinvestigation of the long-standing problem[3a] concerning the surprising thermal *and* photochemical reluctance of 1-pyrazolinone *(1a)* [$\Phi_{313}=0.012$ in benzene at 25 °C[3b]] to lose molecular nitrogen. Furthermore, in the case of the 1-pyrazolinethione *(1d)* photolysis at *low* temperature might provide an opportunity to generate the hitherto unknown cyclopropanethione *(2d)*. So far, the *thermal* generation of reactive $C_3H_4S$-species from other precursors has inevitably led to methylenethiiranes[4], which a should be about 30 kJ/mole more stable than cyclopropanethiones[4d].



*(1)* *(2)*

*(a)*, X = O
*(b)*, X = N–CH$_2$–C(CH$_3$)$_3$
*(c)*, X = N–NH$_2$
*(d)*, X = S
*(e)*, X = SO



In view of the low quantum yield of the 313 nm photolysis of *(1a)* and the fact that the n,π* absorptions of *(1a)*[1] and cyclopropanone[5] occur in the same spectral region, a selective irradiation of *(1a)*, without excitation of the cyclopropanone product, is difficult. Therefore, *(1a)* was irradiated using an intense light source *without* a filter[6a,b]. We obtained 2,3-dimethylbutene *(3)* and acetone azine *(4)* (Table 1), and, in [D$_3$] acetonitrile, also 1—3% of the pyrazolidinone *(6)* *via* photoreduction of *(1a)* ($^1$H-NMR, GC, IR).

Table 1. $^1$H-NMR determined conversion and relative product ratio *(3)*:*(4)* in the photolysis [6a, b] of 1-pyrazolinone *(1a)*.

| Solvent | *T* [°C] | *t* [min] | Conversion [%] | Ratio *(3)* : *(4)* |
|---|---|---|---|---|
| [D$_{12}$]Cyclohexane | 10 | 60 | 52 | 63 : 37 |
| | 90 | 30 | 67 | 57 : 43 |
| [D$_6$]Benzene | 10 | 60 | 37 | 78 : 22 |
| | 90 | 30 | 63 | 64 : 36 |
| [D$_3$]Acetonitrile | 10 | 60 | 27 | 83 : 17 |
| | 90 | 30 | 55 | 68 : 32 |

2,3-Dimethylbutene *(3)* could have been formed *via* photodecarbonylation of *(2a)*. In order to trap *(2a)*, *(1a)* was irradiated in [D$_4$]methanol[6a,c,d], and after 1—6 h at 5 °C (14—97% conversion) we obtained only 1% *(3)*, 4—5% *(4)*, and 6—11% of the expected secondary product *(5)* of *(2a)*; the major products were 30—37% *(6)*, 23—27% *(8)*, and 26—29% *(9)*. Since cyclopropanols, especially alkylated derivatives, are very readily cleaved by *homolysis*[7], *(5)* reacts with triplet-state benzophenone to afford 1,1,2,2-tetraphenyl-1,2-ethanediol and the esters *(8)* and *(9)* in virtually quantitative yield. The latter arise from disproportionation of the radical *(7)*[7a]. Therefore, formation of *(6)*, *(8)* and *(9)* in approximately equal amounts suggests the existence of a relatively long-lived excited state of *(1a)*, most probably $T_1$*(1a)*, which can abstract hydrogen from the photostable[7a] hemiacetal *(5)*. An interaction between azo and carbonyl orbitals, as deduced from the photoelectron spectrum of *(1a)*, has been invoked to account for the accelerated intersystem crossing $S_1$*(1a)*$\rightarrow$$T_1$*(1a)* and hence the reluctance of *(1a)*[1].

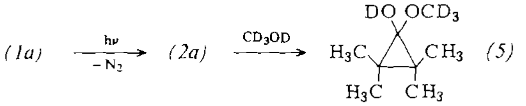
Table 1 shows the influence of solvent and temperature on the remarkable competition between the photoextrusion of $N_2$ and CO from *(1a)*. At 5 °C in methanol, the ratio of [3+2]- versus [4+1]-cycloelimination is (92±1):(8±1). Thus, loss of nitrogen is favored by polar solvents and lower temperatures.

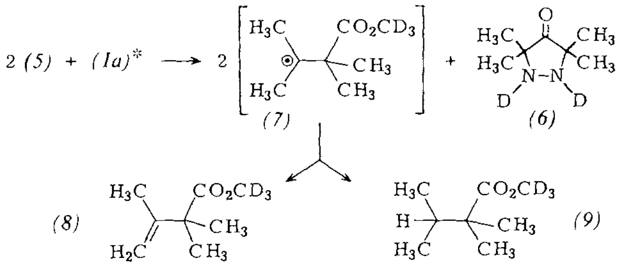
---

[*] Prof. Dr. H. Quast, Dipl.-Chem. A. Fuß
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

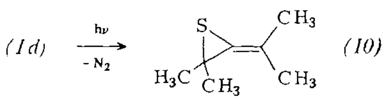
[**] Photochemical formation of methylenecyclopropane analogues. Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. The results are part of the prospective Dissertation of *A. F.* — Part 3: [2].

The much more efficient $[\Phi_{185}=0.63\pm0.05]$ 185 nm photolysis of *(1a)* in pentane yields only 29% *(3)* and 15% *(4)*, but 49% of 2,4-dimethylpenten-3-one, an isomer of *(2a)*[8]. After almost two decades, we have eventually succeeded in completing the final step of *Mock*'s elegant strategy for the generation of *(2a)*[3a].





The thione *(1d)* was prepared conveniently from dichlorodisulfane[9] and the hydrazone *(1c)*[10]. Both n,π* absorptions of the C=S- and N=N-chromophores of *(1d)* exhibit the expected low intensity [$\lambda_{max}$(log ε, in hexane): 234.5 (3.947), 302.5 (2.117), 342 (2.362), 529 (1.102)]. When *(1c)* was irradiated at 5 °C in [$D_{14}$]methylcyclohexane ($\lambda=350$ nm)[6a,c,e], up to 50% conversion, only one compound was formed in 74% yield (in benzene: 65% yield at 29% conversion). NMR spectra (in [$D_6$]benzene: $\delta_H=1.55$ (s, 2CH$_3$), 1.69 and 1.79 (q, $J=0.6$ Hz, CH$_3$); $\delta(^{13}C)=21.1$, 21.3 (CH$_3$), 28.3 (2CH$_3$), 46.5 (quart. C), 114.4, 130.9 (C=C)) and comparison with an authentic sample of *(10)*[4b] established the isopropylidenethiirane structure *(10)* as the photoproduct. On prolonged irradiation of *(1d)*, unidentified products emerged. In contrast to *(1a)* and *(1b)*[2], the photolysis temperature (−60 to +90 °C) had no significant influence. At −195 °C in [$D_{14}$]methylcyclohexane, however, *(1d)* was photostable. The photolysis of *(1d)* using light of wavelengths >330 nm produced a single product only up to 26% conversion. Moreover, on irradiation of 1-pyrazolinethione-*S*-oxides of type *(1e)* at 0 °C in benzene, the corresponding isopropylidenethiirane-*S*-oxides were obtained in 13—17% yields[11].



Received: June 10, 1980 [Z 711 IE]
Revised: February 11, 1981
German version: Angew. Chem. 93, 293 (1981)

---

[1] *P. S. Engel*, Chem. Rev. *80*, 99 (1980).

[2] *H. Quast, A. Fuß, A. Heublein*, Angew. Chem. 92, 55 (1980); Angew. Chem. Int. Ed. Engl. *19*, 49 (1980).

[3] a) *W. L. Mock, Ph. D. Thesis*, Harvard University 1964; b) *P. S. Engel, L. Chen*, Can. J. Chem. *52*, 4040 (1974). CO and $N_2$ were obtained in a 3 : 1 ratio as photolysis products of *(1a)*.

[4] a) *W. J. Middleton*, J. Org. Chem. *34*, 3201 (1969); b) *A. G. Hortmann, A. Bhattacharjya*, J. Am. Chem. Soc. *98*, 7081 (1976); c) *E. Jongejan, T. S. V. Buys, H. Steinberg, T. J. de Boer*, Rec. Trav. Chim. Pays-Bas *97*, 214 (1978); d) *E. Block, R. E. Penn, M. D. Ennis, T. A. Owens, S.-L. Yu*, J. Am. Chem. Soc. *100*, 7436 (1978).

[5] *H. J. Rodriguez, J.-C. Chang, T. F. Thomas*, J. Am. Chem. Soc. *98*, 2027 (1976).

[6] a) 14 mg *(1a)* and 12 mg *(1d)*, respectively, in 0.5 ml solvent were irradiated in Pyrex-NMR-tubes, which had been carefully degassed and sealed at $10^{-5}$ torr. b) The sample was placed at one focal point of the elliptical rhodium-coated mirror of a PRA light source type ALH 220. At the second focal point a 1000 W Hg/Xe high pressure lamp Canrad Hanovia 977B0010 was positioned. c) Focussed 500 W Hg high pressure lamp Osram HBO 500 W/2, quartz optics. d) Filter WG 335 (Schott und Genossen, Mainz). e) Filter UG 1 (Schott und Genossen, Mainz).

[7] a) *C. H. DePuy, H. L. Jones, W. M. Moore*, J. Am. Chem. Soc. *95*, 477 (1973); b) *B. H. Bakker, T. Reints Bok, H. Steinberg, T. J. de Boer*, Rec. Trav. Chim. Pays-Bas *96*, 31 (1977).

[8] *W. Adam, A. Fuss, F. Mazenod, H. Quast*, J. Am. Chem. Soc. *103*, 998 (1981).

[9] Method: *R. Okazaki, K. Inoue, N. Inamoto*, Tetrahedron Lett. *1979*, 3673.

[10] *R. J. Bushby, M. D. Pollard*, J. Chem. Soc. Perkin Trans. 1 *1979*, 2401.

[11] *E. Schaumann, H. Behr, G. Adiwidjaja, A. Tangerman, B. H. M. Lammerink, B. Zwanenburg*, Tetrahedron, *37*, 219 (1981).

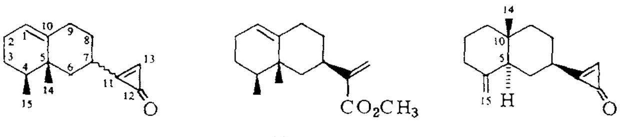
---

## Naturally Occurring Cyclopropenone Derivatives[**]

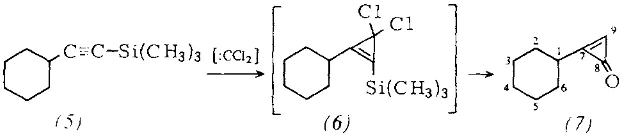
By *Ferdinand Bohlmann, Jasmin Jakupovic, Lutz Müller,* and *Angelika Schuster*[*]

*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

The overground part of *Telekia speciosa* (Schreb.) Baumg. (Compositae, Tribus Innulae) contains, besides numerous sesquiterpene derivatives[1], two difficultly separable, relatively polar compounds of empirical formula $C_{15}H_{20}O$ which, according to the IR spectrum, however, are not alcohols. The main component reacts with methanol in the presence of 4-pyrrolidinopyridine[2] to give the well known methyl ester *(3)*[3]. IR ($\nu$=1840 and 1588 cm$^{-1}$) and $^1$H-NMR spectroscopic data ($\delta$=8.46, d, $J$=1.5 Hz) indicate presence of the cyclopropenone derivative *(1)*. The $^1$H-NMR signals of *(1)* can be completely assigned by spin-decoupling. The $^{13}$C-NMR spectrum is also consistent with structure *(1)*.



*(1)*, 7α-H *(2)*, 7β-H *(3)* *(4)*



Since no data were available for monosubstituted cyclopropenones, we prepared cyclohexylpropenone *(7)* by addition of dichlorocarbene to *(5)*. The dichloro compound *(6)* probably occurring as an intermediate hydrolyzes even during work-up, giving moderate yields of *(7)*, whose $^1$H- and $^{13}$C-NMR spectroscopic data correspond very well with those of the natural product (Table 1). The stereochemistry at 7-H in *(1)* follows from the coupling constants and the stereochemistry of *(3)*. Noteworthy is the extreme downfield shift of the $^{13}$C-NMR signals of C-11 in the case of *(1)* and of C-7 in the case of *(7)*, which may be due, *inter alia*, to the dis-

---

[*] Prof. Dr. F. Bohlmann [+], Dr. J. Jakupovic, Dipl.-Chem. L. Müller, A. Schuster
Institut für Organische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)
[+] Author to whom correspondence should be addressed.

[**] Naturally Occurring Terpene Derivatives, Part 353.—Part 352: *A. Rustaiyan, C. Zdero,* and *F. Bohlmann*, Phytochemistry *20* (1981), in press.

symmetry of the compounds. In disubstituted compounds it is not so extreme[4]. The $^1$H-NMR signals[5] for the cyclopropene protons, like those of the IR bands[6], correspond to the data of well-known compounds (Table 1).

Table 1. $^1$H-NMR data of *(1)*, *(2)*, *(4)*, and *(7)* ($CDCl_3$, 400 MHz, TMS as internal standard), $^{13}$C-NMR data of *(1)* and *(7)* (in $CDCl_3$), and further physical data of *(1)*, *(2)* and *(4)*.

| | $^1$H-NMR ($\delta$ values) [a] | | | |
|---|---|---|---|---|
| | *(1)* | *(2)* | *(4)* | *(7)* |
| 1-H | 5.39 ddd | 5.35 d (br) | | 2.79 dddd |
| 2α-H | 2.01 m | 2.2 m | 1.65—1.35 m | 1.98 m |
| 2β-H | 1.95 m | 1.95 m | | 1.73 m |
| 3-H | 1.41 m | 1.65—1.5 m | 2.1—1.9 m | 1.65—1.35 m |
| 4-H | | | | |
| 5-H | — | — | 2.34 d (br) | |
| 6α-H | 1.56 dd | 1.58 dd | 1.62 m | 1.98 m |
| 6β-H | 2.34 ddd | 2.10 ddd | | 1.73 m |
| 7-H | 3.05 ddddd | 2.98 dddd | 2.78 dddd | — |
| 8α-H | 1.70 dddd | 1.41 dddd | 1.62 m | — |
| 8β-H | 2.20 ddddd | 1.79 d (br) | 2.0 m | — |
| 9α-H | 2.07 d (br) | 2.33 d (br) | 1.62 m | 8.38 s |
| 9β-H | 2.38 ddddd | 2.2 m | | |
| 13-H | 8.46 d | 8.39 s | 8.40 s | — |
| 14-H | 0.88 s | 0.95 s | 0.78 s | — |
| 15-H | 0.89 s | 0.84 d | 4.76 ddd<br>4.44 ddd | — |

| $^{13}$C-NMR ($\delta$ values) | | | | | | | |
|---|---|---|---|---|---|---|---|
| *(1)* | | | | *(7)* | | | |
| C-1 | 122.0 | C-7 | 41.1 | C-1 | 36.7 | C-7 | 173.0 |
| C-2 | 29.1 | C-8 | 29.2 | C-2,6 | 29.3 | C-8 | 159.0 |
| C-3 | 26.6 | C-9 | 25.5 | C-3,5 | 24.8 | C-9 | 146.7 |
| C-4 | 34.0 | C-10 | 144.5 | C-4 | 25.6 | | |
| C-5 | 37.7 | C-11 | 174.9 | | | | |
| C-6 | 41.1 | C-12 | 158.4 | | | | |
| | | C-13 | 147.4 | | | | |
| | | C-14 | 15.4 | | | | |
| | | C-15 | 19.5 | | | | |

Miscellaneous data

*(1)*, IR ($CCl_4$): $\nu = 1840, 1588\ cm^{-1}$ (cyclopropenone); MS: $m/e = 216.151$ ($M^+$, 14%), 201 ($M - {}^{\cdot}CH_3$, 13), 188 ($M - CO$, 13), 173 ($201 - CO$, 45), 131 ($173 - CH_3CH{=}CH_2$, 69, RDA [b]), 91 ($C_7H_7^+$, 100); $[\alpha]^{24} = -78$ ($\lambda = 589$ nm), $-81$ (578), $-93$ (546), $-161$ (436) ($c = 0.65$, $CHCl_3$)

*(2)*, IR ($CCl_4$): $\nu = 1830, 1585\ cm^{-1}$ (cyclopropenone); MS: $m/e = 216.151$ ($M^+$, 12%)

*(4)*, IR ($CCl_4$): $\nu = 1835, 1600\ cm^{-1}$; MS: $m/e = 216.151$ ($M^+$, 3%), 201 (11), 188 (21), 173 (45), 91 (100); $[\alpha]^{24} = +22$ ($\lambda = 589$ nm), $+24$ (578), $+25$ (546), $+34$ (436) ($c = 0.1$, $CHCl_3$)

[a] Coupling constants *J* [Hz]: *(1)*: 1,2α = 1,9 = 2; 1,2β = 5; 2,9 = 2; 4,15 = 6.2; 6α,6β = 14; 6α,7 = 6; 6β,7 = 2.5; 6β,8β = 2.5; 7,8α = 4.5; 7,8β = 8β,9α = 8β,9β = 2.4; 7,13 = 1.5; 8α,9α = 4.5; 8α,9β = 8α,8β = 13; 9α,9β = 14; *(2)*: 1,2 = 5; 4,15 = 6.5; 6α,6β = 13.5; 6α,7 = 11; 6β,7 = 3.5; 6β,8β = 2; 7,8α = 13; 7,8β ≈ 1; 8α,8β = 8α,9β = 13; 8α,9α = 4; 9α,9β = 15; *(4)*: 3,15 = 5,15 = 15,15′ ≈ 1,5; 5,6β = 12.5; 6α,7 = 7,8α = 4; 6β,7 = 7,8β = 12.5; *(7)*: 1,2α = 1,6α = 3.5; 1,2β = 1,6β = 9.5. [b] RDA = Retro-Diels-Alder cleavage.

According to the $^1$H-NMR data (Table 1) the second component is undoubtedly the eudesmane derivative *(4)*. Although, only few signals are interpretable by 1st order rules the spectrum is, nevertheless, very similar to that of the corresponding eudesmane. The allyic coupling for 13-H is missing; however, the chemical shift of 13-H is almost the same as that in the case of *(1)*.

We have also isolated *(1)* from *Lychnophora passerina* Gardn. (Compositae, Tribus Vernonieae), as well as an isomeric cyclopropenone which may have the structure *(2)*. The altered couplings for 7-H show that the cyclopropenone moiety in *(2)* must be arranged equatorially. The $^1$H-NMR data of *(2)* (Table 1) are similar to those of *(1)*. Only the chemical shifts of 6-H and 8-H are somewhat different from those of *(1)*, since the deshielding effects operate differently owing to the changed stereochemistry, as can be deduced from Dreiding models. *(1)*, *(2)* and *(4)*, are the first naturally occurring cyclopropenone derivatives.

*Experimental*

The overground parts of the plants were extracted with ether/petroleum ether and the extracts worked up by column chromatography and by TLC ($SiO_2$). 1.5 kg of overground parts of *Telekia speciosa* gave 25 mg of *(1)* and 3 mg of *(4)* [TLC: ether/petroleum ether (1:1)], 650 g of overground parts of *Lychnophora passerina* gave 10 mg of *(1)* and 6 mg of *(2)*, while 8 mg of *(1)* and 6 mg of *(2)* were isolated from 100 g of roots. *(1)* and *(2)* are colorless oils.

*(7)*: To a solution of 100 mg of *(5)* (prepared by reaction of 1,1-dibromo-2-cyclohexylethylene with *n*-butyllithium at −78 °C and subsequent treatment with chlorotrimethylsilane) in 5 $cm^3$ $CHCl_3$ is added 15 mg of benzyl(triethyl)ammonium chloride and the stirred mixture treated dropwise at 20 °C with 5 $cm^3$ 50% NaOH solution. After 2 h the mixture is poured into 100 $cm^3$ of $H_2O$, taken up in ether, and the residue obtained on evaporation purified by TLC (ether); yield: 60 mg *(5)* and 8 mg *(7)*.

Received: November 28, 1980 [Z 710 IE]
German version: Angew. Chem. 93, 280 (1981)

---

[1] *F. Bohlmann, J. Jakupovic, A. Schuster*, Phytochemistry *20* (1981), in press.
[2] *G. Höfle, W. Steglich*, Synthesis *1972*, 619.
[3] *F. Bohlmann, C. Zdero, M. Silva*, Phytochemistry *16*, 1302 (1977).
[4] *E. V. Dehmlow, R. Zeisberg, S. S. Dehmlow*, Org. Magn. Reson. *7*, 418 (1975).
[5] *P. Crabbé, H. Carpio, E. Velarde, J. H. Fried*, J. Org. Chem. *38*, 1478 (1973).
[6] *R. Breslow, L. J. Altman*, J. Am. Chem. Soc. *88*, 504 (1966).

---

## Biosynthesis of Natural Porphyrins: Studies with Isomeric Hydroxymethylbilanes on the Specificity and Action of Cosynthetase[**]

By *Alan R. Battersby*, *Christopher J. R. Fookes*, *George W. J. Matcham* and *Pramod S. Pandey*[*]

*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

Uroporphyrinogen-III *(4)* is the precursor of the natural porphyrins, chlorins and corrins and its biosynthesis from porphobilinogen *(1)* requires the enzymes deaminase and cosynthetase[1]. The biosynthesis involves the building of an unrearranged tetrapyrrole, the bilane derivative[3,4] *(2)*, followed by a single *intramolecular* rearrangement[2,3]. An enzymic replacement of the amino function of *(2)*, $X = \overset{+}{N}H_3$ and of *(1)* by another nucleophile [shown as X in *(2)*] before the final cyclization with rearrangement is discussed *e.g.* in[3]. With deaminase acting alone on porphobilinogen *(1)*, the product released is the unrearranged hydroxymethylbilane[5,6,7] *(3)*. Natural and synthetic[5] *(3)* were identical substrates for cosynthetase and the product was uroporphyrinogen-III *(4)*.

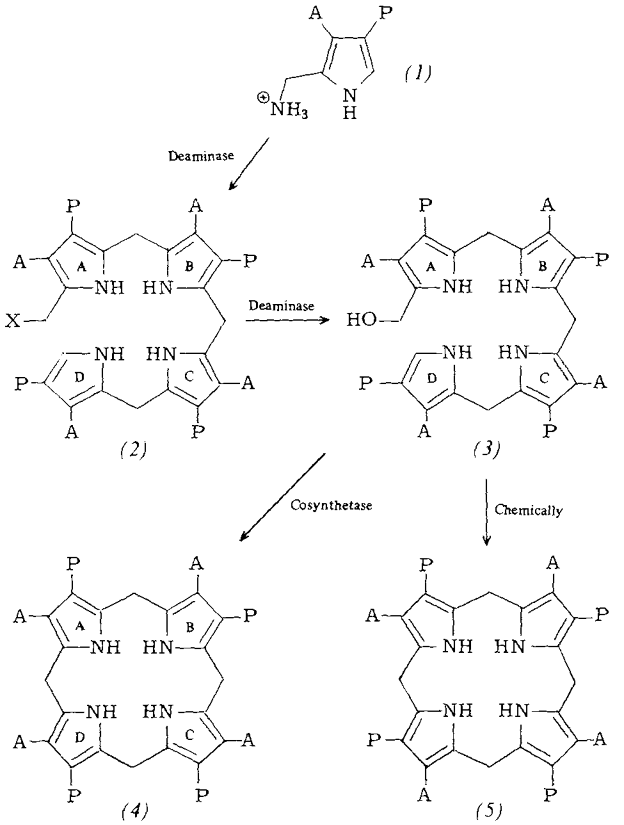
The foregoing knowledge and synthetic methodology made it possible to probe the action of cosynthetase by syn-

---

[*] Prof. Dr. A. R. Battersby, Dr. C. J. R. Fookes, Dr. G. W. J. Matcham, Dr. P. S. Pandey
University Chemical Laboratory
Lensfield Road, Cambridge, CB2 1EW (England)

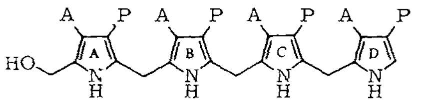
[**] This work was supported by the Science Research Council and by Roche Products Ltd.

thesizing hydroxymethylbilanes, which are isomeric with the natural substrate. Four bilanes were constructed: the reversed ring-B *(6)*, reversed ring-C *(7)*, reversed ring-D *(8)* and *(9)*, in which rings A, B and C have been reversed relative to the natural, unrearranged hydroxymethylbilane *(3)*. Similar synthetic routes were used for all four and the approach for the reversed ring-D bilane *(8)* is illustrated. The five formyl bilane esters as *(10)*, were shown to be isomerically pure by HPLC and were characterized by mass spectrometry and NMR.



Uroporphyrinogen-III Uroporphyrinogen-I

A = $CH_2CO_2H$, P = $CH_2CH_2CO_2H$



A P P A A P A P *(6)*

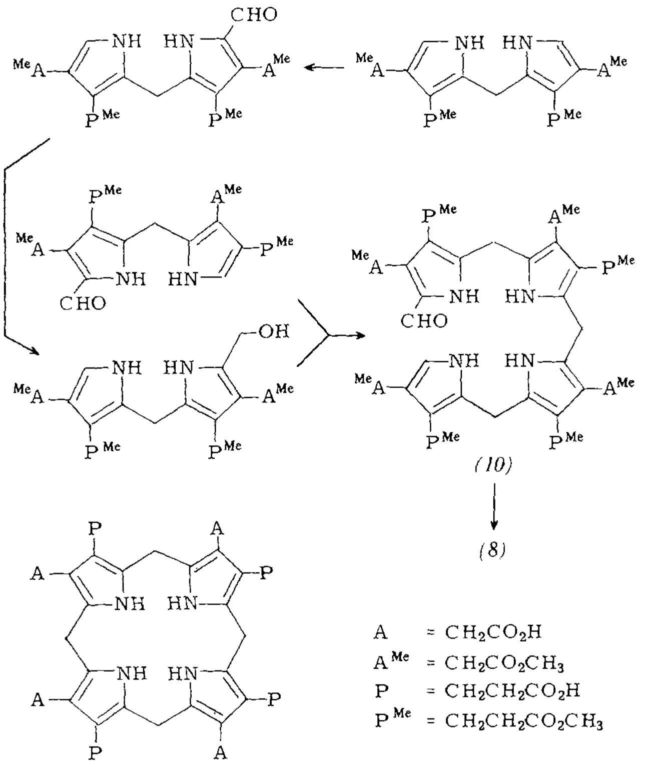
A P A P P A A P *(7)*

A P A P A P P A *(8)*

P A P A P A A P *(9)*

The freshly prepared, derived bilanes *(3)* and *(6)*—*(9)* were then incubated separately (pH = 8.25) with cosynthetase, free from deaminase, which had been isolated from *Euglena gracilis;* non-enzymic ("chemical") ring-closure of each bilane was carried out at the same pH. The unrearranged hydroxymethylbilane *(3)* was included in the set of experiments as a standard.

It was found that the natural unrearranged hydroxymethylbilane *(3)* was by far the best substrate for cosynthetase but interestingly, the cyclizations of reversed-C *(7)* and reversed-D *(8)* bilanes were also enzymically accelerated. In contrast, the reversed-B *(6)* and reversed A, B, C *(9)* bilanes did not



Uroporphyrinogen-IV

A = $CH_2CO_2H$

$A^{Me}$ = $CH_2CO_2CH_3$

P = $CH_2CH_2CO_2H$

$P^{Me}$ = $CH_2CH_2CO_2CH_3$

Table 1. Ring-closure of hydroxymethylbilane *(3)* and isomers *(6)*—*(9)* chemically and by cosynthetase. Products: uroporphyrinogen-I [≡*(5)*]; uroporphyrinogen-III [≡*(4)*]; uroporphyrinogen-IV [≡*(11)*].

| Substrate | $V_{max}$ (rel.) | $K_m$/μM | Uroporphyrinogen isomers yields [%] [a]<br>Chemically<br>I | <br><br>III | <br><br>IV | <br>Enzymically<br>I | <br><br>III | <br><br>IV |
|---|---|---|---|---|---|---|---|---|
| Unrearranged bilane *(3)* [5] | 100 | 11.3 | 100 | — | — | 8 | 92 | — |
| Reversed ring-B *(6)* | <0.5 | — | — | 98 | — | — | 96 | — |
| Reversed ring-C *(7)* | 5 | 105 | — | 99 | — | — | 49 | 51 |
| Reversed ring-D *(8)* | 13 | 11.4 | — | 97 | — | 35 | 64 | — |
| Reversed rings A B C *(9)* | <0.5 | — | — | 98 | — | — | 98 | — |

[a] Yields of uroporphyrinogen-II and of isomers marked with a dash amounted to <3%.

act as substrates (see Table 1). The products from the action of cosynthetase on bilanes *(3)*, *(7)* and *(8)*, and also from chemical ring-closure at pH 8.25, were analyzed by HPLC[5]. The results (see Table 1) showed in each case that chemical ring-closure occurred with essentially no rearrangement. Importantly, *ca.* one third of the enzymic product from the reversed ring-D bilane *(8)* was uroporphyrinogen-I *(5)* arising from enzymic inversion of the terminal ring-D. Knowing the isomeric composition of the product and also the chemical and enzymic rates of ring-closure, it can be calculated that *ca.* 45% of bilane *(8)*, ring-closed by cosynthetase, undergoes ring-D reversal to produce uroporphyrinogen-I *(5)*. Although the reversed ring-C bilane *(7)* is a relatively poor substrate for cosynthetase, similar calculations show that in this case, the ring-closure promoted by cosynthetase, nevertheless, occurs with efficient formation (>95%) of uroporphyrinogen-IV *(11)*, presumably from inversion of the terminal ring[8].

These results interlock with those obtained earlier[9], in which deaminase and cosynthetase acted together on members of a set of isomeric aminomethylbilanes (*2*, $X{=}\overset{+}{N}H_3$ and isomers). Interpretation of these early experiments was complicated by the fact that two enzymic steps were involved; thus, conversion of any of the aminomethyl into hydroxymethyl bilanes by deaminase[4] would enhance the rate of uroporphyrinogen formation, even when cosynthetase is not involved, as is the case for the reversed ring-B bilane *(6)*. The present work focuses attention on cosynthetase alone and shows the following: (a) Cosynthetase is not an absolutely specific enzyme, but all the studied modifications of pyrrole rings produced a substantial adverse effect on affinity, rate of reaction and/or efficiency of the inversion process. (b) Cosynthetase has evolved to invert the terminal ring during ring-closure of the natural hydroxymethylbilane *(3)* and will do a similar inversion when an isomeric hydroxymethylbilane acts as a substrate *e.g.* it does so efficiently (but slowly) with bilane *(7)* as substrate. (c) Cosynthetase will even partially turn back the terminal ring of bilane *(8)* in which ring-D had already been inverted by synthesis. This result excludes the possibility that formation of uroporphyrinogen-III *(4)* from the regular hydroxymethylbilane *(3)* involves rearrangement of *(3)* into *(8)* as a first step.

Received: December 1, 1980 [Z 708 IE]
German version: Angew. Chem. 93, 290 (1981)

---

[1] Review: *A. R. Battersby, E. McDonald*, in *K. M. Smith:* Porphyrins and Metalloporphyrins, Elsevier, Amsterdam, 1975, p. 61.

[2] *A. R. Battersby, G. L. Hodgson, E. Hunt, E. McDonald & J. Saunders*, J. Chem. Soc. Perkin Trans. I, *1976*, 273.

[3] *A. R. Battersby, E. McDonald, D. C. Williams, H. K. W. Wurziger*, J. Chem. Soc. Chem. Commun. *1977*, 113; *A. R. Battersby, C. J. R. Fookes, E. McDonald, M. J. Meegan, ibid. 1978*, 185; *H.-O. Dauner, G. Gunzer, I. Heger, G. Müller*, Z. Physiol. Chem., *357*, 147 (1976).

[4] *A. R. Battersby, C. J. R. Fookes, G. W. J. Matcham, E. McDonald*, J. Chem. Soc. Chem. Commun. *1979*, 539; *P. Jordan & J. S. Seehra*, FEBS Lett. *104*, 364 (1979).

[5] *A. R. Battersby, C. J. R. Fookes, G. W. J. Matcham, E. McDonald & K. E. Gustafson-Potter*, J. Chem. Soc. Chem. Commun. *1979*, 316; *A. R. Battersby, C. J. R. Fookes, K. E. Gustafson-Potter, G. W. J. Matcham, E. McDonald, ibid. 1979*, 1155.

[6] *A. R. Battersby, R. G. Brereton, C. J. R. Fookes, E. McDonald, G. W. J. Matcham*, J. Chem. Soc. Chem. Commun. *1980*, 1124.

[7] The intermediate released by deaminase was also observed independently in Texas and the natural material was shown to be a substrate for cosynthetase (see *G. Burton, P. E. Fagerness, S. Hosozawa, P. M. Jordan, A. I. Scott*, J. Chem. Soc. Chem. Commun. *1979*, 202) but it was wrongly concluded that its structure is an *N*-alkylpyrrole macrocyclic system (see *G. Burton, H. Nordlöv, S. Hosozawa, H. Matsumoto, P. M. Jordan, P. E. Fagerness, L. M. Pryde, A. I. Scott*, J. Am. Chem. Soc. *101*, 3114 (1979).

[8] In principle, uroporphyrinogen-IV could also be formed from bilane *(7)* by inversion of ring-B but the sum of evidence points to this being highly unlikely.

[9] *A. R. Battersby, C. J. R. Fookes, G. W. J. Matcham, E. McDonald*, J. Chem. Soc. Chem. Commun. *1978*, 1064.

---

## "Chemical Mutation" by Amino Acid Exchange in the Reactive Site of a Proteinase Inhibitor and Alteration of Its Inhibitor Specifity[**]

By *Herbert R. Wenzel* and *Harald Tschesche*[*]

*Dedicated to Professor Gerhard Pfleiderer on the occasion of his 60th birthday*

Low-molecular weight protein proteinase inhibitors inhibit serine-proteinases by reversible, substrate-analogous association at the active center of the enzyme[2]. The specificity of an inhibitor is determined by the geometry of the amino acid residues at the contact surface and in most cases dominated by the amino acid $P_1$[3a,3b] in its reactive center. This is supported by comparison of the sequences of homologous inhibitors[4a] and in two cases by semisynthetic amino acid replacements[4b]: thus, by enzymatic reactions $P_1 = Arg$ could be replaced by Lys in the soybean inhibitor (Kunitz) and $P_1 = Lys$ by Arg in the inhibitor from bovine organs. The anti-tryptic activity of both proteins was preserved. Replacement of the basic amino acids by Trp converted the two inhibitors with primary specificity against trypsin into inhibitors with primary specificity against chymotrypsin. The "enzymatic mutation" has so far only been used with success in the case of basic and aromatic amino acids, since no suitable enzyme system could be found for other amino acids.

We describe here a method which enables insertion of almost every amino acid in the position $P_1$ of the inhibitor (Kunitz) from bovine organs by a peptide-chemical method. The natural inhibitor ($P_1 = Lys^{15}$) inhibits trypsin extremely strongly, chymotrypsin strongly, leukocytic elastase scarcely, and pancreatic elastase not at all. (A projection of the α-carbon atoms of the inhibitor is shown in[5].)

The $Lys^{15}$—$Ala^{16}$ peptide bond in the reactive site of the native inhibitor is hydrolyzed according to previously described methods; with carboxypeptidase B one then obtains the inactive modified des-$Lys^{15}$ inhibitor[6]. Water-soluble carbodiimides enable coupling of Val—OMe with the free carboxyl group of $Cys^{14}$[7] (Scheme 1).

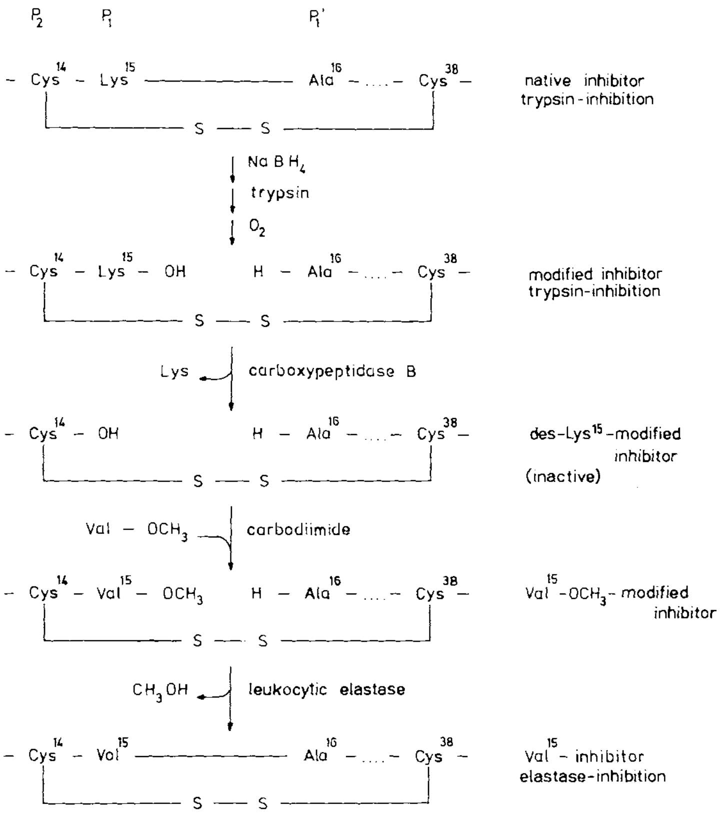
The product is an excellent inhibitor for elastase from human leukocytes. The maximum inhibition is only reached after several minutes; obviously the complex between elastase and $Val^{15}$-inhibitor is formed relatively slowly. If this complex is dissociated by drastic lowering of the pH (kinetically controlled dissociation), an inhibitor is obtained which immediately inhibits elastase to the maximum. This finding suggests resynthesis of the peptide bond $Val^{15}$—$Ala^{16}$ by the proteinase during the complex formation[8].

The semisynthesis has so far also been carried out according to the same procedure with the methyl esters of Arg, Phe, Met, Leu, Ala and Gly. According to the amino-acid analysis of the crude material about 2.2 to 4.1 amino acids were inserted per inhibitor molecule, up to 0.3 thereof in the decisive position $P_1$, *i.e.* 30% yield. The other part was coupled to the five carboxy groups ($Asp^3$, $Glu^7$, $Glu^{49}$, $Asp^{50}$, $Ala^{58}$) already present in the unmodified inhibitor. These are so far removed from the reactive site, that their derivatization has hardly any influence on the inhibitor activity.

---

[*] Prof. Dr. H. Tschesche, Dr. H. R. Wenzel
Fakultät für Chemie, Lehrstuhl Biochemie der Universität
Postfach 8640, 4800 Bielefeld 1 (Germany)

[**] Delivered in part in a lecture at the Spring Conference of the Gesellschaft für Biologische Chemie, Münster, March 1980 [1]. This work was supported by the Deutsche Forschungsgemeinschaft, the Stiftung Volkswagenwerk, and the Fonds der Chemischen Industrie. We thank Bayer AG for supplying us with Trasylol® [Trypsin-Kallikrein® inhibitor (Kunitz) from bovine lung].



Scheme 1. Replacement of Lys$^{15}$ by Val in the position P$_1$ of the inhibitor (Kunitz) from bovine organs.

The inhibitor specificity of the new semisynthetic inhibitors can be largely predicted from the residue P$_1$ and from the known cleavage specificity of the individual proteinases: The insertion of Arg restores the original anti-tryptic activity. Introduction of Phe or Met leads to strong chymotrypsin inhibitors which also still weakly inhibit trypsin. Moreover the Met$^{15}$ inhibitor also weakly inhibits the elastases from porcine pancreas and human leukocytes. A strong inhibitor against both elastases and chymotrypsin is obtained by insertion of Leu, trypsin is then only weakly inhibited. The Val$^{15}$-inhibitor appears to be more specific; it shows strong activity against human leukocyte-elastase and weak activity against trypsin, chymotrypsin, and porcine pancreas-elastase. All four enzymes are only weakly inhibited by the Ala$^{15}$ inhibitor. Surprisingly the Gly$^{15}$ inhibitor shows no elastase-, but good chymotrypsin-, and excellent trypsin-inhibition.

The peptide-chemical method represents an important extension to the methods for the semisynthesis of proteinase inhibitors, and allows further detailed investigation of the relationship between sequence and reactivity of these proteins.

### *Procedure*

A solution of 100 mg of modified des-Lys$^{15}$ inhibitor (Kunitz) from bovine organs[6], 20 mmol amino acid methyl ester hydrochloride, 200 mg *N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride, and 400 mg *N*-cyclohexyl-*N'*-(2-morpholinoethyl)carbodiimide-methyl *p*-toluenesulfonate in 20 cm$^3$ water is allowed to react with stirring in an autotitrator at constant pH = 4.75 (addition of 0.5 M HCl)[7]. After cessation of reaction the inhibitor is separated by gel filtration on Sephadex G-25 fine (eluting reagent 0.1 M acetic acid) from low-molecular substances and high-molecular protein aggregates.

Received: September 25, 1980 [Z 709 IE]
German version: Angew. Chem. 93, 292 (1981)

---

[1] *H. R. Wenzel, H. Tschesche*, Hoppe-Seylers Z. Physiol. Chem. *361*, 345 (1980).
[2] a) *M. Laskowski, Jr., R. W. Sealock* in *P. D. Boyer*: The Enzymes. Vol. III, Academic Press, New York 1971, p. 375; b) *H. Tschesche*, Angew. Chem. *86*, 21 (1974); Angew. Chem. Int. Ed. Engl. *13*, 10 (1974).
[3] a) *I. Schechter, A. Berger*, Biochem. Biophys. Res. Commun. *27*, 157 (1967); b) *M. Laskowski, Jr.*, Biochem. Pharmacol. *29* (1980).
[4] a) *M. Laskowski, Jr., I. Kato*, Annu. Rev. Biochem. *49*, 593 (1980); b) *R. W. Sealock, M. Laskowski, Jr.*, Biochemistry *8*, 3703 (1969); *H. Jering, H. Tschesche*, Eur. J. Biochem. *61*, 453 (1976).
[5] *R. Huber, D. Kukla, A. Rühlmann, O. Epp, H. Formanek*, Naturwissenschaften *57*, 389 (1970).
[6] *H. Jering, H. Tschesche*, Eur. J. Biochem. *61*, 443 (1976).
[7] *G. E. Means, R. E. Feeney*: Chemical Modification of Proteins. Holden-Day, San Francisco 1971.
[8] *U. Quast, J. Engel, E. Steffen, H. Tschesche, S. Kupfer*, Biochemistry *17*, 1675 (1978).

---

## Novel 4-Amino-2-azabutadienes and 1-Aminobutadienes; Syntheses of Pyridines, Benzenes, and Azoles[**]

By *Rudolf Gompper* and *Ulrich Heinemann*[*]

2-Aza-1,3-butadienes have been prepared for a variety of purposes during the past ten years; only very few 1-amino-[1] and 1-alkoxy-2-azabutadienes[2] have so far been used for the preparation of pyridines by Diels-Alder reactions. On the other hand, numerous interesting [4+2]-cycloadditions of donor-substituted 1,3-dienes are known (cf. [3]). Further methods for the preparation of donor-substituted 2-azabutadienes would therefore seem desirable.

In connection with our studies on the reactions of 1-acceptor-substituted vinamidinium salts[4] we have found that the azomethines *(1)*[5] can be converted into 4-amino-2-azabutadienes *(2)* by heating with dimethylformamide diethylacetal (Tables 1 and 2).

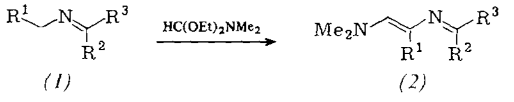


Table 1. Synthesized 4-amino-2-azabutadienes *(2)*.

| *(2)* | R$^1$ | R$^2$ | R$^3$ | Yield [%] | M.p. [°C] |
|---|---|---|---|---|---|
| *a* | $CO_2Me$ | H | $C_6H_5$ | 83 | 99—100 |
| *b* | $CO_2Me$ | H | $p$-$ClC_6H_4$ | 70 | 112—114 |
| *c* | $CO_2Me$ | H | $p$-$MeC_6H_4$ | 82 | 86—88 |
| *d* | $CO_2Me$ | H | $p$-$Me_2NC_6H_4$ | 58 | 138—139 |
| *e* | CN | H | $C_6H_5$ | 35 | 120—121 |
| *f* | $CO_2Me$ | SMe | SMe | 87 | 75 |
| *g* [a] | $CO_2Me$ | H | $NMe_2$ | 47 | [b] |

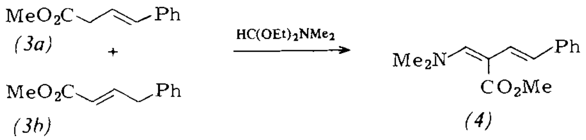
[a] *(2g)* could only be obtained with $[Me_2NCHCl]^+Cl^-$ in presence of $NEt_3$ [8].
[b] B.p. 140 °C/10$^{-2}$ mbar (Kugelrohr).

By the same method a mixture of the esters *(3a)* and *(3b)*[6] affords the 1-aminobutadiene *(4)*. Preliminary experiments

---

[*] Prof. Dr. R. Gompper, Dr. U. Heinemann
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.



have also shown that other orthocarboxylic acids and orthocarboxylic acid derivatives as well as carbenium salts derived therefrom can be condensed with *(1)* and related compounds.

The novel 4-amino-2-azabutadienes *(2)* and the aminobutadiene *(4)* are suitable as starting materials for the preparation of heteroarenes and arenes, respectively. On reaction with acetylenedicarboxylate, *(2a, b, c)* afford the 6-aryl-2,4,5-pyridinetricarboxylates *(5a, b, c)*, while *(4)* affords the 2,3,5-biphenyltricarboxylate *(6)*, which on treatment with conc. sulfuric acid furnishes the anhydride *(7)* (Table 2).

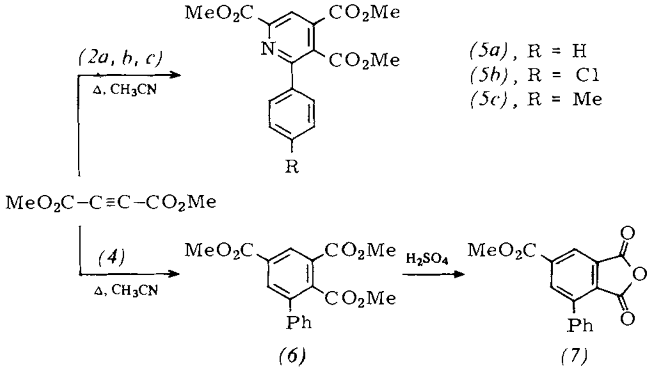


Table 2. Some data of the compounds of type *(2)* and *(4)* to *(10)*.

*(2a)*: IR (KBr): 1672, 1625 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 3.31$ (s, 6 H, $N(CH_3)_2$), 3.71 (s, 3 H, $OCH_3$), 7.19 (mc, 4 H, H-4 and aromatic H), 7.65 (mc, 2 H, aromat. H), 9.07 (s, 1 H, H-1); UV/VIS ($CH_2Cl_2$): $\lambda_{max}$ (lg $\varepsilon$) = 241 (4.1), 300 (4.2), 358 (4.3)

*(2f)*: IR (KBr): 1683, 1608 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 2.48$ (s, 6 H, $SCH_3$), 2.93 (s, 6 H, $N(CH_3)_2$), 3.66 (s, 3 H, $OCH_3$), 6.89 (s, 1 H, H-4)

*(2g)*: IR (Film): 1685, 1620—1640 $cm^{-1}$; UV ($CH_2Cl_2$): $\lambda_{max}$ (lg $\varepsilon$) = 321 (4.2)

*(4)*: yield 71%; b.p. = 250 °C/$10^{-2}$ mbar (kugelrohr); IR (film): 1685, 1590 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 3.03$ (s, 6 H, $N(CH_3)_2$), 3.73 (s, 3 H, $OCH_3$), 6.70 (d, 1 H, $J = 15$ Hz), 7.01—7.57 (m, 7 H)

*(5a)*: yield 41%; m.p. = 127—128 °C; IR (KBr): 1738 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 4.00$ (s, 3 H, $OCH_3$), 4.02 (s, 6 H, $OCH_3$), 7.56 (mc, 3 H), 8.12 (mc, 2 H), 8.41 (s, 1 H, pyridine-H)

*(5b)*: yield 38%; m.p. = 96—98 °C

*(5c)*: yield 15%; m.p. = 88—90 °C

*(6)*: yield 35%; m.p. = 79—80 °C

*(7)*: yield 96%; m.p. = 189—191 °C; $^1H$-NMR ($CDCl_3$): $\delta = 4.07$ (s, 3 H, $OCH_3$), 7.61 (s, 5 H), 8.56 (d, $J = 1$ Hz; 1 H), 8.66 (d, $J = 1$ Hz, 1 H)

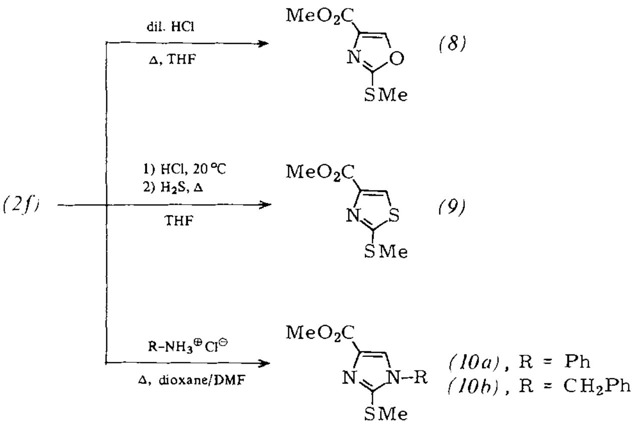
*(8)*: yield 86%; m.p. = 90—91 °C; IR (KBr): 1720 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 2.74$ (s, 3 H, $SCH_3$), 3.96 (s, 3 H, $OCH_3$), 8.25 (s, 1 H)

*(9)*: yield 85%; m.p. = 88—89 °C

*(10a)*: yield 22%; m.p. = 128—129 °C

*(10b)*: yield 38%; m.p. = 72—74 °C

The azabutadienes *(2f, g)* can also be used for the synthesis of azoles. For example, if the solution of *(2f)* in tetrahydrofuran is treated with dil. hydrochloric acid and the mixture heated to boiling the methyl 2-methylthio-4-oxazolecarboxylate *(8)* is obtained. The thiazole derivative *(9)*[7] is formed in the same way in high yields when hydrogen chloride is passed into the solution of *(2f)* in tetrahydrofuran at room temperature followed by hydrogen sulfide at elevated temperature. Finally, the imidazoles *(10a)* and *(10b)*, respectively, are obtained on heating *(2f)* with the respective amine hydrochlorides in dioxane-dimethylformamide or dimethylformamide.



Received: February 8, 1979 [Z 717a IE]
Publication delayed at authors' request
German version: Angew. Chem. *93*, 297 (1981)

CAS Registry numbers:
*(1a)*, 66646-88-6; *(1b)*, 76862-09-4; *(1c)*, 76862-10-7; *(1d)*, 76862-11-8; *(1e)*, 34039-84-4; *(1f)*, 58091-08-0; *(1g)*, 62448-39-9; *(2a)*, 76862-12-9; *(2b)*, 76862-13-0; *(2c)*, 76862-14-1; *(2d)*, 76862-15-2; *(2e)*, 76862-16-3; *(2f)*, 76862-17-4; *(2g)*, 76862-18-5; *(3a)*, 24891-74-5; *(3b)*, 63158-17-8; *(4)*, 76862-19-6; *(5a)*, 76862-20-9; *(5b)*, 76862-21-0; *(5c)*, 76862-22-1; *(6)*, 76862-23-2; *(7)*, 76862-24-3; *(8)*, 76862-25-4; *(9)*, 76862-26-5; *(10a)*, 76862-27-6; *(10b)*, 76862-28-7; dimethylformamide diethylacetal, 1188-33-6

---

[1] *A. Demoulin, H. Gorissen, A.-M. Hesbain-Frisque, L. Ghosez*, J. Am. Chem. Soc. *97*, 4409 (1975).

[2] *D. H. Aue, D. Thomas*, J. Org. Chem. *40*, 1349 (1975).

[3] *R. Gompper, R. Sobotta*, Tetrahedron Lett. *1979*, 921.

[4] *R. Gompper, R. Sobotta*, Angew. Chem. *90*, 808 (1978); Angew. Chem. Int. Ed. Engl. *17*, 760 (1978).

[5] *D. Hoppe*, Angew. Chem. *87*, 449, 450 (1975); Angew. Chem. Int. Ed. Engl. *14*, 424, 426 (1975); *D. F. Sullivan, D. I. C. Scopes, A. F. Kluge, J. A. Edwards*, J. Org. Chem. *41*, 1112 (1976); *G. Stork, A. Y. W. Leong, A. M. Touzin, ibid. 41*, 3491 (1976); *J. J. Fitt, H. W. Gschwend, ibid. 42*, 2639 (1977).

[6] *R. F. Heck, J. P. Nolley, Jr.*, J. Org. Chem. *37*, 2320 (1972).

[7] 2-Mercapto-4-thiazolecarboxylates, see *J. J. D'Amico, T. W. Bertram*, J. Org. Chem. *25*, 1336 (1960); *J. M. Sprague, C. Ziegler*, US-Pat. 2994701 (1959), Merck & Co., Inc.; Chem. Abstr. *56*, P 1458 d (1962); *H. Hayashi, R. Ohi, T. Shishido*, DOS 2148667 (1972), Fuji Photo Film; Chem. Abstr. *78*, 36272 q (1973).

[8] *Note added in proof:* In the meantime preparation of the ethyl ester corresponding to the compound *(2g)* has been described by *W. Kantlehner, F. Wagner, H. Bredereck*, Liebigs Ann. Chem. *1980*, 344.

---

## Aminopyridines, Aminpyrimidines, and Tris(dimethylamino)benzene from (Aza)Vinamidinium and (Aza)Pentamethinium Salts[**]

By *Rudolf Gompper* and *Ulrich Heinemann*[*]

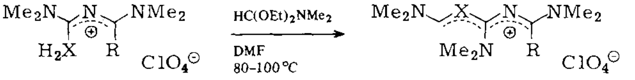
Pentamethinium salts, which can be prepared, *inter alia*, by reaction of 1-methylvinamidinium salts with dimethylformamide-diethylacetal[1a], can be converted by ammonium chloride into pyridines[1]. According to this synthetic principle, pyrimidines should be obtainable *via* 2-azapentamethinium salts *(2)* if 1-methyl-2-azavinamidinium salts *(1)*[2] are used as starting materials. 1-Methylvinamidinium salts and the corresponding 2-aza-derivatives, on the other hand,

---

[*] Prof. Dr. R. Gompper, Dipl.-Chem. U. Heinemann
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

should also react directly *via* intermediary (2-aza)hexatrienes to give benzene- and pyridine-derivatives, respectively. This would provide a simple method for the synthesis of electron-rich six membered (hetero)arenes.



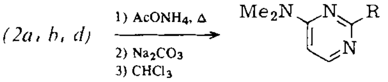
*(1)*, X = CH
*(3)*, X = N
*(2)*, X = CH
*(4)*, X = N

Table 1. Synthesized azamethinium salts *(2)* and *(4)*.

| | R | M.p. [°C] | UV (CH$_2$Cl$_2$) $\lambda_{max}$ [nm] (lg $\varepsilon$) | Yield [%] |
|---|---|---|---|---|
| *(2a)* | H | 125—126 | 278 (4.17), 319 (4.56) | 84 |
| *(2b)* | Ph | 148—149 | 283 (4.04), 325 (4.51) | 74 |
| *(2c)* | Me | 95—97 | 320 (4.55) | 83 |
| *(2d)* | NMe$_2$ | 99 | 268 (4.11), 319 (4.42) | 89 |
| *(4)* | H | 107—108 | 269 (4.55) | 90 |

Reaction of the 1-methyl-2-azavinamidinium salts *(1)* with dimethylformamide diethylacetal affords the 2-azapentamethinium salts *(2)* in good yields. In an analogous way the 1-amino-2-azavinamidinium salt *(3)*[3] affords the 2,4-diazapentamethinium salt *(4)* (Table 1).

On heating with ammonium acetate the salts *(2a, b, d)* are converted into the pyrimidines *(5)* (Table 2).



*(5a)*, R = H
*(5b)*, R = Ph
*(5c)*, R = NMe$_2$

Table 2. Some data of the compounds of type *(5)*—*(7)*.

*(5a)*: yield 56%, b.p. 60 °C/0.1 mbar ([4a] 131—132 °C/67 mbar)

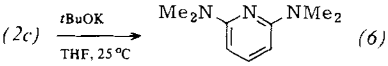
*(5b)*: yield 70%, m.p. 71—72 °C ([4b] 70 °C)

*(5c)*: yield 43%, m.p. 54—55 °C ([4c] 47—49 °C)

*(6)*: yield 57%, b.p. 140 °C/0.01 mbar, m.p. 33—34 °C

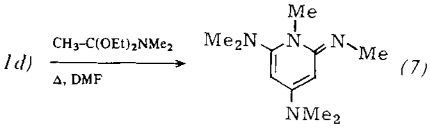
*(7)*: yield 66%, m.p. 90—93 °C (dec.); IR (KBr): 1588, 1563 cm$^{-1}$; $^1$H-NMR (CDCl$_3$): $\delta$ = 2.96 (s) and 3.06 (s) (18 H), 5.22 (s, 1 H), 5.73 (s, 1 H)

The last ring member required for the cyclization of *(2)* to a six-membered ring—introduced by ammonia in the case of *(2a, b, d)*—is already contained in the molecule as methyl group in the case of *(2c)*. Accordingly, treatment of *(2c)* with potassium *tert*-butoxide in tetrahydrofuran leads, presumably *via* an azahexatriene as intermediate[5], to the (no physical data given[6]) 2,6-bis(dimethylamino)pyridine *(6)* (Table 2).

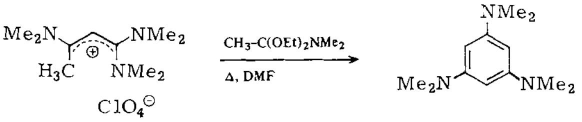


The reaction of *(2c)* to give *(6)* has a parallel in the formation of 3-chloroanisole along with 2,4-dichlorobenzaldehyde from 4-methoxy-3-penten-2-one and dimethylformamide-phosphorus oxide chloride[7], when, however, no intermediates were isolated.

A modification of the method for the preparation of *(6)* and related compounds consists, *e.g.* in heating *(1d)* with *N,N*-dimethylacetamide diethylacetal instead of with dimethylformamide acetal. Reaction *via* azapentamethinium and azahexatriene intermediates, however, does not lead to the expected 2,4,6-tris(dimethylamino)pyridine, but to 4,6-bis(dimethylamino)-1-methyl-2-methylimino-1,2-dihydropyridine *(7)* (Table 2).



This method can also be used for the formation of a pyridine ring according to the [4+2]-scheme, and for preparation of benzene derivatives. On heating the vinamidinium salt *(8)*—prepared in analogy to the method described in ref. [8] from 1,1-bis(dimethylamino)ethylene and *N,N*-dimethylacetamide- dimethyl sulfate in dichloromethane (yield 70%, m.p. 104—105 °C)—with an excess of *N,N*-dimethylacetamide diethylacetal in dimethylformamide, the 1,3,5-tris(dimethylamino)benzene *(9)*, first synthesized by *Effenberger* and *Niess*[9], is obtained in quantitative yield. The process can also be carried out as a "one-pot" reaction by heating the *N,N*-dimethylacetamide-dimethyl sulfate adduct with an excess of 1,1-bis(dimethylamino)ethylene and *N,N*-dimethylacetamide diethylacetal in dimethylformamide; *(9)* is formed in 77% yield. *(9)* is even obtained, though so far only in a yield of 15%, on heating *N,N*-dimethylacetamide diethylacetal with a catalytic amount of boron trifluoride-ether.



*(8)* *(9)*

Received: November 30, 1979 [Z 717 b IE]
Publication delayed at authors' request
German version: Angew. Chem. *93*, 298 (1981)

CAS Registry numbers:
*(1a)*, 72953-15-2; *(1b)*, 72953-19-6; *(1c)*, 72953-21-0; *(1d)*, 72953-23-2; *(2a)*, 76916-32-0; *(2b)*, 76916-34-2; *(2c)*, 76916-36-4; *(2d)*, 76916-38-6; *(3)*, 76916-40-0; *(4)*, 76916-42-2; *(5a)*, 31401-45-3; *(5b)*, 33630-27-2; *(5c)*, 1076-94-4; *(6)*, 40263-66-9; *(7)*, 76916-43-3; *(8)*, 76916-45-5; *(9)* 16857-99-1; dimethylformamide diethylacetal, 1188-33-6; 1,1-bis(dimethylamino)ethylene, 815-62-3; *N,N*-dimethylacetamide dimethyl sulfate, 920-98-9; *N,N*-dimethylacetamide diethylacetal, 19429-85-7.

---

[1] a) *Z. Arnold, A. Holý*, Collect. Czech. Chem. Commun. *28*, 2040 (1963); b) *ibid. 30*, 47 (1965).

[2] *R. Gompper, U. Heinemann*, Angew. Chem. *92*, 208 (1980); Angew. Chem. Int. Ed. Engl. *19*, 217 (1980).

[3] *K. Bichlmayer*, Dissertation, Universität München 1979.

[4] a) *D. J. Brown, L. N. Short*, J. Chem. Soc. *1953*, 331; b) *P. Lardenois, M. Sélim, M. Sélim*, Bull. Soc. Chim. Fr. *1971*, 1858; c) *D. J. Brown, T. Teitei*, J. Chem. Soc. *1965*, 755.

[5] *C. Jutz*, Top. Curr. Chem. *73*, 125, 194 (1978).

[6] *P. R. Hammond*, US-Pat. Appl. 589489 (1975), U. S. Dept. of the Navy; Chem. Abstr. *84*, P137228j (1976).

[7] *A. Holý, Z. Arnold*, Collect. Czech. Chem. Commun. *30*, 53 (1965).

[8] *C. Jutz, E. Müller*, Angew. Chem. *78*, 747 (1966); Angew. Chem. Int. Ed. Engl. *5*, 724 (1966).

[9] *F. Effenberger, R. Niess*, Angew. Chem. *79*, 1100 (1967); Angew. Chem. Int. Ed. Engl. *6*, 1067 (1967); Chem. Ber. *101*, 3787 (1968).

## σ-Framework Radical Cations — A Novel Type of Reactive Intermediates[**]

By *Peter Gölitz* and *Armin de Meijere*[*]

*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

In polycyclic systems containing both a carbenium ion and a radical center at two bridgehead positions, an interaction

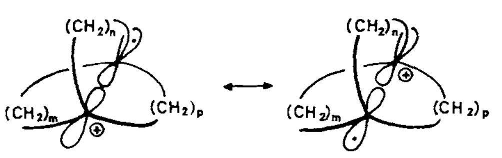
---

[*] Prof. Dr. A. de Meijere, Dr. P. Gölitz
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

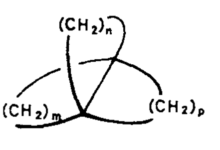
[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and by Deutsche Shell Chemie.

0570-0833/81/0303-0298 $ 02.50/0

between these could lead to a delocalization of the unpaired electron. Such radical cations *(1)* would then correspond to propellanes *(2)*, whose molecular orbital responsible for the central bond is occupied by only one electron.



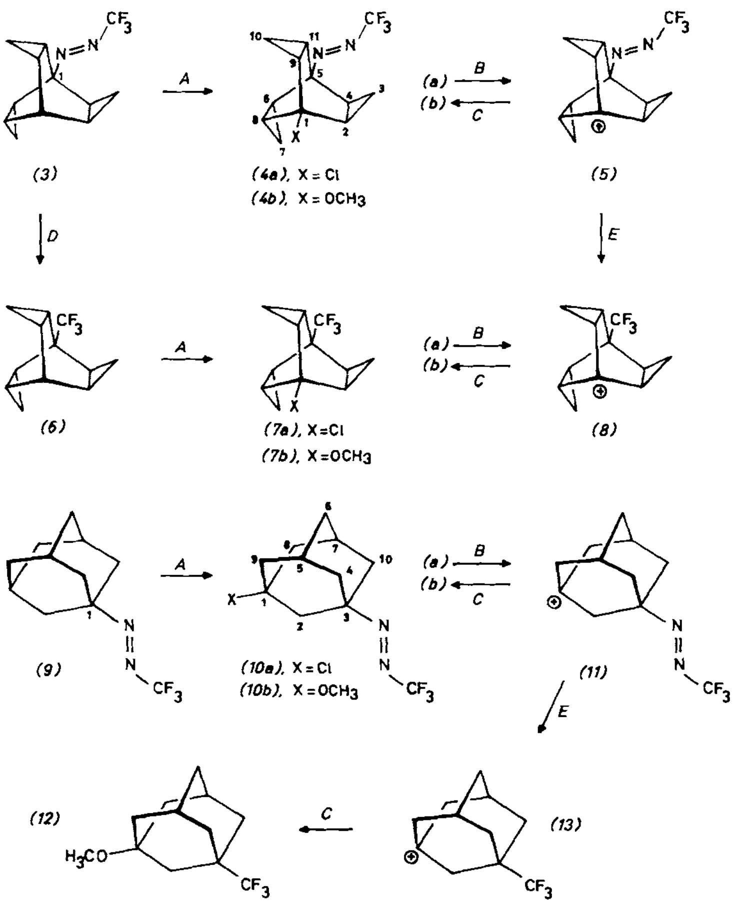
*(1)*



*(2)*

Although numerous propellanes[1], bridgehead carbenium ions[2] and also bridgehead radicals[3] have been generated and investigated, no example of type *(1)* has yet been described in the literature; so far only semiempirical quantum chemical calculations for such a system have been mentioned[4].

This is a report on a novel general method by which radical cations of hydrocarbons with a pure $\sigma$-bond framework can be generated. Possible precursors for such species are polycyclic molecules which contain a "nucleofugic" and a "radicofugic" leaving group on two bridgehead positions. The trifluoromethylazo group is particularly well suited as a radicofugic leaving group. Thus, because of their relatively high photostability, the trifluoromethylazo-derivatives[5] of trishomobarrelene *(3)* and adamantane *(9)* can readily be photochlorinated with *tert*-butyl hypochlorite to their difunctional derivatives *(4a)* (59% yield) and *(10a)* (25%), respectively (Scheme 1)[6]. In the reaction of *(4a)* and *(10a)* with antimony pentafluoride in sulfonyl chloride fluoride[7] the trifluoromethylazo group shows excellent stability towards Lewis acids; at −100 to −80 °C, solutions of the bridgehead carbenium ions *(5)* and *(11)*, respectively, were obtained with intact $CF_3N_2$ groups, which were characterized by their $^1$H- and $^{13}$C-NMR spectra (see Table 1). The solution of *(5)*—but not of *(11)*—could be kept at −10 °C for 1 h without any observable decomposition, yet another confirmation of the unusual stability of bridgehead carbenium ions with the trishomobarrelene skeleton[8]. Reactions of *(5)* and *(11)* with sodium methoxide/methanol solution at −70 °C afforded only the unrearranged methoxy(trifluoromethylazo) derivatives *(4b)* and *(10b)*, respectively.



Solutions of the carbenium ions *(5)* and *(11)* were each irradiated at −80 °C for 18 h with a 500-W mercury high-pressure lamp[9]. Although a considerable amount of polymeric products was formed in both cases, the newly recorded $^{13}$C-NMR spectrum of the solution of *(5)* showed all the signals doubled except that for the substituted bridgehead C-atom. The $^{13}$C-NMR spectrum of the 5-trifluoromethyltrishomobarrelenyl cation *(8)* independently generated from *(6)*[5] *via (7b)* proved that the new signals in the spectrum of the irradiated solution of *(5)* belonged to *(8)*. Upon quenching, this solution yielded 1-methoxy-5-trifluoromethyltrishomobarrelene *(7b)* (7%) besides *(4b)* (15%). The irradiated solution of the adamantyl cation *(11)* was treated analogously, but, due to a large proportion of polymeric substances, no $^{13}$C-NMR spectrum could be recorded. The reaction with sodium methanolate/methanol, however, afforded both *(10b)* (14%) as well as the methyl ether *(12)* (12%).

The formation of trifluoromethyl radical-recombination products *(8)* and *(13)* during photolytic cleavage of the $CF_3N_2$-substituted carbenium ions *(5)* and *(11)*, is a clear indication of the intermediary cage radical cations *(14a)* and *(15a)*. So far, nothing is known about the lifetime of these

Table 1. $^1$H- and $^{13}$C-NMR spectroscopic data ($\delta$ values, TMS int.) and melting points of the novel trishomobarrelene and adamantane derivatives. All the new compounds gave correct elemental analyses and IR spectra.

*(3)*, $^1$H-NMR ($CDCl_3/C_6H_6$): 2.44 (q, 5-H), 0.90 (m, 2,8,9-H), 0.66 (m, 4,6,11-H; 3,7,10-$H_{endo}$), 0.18 (m, 3,7,10-$H_{exo}$); $^{13}$C-NMR ($CDCl_3$): 74.5 (C-1), 23.6 (C-5), 13.8 (C-2,8,9), 11.0 (C-4,6,11), 1.5 (C-3,7,10), 121.15 (q, $CF_3$, $^1J_{CF}=274.6$ Hz)

*(4a)*, m.p. 91 °C; $^1$H-NMR ($CDCl_3/C_6H_6$): 1.09 (m, 3,7,10-$H_{endo}$; 4,6,11-H), 0.87 (m, 2,8,9-H), 0.36 (m, 3,7,10-$H_{exo}$); $^{13}$C-NMR ($CDCl_3$): 72.1 (C-5), 66.6 (C-1), 20.3 (C-2,8,9), 17.4 (C-4,6,11), 2.2 (C-3,7,10), 120.6 (q, $CF_3$, $^1J_{CF}=275.0$ Hz)

*(4b)*, $^1$H-NMR ($CDCl_3/C_6H_6$): 3.31 (s, $OCH_3$), 0.80—1.15 (m, 2,8,9-H; 3,7,10-$H_{endo}$; 4,6,11-H); 0.24—0.51 (m, 3,7,10-$H_{exo}$)

*(5)*, $^1$H-NMR ($SO_2ClF/SbF_5$/TMS): 3.60—3.92 (m, 6 H); 3.21—3.50 (m, 3 H); 2.36—2.64 (m, 3 H); $^{13}$C-NMR ($SO_2ClF/SbF_5$/TMS): 296.7 (C-1), 71.5 (C-2,8,9), 67.3 (C-5), 41.6 (C-4,6,11), 13.8 (C-3,7,10), 119.8 (q, $CF_3$)

*(6)*, $^1$H-NMR ($CDCl_3/C_6H_6$): 2.42 (q, 5-H), 0.89 (m, 2,8,9-H), 0.60 (m, 3,7,10-$H_{endo}$; 4,6,11-H), 0.17 (3,7,10-$H_{exo}$); $^{13}$C-NMR ($CDCl_3$): 128.2 (q, $CF_3$, $^1J_{CF}=279.1$ Hz), 39.1 (q, C-1, $^2J_{CF}=27.3$ Hz), 22.5 (q, C-5, $^5J_{CF}=0.5$ Hz), 9.75 (q, C-2,8,9, $^3J_{CF}=2.8$ Hz), 9.5 (s, C-4,6,11), 1.1 (s, C-3,7,10)

*(7a)*, m.p. 115—116 °C; $^1$H-NMR ($CDCl_3/C_6H_6$): 0.74—1.26 (m, 2,4,6,8,9,11-H; 3,7,10-$H_{endo}$), 0.29—0.57 (m, 3,7,10-$H_{exo}$); $^{13}$C-NMR ($CDCl_3$): 128.3 (q, $CF_3$, $^1J_{CF}=279.5$ Hz), 66.3 (q, C-1, $^5J_{CF}=0.8$ Hz), 38.0 (q, C-5, $^2J_{CF}=29$ Hz), 18.5 (s, C-2,8,9), 13.3 (q, C-4,6,11, $^3J_{CF}=2.74$ Hz), 1.4 (s, C-3,7,10)

*(7b)*, $^1$H-NMR ($CDCl_3/C_6H_6$): 3.26 (s, $OCH_3$), 0.84–1.01 (m, 3, 7, 10-$H_{endo}$), 0.61–0.79 (m, 2, 4, 6, 8, 9, 11-H); 0.12–0.31 (m, 3, 7, 10-$H_{exo}$)

*(8)*, $^{13}$C-NMR ($CDCl_3$): 299.7 (s, C-1), 74.5 (s, C-2, 8, 9), 42.9 (s, C-4, 6, 11), 13.9 (C-3, 7, 10); C-5 and $CF_3$ were too weak

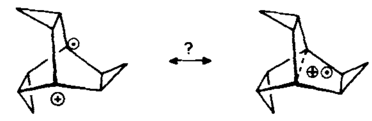
*(9)*, m.p. = 36 °C; $^1$H-NMR ($CDCl_3$/TMS): 2.24 (s, 3, 5, 7-H), 1.86 (d, 2, 8, 9-H), 1.78 (s, 4, 6, 10-H); $^{13}$C-NMR ($CDCl_3$/TMS): 120.5 (q, $CF_3$, $^1J_{CF}=273.7$ Hz), 71.4 (C-1), 39.8 (C-2, 8, 9), 36.3 (C-4, 6, 10), 29.1 (C-3, 5, 7)

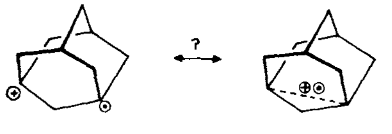
*(10a)*, $^1$H-NMR ($CDCl_3$/TMS): 2.42 (br. s, 2-H), 2.22 (s, 5, 7-H), 2.12 (s, 4, 10-H), 1.83 (br. s, 6-H); $^{13}$C-NMR ($CDCl_3$/TMS): 119.3 (q, $CF_3$, $^1J_{CF}=274.4$ Hz), 73.6 (C-3), 66.4 (C-1), 48.9 (C-2), 46.4 (C-8, 9), 38.1 (C-4, 10), 34.3 (C-6), 31.2 (C-5, 7)

*(10b)*, $^1$H-NMR ($CDCl_3$/TMS): 3.25 (s, $OCH_3$), 2.44 (br. s, 2-H), 1.86 (s, 5, 7-H), 1.79 (s, 4, 8, 9, 10-H), 1.65 (6-H)

*(11)*, $^1$H-NMR ($SO_2ClF/SbF_5$/TMS): 5.08 (5, 7-H), 4.26 (2, 8, 9-H), 3.07 (4, 10-H), 2.28 (6-H); $^{13}$C-NMR ($SO_2ClF/SbF_5$/TMS): 299.0 (C-1), 116.3 (C-3), 75.0 (C-5, 7), 67.0 (C-2), 64.2 (C-8, 9), 37.0 (C-4, 10), 33.8 (C-6)

*(12)*, $^1$H-NMR ($CDCl_3$/TMS): 3.24 (s, $OCH_3$), 2.32 (2-H), 1.75 and 1.72 (4, 5, 7, 8, 9, 10-H), 1.62 (6-H)


(14a) (14b)


(15a) (15a)

novel species. Experiments on the direct ESR spectroscopic detection should also clarify whether the unpaired electrons in *(14a)* and *(15a)* are delocalized in the sense of *(14b)* and *(15b)*, respectively.

Received: September 11, 1980 [Z 721 IE]
German version: Angew. Chem. *93*, 302 (1981)

CAS Registry numbers:
*(3)*, 64253-02-7; *(4a)*, 76916-00-2; *(4b)*, 76916-01-3; *(5)*, 76916-02-4; *(6)*, 76984-83-3; *(7a)*, 76916-03-5; *(7b)*, 76916-04-6; *(8)*, 76916-05-7; *(9)*, 64253-00-5; *(10a)*, 76916-06-8; *(10b)*, 76916-07-9; *(11)*, 76916-08-0; *(12)*, 76916-09-1

---

[1] a) *D. Ginsburg:* Propellanes, Structure and Reactions. Verlag Chemie, Weinheim 1975; b) *A. Greenberg, J. F. Liebman:* Strained Organic Molecules. Academic Press, New York 1978, pp. 342ff.
[2] *R. C. Fort, Jr.* in *G. A. Olah, P. v. R. Schleyer:* Carbonium Ions. Vol. 4. Wiley-Interscience, New York 1973, p. 1783.
[3] *T. Y. Luh, L. M. Stock*, J. Org. Chem. *43*, 3270 (1978), and references cited therein.
[4] See [1b], p. 360f.
[5] *P. Gölitz, A. de Meijere*, Angew. Chem. *84*, 892 (1977); Angew. Chem. Int. Ed. Engl. *16*, 854 (1977).
[6] *E. S. Huyser* in *S. Patai:* The chemistry of the carbon-halogen bond. Vol. 1. Wiley, New York 1973, p. 549.
[7] *G. A. Olah*, Angew. Chem. *85*, 183 (1973); Angew. Chem. Int. Ed. Engl. *12*, 173 (1973).
[8] *A. de Meijere, O. Schallner*, Angew. Chem. *85*, 400 (1973); Angew. Chem. Int. Ed. Engl. *12*, 399 (1973).
[9] High-pressure mercury vapor lamp SP 500 W (Philips GmbH, Hamburg).
[10] In collaboration with Dr. *K. U. Ingold*, National Research Center, Ottawa.

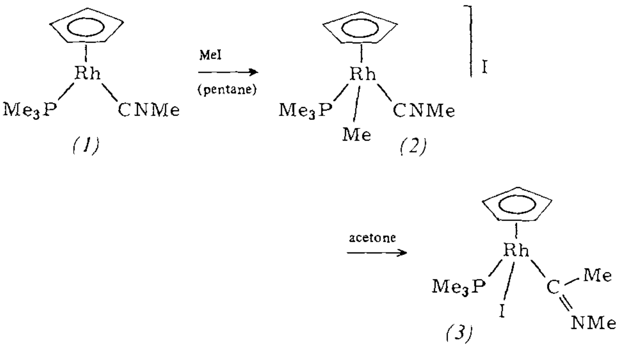
## Cobaltaheterocycles by [3+2]-Cycloaddition of an Acetimidoylcobalt Complex with Acetone and Acetonitrile[1]

By *Helmut Werner, Bernd Heiser*, and *Alfred Kühn*[*]

*Dedicated to Professor Alfred Roedig on the occasion of his 70th birthday*

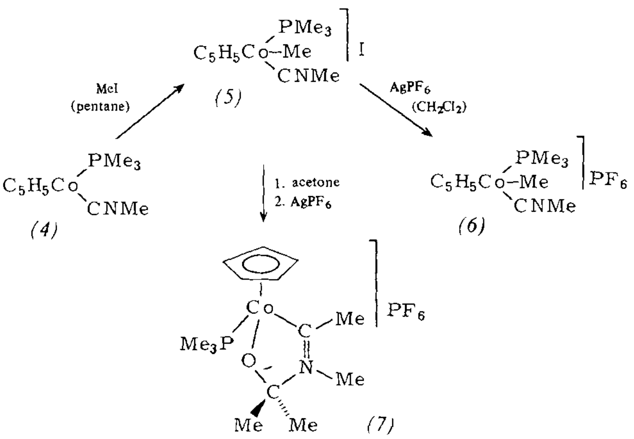
The series of Lewis-base half-sandwich compounds of the type $C_5H_5Co(PMe_3)L$ ($L = PMe_3$, $PPh_3$, $P(OR)_3$[2], CO, CS[3]) was recently extended by the synthesis of the isocyanide complexes $C_5H_5M(PMe_3)CNR$ (M = Co, Rh; R = Me, *t*Bu, Ph)[1]. Since the donor-acceptor properties of isocyanides and CO are similar[4], we expected that the reactions of $C_5H_5M(PMe_3)CNR$, *e.g.* with iodomethane, would proceed analogously to those of the carbonyl complexes $C_5H_5M(PMe_3)CO$ (M = Co[3a], Rh[5]).

This expectation is fulfilled in the case of the methyl isocyanide-rhodium complex *(1)*. Reaction with iodomethane in pentane initially yields initially the salt-like compound *(2)*, which on stirring in acetone (4 h, 50 °C) is transformed, with migration of the methyl group from the metal to the isocyanide carbon, into the acetimidoyl complex *(3)*.



(1) (2) (3)

The first step in the reaction of the methyl isocyanide-cobalt complex *(4)* with iodomethane probably proceeds analogously to that of *(1)*. A yellow solid is obtained whose IR spectrum [$\nu(CN) = 2203\ cm^{-1}$, in nujol] is consistent with the composition *(5)*. The complex *(5)* is unstable in solvents such as $CH_3NO_2$ or $CH_2Cl_2$, but can be converted into the



(4) (5) (6) (7)

Table 1. Spectroscopic data of the reaction products ($^1$H-NMR: $\delta$ values, TMS int., $J$ in Hz; IR nujol, values in $cm^{-1}$).

| Complex | $^1$H-NMR Solvent | $C_5H_5$ | $P(CH_3)_3$ | $NCH_3$ [a] | $XCH_3$ | IR $\nu$(CN) |
|---|---|---|---|---|---|---|
| *(2)* | $(CD_3)_2CO$ | 5.80 "t"<br>$J_{RhH} = J_{PH} = 0.6$ | 1.85 d × d<br>$J_{RhH} = 1.0$<br>$J_{PH} = 11.7$ | 3.75 | 0.83 d × d (X = Rh)<br>$J_{RhH} = 1.1$<br>$J_{PH} = 2.5$ | 2200 |
| *(3)* | $(CD_3)_2CO$ | 5.43 d × d<br>$J_{RhH} = 0.6$<br>$J_{PH} = 1.6$ | 1.78 d × d<br>$J_{RhH} = 0.9$<br>$J_{PH} = 11.5$ | 3.20 | 2.87 (br) (X = C) | |
| *(6)* | $CD_3NO_2$ | 5.17 d<br>$J_{PH} = 0.5$ | 1.57 d<br>$J_{PH} = 11.1$ | 3.47 | 0.73 d (X = Co)<br>$J_{PH} = 3.0$ | 2203 |
| *(7)* | $CD_3NO_2$ | 5.30 d<br>$J_{PH} = 0.5$ | 1.55 d<br>$J_{PH} = 11.8$ | 3.03 | 3.33 (br) [b]<br>1.37 s<br>1.30 s | 1560 |
| *(9)* [c] | $(CD_3)_2CO$ | 5.19 d<br>$J_{PH} = 0.4$ | 1.44 d<br>$J_{PH} = 11.5$ | 3.14 s | 2.20 s (X = C) | [d] |

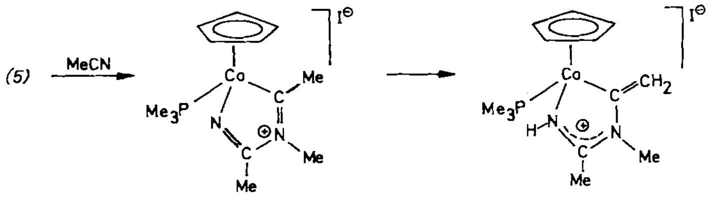
[a] Relative to broad signal, except in the case of *(9)*. [b] Signal of the methyl group on the C-atom $\alpha$ to cobalt. [c] Protons of the exocyclic $CH_2$-group give rise to two doublets of doublets at $\delta = 5.01$ ($J_{PH} = 4.4$, $J_{HH} = 2.5$ Hz) and 4.59 ($J_{PH} = 3.2$, $J_{HH} = 2.5$). [d] Three bands for $\nu$(CN) and $\nu$(CC) at 1610, 1570, and 1520 $cm^{-1}$.

---

[*] Prof. Dr. H. Werner, Dipl.-Chem. B. Heiser, Dr. A. Kühn
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

yellow, air-stable salt *(6)* with $AgPF_6$ (in $CH_2Cl_2$). Treatment of *(5)* with acetone leads to precipitation of a brown, microcrystalline powder which, according to elemental analysis, is formally a 1 : 1 adduct of acetone and *(5)*. On the basis of $^1$H-NMR data (Table 1) we ascribe the hexafluorophosphate formed on reprecipitation with $AgPF_6$ the structure *(7)*.

The compound *(5)* also reacts with acetonitrile in the same fashion as with acetone. Possibly the initial product formed in the reaction is the compound *(8)*, analogous to *(7)*, which very rapidly forms the tautomeric complex *(9)*. The corresponding $PF_6$ salt is obtained on reaction with $AgPF_6$ (in $CH_3NO_2$) or on addition of acetonitrile to *(7)*.



*(8)*  *(9)*

The structure of the cation of *(9)* is shown in Figure 1. The cobalt-containing heterocycle is completely planar (maximum deviation of the atoms from the ring plane 1 pm), and the C-atoms C11, C12 and C13 also lie in the ring plane. The presence of the exocyclic double bond is confirmed by the length of the C10—C13 bond (134 pm). On the basis of the relatively small difference in the C9—N1 and C9—N2 bond lengths the positive charge in the NCN fragment of the ring should be delocalized.

Acetone and acetonitrile have only slightly activated multiple bonds and are therefore generally not capable of undergoing [3+2]-cycloadditions[7]. The observation that the acetimidoylcobalt group formed by the electrophilic attack of MeI at the Co—CNMe bond of *(4)* rapidly reacts both with $Me_2C{=}O$ as well as with $MeC{\equiv}N$ points to a high nucleophilicity of the acetimidoyl N-atom, probably owing to the electron supply of the electron-rich $C_5H_5(PMe_3)Co$ fragment.

Received: July 18, 1980 [Z 724 IE]
German version: Angew. Chem. *93*, 305 (1981)

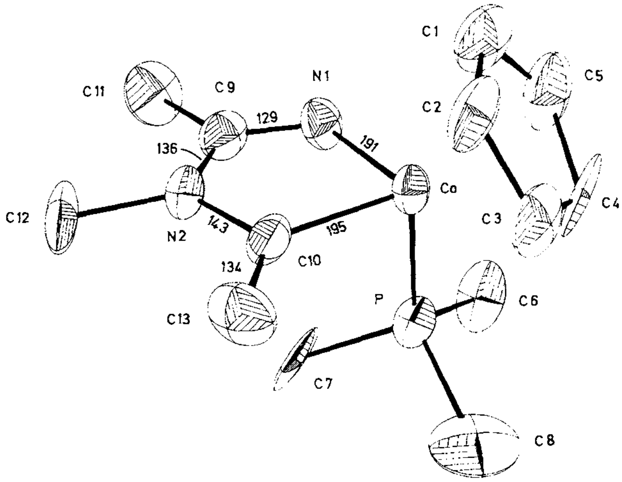


Fig. 1. Structure of the cation of *(9)* in the crystal, with bond lengths [pm] and bond angles [°].

CAS Registry numbers:
*(1)*, 77097-48-4; *(2)*, 77097-49-5; *(3)*, 77097-50-8; *(4)*, 77097-51-9; *(5)*, 77097-52-0; *(6)*, 77097-54-2; *(7)*, 77097-56-4; *(9)*, 77097-57-5; me$_2$C=O, 67-64-1; mel, 74-88-4.

---

[1] Basic Metals, Part 27. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and by BASF AG, Ludwigshafen, and DEGUSSA, Hanau.—Part 26: *S. Lotz, B. Heiser, H. Werner*, J. Organomet. Chem., in press.

[2] *H. Werner, W. Hofmann*, Chem. Ber. *110*, 3481 (1977); *K. Leonhard, H. Werner*, Angew. Chem. *89*, 656 (1977); Angew. Chem. Int. Ed. Engl. *16*, 649 (1977); *B. Juthani*, Dissertation, Universität Würzburg 1980.

[3] a) *A. Spencer, H. Werner*, J. Organomet. Chem. *171*, 219 (1979); b) *H. Werner, O. Kolb*, Angew. Chem. *91*, 930 (1979); Angew. Chem. Int. Ed. Engl. *18*, 865 (1979).

[4] *F. A. Cotton, G. Wilkinson:* Anorganische Chemie, 3rd Ed. Verlag Chemie, Weinheim 1974, Chap. 22; Advanced Inorganic Chemistry, 4th Ed. Wiley-Interscience, New York 1980, Chap. 25.

[5] *H. Werner, R. Feser*, Angew. Chem. *91*, 171 (1979); Angew. Chem. Int. Ed. Engl. *18*, 157 (1979).

[6] Crystallographic data: space group $P2_1/c$, $a=12.595(5)$, $b=8.573(4)$, $c=15.867(5)$ Å, $\beta=98.03°$, $V=1696$ Å$^3$, $Z=4$, $\rho_{calc}=1.66$, $\rho=1.68$ g/cm$^3$; 1592 independent reflections ($2\theta \leq 40°$, Syntex $P2_1$, $Mo_{K\alpha}$), solution by direct methods (SHELX), refinement to $R=0.037$ (anisotropic temperature factors).

[7] *R. Huisgen*, Angew. Chem. *75*, 604 (1963); Angew. Chem. Int. Ed. Engl. *2*, 565 (1963).

# BOOK REVIEWS

**The Biosynthesis of Mycotoxins.** Ed. by *P. S. Steyn.* Academic Press, New York 1980. x, 432 pp., bound, $ 44.00.

A clear distinction must always be drawn between primary and secondary metabolism. Primary metabolism is absolutely essential, while secondary is not. In secondary metabolism a very wide range of compounds is synthesized (without aim or purpose?) and we can regard this area as a "playground for evolution". From a consideration of their mode of action, the secondary metabolic products which are synthesized by microorganisms and which inhibit or kill microorganisms are known as antibiotics. To them has recently been added the large group of mycotoxins, the toxic secondary metabolites of fungi. The particular interest in this group of substances started at the beginning of the sixties with the discovery of aflatoxin, a metabolic product of *Aspergillus flavus* and *Aspergillus parasiticus* that turned out to be a highly active carcinogen. It is not surprising that since then the analysis of this class of substances has been worked out very thoroughly and a firm recommendation has been made to destroy all moldy food.

The present work is an excellent survey of the latest stage of research into the biosynthesis of mycotoxins. The first paper, by *Bu'Lock*, gives an introduction to the field that is well worth reading. The summary reports are written by authoritative experts: *Floss* reports on the biosynthesis of the ergot alkaloids, *Tamm* on the biosynthesis of trichothecin mycotoxins and cytochalasines; *Steyn, Vleggaar* and *Wessels* provide an important contribution on aflatoxins, *B. Franck* reports on the biosynthesis of ergochrome, and *Yamazaki* on neurotropic mycotoxins; *Lolita Zamir* on patulin and penicillic acid; *Kirby* and *Robins* write a contribution on gliotoxin and related epipolythiodioxopiperazines; *Holzapfel* reports on the biosynthesis of cyclopiazonic acid and related compounds, *Sankawa* on mycotoxins of the anthraquinone series, and *Vleggaar* and *Steyn* conclude with a study of those mycotoxins that up to now have been considered to be of smaller importance.

The mycotoxins are of chemical interest both from the analytical and the synthetic point of view, since they are generally complex molecules belonging to diverse classes. The present book will be of use to chemists, biochemists, food chemists, biologists, toxicologists, and pharmacists.

*Franz Lingens* [NB 532 IE]

**Biotransformation von Arzneimitteln** (Biotransformation of Pharmaceuticals). By *S. Pfeifer*. Vol. 3. Verlag Chemie, Weinheim 1979, 560 pp., bound, DM 118.—.

The third volume of this series of monographs[*] deals with the metabolism of 311 compounds, particular attention being paid to members of the following groups: antiallergics, antibiotics, bronchodilators, diuretics, local anaesthetics, sweetening agents, and cytostatics. The literature is covered up to the beginning of 1978; supplements to the literature in volumes 1 and 2 update these to the same point in time.

A total of 851 substances is described in this three-volume work, including not only drugs in general usage but also pharmaceuticals no longer used in therapy and substances still at the stage of clinical trials. The nomenclature is not completely uniform. In general the Latin versions of the international short names are used (for example acidum etacrynicum). This may be the usual nomenclature in the German and European pharmacopeias, but it sounds very strange to those who are not pharmacists. For unambiguous identifications the reader is referred to reference works.

The telegraphic style and the extensive use of abbreviations and symbols result in compressed descriptions not always easy to follow. Each monograph has a similar structure. A set of formulas is presented (the metabolites are generally given as partial formulas), with no differentiation between the main and the subsidiary biotransformation reactions. This is followed by data on separation techniques, species, and analysis. In the next section, "Comments", information in keyword form is given on the pharmacokinetics, together with supplementary data on the metabolites. No claims are made to completeness. The literature references used are given (without titles) at the end, in alphabetical order by authors.

These monographs should not be regarded as critical summaries presenting the metabolic behavior of the individual pharmaceuticals. However, they could be useful as a preliminary source of information for the nonspecialist, for some essential information appears with equal validity side by side with unverified data. The work does, however, constitute a very comprehensive compilation of the literature on the substances in question, with some general explanations and additional comments, which is what the reader might expect in a study of the literature cited. The author and his associates have thus made a very important contribution to this specialist field, particularly when we consider the effort still required in making a literature search in the field of biotransformation of pharmaceuticals, even with all the aids of modern technology.

The collection as a whole forms a very useful reference work, and should be welcomed by all concerned with the biotransformation of drugs. The authors should be encouraged in their intention of keeping this work as up-to-date as possible by literature supplements. If at a later date a new edition is brought out, it might be possible to make it appeal to a wider circle of readers, especially if the format could be modified.

*K.-O. Vollmer* [NB 533 IE]

**Recent Books**

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**The Handbook of Environmental Chemistry.** Edited by *O. Hutzinger*. Springer-Verlag, Berlin 1980. **The Natural Environment and the Biogeochemical Cycles.** Vol. 1. Part A. xii, 258 pp., bound, DM 98.00.—ISBN 3-540-09688-4.—**Reactions and Processes.** Vol. 2. Part A. xiv, 307 pp., bound, DM 126.00.—ISBN 3-540-09689-2.—**Anthropogenic Compounds.** Vol. 3. Part A. xiii, 274 pp., bound, DM 98.00.—ISBN 3-540-09690-6

**Controlled Release of Bioactive Materials.** Edited by *R. Baker*. Academic Press, New York 1980. xii, 473 pp., bound, $ 34.50.—ISBN 0-12-074450-3

**Synthese, Einkristallzüchtung und Untersuchung akustoopischer Materialien.** By *K. Recker* and *F. Wallrafen*. Westdeutscher Verlag, Opladen 1980. 45 pp., carton, DM 12.00.—ISBN 3-531-02983-5

**Phosphorus Chemistry.** Edited by *M. Grayson* and *E. J. Griffith*. John Wiley & Sons, New York 1980. 517 pp., bound, £ 37.50.—ISBN 0-471-05890-4

---

[*] Cf. Angew. Chem. 90, 923 (1978); Angew. Chem. Int. Ed. Engl. 17, 871 (1978).

**Editorial office:** Boschstrasse 12, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

**Editor:** *O. Smrekar*. **Translation Editors:** *I. G. Neil* and *A. Stimson*.

**Publishers:** Verlag Chemie GmbH, (Managing Directors *Dr. Helmut Grünewald* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH, (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany, Telephone Weinheim (06201) 14031 (602-1), Telex 465516 vchwh d.

ANGEWANDTE
CHEMIE

Volume 20 · Number 4
April 1981
Pages 303–412

International Edition in English

# Macromolecular Chemistry Today—Aging Roots, Sprouting Branches

By Hermann F. Mark[*]

In the early twenties, I did research in a small team (together with *R. Brill, I. R. Katz, M. Polanyi* and *R. Weissenberg*) at the Kaiser-Wilhelm-Institut für Faserstoffchemie (Chemistry of Fibers) in Berlin-Dahlem, in *R. O. Herzog*'s group. We investigated the structures of industrial textile fibers (cotton, wool, silk, hemp) and of other natural products such as starch, rubber, leather and wood. In those days, each of these important products was the subject of a large, separate research field—both in science and engineering. There were textbooks on cellulose, on proteins, on rubber, on starch; each of the fields had its own journals and there were special societies and conferences for chemists working on starch, rubber, proteins and cellulose. Similarities were not considered—even if they were obvious; each of the different areas was a world of its own, and little if any overlap existed, which might have led to mutual stimulation.

This situation suddenly changed when *Hermann Staudinger* established the concept of *macromolecules,* setting his face against strong and broad opposition. It now became clear that all the many products were structurally similar: they consisted of *long chain* molecules. Chain length itself was initially not considered to be so important—there ought to be more than eight or ten, perhaps there were more than one hundred repeating units. But what was the structural basis for the vast range of properties and behavior of these natural products? The *microstructure* of the main chains and the type of *substituents* linked to them! The latter could be hydrophilic or hydrophobic, small or large, basic or acidic; one was back again in the well-known field of classical organic chemistry. A new, unifying principle had emerged which made things marvelously clear and easy. Half a century before, the confusing manifoldness of thousands of synthetic dyes had become explicable by the unifying principle of chromophoric groups, and all colors of the spectrum could be prepared by simply adding auxochromic moieties to the molecules. Now again, a unifying principle—the concept of long main chains (hydrocarbons, polyethers, polyesters, polyamides) and the presence of different side chains and substituents—explained the confusing variety in the behavior of many important natural products. From the chemist's point of view, the difference between rubber and wool had become basically as small as the difference between a yellow and a blue dye.

A unifying principle, once accepted, creates order where confusion reigned and understanding where uncertainty prevailed: consider how the work of *Lavoisier* and *Mendeleev* influenced chemistry!

A few years later, I worked in *K. H. Meyer*'s group in Ludwigshafen in the central laboratories of IG Farben together with *M. Dunkel, H. Fikentscher, E. Dorrer* and *C. Wulff.* Trying to make synthetic polymers, we all realized the enormous advantage the macromolecular model had for our way of thinking and for the design of new experiments: so did innumerable chemists in other laboratories. A boom began no one had dreamt of—a boom in the understanding, production and manifold applications of macromolecular products of all kinds. New ideas and methods kept progress in motion.

If today, 60 years later, we look back at this development of chemical science and industry, the question arises: has it lost momentum, or can we notice new impulses?

One answer to this question is given by the reports on recent advances published in the current issue of this journal. Many macromolecular substances and classes of compounds have already been highly developed; their further develop-

---

[*] Prof. Dr. H. F. Mark
Polytechnic Institute of New York
333 Jay Street, Brooklyn, N. Y. 11201 (USA)

0570-0833/81/0404-0303 $ 02.50/0

ment will be slow and lead mainly to more elaborate and cheaper products. Other fields exist, however, in which the as yet unattainable is sought.

The article "Half a Century of Polystyrene—a Survey of the Chemistry and Physics of a Pioneering Product" by *A. Echte et al.,* goes back to work carried out in the middle of the twenties for which two patents were granted to *C. Wulff* and myself and to *E. Dorrer* and *C. Wulff.* The original "Sumpfphasen" ("swamp phase")-polymerization had already been remarkably stimulated by the concept of long chain molecules and yielded a product which at the time was commercially highly successful. During the next five decades, the regularity and reproducibility of molecular weights were constantly improved. Later, copolymerization and polymer blending were used (together with many new methods in synthesis and processing) to expand the range of applications, in order to compete with other polymeric products. From the three or four prototypes of the early years, a vast variety of more than a hundred useful products has emerged; one can hardly imagine doing without them in the household, electrical industries (telephone, radio, television) and for the interior equipment of all kinds of vehicles. Polystyrene will continue to flourish, further improvements will be necessary, but one can handly expect striking innovations.

In contrast, the articles by *H. Ringsdorf et al.* and *U. Zimmermann et al.* report on the breaking of new ground. Some 40 years ago, *I. Langmuir* considered the structural analysis of proteins and the synthesis of one of these compounds to be an important long-term objective in chemistry. Much has happened since, and even the macromolecular structure of complicated proteins like hemoglobin has been largely explained. As a next long-term objective in macromolecular biochemistry, "synthesis" of a cell was aspired. Before there is a chance to synthesize, one has to become familiar with the target structure by *e.g.* deliberately altering it and studying the resulting effects. Such investigations have been started in Mainz *(H. Ringsdorf),* London *(D. Chapman)* and Jülich *(U. Zimmermann).* In order to stabilize cell membranes *Ringsdorf* tries to introduce polymerizable molecules, which due to their structure are compatible with membrane constituents. Their polymerizable groups can be activated whenever desired. In this way, ***stabilized cell models*** are available which may serve as models for studies of membrane properties and membrane transport or even as antitumor agents. The solution of this problem requires exceptional skill in the synthesis of new, complicated monomers which consist of *e.g.* a sugar- and a lipid-moiety covalently bound to a polymerizable group (diacetylene, butadiene). *Zimmermann*'s method of fusing cells and incorporating different substances into them requires knowledge of electronics and electrical engineering. Synthetic work and the application of biophysical methods can, however, only be successful if the cooperating cell biologists and membrane physiologists give the right "instructions": there is a "multilingual" borderland, beyond which only a well established interdisciplinary team can expect to progress. This cooperation may give rise to an entirely new discipline which survives the old ones. "Material science" thus originated from metallurgy, ceramics and plastics technology. What about "Life Science"? Can polymer chemistry, cell biology and medicine overlap and strive together for new goals?

Similar pioneering work with quite different objectives is reported by *G. Wegner* in his contribution on "Polymers with Metal-like Conductivity—A Review of their Synthesis, Structure and Properties". The production and application of macromolecular substances has so far tried to achieve certain thermal and mechanical properties—high melting points, resistance to solvents, elasticity, toughness—because these are essential for fibers, films, molded shapes *etc.* A polymer scientist would say they are consequences of the movement of chain segments and atoms. The phenomena discussed by *Wegner,* however, are based on the movement of *electrons* in organic solids—especially in macromolecular systems. In contrast to metallic solids, which contain many mobile electrons and are therefore conductors or semiconductors, organic solids, like cellulose, rubber, polystyrene or nylon have no mobile charges; they are typical insulators and have long been used successfully as insulating materials. Nevertheless it seems worthwhile to try to produce conducting or semiconducting organic polymers: easy processing, low specific weight and resistance to corrosion are appealing advantages. Indeed, in recent years, it has been discovered that by loosening binding electrons or by creating additional charges (doping) remarkable degrees of conductivity can be realized. In *Wegner's* article, remarkable thoughts and experiments are presented which are situated between two established disciplines: physics of metals and chemistry of macromolecules. Only well-organized team-work will be successful in this new and eminently promising field.

To sum up, these contributions (written in the year of *Hermann Staudinger*'s 100th birthday) clearly show that macromolecular chemistry has become a huge tree with new branches still sprouting.

Received: March 13, 1981 [A 364 IE]
German version: Angew. Chem. *93,* 309 (1981)

# Polymeric Antitumor Agents on a Molecular and on a Cellular Level?

By Leo Gros, Helmut Ringsdorf, and Hans Schupp[*]

"Chemistry has become a mature science, with all the advantages and handicaps of maturity: harvest is abundant, but many people think future and adventure are to be found elsewhere"[1a]. This holds true—in 1981, the year of *Hermann Staudinger*'s 100th birthday—for macromolecular chemistry, too. Where can the polymer chemists seek adventures? Unsolved problems in neighboring fields like medicine and molecular biology attract his zeal. Cancer chemotherapy is such a field. Can the polymer chemist help to solve its problems?

Polymers may be pharmacologically active as such. If used as carriers, they may, due to their intrinsic properties, influence body distribution, excretion or cell uptake of the pharmaca they carry. Hence, there is a chance for new ways in therapy, including affinity chemotherapy using synthetic macromolecules.

Our own body has a perfect biological system for affinity therapy: immune response to infection selectively attacks foreign cells. It is fascinating to observe what the immune system does to a tumor cell which could not escape immune surveillance (cf. Fig. 14). Can these specific cell-cell interactions be mimicked? What do we have to learn for an experimental approach to this adventure? Stable membrane and cell models can be synthesized, a first step towards this goal.

Macromolecular chemistry is far from being able to offer satisfying solutions for a specific tumor therapy; striving for it, polymer chemists can learn lots of things. In order to do so, they will have to enter neighboring fields and they will have to be willing and able to cooperate.

*Irrtümer haben ihren Wert;*
*Jedoch nur hie und da.*
*Nicht jeder, der nach Indien fährt,*
*Entdeckt Amerika.*[**]
*(Erich Kästner)*

## 1. Introduction

Interdisciplinary thinking is no longer regarded as poaching in other people's territory; a modern scientist must enter neighboring fields. When doing so, he may need the help of model concepts, which, far from being perfect definitions, can serve as sign posts in the thicket of facts. This is what the authors have in mind when they talk about antitumor agents on a molecular and on a cellular level, trying to characterize different modes of action of these drugs.

Most of the antitumor agents presently used may be regarded as drugs acting on a molecular level: Let us imagine a cell-killing drug which enters a cell and for example cross-links DNA or inhibits a key enzyme. Cell metabolism is thus disturbed on a molecular level; the internal medium of the cell is damaged causing a series of events. "Death", *i.e.* destruction of the cell is the final result of this series of chemical reactions. Drugs of this type may be called drugs acting on a *molecular level.*

Mother Nature, however, often combats tumor cells in a different way: the immune system recognizes degenerate cells; antibodies together with a protein complex (complement system) or, alternatively, killer cells interact with and destroy the tumor cell membrane. Membrane destruction, although perhaps induced chemically (*e.g.* by membrane destabilizing agents), is ultimately a physical phenomenon: the internal medium of the cell can no longer exist because the crucial compartment-forming structure (the cell membrane), which separated the cell from its environment, is destroyed (cf. Fig. 14). Systems which in this manner destroy a cell as a whole may be called antitumor agents acting on a *cellular level.*

In recent years, chemists have tried to develop not only low molecular, but also polymeric antitumor agents. The present survey attempts to review current activity and to discuss possible developments in the field of polymeric antitumor agents on a molecular and on a cellular level from a polymer chemist's point of view.

After a short description of guidelines in the design of antitumor agents and of chances in the "tailoring" of such drugs (Section 2), we will discuss in Section 3 why and how polymeric antitumor agents on a molecular level have been developed. Section 4 deals with possible starting points for a different approach; the question is whether one can design polymeric antitumor agents on a cellular level, imitating the final step of natural immune response.

## 2. Tailor-Made Antitumor Agents?

Surgical and radiation treatments are the most common tumor therapies. Their effect is optimal only when the tumor

---

[*] Prof. Dr. H. Ringsdorf, Dipl.-Chem. L. Gros, Dipl.-Chem. H. Schupp
Institut für Organische Chemie der Universität
J.-J.-Becher-Weg 18-20, D-6500 Mainz 1 (Germany)

[**] A translation in Brokish (broken English):
*Errors may sometimes bring success,*
*sometimes more, and sometimes less.*
*Not many bound for India,*
*will end up in America.*

*0570-0833/81/0404-0305 $ 02.50/0*

is localized. If the tumor cells are spread over the body, a therapy is needed which can reach them wherever they may be situated. This is (at least in theory) the domain of cancer chemotherapy[1b]. Although in recent years, considerable progress has been achieved in this field, the main problem of chemical treatment of tumors remains largely unsolved: most antitumor drugs are not selective, they are highly toxic for both cancer and normal cells.

Chemists who set about developing antitumor active substances may either isolate natural products or synthesize new compounds and then test their activity on cell cultures and animal models. This procedure, however, does not satisfy the scientist searching for causal relationships, and is in any case extremely expensive. Nevertheless, this screening plays an important role: at the National Cancer Institute (USA), 30800 new compounds were screened in 1972[2].

At the beginning of this century, *Paul Ehrlich* proposed targeting to affected tissues[*] by means of appropriate receptors[3]. Interest in tackling the tumor problem in this way, *i. e.* immunologically, has constantly grown, due to the increasing knowledge of high specifities of cell-cell-recognition and immune response. Thus, in the past years a large number of investigations have been carried out with the goal of replacing unspecific antitumor agents (toxic to all cells) by tailor-made, specific drugs which act selectively on tumor cells.

"Drug design"[4]—*i. e.* tailoring of pharmaca—presupposes "taking the target's measurements". A thorough knowledge of structure-activity relationships and a detailed understanding of biochemical and morphological characteristics of the target cell are required. Here we encounter a crucial problem: Despite the fact that innumerable investigations have been done in the field, we are still far from a true understanding of the origin and spread of tumors. The possibilities of "rational drug design" should not be overestimated[5]. Nevertheless, the idea of investigating the differences between tumor and normal cells in order to develop a therapeutic potential remains a suitable guideline[1,6].

It must be considered, however, that there is no such thing as "the tumor cell". The about 100 human tumors known are significantly different from each other. Even in any one tumor there are several different cell-subpopulations (phenotypes) which themselves can change during tumor development[7]. Table 1 shows several differences between normal and malignant cells of a given tissue. Not all of these characteristics, however, apply to all tumor types[8].

This survey of typical tumor cell properties may seem impressive; yet one has to note that although these differences may be used diagnostically, they provide only a narrow basis for selective chemotherapy.

Among these, the high mitotic activity of many tumors must be emphasized. Most antitumor agents used clinically act upon metabolic pathways related to cell growth. Rapidly dividing tumor cells are therefore effectively attacked by cytostatic agents and radiation therapy, but normal tissues which divide rapidly, too—*e. g.* liver, lymph system *etc.*—are equally damaged.

Table 1. Characteristics of tumor cells as compared with normal cells.

| Properties | Ref. |
|---|---|
| *Cellular metabolism and intracellular environment* | |
| 1. increased content of methylated nucleosides | [9] |
| 2. different enzyme patterns | [10] |
| – increased activity of DNA-synthesizing and decreased activity of DNA-catabolizing enzymes | [10] |
| – lack of asparagine-synthetase (several types of leukemia) | [11] |
| – increased activity of proteolytic lysosomal enzymes | [12] |
| – strongly decreased activity of $Mn^{2+}$-superoxide dismutase | [13] |
| 3. higher need for exogenous $Zn^{2+}$ | [14] |
| 4. lower $Ca^{2+}$ and higher $K^{+}$-concentrations | [15] |
| 5. lower pH of cytoplasm (after injection of glucose) | [16] |
| *Membrane structure and properties* | [17] |
| 6. higher rate of endocytosis | [18] |
| 7. altered phospholipid contents | [17d] |
| 8. different glycoproteins (lectin receptors) of the membrane | [7, 19] |
| 9. tumor associated surface antigens | [20] |
| *Cell growth and behavior of cells in tissues* | |
| 10. impaired cell proliferation | [21] |
| 11. lower cohesion in tissues | [22] |
| 12. lower contact inhibition | [22] |
| 13. metastasizing activity | [23] |
| 14. "invasiveness" = active penetration into other tissues | [22] |

It is out of the question that a tumor cell-specific chemotherapy has not been achieved so far. Nevertheless, besides high mitotic activity, some of the differences between normal and tumor cells mentioned in Table 1 have proved to be helpful in "rational drug design". We will come back to endocytotic activity (point 6 in Table 1) and tumor-associated antigens (point 9 in Table 1) later and just mention the exploitation of different enzyme patterns (point 2 in Table 1). An enzyme therapy with asparaginase has already been used in the treatment of certain leukaemias[11,24]: These leukaemic cells are unable to produce asparagine and need an extracellular asparagine supply. Asparaginase used as a therapeutic agent degrades asparagine and thus deprives the cells of a substance which is essential for protein biosynthesis.

This example of a relatively high degree of specificity is an exception. Many attempts have therefore been made[2,6,25] to obtain antitumor agents of a high selectivity:

1) Isolation or synthesis of new active compounds, *e. g.* hormones, plant products, interferones, antimetabolites.
2) Further development of known antitumor agents with the aim to improve selectivity, *e. g.* by fixation to tissue-specific substances (like hormones[26]) or applying the transport form—active form concept[27].
3) Use of carrier systems designed to more selectively carry the antitumor agent to the target (the tumor)[28]. In particular, the following carriers have been proposed:
    - polymers (cf. Section 3)
    - liposomes[29]
    - cells[30]

During the last decade many scientists have placed their hopes in the carrier approach, the increasing number of papers and reviews[28-30] speaks for itself. In the following, we would like to discuss some essential aspects of one of these carriers, namely polymers.

---

[*] Much earlier, in the 14th century, drug targeting was familiar to physicians. In the preface to his collection of tales, *Don Juan Manuel* (El Conde de Lucanor, Editorial Castalia, Madrid 1976) tells us why he teaches practical philosophy through pleasant stories: "I did as physicians do when they, in order to make a medicament for the benefit of the liver, add sugar, honey or some other sweet stuff, because the liver likes sweet things. And due to this preference for the sweet, the liver attracts the sweet and the medicament with it. The same is done with every organ which needs a medicament: the drug is mixed with something the organ naturally is inclined to".

## 3. Polymeric Antitumor Agents on a Molecular Level

### 3.1. Polymeric Antitumor Agents—Why?

The investigation of polymers in medicine[31] (biomaterials) is one of the new and fascinating areas in polymer science. One of the interesting topics is the investigation of pharmacologically active polymers, *i. e.* macromolecules which are pharmacologically active by themselves or which can be used as carriers for low molecular weight pharmaca.

Although polymers have been widely used in medicine, *e. g.* as materials for artificial organs and implants[32], pharmacologically active polymers are still subject to considerable scepticism. Nevertheless, much has been achieved, and a growing number of papers and review articles on the subject have been published[33-43]. Many of these publications deal with the development of polymeric antitumor agents[28,44,53]. Why? *Harris Busch* gives quite a simple answer: "Everybody wants to contribute to the cancer problem..."[45]—and so do polymer chemists!

One of the first considerations leading to the development of pharmacologically active polymers was the hope that one might achieve depot effects due to high molecular weights[46]. This hope had been cherished by experience with synthetic polymeric plasma expanders[47]. But taking into account that there is a great variety of possible interactions between polymers and biological systems, the depot effect is just one of many promising applications of pharmacologically active polymers.

As discussed before, specificity of antitumor drugs is a crucial problem in tumor chemotherapy[48]. One approach to the synthesis of specific low molecular weight antitumor agents—the use of tumor cell-specific transport moieties attached to the drug—often meets with substantial difficulties. The following example will illustrate this and show why macromolecular science might be able to contribute to a solution of this problem.

*Connors et al.*[49] investigated the influence of substituents on the cell-specific uptake of sulfadiazines by tumor tissue in rats.

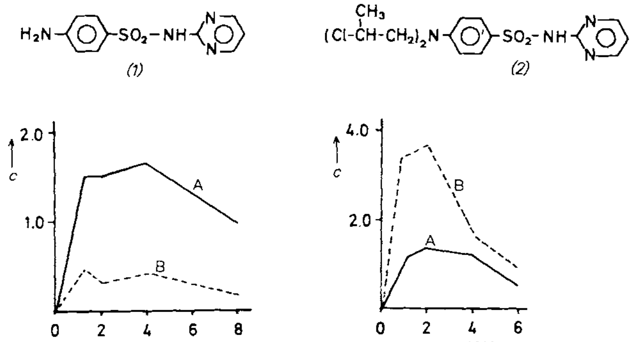


Fig. 1. Different cell uptake of sulfadiazines *(1)* and *(2)* by liver and tumor cells (Walker tumor in rats) [49]. *c*: μg of compound per mg tissue, *t*: time after intraperitoneal injection (i.p.), A: tumor cells, B: liver cells.

Figure 1 shows that the sulfadiazine derivative *(1)* is preferentially taken up by Walker tumor tissue compared to liver tissue (left). *Connors et al.* concluded that linkage of this tissue-specific compound to the cytotoxic Lost-system might result in a combined tumor-specific and cytotoxic activity and thus synthesized the sulfadiazine-Lost conjugate *(2)*. This substance is indeed an antitumor agent. However, instead of being taken up into tumor tissue, it was found to be enriched in the liver (Fig. 1, right).

This means that, in this particular case, chemical linkage of two structural units in a small molecule (the properties of which are highly dependent on its structure) does *not* result in a combination of the desired functions[50]. This problem does not always occur[51], but is found very often[52]. Nature achieves high specifities by, for example, building up high molecular weight compounds with different functional units (which are very often localized seperately). Structural complexity affords functional specificity.

As an approach, one might try to achieve a combination of desired properties (*e.g.* cell toxicity, solubility, tumor cell specificity) by linking the appropriate structural units to different domains along a polymer chain. Figure 2 shows a model[36,53] of such a compound.

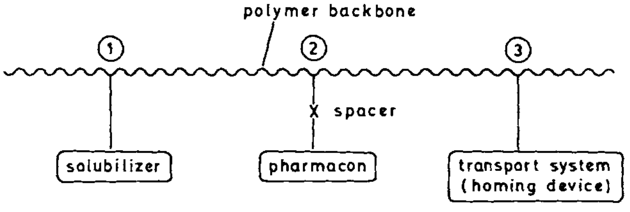


Fig. 2. Model of a pharmacologically active polymer [36, 53].

One domain within the model macromolecule ① contains units which may influence *solubility* (lipophilicity, hydrophilicity), body distribution and acute toxicity of the whole molecule. In a second domain ②, the *drug* is linked to the polymer chain by a *bond*, which may be cleaved or may be stable under *in vivo* conditions. A *spacer group* may be necessary to separate the drug from the main chain in order to make it accessible to enzymes or receptors. Finally, a unit which assures preferential uptake into a target tissue *("homing device")* may be conceived.

Function and biological activity of pharmacologically active polymers are especially influenced by polymer specific structural parameters:

- Molar mass and molar mass distribution influence body distribution of polymeric pharmaca[54]. High molecular weight compounds for example cannot enter the brain (blood-brain barrier[55]) and generally are not resorbed after oral administration. Renal clearing depends on molar mass[56]. As a result, high molecular weight compounds in particular are excreted slowly and stored, especially in the cells of the reticuloendothelial system (RES)[57].
- Stereochemistry of polymers may influence their biological properties. Isotactic poly(acrylic acid) shows a higher antiviral activity than the heterotactic compound[58]. Poly(D-lysine) is not degraded, poly(L-lysine) is degraded inside the cell[59].
- Copolymerization allows systematic variation of the distribution of active units along a polymer chain. Moreover, copolymers can be tailor-made in order to vary hydrophilicity or lipophilicity of the entire molecule and of single domains (block systems). Properties of the microenviron-

ment in a polymer coil can differ drastically from those of the bulk solution and are strongly influenced by comonomer composition[60]. Thus, time of release of polymer-fixed drugs can be varied.

- Incorporation of labile groups into the main chain renders hydrolytic or enzymatic degradation possible, and hence leads to a slow release of polymer-fixed or incorporated drugs (chronomers)[61].
- Careful selection of appropriate spacer length and structure allows a wide variation of cleavability[62].
- Toxicity of low molecular weight compounds can be masked by fixing them to a polymer chain[62b,63].
- Binding of haptens (low molecular weight molecules which, when attached to certain macromolecular carriers, elicit an immune response) to synthetic polymers leads in almost every case to substantially reduced[62b] immune response or even blocks it totally[64].
- Moreover, one can consider macromolecules to show pharmacological (*e.g.* antitumor) activity as such, without a drug (*e.g.* antitumor agent) fixed to it. This is indeed the case, as will be shown in Section 3.3.1.

In contrast to the advantages of polymer specific properties mentioned so far, there are important disadvantages, objections and problems[62c].

- Biocompatibility of water soluble polymers has so far only been tested in a few isolated cases. We still lack overall experience with hemolytic activity, pyrogenicity, osmotic properties, and interaction with plasma constituents under *in vivo* conditions.
- Non-degradable synthetic polymers can be used in order to obtain depot-effects. A long-lasting systemic storage of high molecular weight compounds can however not be accepted from pharmacological and toxicological points of-view. Therefore, the development of bio-degradable polymers is becoming more and more important[66]; oligomers or polymers of low molecular weight which can be excreted may be also used.
- There have been few systematic investigations on the body-distribution of polymers and its change with time[54].
- Little attention has been paid to immunological reactions against pharmacologically active polymers[64b].
- Synthetic polymers investigated so far are not resorbed from the gastrointestinal tract; a fact which decisively limits the choice of appropriate drug formulations.

Nothing at all could be said in favor of polymeric pharmaca if they were just "me-too drugs"[4]—drugs which can do a job that low molecular weight pharmaca can do just as well. Therefore it is reasonable to concentrate efforts on the development of pharmacologically active polymers in such areas where low molecular weight drugs have failed or have given only insufficient therapeutic results. One such area is the chemotherapy of cancer. There is no doubt that the use of polymeric antitumor agents has only been moderately successful up to now. Investigations carried out so far, however, give clear-cut evidence that these drugs open up new possibilities which could not be realized by the use of low molecular weight drugs.

### 3.2. How Do Macromolecules Enter Cells?

Besides diffusion and active transport, there is one other way in which cells take up material: endocytosis[67] (phagocytosis, pinocytosis). Cell uptake of polymers is normally limited to this mechanism[68], which resembles the ingestion of material by amoebae:

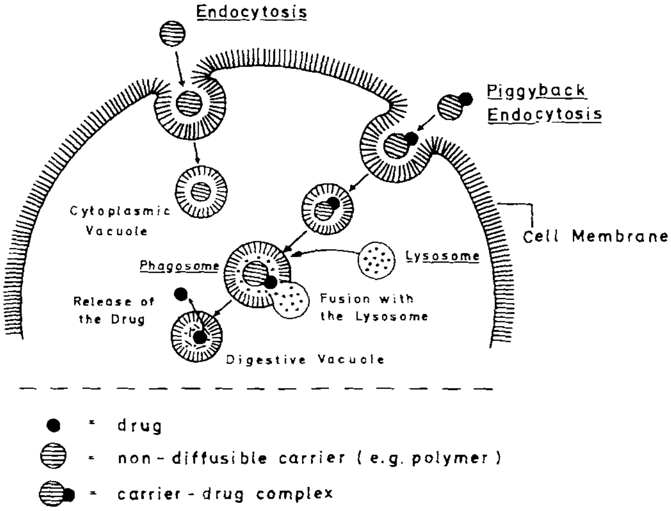
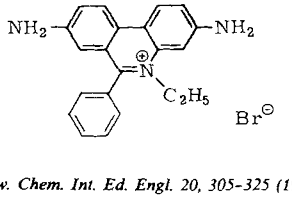


Fig. 3. Schematic representation of cell-uptake of polymers by endocytosis and piggyback-endocytosis.

The endocytosis of polymers is normally initiated at the cell membrane. Subsequently, membrane invaginations are formed which are then separated from the membrane. The vacuoles thus formed can fuse intracellularly with a lysosome. The about 40 lytic lysosomal enzymes will then attack the endocytosed macromolecule. Many investigators have studied the influence of charge, hydrophobicity and molecular weight on endocytotic uptake and have obtained contradictory results[69].

A special case of endocytosis is called piggyback-endocytosis[70] (Fig. 3): a pharmacon is attached to a macromolecule which can be taken up by endocytosis. This, on the one hand, prevents diffusion of the drug through the membrane and therefore leads to a first degree in cell specificity (because the drug-carrier-complex will only be taken up by cells having endocytotic activity). As tumor cells in general have a higher rate of endocytosis than the corresponding normal cells (see Table 1), it was expected that the use of polymeric carriers might lead to a certain tumor cell specificity. On the other hand, antitumor agents which cannot enter the cell through the membrane can be transported into the cell *via* endocytosis when linked to a polymer (cf. Section 3.3.3).

*A. Trouet et al.*[71] presented an interesting example for therapeutic usefulness of piggyback endocytosis. They studied the effect of ethidium bromide *(3)* on *Trypanosoma Cruzi*. If added to a cell culture *(in vitro)* of this parasite, *(3)*, is highly toxic for *T. cruzi* cells. However, when administered *in vivo* to a mouse infected by *T. cruzi*, the drug has hardly any



*(3)*

effect at all. Figure 4 shows why the parasite can escape the toxic drug *in vivo* and how, by means of piggyback endocytosis, it can be attacked effectively: *T. cruzi* is taken up by endocytosis and thus ultimately resides inside the lysosomes. Due to a special cell wall structure, it there resists the lytic enzymes (Figure 4).

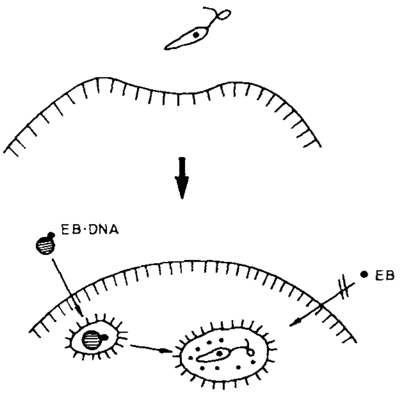


Fig. 4. Schematic representation of cell-uptake of the parasite *Trypanosoma cruzi* *via* endocytosis; effect of the ethidium bromide-DNA complex (EB-DNA) on a cell attacked by the parasite (cf. [71]).

While free ethidium bromide *(3)* cannot enter the cell, it is taken up as a complex with DNA, probably *via* piggyback endocytosis. After fusion of the ethidium bromide-loaded vacuole with a lysosome inhabited by a parasite, the DNA carrier will be degraded by lysosomal enzymes and the drug can attack the parasite.

Experimental results shown in Figure 5[71] show that mice infected with *T. cruzi* have much better chances of survival when *(3)* is not administered in a free form but rather as a complex with the carrier molecule DNA.

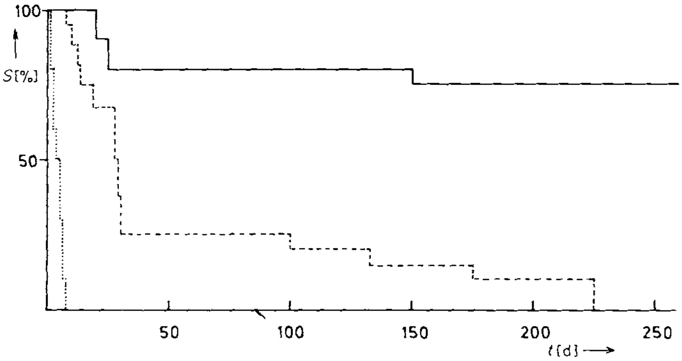


Fig. 5. Survival of mice infected by *Trypanosoma cruzi* [71]. Treatment: 3 injections (on days 2, 3, 4). (······) control animals, no treatment; (– – – – – –) 3 × 0.5 mg ethidium bromide *(3)*; (———) 3 × 0.5 mg ethidium bromide-DNA complex; $S$ = percent surviving animals; $t$ = time after i.p. injection of *T. cruzi*.

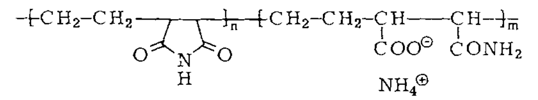
Systems of this type which can be targeted to lysosomes *via* endocytosis are called "lysosomotropic" and discussed as carriers for pharmaca by *de Duve et al.*[72].

## 3.3. Polymeric Antitumor Agents on a Molecular Level—Selected Examples

After having briefly discussed the special mode of uptake of polymeric molecules into cells, we shall now select a few of the numerous examples of polymeric antitumor agents; though far from being exhaustive, these will serve to illustrate the relevant possibilities and problems.

### 3.3.1. Synthetic Polymers Themselves Are Active Against Tumors

As pointed out previously (Section 3.1), it was found that synthetic polymers as such act upon cells and organisms without any low molecular weight drugs linked to them. Poly(acrylic acid), for example, shows antiviral activity, which is highly dependent on both molecular weight and tacticity[58]. DIVEMA, a copolymer of maleic anhydride and divinyl ether[73], stimulates the immune system and is discussed as a possible interferon inducer[74]. Recently, a comprehensive treatise on anionic polymeric drugs has been published[75]. Some cationic drugs show antitumor activity, too[76]. Recently, a random copolymer of low molecular weight *(4)* attracted special attention. It consists of ethylene and modified maleic acid units[77].


*(4)*

When tested against a methylcholanthrene-induced bladder carcinoma of rats, *(4)* caused an increased lifespan and almost totally inhibited the formation of the lung metastases found in untreated control animals. When *(4)* was administered after operative removal of the tumor, animals not only were free of metastases but also showed no recurrence of the tumor, when the polymer was administered repeatedly every 6 weeks (Fig. 6)[77].

The authors could show that *(4)* enhances immune response of the animals and that this effect is due to a stimulation of the antibody-producing B-cells. *(4)* is not toxic, nor immunogenic. First clinical trials[78] on patients with gastrointestinal tumors show that *(4)* is also non-toxic in humans. The results published so far suggest an increase in lifespan. Another copolymer which shows antitumor activity without being cytotoxic itself has been published recently[79].

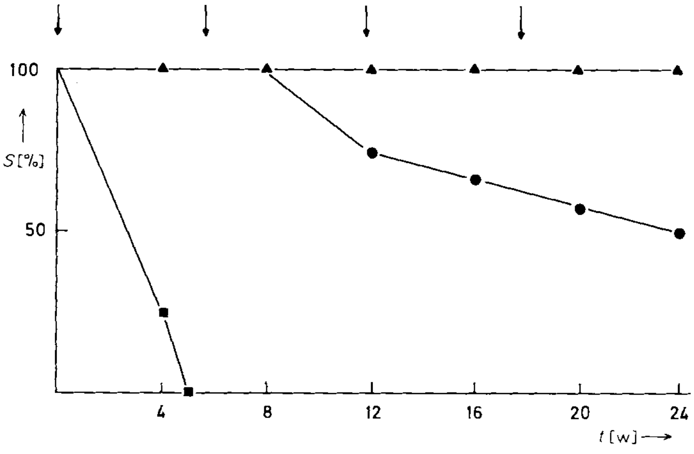
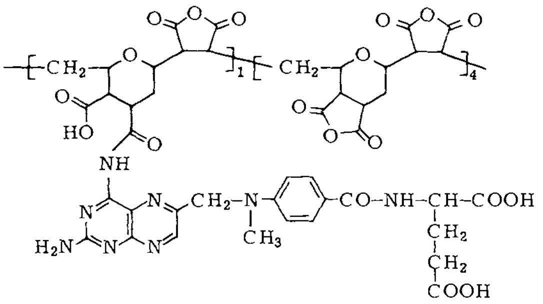


Fig. 6. Survival of rats after surgical removal of a primary carcinoma of the bladder and subsequent treatment with copolymer *(4)*. (■—■) untreated controls, death caused by lung metastases; (●—●) single dose of *(4)* (day 1): recurrence of local tumor; (▲—▲) four doses of *(4)* at 6 week intervals (see arrows); $S$ = percent survivors; $t$ = time after excision of primary tumor.

Thus, the idea of enhancing the body's own immune response with suitable immune-stimulating polymers has found more experimental support.

### 3.3.2. Fixation of Methotrexate to an Immune-Stimulating Carrier Polymer

The immune-modulating effect (*e.g.* activation of macrophages) of the cyclo-copolymer of divinylether and maleic anhydride (DIVEMA) stimulated the idea of using this polymer as a carrier for the folic acid antagonist methotrexate (MTX). MTX is an antitumor agent used clinically; its immunosuppressive properties often give rise to therapeutic problems.



*(5)*

Polymer DIVEMA-MTX *(5)* was synthesized by covalent binding of the pteridinyl group of MTX to DIVEMA[80]. The effect of *(5)* on the macrophage system (macrophages are immune cells which literally eat up foreign material) was tested. It showed a stimulating effect which was, however, slightly inferior to that of DIVEMA itself[81].

In spite of the lability of the linkage of MTX to DIVEMA, copolymer *(5)* showed higher antitumor activity (as tested against L1210 leukaemia in mice). This may be due to sustained release and longer systemic circulation of MTX (Fig. 7)[82].

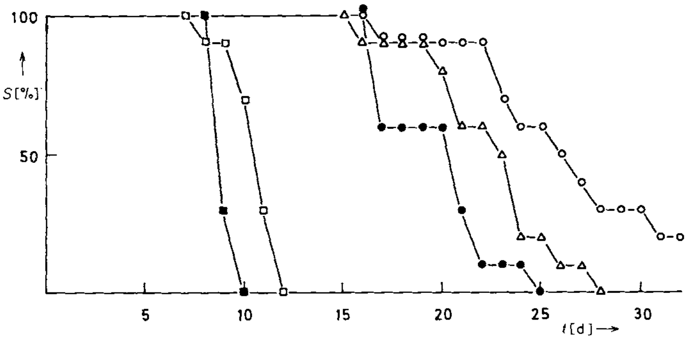


Fig. 7. Survival of CDF$_1$-mice (male) after i.p. injection of $10^5$ L1210-tumor cells and subsequent treatment with polymer-fixed methotrexate *(5)* on days 1,5,9,13,17 [82]. (■—■) untreated controls; (□—□) treatment with DIVEMA (80 mg/kg body weight); (●—●) treatment with DIVEMA + MTX (29 + 10 mg/kg body weight); (△—△) treatment with MTX (20 mg/kg body weight, optimum dose); (○—○) treatment with DIVEMA-MTX *(5)* (31 mg/kg body weight) ≙ 8 mg MTX/kg body weight); S = percent survivors; *t* = time after tumor inoculation.

One undesired effect of polymer fixation is a marked increase in toxicity of DIVEMA-MTX in a therapeutic dose range. This is probably due to uptake of the polymer into the macrophages, where MTX is cleaved from the carrier and exhibits toxic effects. Moreover, the *in vitro* inhibition of tetrahydrofolic acid dehydrogenase by *(5)* was evaluated (Murine L5178 Y-tumor cells being used as model system)[83]. The results suggest that MTX is cleaved rapidly from the carrier polymer.

### 3.3.3. Combination of MTX with a Lysosomotropic Carrier

Besides being immuno-suppressive, MTX shows one more disadvantage: some tumor cells are resistant against the drug.

This is probably due to the lack of the appropriate transmembrane transport system for MTX[84]. *Ryser* and *Shen*[84] showed that MTX linked covalently to poly-(D-lysine) and poly-(L-lysine) is taken up equally well by resistant and nonresistant cells. MTX linked to a polymer of molecular weight 60000—70000 is taken up 200 times better than free MTX. Cell growth is, however, only inhibited if a poly-(L-lysine) carrier is used (Fig. 8)[84].

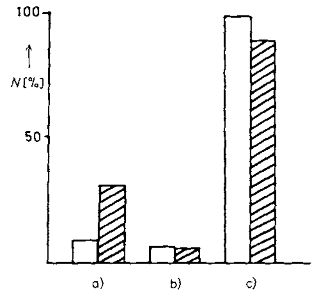
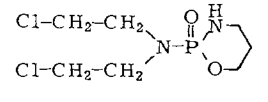


Fig. 8. Growth inhibition of Chinese hamster ovary (CHO) cells after application of $10^{-6}$ moles of MTX [84]: a) low molecular weight MTX; b) poly(L-lysine)-MTX, MW 70000; c) poly-(D-lysine)-MTX, MW 60000; unshaded: non-resistant cell line; shaded: MTX-resistant cell line; $N$ = number of residual cells after 4 days (% of cells in untreated control culture).

The authors showed that only this polymer and not the poly-D-isomer, is degraded intracellularly. Polymer-bound MTX being only a weak inhibitor of dihydrofolic acid reductase, enzymatic degradation of the polymer is essential for an inhibiting effect. The MTX-poly-(L-lysine) conjugate is a lysosomotropic system (cf. Section 3.2.) which is only activated in the secondary lysosomes (phagosomes). Thus, MTX-resistance of tumor cells can be overcome. Moreover it seems that, due to higher activities of proteolytic enzymes in some solid tumors (see Table 1), a certain tumor cell specificity can be obtained. These investigations show that stereochemistry of the polymer main chain may play an important role in antitumor activity.

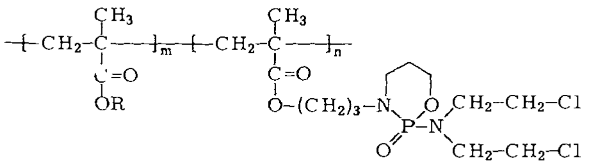
### 3.3.4. A Way Out of an Impasse

2-[Bis-(2-chloroethyl)amino]-1,3,2-oxazaphosphorinane 2-oxide (cyclophosphamide, cytoxane) *(6)* is a well known antitumor agent[85] and can be regarded as a non-toxic pro-drug of the ultimately active *N,N*-bis(2-chloroethyl)phosphoric diamide (Friedman acid) *(10)*[27].



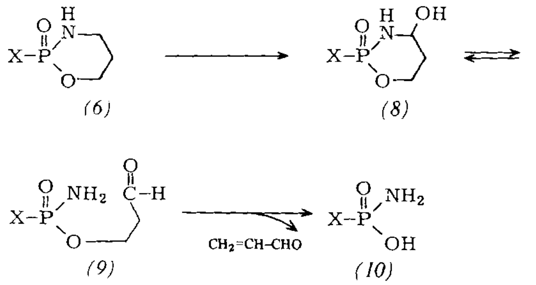
*(6)*

According to the model discussed above (Fig. 2), polymeric derivatives of cyclophosphamide (CP) of the type *(7)* were synthesized[86].



(7a), $R = -(CH_2)_2-SO-CH_3$; (7b), $R = -(CH_2)_2-\overset{\oplus}{N}(CH_3)_3\ Cl^{\ominus}$

These compounds turned out to be only weakly active in animal tests. In order to understand why this is the case, we have to consider the metabolism of CP *(6)* (Fig. 9).



$X = (Cl-CH_2-CH_2)_2N$

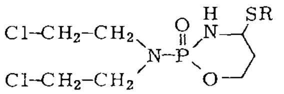
Fig. 9. Metabolic activation of cyclophosphamide *(6)* in the organism by hydroxylation and release of acrolein.

Investigations concerning the metabolism of transport form and active form of CP by *Hohorst* and *Brock*[87] as well as by *Connors et al.*[88] showed that *(6)* is hydroxylated preferentially by liver enzymes whereupon acrolein is spontaneously released, yielding Friedman acid *(10)*.

While *(6)* is inactive *in vitro* (due to the lack of hydroxylating enzymes), it shows high cell toxicity *in vivo* after oxidation to the labile 4-OH-CP *(8)*. Accordingly, the primary metabolite *(8)* is not only active *in vivo* but also in cell cultures.

Polymers *(7)* contain CP in a covalently fixed form which, even if it is cleaved from the polymer after transport to a tumor cell, is inactive: it has to go to the liver for hydroxylation. So polymers *(7)* are almost inactive.

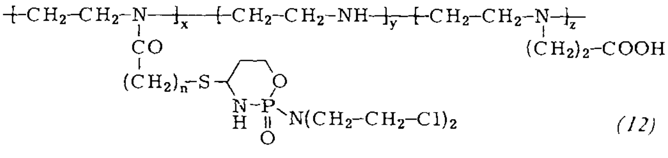
What can be learned from this impasse? A covalent fixation of an antitumor agent to a polymeric carrier has to be achieved in such a way that a directly active species can be cleaved off. After *Takamizawa et al.*[89] had found a way to synthesize the active labile metabolite *(8)*, *Hohorst et al.*[90] were able to prepare stabilized derivatives *(11)* which can be hydrolytically cleaved to yield *(8)*.



*(11)*

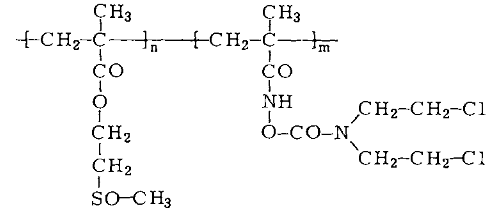
Now it was possible to fix the active metabolite in its stable form *via* derivatives with reactive groups R ($R = -(CH_2)_n-OH$ and $-(CH_2)_n-COOH$)[91] to a polymer carrier, *e.g.* modified poly(ethylenimine).

Polymers *(12)* can, after transport to tumor cells and cleavage of the active metabolite *(8)* from the carrier, directly act cytotoxically. The antitumor activity of low molecular weight derivatives of type *(11)* is comparable to the activity of CP itself[91c]. When DIVEMA is used as a carrier polymer, activity decreases[91c]. Polymers *(12)* are currently being tested.



*(12)*

Similar considerations governed fixation of bis(2-chloroethyl)amine (N-Lost) to polymers. If fixed as an amide, this highly cytotoxic compound is inactive. Therefore, polymer fixation was carried out using labile bonds (*O*-acyl-hydroxamic acids, urethanes), *e.g.* *(13)*[92].



*(13)*

First investigations show that compounds *(13)* are active *in vitro*[92].

These two examples suggest that cleavability of the polymer-pharmacon bond[62] and bio-availability of cytotoxic units play a decisive role in the use of polymeric carrier systems.

### 3.3.5. Affinity Chemotherapy—
### An Attempt at Targeting Antitumor Agents

As a last example for antitumor agents on a molecular level, we will describe a system which includes a homing device (as discussed in the model, Fig. 2).

Animal cells contain specific surface proteins (surface antigens), which are involved in many biological processes (cell-cell recognition, immune response, cell differentiation). If we are able to produce antibodies against a certain target tissue (*i.e.* against surface antigens of cells of this tissue), the antibodies should be able to recognize the target tissue specifically. Such an antibody might be loaded with antitumor agent and serve as a specific transport vehicle to target cells which bear the corresponding antigen on their surface. This is the principle of affinity chemotherapy which was proposed by *Paul Ehrlich* as early as 1906[3] and was developed, *inter alia*, by *Wilchek et al.*[93]. It is shown schematically in Figure 10.

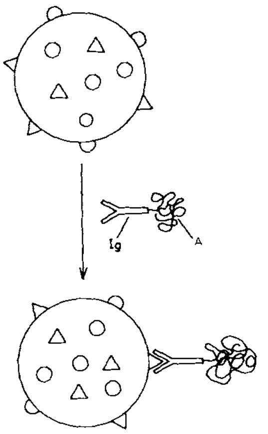


Fig. 10. Schematic representation of affinity chemotherapy of a *tumor cell*. A: polymeric antitumor agent; Ig: Immunoglobulin; △: tumor associated antigens; ○: antigens of a normal cell.

Apart from problems with preparation and isolation of pure, tumor-specific antibodies, one main difficulty is to find the optimum concentration of antitumor agent fixed to the antibody. If the amount of antitumor agent is too low, the tumor cell may be recognized, but antitumor activity will be insufficient. If it is too high, as shown schematically in Figure 11a, the combining site of the antibody may be blocked and recognition of the antigen becomes impossible.

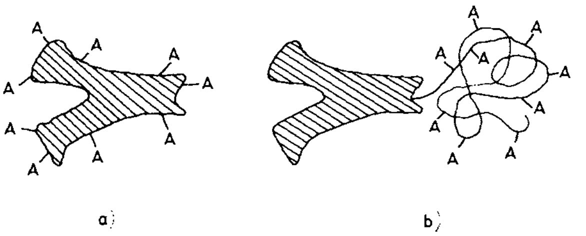


Fig. 11. Schematic representation of the binding of an antitumor agent (A) to an antibody. a) Direct fixation of antitumor agents to immunoglobulins; b) fixation of a polymer loaded with antitumor agent to an immunoglobulin.

One might avoid the difficulties described above by binding the antitumor agent to a polymer which (as discussed in the model, Fig. 2) itself is linked to an antibody serving as homing device (Fig. 11b) and which does not interfere with the combining site of the antibody. Such a polymer has *e.g.* been synthesized by *Rowland, O'Neill* and *Davies* (Fig. 12)[94].

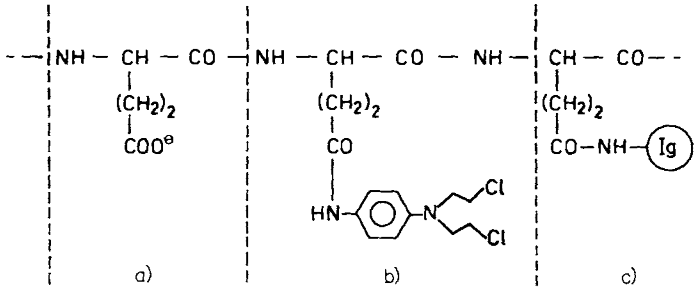


Fig. 12. Polymeric, tumor cell-specific alkylating antitumor agent (cf. Fig. 2 and 13). a) Solubilizer, poly(glutamic acid) (PGA); b) pharmacon, *p*-phenylenediamine-lost (PDM); c) homing device, immunoglobulin (Ig).

Poly(glutamic acid) (PGA) serves as a macromolecular carrier. The carboxylate groups of glutamic acid (a) may be regarded as the solubilizer described in the model (Fig. 2). *p*-Phenylenediamine-lost (PDM) fixed as an amide to the polymer chain is the antitumor agent (b). As a homing device (c) a protein (Ig) was used which had been isolated from the serum of rabbits "vaccinated" with lymphoma tumor cells. (These rabbits should have produced tumor specific antibodies.) When tested *in vivo* against EL-4 lymphoma of mice, this system was superior to the corresponding control systems. None of the animals treated with the terpolymer died within 60 days after inoculation of tumors (Fig. 13).

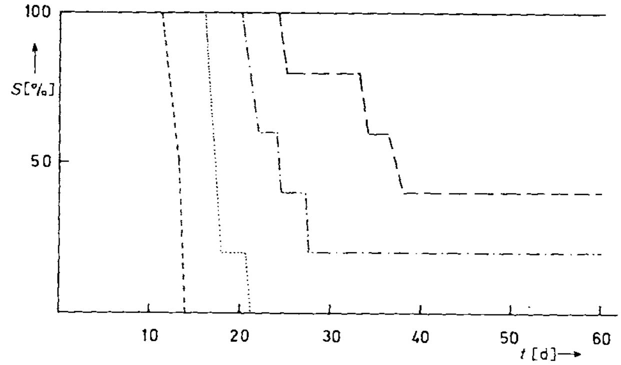


Fig. 13. Survival of mice bearing an EL-4-lymphoma after treatment with polymeric antitumor agents (cf. Fig. 12) [94]. (– – – – – – – –) untreated controls; (·········) 4 mg Ig; (–·–·–·–·) 750 μg PGA-PDM; (— — — —) 4 mg Ig + 750 μg PGA-PDM; (————) PGA-PDM-Ig (≙4 mg Ig and 750 μg PGA-PDM; *S* = percent survivors; *t* = time after tumor inoculation.

On the basis of control experiments, the authors conclude that the effect is due to the carrier and is not merely a synergistic effect (*i.e.* an effect which can just as well be obtained by administration of a mixture of free immunoglobulin (Ig) and lost-polymer). Later, *Rowland* reported similar experiments with dextran as carrier system and could not completely exclude synergistic effects in this case[95]. The concept of affinity chemotherapy is likely to bring about useful results in the development of antitumor agents[20,96]. The first positive results obtained in animal tests justify further research in the area of targeting of antitumor agents using a homing device.

### 3.4. From Research Lab to Clinic?

An unprejudiced reader may conclude from the five examples given in Section 3.3 that polymeric antitumor agents on a molecular level will soon be or are already used clinically in chemotherapy. This is, however, not the case; some of the relevant problems have already been mentioned in Section 3.1. What has been achieved so far? Concepts for pharmacologically active polymers have been developed. Numerous substances have been synthesized. Model considerations and a broad spectrum of molecular structures have opened a vast field which has to be investigated more systematically and in close interdisciplinary team-work.

Same old story: there is an idea, one can show that it works "in principle", and then the tedious and laborsome phase of optimization and adaption towards a biological target system begins. Accordingly, our knowledge of tumor cells and of interactions between an organism and pharmacologically active polymers must be substantially improved. Great care has to be taken in the transfer of results from animal tests to clinical trials[97]: many of the drugs active in animal models turned out to be inactive in humans. Regarding the nice graphs showing increase in lifespan (Fig. 13), one should not forget that affinity chemotherapy in human patients requires detection and isolation of human tumor-specific antibodies—a problem not yet solved. Recent progress in membrane biology, immunology, and gene technology (isolation of monoclonal antibodies) raises hopes for further advancements.

## 4. Polymeric Antitumor Agents on a Cellular Level?

### 4.1. Can the Immune Response to Tumor Cells Be Mimicked?

Of all parts of a cell which change during the transition from a normal to a malignant cell (carcinogenesis), the biomembrane is affected to a great extent (cf. Table 1). Many signals controlling cell growth, mitosis and cell uptake originate in the membrane. It is therefore not surprising that minor changes in the cell surface have major consequences for cell behavior. In this context, the cell membrane with its associated antigens[98] plays a key role as a starting point for considerations to solve the tumor problem by mimicking parts of the immunological process.

### 4.1.1. Death of a Tumor Cell

Although tumor cells can normally escape the immune system, it is very impressive to see what happens, if they fail to circumvent the immune defense of the body. Figure 14[99] demonstrates this and shows the death of a tumor cell, a process which takes place on a cellular level and which may teach us how to develop antitumor agents on this cellular level.

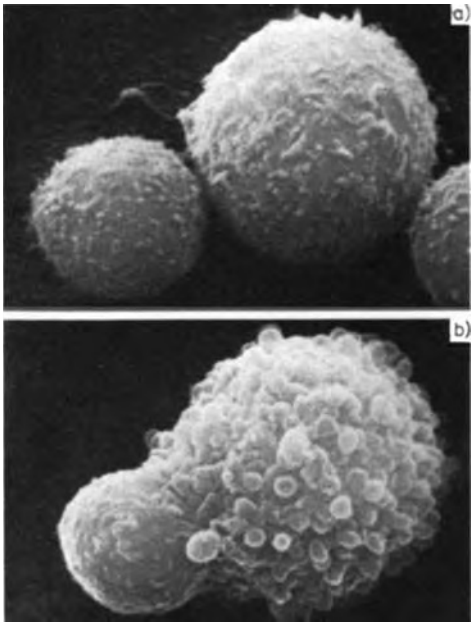


Fig. 14. Electron microscopic picture showing a T-lymphocyte attacking a tumor cell [99]. a) The tumor cell (right) has antigens on its surface which are recognized selectively by the activated lymphocyte (*i.e.* by the antibodies in the lymphocyte membrane). b) Death of a tumor cell. Destruction by the lymphocyte occurs by membrane destabilization—"bubbles" are formed.

These two pictures (Fig. 14) show the sequence of an attack of a T-lymphocyte on a malignant cell. The tumor-associated antigens are recognized by the attacking lymphocyte. This corresponds to the principle of affinity chemotherapy described in Section 3.3.5, but in this case on a cellular level. The subsequent destruction of the tumor cell is not a molecular process (as defined in Section 1), but is the consequence of the membrane destruction (formation of bubbles) after contact of the T-lymphocyte with the tumor cell. This mechanism of destruction by a membrane destabilization is not well understood in all details; three possibilities at least are discussed: a locally high concentration of lysophospholipids[100], release of toxic (*i.e.* membrane destructive) substances by the lymphocyte[101] or spontaneous membrane destabilization by a change of protein conformation[102].

The basis of all hypotheses is destruction on a purely physical level. Although there is not yet any exact proof, there are a number of hints supporting this assumption: a mere adsorption of liposomes, *i.e.* closed spherical structures, to a cell can destabilize both membranes to an extent that allows a penetration of low molecular substances into the cell[103]. A cell fusion, which can take place only after a strong destabilization of the membranes, can be induced in several ways, for example biologically (by means of the Sendai virus[104]), chemically (by the presence of calcium ions[105] or by incorporation of lysophospholipids[100] into a membrane), or physically (by applying an electric field[106]).

Bearing in mind the picture of the death of a tumor cell, one wonders whether antitumor agents on a cellular level can be conceived and whether they would be able successfully to mimic such a process.

A possible starting point for solving this problem could be the interaction of a tumor cell with a synthetic vesicle, which would have to fulfill the following criteria:

1. Possibility of cell-specific recognition.
2. Ability to destabilize the tumor cell membrane.
3. Similar or higher stability than the tumor cell membrane.

All three points are largely unsolved problems in the investigation of the use of liposomes in medicine described in the literature. Attempts to mimic the above-described interaction of a lymphocyte with liposomes from natural or synthetic phospholipids will lead to the destruction of the liposome rather than of the malignant cell: the liposome is fused, undergoes endocytosis, or its membrane is destabilized[107]. This is of course not what one expects from an antitumor agent on a cellular level. Even less is known about the problems of cell specific recognition (cf. Section 4.3.3.) and of destabilization of the tumor cell membrane (cf. Section 4.3.4.). Membrane-destroying compounds would also destroy the liposomes. It is essential, therefore, to increase the stability of synthetic liposomes. Among the three problems mentioned, this particular one seems to have the best chance of being realized. In addition, stabilized cell models are of interest *per se*, *e.g.* for the investigation of cell recognition[108], cell-cell interaction[109] *etc.* The problem of stability is also essential for the use of liposomes as drug carrier systems. Liposomes used so far, exhibit a relatively high permeability for entrapped drugs when exposed to blood, since they are destabilized by adsorption of proteins and destroyed by the action of lipase[110]. In the following Section we will describe current considerations on, and experiments designed for, the creation of models of biomembranes and cells with high and variable stability.

### 4.1.2. Mother Nature Forms Stable Membranes. Can a Chemist Reach Her Standards?

The well-known membrane model of *Singer* and *Nicolson* (Fig. 15) pictures a double layer formed by a lipid matrix and proteins, *e.g.* enzymes as informational and functional units "floating" in this lipid matrix[111].

However, this intuitive representation is oversimplified: Vesicles from natural phospholipids have the same lipid matrix, but are rather unstable; some biomembranes contain only 25% of lipids[112]. Obviously Nature finds additional means for creating membranes of high stability. Let us look at two of these in more detail:

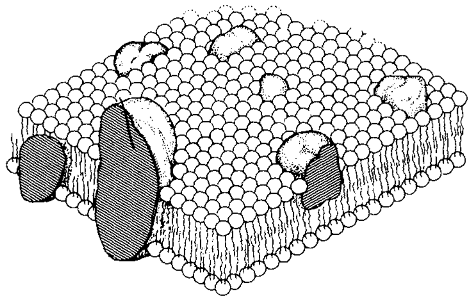


Fig. 15. Fluid mosaic model of biological membranes after *Singer* and *Nicolson* [111].

1. Besides the so-called "integral" membrane proteins (which are embedded in the hydrophobic part of the membrane), there are peripheral proteins, only found in the hydrophilic part of the membrane. Some of these peripheral proteins act as a support, because they are associated with several integral proteins. A well-known example is spectrin situated at the inside of the erythrocyte membrane[113].
2. As an example of an enveloped vesicle we have the so-called "coated vesicles"[114]. Here a phospholipid vesicle within a cell is coated by a polypeptide and resembles a football in a basket. A comparable form of membrane coating is found in the cell walls of bacteria[115]. Here too, macromolecules provide an envelope similar to a basket, but they consist of polysaccharides cross-linked by oligopeptides. It is remarkable that this extreme stabilization by an exogeneous support is found in bacteria, which (as parasites in foreign tissues) have to be especially resistant.

How can a stabilization of biomembranes be achieved synthetically? The attempt to mimic a support similar to the spectrins seems unlikely, for very little is known, as yet, about the interactions between peripheral and integral proteins. An increase of stability *via* polymer coating, as in the case of a bacterial membrane, sounds more realistic and is in fact used to immobilize living cells. This coating however prevents contact and hence interaction of different cells[116].

The most convenient and realistic attempt seems to be a method which uses membrane lipids for stabilization. One experiment of this type (though having a different purpose) has been described by *Khorana et al.*[117]. These authors incorporated lipids carrying photoreactive groups into a membrane and could (by irradiation) covalently fix proteins to these lipids. Another method with much greater potential uses polyreactions of lipids carrying polymerizable groups.

Before we report on investigations of such systems in the next Section, we will introduce models used to study membrane properties.

### 4.1.3. Membrane Models

A knowledge of the bulk properties of lipids and surfactants is not sufficient to gauge their ability to form membranes. The interaction with an aqueous phase results in totally different properties, which can be described by terms like amphiphilic behavior, micelle and liposome formation, and formation of lyotropic phases[118]. For thermodynamic reasons lipids undergo self-organization to membrane-like structures when brought into an aqueous medium. Several methods have been developed in recent years for investigations on those structures. The most common membrane models, namely monolayers[119], black lipid or bilayer membranes (BLM)[120], and liposomes[121], are shown schematically in Figure 16[122].

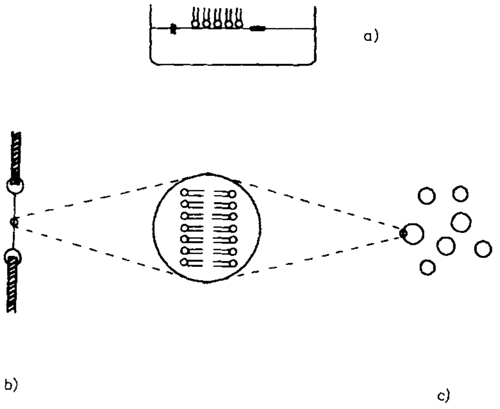


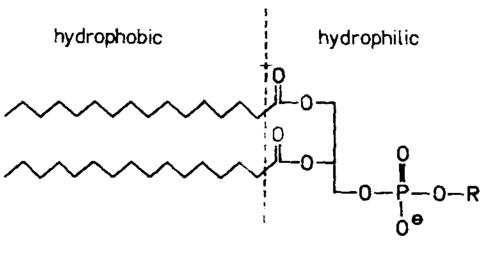
Fig. 16. Orientation of amphiphilic compounds in model membranes: a) monolayer; b) bimolecular lipid membrane (BLM); c) liposome. Between b) and c) a cross-section through the BLM or liposome wall is shown.

In all three cases amphiphilic lipids orient spontaneously to form a structure which resembles the phospholipid structure in a biomembrane. These membrane models permit investigations of physical properties of oriented systems in a variety which cannot be performed with complex natural membranes. A comparison and discussion of these models is given by *Noell*[122].

## 4.2. Polymeric Membrane Models

### 4.2.1. Polymerizable Lipids

The main component of lipids in a membrane consists of phospholipids. The structure of typical representatives of these amphiphilic systems (with hydrophobic alkyl chains and a hydrophilic head group) is shown in Figure 17.



Lecithin $R = -(CH_2)_2-\overset{\oplus}{N}(CH_3)_3$

Cephalin $R = -(CH_2)_2-\overset{\oplus}{N}H_3$

Phosphatidylserine $R = -CH_2-\underset{\oplus NH_3}{CH}-COO^{\ominus}$

Fig. 17. Structures of the most common biomembrane phospholipids.

If one intends to synthesize polymerizable lipids to build up membranes of high stability, the polymerizable group can be introduced into different parts of the lipid molecules, *i.e.*

into the hydrophilic head group or into the hydrophobic alkyl chain (Fig. 18)[123].

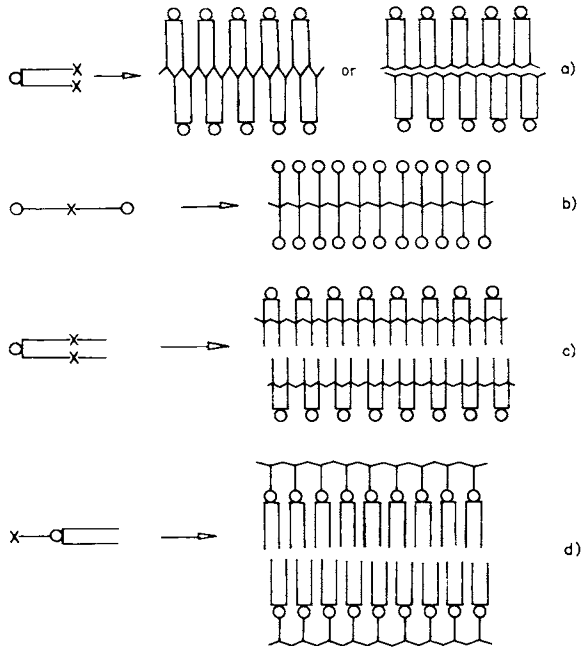


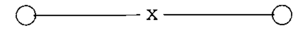
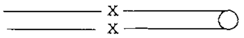
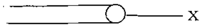
Fig. 18. Possible ways to synthesize polymeric model membranes [123] (x = polymerizable group). a)—c) Polymerization with preservation of head group properties; d) polymerization with preservation of chain mobility. For examples of appropriate monomers, see Table 2.

All four principles in Figure 18 result in systems which have properties differing from those of cell membranes. Methods a—c have no influence on the head groups and hence preserve physical properties (such as charge, charge density, *etc.*) but change the fluidity of the hydrophobic chains. In case d the fluidity is not affected, but there is no free choice of the head groups. All polymeric lipid systems will show an increase in viscosity and a decrease in the lateral mobility of the molecules.

All four possibilities shown in Figure 18 for the formation of polymerizable lipids have been realized synthetically[123]. To choose the proper lipid to start with, "one need not attempt to reproduce Mother Nature slavishly" *(Fendler)*[124]. *Kunitake* (1977)[125] was able to show that simple molecules like dialkylphosphates or dialkyldimethylammonium salts can form liposomes. *Fuhrhop*[126] and *Kunitake*[127] could realize liposome formation with molecules consisting of one chain with two hydrophilic head groups (cf. Table 2, type b). Acrylic and methacrylic groups (type a and d in Table 2) as well as diacetylene and diene groups (type b and c) have been used as polymerizable groups. Some of the synthesized polymerizable lipids are listed in Table 2.

The compounds shown in Table 2 have been investigated regarding their ability to undergo polymerization in a membrane-like orientation. The formation of monolayers at the gas-water interface is the oldest and most simple of the membrane models in Figure 16. A monolayer permits a variety of investigations and is especially suited for studying polymerizations. This method will therefore be described in more detail.

Table 2. Several examples of polymerizable, liposome-forming lipid analogues (cf. Fig. 18).

| Type | Compound | | Ref. |
|---|---|---|---|
| a) |  | | |
| | $CH_2{=}C(CH_3){-}CO{-}NH{-}(CH_2)_{10}{-}CO{-}O{-}(CH_2)_2\diagdown\ \ CH_3$<br>$\overset{\oplus}{N}\quad Br^{\ominus}$<br>$CH_2{=}C(CH_3){-}CO{-}NH{-}(CH_2)_{10}{-}CO{-}O{-}(CH_2)_2\diagup\ \ CH_3$ | *(14)* | [123] |
| | $CH_2{=}C(CH_3){-}CO{-}O{-}(CH_2)_{11}\diagdown\ \ CH_3$<br>$\overset{\oplus}{N}\quad Br^{\ominus}$<br>$CH_3{-}(CH_2)_{15}\diagup\ \ CH_3$ | *(15)* | [128] |
| b) |  | | |
| | $HOOC{-}(CH_2)_8{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}COOH$ | *(16)* | [123] |
| | $HO{-}(CH_2)_9{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_9{-}OH$ | *(17)* | [123] |
| | $H_2O_3P{-}O{-}(CH_2)_9{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_9{-}O{-}PO_3H_2$ | *(18)* | [129] |
| c) |  | | |
| | $CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}CO{-}O{-}CH_2$<br>$CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}CO{-}O{-}CH$<br>$CH_2{-}O{-}\overset{O}{\overset{\Vert}{P}}{-}O{-}(CH_2)_2{-}\overset{\oplus}{N}(CH_3)_3$<br>$O^{\ominus}$ | *(19)* | [130] |
| | $CH_3{-}(CH_2)_{12}{-}CH{=}CH{-}CH{=}CH{-}CO{-}O{-}CH_2$<br>$CH_3{-}(CH_2)_{12}{-}CH{=}CH{-}CH{=}CH{-}CO{-}O{-}CH$<br>$CH_2{-}O{-}\overset{O}{\overset{\Vert}{P}}{-}O{-}(CH_2)_2{-}\overset{\oplus}{N}(CH_3)_3$<br>$O^{\ominus}$ | *(20)* | [130] |
| | $CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}CO{-}O{-}(CH_2)_2\diagdown\ \ CH_3$<br>$\overset{\oplus}{N}\quad Br^{\ominus}$<br>$CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}CO{-}O{-}(CH_2)_2\diagup\ \ CH_3$ | *(21)* | [132] |
| | $CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_9{-}O\diagdown\ \ O$<br>$\overset{\Vert}{P}{-}OH$<br>$CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_9{-}O\diagup$ | *(22)* | [133] |
| | $CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}CO{-}O{-}(CH_2)_2\diagdown$<br>$N{-}(CH_2)_2{-}SO_3H$<br>$CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}CO{-}O{-}(CH_2)_2\diagup$ | *(23)* | [134] |
| d) |  | | |
| | $CH_3{-}(CH_2)_{16}{-}CO{-}O{-}CH_2$<br>$CH_3{-}(CH_2)_{16}{-}CO{-}O{-}CH$<br>$CH_2{-}O{-}CO{-}C(CH_3){=}CH_2$ | *(24)* | [123] |
| | $CH_3{-}(CH_2)_{17}{-}O{-}CH_2$<br>$CH_3{-}(CH_2)_{17}{-}O{-}CH$<br>$CH_2{-}O{-}CO{-}(CH_2)_5{-}NH{-}CO{-}C(CH_3){=}CH_2$ | *(25)* | [123] |
| | $CH_3{-}(CH_2)_{17}{-}O{-}CO{-}CH_2$<br>$CH_3{-}(CH_2)_{17}{-}O{-}CO{-}CH{-}NH{-}CO{-}C(CH_3){=}CH_2$ | *(26)* | [123] |

### 4.2.2. Investigations of Polymerizable Amphiphiles in Monolayers

The earliest reports on the behavior of oil on water were given by the Babylonians. They spread oil droplets on a water surface and used the behavior of the films for soothsaying on health, war or wealth[135]. (The progress of science is obvious: Today lipids are spread on water and one attempts soothsaying—on the lipids.)

As early as 1917 *Irving Langmuir* recognized that amphiphilic substances can form a film on a water surface with a thickness of exactly one molecular layer[136]. Such a monomolecular film forms a two-dimensional system, which by variation of surface pressure, area and temperature permits the measurement of phase diagrams. The most common form of recording diagrams is the so-called pressure-area diagram measured with a Langmuir film balance (Fig. 19)[119].

Different states can be seen in the monolayer by analogy to pV-diagrams of three-dimensional systems: At to pressures

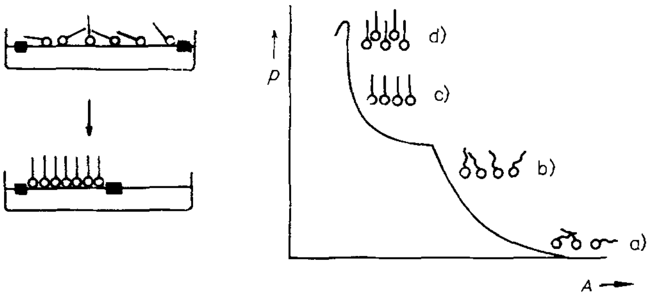
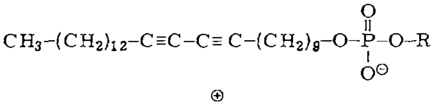


Fig. 19. Left: Langmuir film balance, schematic; right: representation of surface pressure area diagram of a monolayer at the gas-water interface [a)—d), explained in the text]. $p$ = surface pressure, $A$ = area.

a gas-analogous phase (a) is formed, which obeys a two-dimensional gas law. Compression leads to an expanded or liquid-analogous state (b) with a contact of head groups, but a high mobility of the hydrophobic chains. Further compression results in a condensed or solid-like phase with head-packing (c) or chain-packing (d). The smallest area of a solid film is in the order of 0.18 nm$^2$ per alkyl chain and corresponds to the occupied area of a paraffin chain in a crystal. A further decrease in the area of the film results in a collapse of the monolayer; beyond this collapse-point there is no well-defined system and the molecules lose their high degree of orientation.

The measurement of surface pressure-area diagrams provides a method for studying the influence of variables like temperature, head group, alkyl chain length and pH on membrane properties (*e.g.* stability). This can be demonstrated by amphiphilic compounds *(27)—(29)* with different biological headgroups (lysophospholipid analogues)[137] (Fig. 20):



$$CH_3{-}(CH_2)_{12}{-}C{\equiv}C{-}C{\equiv}C{-}(CH_2)_8{-}O{-}\underset{O^{\ominus}}{\underset{|}{\overset{O}{\overset{\|}{P}}}}{-}O{-}R$$

*(27)*, R = $CH_2{-}CH_2{-}\overset{\oplus}{N}(CH_3)_3$
*(28)*, R = $CH_2{-}CH_2{-}NH_3^{\oplus}$
*(29)*, R = H

A decrease in the occupied area of the head group results in an increase in the packing density of the molecules: *(27)* exhibits only an expanded film; *(28)* forms a liquid-analogous as well as a solid-like phase. *(29)* exhibits only a condensed phase.—Monolayer properties of many natural phospholipids and synthetic lipids are described in the literature[138,144].

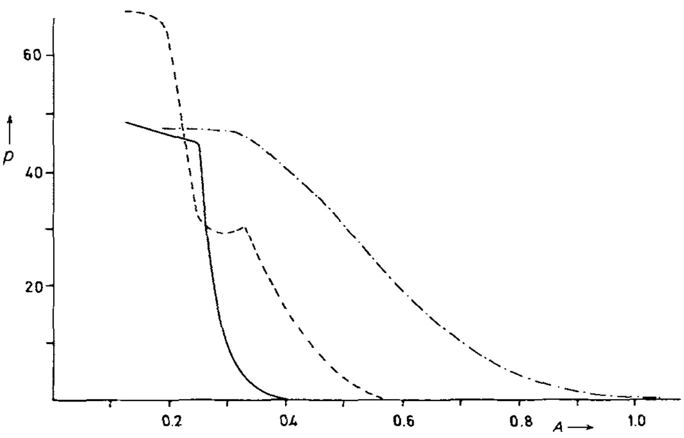


Fig. 20. Influence of the head group of lysophospholipid analogues *(27)—(29)* on their properties in monolayers [137]. Surface pressure-area diagram of *(27)* (–·–·–); *(28)* (– – –), and *(29)* (——). $p$ = surface pressure (in mN/m); $A$ = area (in nm$^2$/molecule).

Apart from the characterization of lipids in a monolayer, several other examples of the versatility of this method have been described. *Gorter* and *Grendel* postulated the existence of a double layer in biomembranes from the occupied area of membrane extracts in monolayers[139]. Many membrane reactions can be monitored in monolayers, for example adsorption of proteins at a monolayer and insertion into the lipid matrix[140]. Another example is the investigation of the activity of the enzyme lipase as a function of the surface pressure[141]. The investigation of the miscibility of different phospholipids and the characterization of phospholipid-cholesterol mixtures provides a method for the interpretation of their action in biomembranes[142]. Interactions of local anesthetics with membranes have been studied in monolayers as a model[143].

The correlation of monolayer properties and spherical membranes (liposomes, cells) has been discussed by *Blume*[144].

### 4.2.3. Polymerization in Monomolecular Layers

Since the orientation and packing density of the monomers in monomolecular layers can be varied, this method allows the investigation of a polyreaction in such systems, as is shown schematically in Figure 21[145].

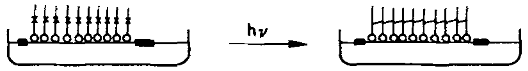


Fig. 21. Schematic representation of the synthesis of polymeric monolayers by UV-irradiation, orientation of the molecules being preserved (x = polymerizable groups).

The orientation of the monomer units remains unchanged; the reaction results in a highly oriented stable polymer film with a degree of orientation not realizable by other methods, *e.g.* the spreading of the same substance after polymerization in solution[146]. UV-initiated monolayer polymerization has been studied intensively in recent years[145-148]. Normally the reactions involve contraction of the film; the surface pressure-area diagrams of the polymers exhibit a smaller occupied area, a steeper slope, and a higher collapse pressure[146]. Hence the polyreaction can be followed by measuring the film contraction versus time at constant pressure. This can be shown in the case of the diacetylene lipid *(21)* (Fig. 22)[132].

In recent years another method has been developed for monitoring the polymerization kinetics by measuring the UV absorption in monolayers[148]. A special Langmuir film balance was constructed to fit a commercial UV spectrometer. This polyreaction can be easily monitored by the new device (Fig. 27), since the polydiacetylenes exhibit a high extinction coefficient in the visible region. The polymerization of diacetylenes in the solid state has long been known[149]. The polyreaction is topochemically controlled; *i.e.* the structure of the monomer crystal determines the reactivity and structure of the polymer. The color of the polymer (blue/red, cf. Fig. 26) with conjugated double and triple bonds depends on the conformation of the polymer backbone in the solid state[150] and in solution[151].

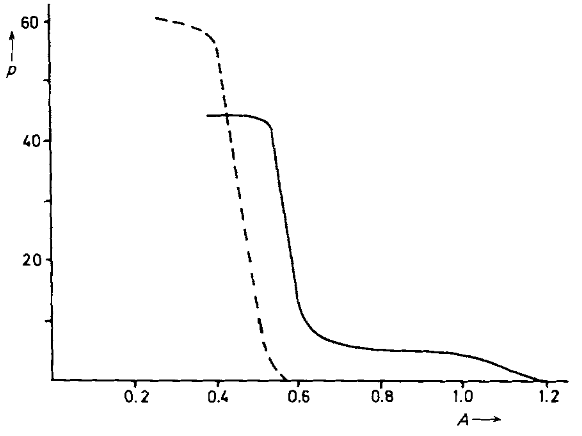
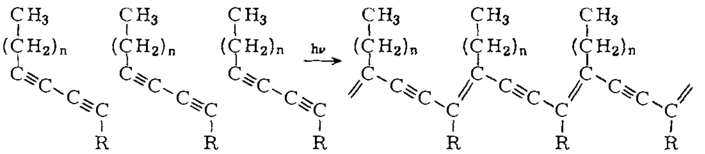


Fig. 22. Surface pressure-area diagram of monomeric and polymeric ammonium lipid *(21)* [132] (Table 2). (————) monomer; (--------) polymer; $p$ = surface pressure (in mN/m); $A$ = area (in nm$^2$/molecule).

The spectroscopic investigation of the polymerization of diacetylene surfactants and lipids in monolayers shows that it is comparable to the polyreaction of these systems in a crystal[148]. The blue ($\lambda_{max}$ = 620 nm) as well as the red ($\lambda_{max}$ = 540 nm) form of the polymer can be detected, depending on irradiation time. The polymerizability of the diacetylene lipid *(21)* proves that the required packing density for a topochemical reaction is realizable in monolayers. It can be shown that a polyreaction is only possible in a solid-analogous monomer film, *i. e.* in our example at surface pressures above 10 mN/m[132, 134, 148]. Irradiation of a liquid-analogous film ($p$ < 10 mN/m) does not lead to a polymer.



In contrast to the topochemically polymerizable diacetylenes, the methacrylic and diene derivatives of lipids and surfactants are polymerizable not only in the solid-like but also in the liquid-like state[123, 130]. Figure 23 shows the contraction behavior of the diene lecithin *(20)* during irradiation in the liquid-analogous state ($p$ = 7 mN/m)[130].

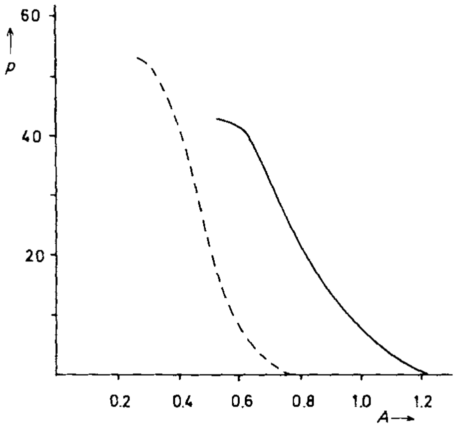


Fig. 23. Surface pressure-area diagram of monomeric and polymeric lecithin derivative *(20)* [130] (Table 2). (———) monomer; (------) polymer; $p$ = surface pressure (in mN/m); $A$ = area (in nm$^2$/molecule).

Compared to the diacetylenes, the methacrylic and diene systems exhibit a higher mobility of the non-conjugated polymer chains and are therefore more suitable for the formation of flexible membranes.

For all investigated systems, the surface pressure-area diagrams of the polymer exhibit a higher packing density and a higher collapse pressure than those of the corresponding monomers, thus supporting the concept of a higher film stability of the polymerized membranes. This is demonstrated in Figure 24:

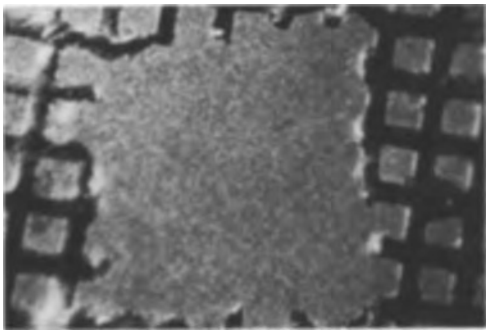


Fig. 24. Bilayer of a polymerized diacetylenecarboxylic acid deposited on an electron microscope grid. The stable bilayer spans an area of about 0.25 mm$^2$.

A double layer of a poly(diacetylenecarboxylic acid) spans a width of 0.5 mm in diameter in an electron microscope grid. This bilayer membrane remains stable for weeks in air or in water[147d].

So far these investigations show that a polyreaction in oriented planar systems is possible and leads to highly oriented and very stable model membranes. It remains to be seen whether polymerization is possible in spherical bilayers such as liposomes and whether the vesicles thus formed exhibit a higher stability than the low molecular systems.

## 4.3. Polymeric Liposomes as Cell Models

### 3.2.1. Structure and Formation of Liposomes

Liposomes are the nearest approach to biomembranes; they are closed, spherical structures having an aqueous interior and one or several lipid double layers[152].

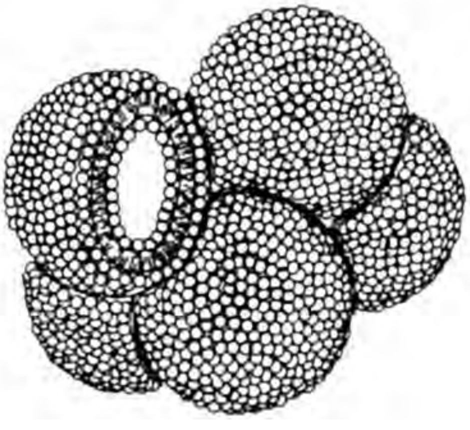


Fig. 25. Schematic representation of unilamellar liposomes (*i. e.* consisting of one bilayer).

Such vesicles can be formed from synthetic amphiphiles and membrane extracts; reconstituted membranes, *i. e.* liposomes of cell membrane constituents, contain nearly all components of cell membranes (lipids, proteins, glycolipids *etc.*). Erythrocyte ghost-cells formed by osmotic shock constitute one further example[153].

Vesicles of synthetic lipids or lipid analogues have a much simpler composition and, depending on the method of formation, one obtains double- or multilayered vesicles of different sizes[121].

The most common methods to prepare liposomes[121]—which are not discussed in detail here—are the ultrasonication of lipid suspensions in water, the injection of methanolic or ethereal solutions of lipid into water, the dialysis of surfactant-lipid mixtures and the shaking (by hand) of lipid films on glass surfaces in water.

The polymerizable lipids and lipid analogues *(14)*—*(25)* (Table 2) described in Section 4.2.1. have been transformed into liposomal solutions by ultrasonication of their crystal suspensions[123,154b]. Long chain diacetylenecarboxylic acids and their derivatives could be transformed into liposomes[154b], by analogy to the investigations of *Gebicki* and *Hicks*[155], with unsaturated surfactants. Small and relatively homogeneous vesicles with a single bilayer are formed after long sonication times. On filtration through a Millipore filter, clear or slightly opaque solutions are obtained. The monomeric liposomes are relatively unstable: like vesicles from normal lipids their solutions turn turbid after some days.

### 4.3.2. Polymerization in Liposomal Systems

The clear monomeric vesicle solutions of methacrylic, diene and diacetylene lipids and surfactants can be polymerized by UV-irradiation. In the case of diacetylene lipids, the transition from monomeric to polymeric liposomes can be observed visually and spectroscopically by the color change mentioned above (Fig. 26). As with the monolayer polymerization, deep-colored polymer solutions are obtained[154b].

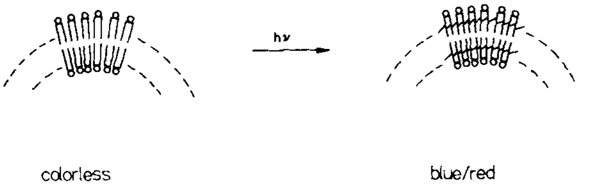


Fig. 26. Polymerization of liposomes of the diacetylene lipid *(21)* (Table 2, cf. Fig. 27). The colorless monomer solution is converted into deep-blue or brilliant red polymer solutions.

The color change from blue to red (Fig. 26) occurs on prolonged irradiation or at high temperatures. The visible spectra of the red form in monolayers and liposomes are identical with regard to the wavelengths, as can be seen in Figure 27.

Electron microscopy can provide direct evidence that the polymers are still liposomal structures. Figure 28 shows a solution of the monomeric vesicle of the ammonium lipid *(21)*[154b].

The structure remains unchanged during polymerization, as can be seen by a comparison with the corresponding polymer solutions. This is consistent with the investigations of *Regen et al.*[128] for the case of the polymethacrylic lipid *(15)*.

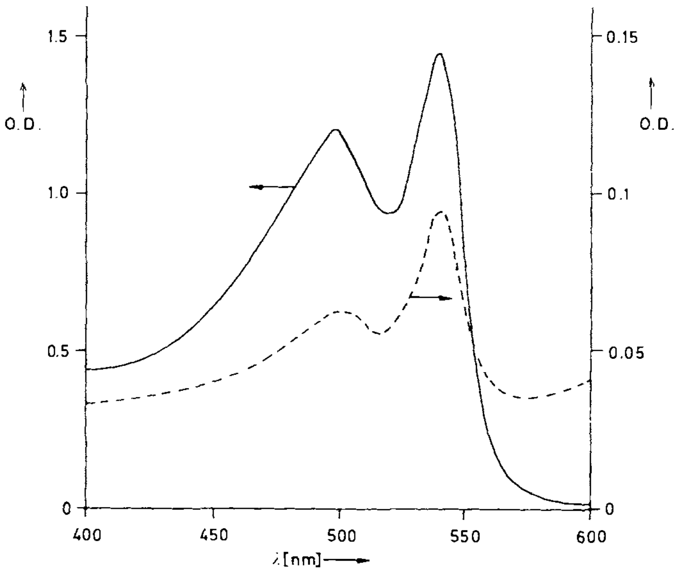


Fig. 27. Visible spectra of the red species of a polymerized monolayer and polymerized liposomes of diacetylene lipid *(21)* [154b]. (----) spectrum of monolayer (cf. Fig. 22); (——) spectrum of liposome solution (cf. Fig. 26); O.D. = optical density.

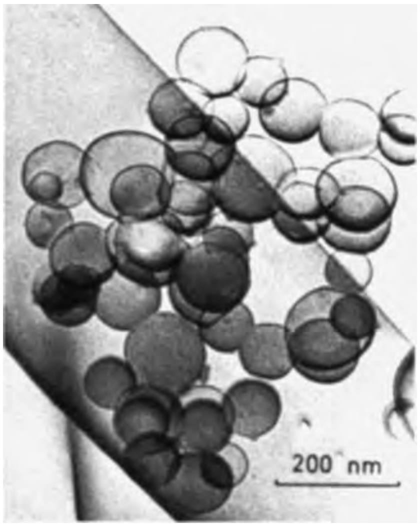


Fig. 28. Electron microscopic picture of small, unilamellar monomer liposomes formed by the diacetylene lipid *(21)* after ultrasonication. Negative stain (uranyl acetate) [154b].

The size distribution of monomeric and polymeric vesicles is essentially the same, as shown for liposomes of the diene lipid *(20)* by GPC measurements[156].

Polymerization of liposomes affects the stability. In contrast to monomeric liposomes, the polymers remain stable for weeks. Entrapped substances are released to a much smaller extent from polymeric liposomes than from monomeric ones. This has been studied in the case of the diene lipid *(20)*: Entrapped 6-carboxyfluorescein (6-CF), in high concentration, exhibits self-quenching; release into the surrounding aqueous medium results in a strong fluorescence due to the dilution[154a]. Below the phase transition temperature, liposomes made from dipalmitoylphosphatidylcholine exhibit an 8% release after 40 hours. Liposomes made of monomeric *(20)* are in the liquid state and release the dye much more rapidly. Polymeric liposomes, however, showed no significant release after 40 hours (Fig. 28a)[156].

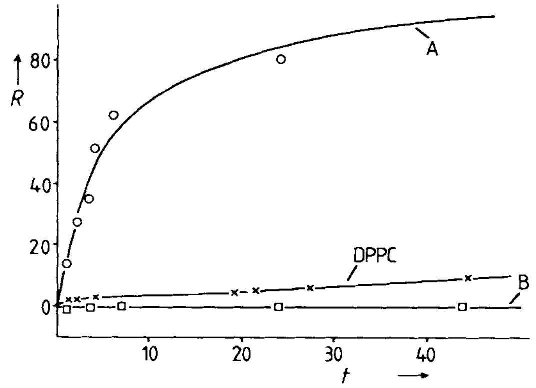


Fig. 28a. Release of entrapped 6-carboxyfluorescein from liposomes of monomeric and polymeric *(20)*. For comparison: DPPC (dipalmitoylphosphatidylcholine). R = % relase: t = time in h

Vesicle solutions can be diluted with ethanol without precipitation[154b]. The solutions of polymeric liposomes of *(21)* and *(14)* are stable in 80% ethanol for weeks. This could also be shown by *Regen* for the case of the polymerized methacrylic lipid *(15)* (Fig. 29)[129].

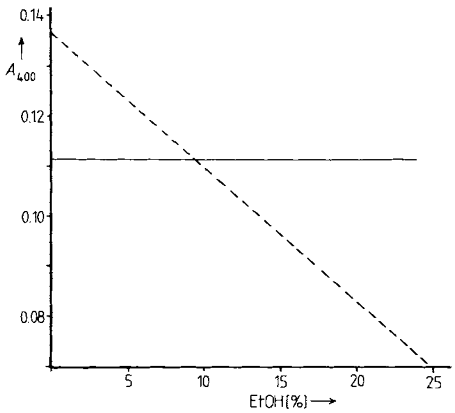


Fig. 29. Comparison of the stability of monomeric (-----) and polymeric (———) liposomes of the methacryloyllipid *(15)* after addition of ethanol [128]; $A_{400}$ = absorption at 400 nm.

A precipitation can be achieved by addition of salts, *e.g.* KCl. Here, too, the polymeric liposomes are not destroyed osmotically. Electron micrographs of the precipitate still show spherical vesicles[154b].

Another indication of the high stability of polymeric liposomes is obtained by scanning electron microscopy (Fig. 30). While monomeric vesicles are destroyed due to the drastic preparation conditions (high vacuum), pictures of polymeric liposomes showing spherical structures can be obtained[154b].

Among the different possibilities for model membrane investigations described in Section 4.1.3., up to now polymerization in monolayers and liposomes have been realized and discussed. Polymerization of surfactants and lipids in a bimolecular lipid membrane (BLM) has not yet been described in the literature. It could be shown, however, that polymerizable surfactants and lipids form BLM's comparable to phospholipids[157]. Mixtures of polymerizable lipids with phospholipids could also be realized. In the case of a methacrylic lipid a polymerization has already been achieved[157].

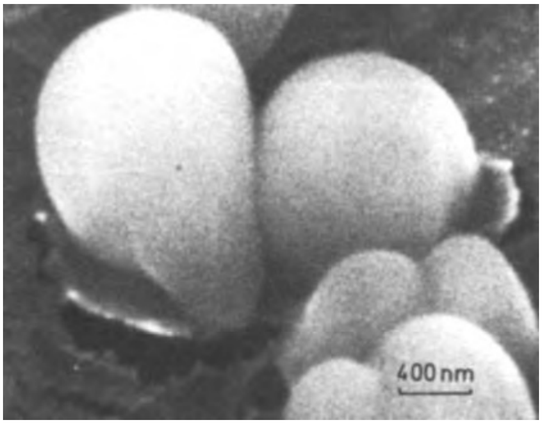


Fig. 30. Scanning electron microscope picture of large multilamellar polymer vesicles from the diacetylenelipid *(21)* [154].

4.3.3. Surface Recognition Experiments with Polymeric Liposomes

In Section 4.1.1. three criteria have been laid down for an hypothetical polymeric antitumor agent on a cellular level. High stability—the most simple condition— has been realized.

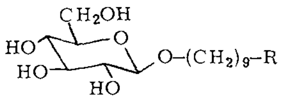
The next problem, namely the specific recognition, has been investigated in the case of low molecular liposomes in numerous experiments.

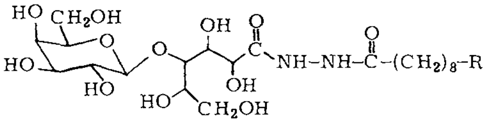
The structural composition of liposomes already influences the *in vivo* behavior. Size, charge and lipid composition influence the clearing time from biological systems and the ability for the uptake into certain organs[158]. However, a specific targeting cannot be achieved by variation of these parameters.

In recent years attempts to achieve a more specific transport of liposomes have been described. *Cohen et al.* coated liposomes with aggregated immunoglobulin[159]. The uptake into phagocytes could be increased by a factor of 60 compared to uncoated liposomes. *Gregoriadis* and *Neerunjun* achieved a "homing" of antibodies with cell cultures[160]. The uptake of liposomes by the corresponding cells showed a 25-fold increase if the liposomes carried the antibodies. Similar attempts had been made using lipid-fixed antibodies[161]. In spite of these encouraging attempts a direct targeting has not yet been achieved. Liposomes are mainly accumulated in liver and spleen and are cleared from the blood too rapidly.

With polymeric liposomes, only simple model reactions have been carried out so far. The interactions of membrane-bound sugars and lectins offered a promising perspective to study the feasability of specific recognition: in the biological membrane, sugar residues located at the outside fulfill many important functions[162]. Some sugar molecules can be recognized and bound specifically by various plant proteins, the so-called lectins[163]. The binding of lectins to glycoproteins and glycolipids incorporated into normal liposomes and the agglutination of the lectin-liposome complex have been intensively investigated[164]. The lectin most widely used is Concanavalin A (Con A), which at pH 7 forms a tetramer and has four binding sites for sugars such as D-mannopyranose and D-glucose[163].

The amphiphilic monomers *(30)* and *(31)* with gluco- and glycopyranose ring, respectively, as head group have been synthesized and investigated in order to achieve a model reaction with Con A[129,165]:


*(30)*


*(31)*

R = $C{\equiv}C{-}C{\equiv}C{-}(CH_2)_{12}{-}CH_3$

*(30)* could be transformed into liposomes by ultrasonication and subsequently polymerized, yielding the typical blue and red solutions. On addition of Con A to monomeric and polymeric liposomes, agglutination and precipitation of the liposomes takes place within a few seconds. This effect did not occur with polymerized vesicles not containing sugars at their surface[129,165].

The incorporation of non-polymerizable glycolipids into polymeric liposomes has been realized, too[129]. These liposomes bearing sugar molecules at the membrane surface are recognized and precipitated by the lectin. It is remarkable that by addition of the corresponding free sugar the lectin-liposome complex can be dissociated and the red precipitate dissolved. This means that the sugar bearing polymeric liposomes are not destroyed during the recognition and precipitation processes. These experiments demonstrate that glycolipids can be specifically recognized even in polymeric liposomes. At present, investigations are being carried out with polymeric liposomes carrying only a small amount of sugar moieties and attempts are under way to incorporate lectins into polymeric vesicles. In this context, the question of the use of mixed systems is interesting, and in the next Section possibilities are discussed for achieving a more biomembrane-like behavior of synthetic polymeric liposomes by using mixtures of natural phospholipids, polymerizable phospholipids, and proteins.

### 4.3.4. On the Way to Cell Models?

Polymeric antitumor agents on a cellular level? The question remains.

We have mentioned three important requirements such systems would have to meet: stability, ability to recognize and to destroy cells. Synthesis of sufficiently *stable* liposomes from amphiphilic monomers has been achieved. An example for a specific *recognition* of these polymeric liposomes could be shown (lectin-sugar interaction). Although one has to admit that it is still a long way to real "targeting", considering the successful incorporation of monoclonal antibodies[166a] into low molecular weight liposomes[166b], one can be hopeful.

As far as the third requirement *(cell-destroying principle)* is concerned, we can only speculate on the basis of biochemical knowledge: one could incorporate lysophospholipid-producing enzymes (*e.g.* phospholipase A) into a stable vesicle which itself resists enzymatic attack; one could also prepare mixed liposomes with high lysophospholipid content, because the polymeric membrane components should not be affected by lysis. Attempts to destroy tumor cells selectively by synthetic alkyl-lysophospholipids have been reported[167]. One more possibility is the transport of polymeric surfactants to a tumor cell membrane, using carrier liposomes which are resistant to polysoaps. The latter example resembles that which is called "humoral immune answer"[168].

In order to acheive release of entrapped material from polymeric liposomes, these stable liposomes must have areas which can be destabilized or "opened"—just like a bottle is uncorked (see Scheme in Figure 31).

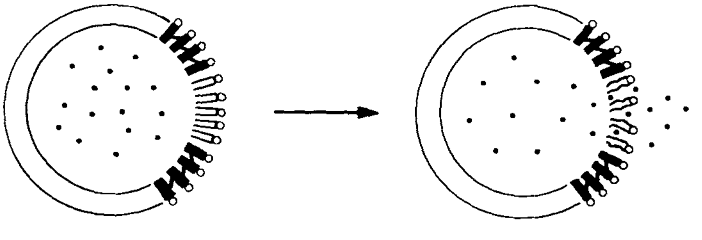


Fig. 31. Destabilization of labile parts in polymerized liposomes (schematic); liposome contents are released (mechanisms of destabilization are explained in the text).

One can think about different mechanisms which allow opening (increase in permeability, uncorking) of stable, polymeric liposomes:

- photochemical membrane destabilization[169]
- pH-dependent opening under acidic conditions[170]
- temperature-dependent opening by exceeding phase transition temperatures (hyperthermia)[171]
- enzymatic procedures

The corresponding investigations on low molecular weight liposomes have been published[169-171].

Thus, the increased stability of polymerized liposomes is only a first, though crucial, step on the way towards the hypothetical antitumor agents on a cellular level.

Apart from the special goals discussed in this report, polymerized vesicles open new applications wherever stable compartments are required. The use of microenvironments[60,172] and microcompartments is one major principle of life. Biomimetic[173] application of the compartment principle meets with ever-increasing interest and has already been successful in a number of cases, *e.g.* solar energy conversion[174,124], synthesis of enzyme models[175] and use of liposomes as drug carriers[29a-c] and in clinical analysis. Not all possible avenues have been explored so far. Compartmentation is a useful principle for microencapsulation[176] and optimization of catalytic processes. *Stabilization* of such compartments (*e.g.* liposomes, micelles) by polymerization may considerably extend the scope of applications. On polymerized liposomes, one can carry out reactions which selectively occur at the outer membrane layer and thus produce different inner and outer membrane structures[126b] without destruction of the liposome. More complex systems are however required in order to move from simple compartments to specifically active vesicles.

Membranes consisting of polymerizable units, areas which can be destabilized, proteins, and recognition units allow the "formation" of liposomes which may be regarded as single cell models.

Model discussions have in general proved to be very useful in modern cell membrane research[177]. Current membrane models—though perhaps oversimplified—are of high potential value for an understanding of important biological processes[178], *e. g.* intercellular communication, cell uptake of extracellular material, and transformation of external impulses into intracellular effects. Figure 32 shows four possible paths to cell models with polymerizable units.

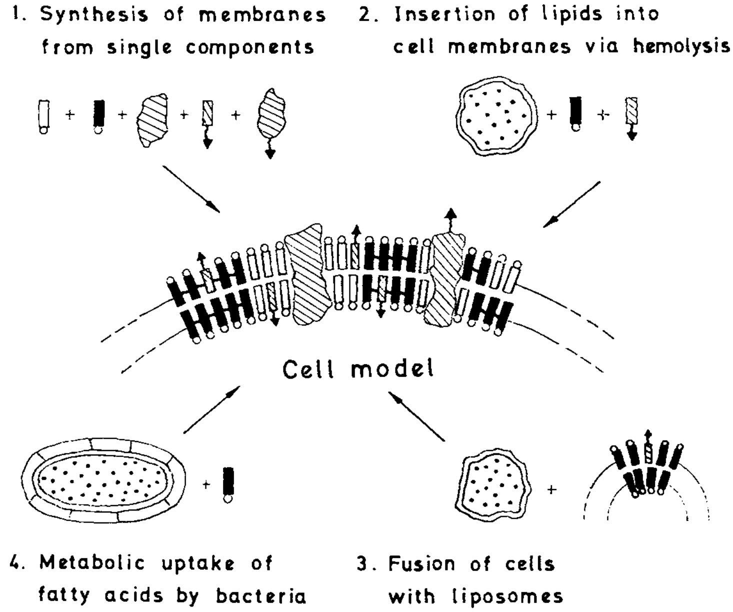


Fig. 32. Schematic representation of few possible ways to build up highly stable cell models by partial polymerization of the cell membrane. a) Natural or synthetic lipids; b) polymerizable lipids; c) proteins; d) protein or lipid bearing a recognition unit.

*First* of all, a mixture of synthetic or natural phospholipids, polymerizable lipids, and proteins can be converted into liposomes (by one of the methods described in Section 4.3.1.) and then be polymerized. First experiments with $F_0F_1$-ATPase (from *Rhodospirillum Rubrum*) show that complex proteins can be incorporated into such liposomes; the activity of the ATPase is retained[179]. Activity depends on time of polymerization, *i. e.* on the amount of polymerized lipid in the membrane. ATPase activity in a monomeric liposome (from compound *(23)*) is lower than in a liposome consisting of natural phospholipids. With increasing polymerization time, however, activity of the enzyme entrapped in liposomes formed by *(23)* increases and reaches the value found for lecithin liposomes. In contrast to the latter ATPase-containing polymer liposomes are more stable over a longer period.

A *second* possibility is the introduction of polymerizable lipids into, *e. g.*, erythrocyte ghost cells by controlled hemolysis and subsequent polymerization (UV). While osmotic hemolysis[153] has several decisive disadvantages, electric hemolysis as described by *Zimmermann et al.* allows the convenient variation of ghost cell membranes. This technique is based on a reversible dielectric breakdown of the cell membrane[106c, 180].

Dielectric breakdown also provides a *third* possible path to the production of cell models: *Zimmermann et al.* could show that under certain conditions cells can be fused with other cells or with liposomes[181]. Thus lipids from artificial liposomes can be incorporated into a cell membrane.

A *fourth* approach has been published by *Chapman et al.*[131]: bacterial cells incorporate polymerizable diacetylene fatty acids into their membrane lipids. The diacetylene units can be UV-polymerized *in vivo*.

The four paths to cell models sketched in Figure 32 may provide useful approaches to stabilized cell models for the investigation and characterization of cell properties and for the simulation of biological interactions.

## 5. Concluding Remarks

In the present paper we have attempted to report on the possible contributions of polymer science to the development of new antitumor agents. We have done so from a polymer chemist's point of view—which is necessarily a limited one.

The aim of our considerations was to point out some solved and unsolved problems and to speculate on possible further solutions. We are aware of the fact that the joint treatment of two entirely different fields (namely the development of polymeric antitumor agents on a molecular level and first attempts to build up stable cell models), may seem rather arbitrary to the reader. Indeed, development of the former has advanced to a point where first successes are seen—together with the corresponding difficulties. One can surely say that this field is a promising one, and needs further intensive research. In the case of cell models and hypothetical antitumor agents on a cellular level, only the very first steps have been undertaken and it remains to be seen whether this concept is a realistic one. Both approaches have one crucial point in common: targeting to tumor cells in the human body is still an unsolved problem: "The development of comparative biochemistry of various tissues and cells has lagged behind the ingenuity of the synthetic chemist, so that although in many cases the gun could be loaded with suitable ammunition, we lack information about the target"[182].

Considering this situation, one might object that it does not make sense to further load the gun before the target is exactly known. The cancer problem, however, is such an urgent one that we cannot give up empirical or rational search for antitumor agents. If this search is done in cooperation with chemists, pharmacologists, immunologists and molecular biologists, it should help in gaining more detailed information about tumor cells. Thus, development of antitumor agents can help to characterize and to treat tumors. The reader may consider that a great deal of the concepts presented here is speculative—he is right. We do feel, however, that this particular area of research merits stimulation and further collaborative investigation.

Macromolecular science can perhaps make modest contributions. In 1978 *C. C. Zubrod*, an expert in chemotherapy, compared minimal success in the chemotherapy of tumors with the triumph of antimicrobial therapy and added: "Remember, however, that with regard to infectious disease, quinine was discovered in the 17th century, and Salvarsan in 1910, and now, in 1978, we still lack curative agents for viral diseases. The only treatment for my grandchildren's chickenpox is watching TV. So the short list of cures of metastatic disease compiled in these 37 years should not be discouraging. I feel optimistic that wider success will follow in years or decades, rather than in centuries, as with chemotherapy of infection"[48].

Thus, neither uncritical optimism nor obstructive pessimism seems justified. As far as our "standpoint" is concerned, we feel that for the present attempt (as for all attempts to describe a field from an "elevated" perspective) the quote from *H. von Saalfeld* (Fig. 33) bears repetition: "You just can't do without the proper perspective these days!"

„Ohne den nötigen Überblick ist es heute einfach nicht mehr zu schaffen!"

*We are grateful to the Deutsche Forschungsgemeinschaft (Sonderforschungsbereich 41, Chemie and Physik der Makromoleküle, Mainz/Darmstadt), the Bundesministerium für Forschung und Technologie (Forschungsprogramm Arzneimittelentwicklung und -testung für die Krebstherapie) and the Fonds der Chemischen Industrie for support of our work.*

Received: January 30, 1981 [A 357 IE]
German version: Angew. Chem. 93, 311 (1981)

## Glossary

| | |
|---|---|
| Antibodies: | Proteins of the immunoglobulin type which specifically recognize antigens. They contain an antigen binding site which can bind to certain structural units of the antigen (antigenic determinants). |
| Antimetabolite: | Compound which blocks a metabolic pathway by competing with a normal metabolite (*e.g.* the substrate of an enzyme). Antimetabolites are also used as anticancer drugs (*e.g.* methotrexate). |
| Chronomers: | Bio-degradable polymers which release a drug in a controlled manner. |
| Endocytosis: | Process by which certain cells take up extracellular materials (see Fig. 3). Two types of endocytosis can be discriminated: phagocytosis (uptake of material visible in a normal light microscope) and pinocytosis (uptake of sub-microscopic material). |
| Hemolysis: | Loss of hemoglobin by lysed red blood cells (cell membrane lysis). Controlled hemolysis (induced osmotically or electrically) yields hemoglobin-free "erythrocyte ghosts". |
| Immunogen: | Antigen which induces an immune answer. |
| Immunostimulating: | Stimulating immune response, *e.g.* by stimulation of macrophages or antibody producing B-cells. |
| Immunosuppressive: | Suppressing immune response. |
| Interferons: | Proteins which are active against virus infections. |
| Liposome: | Closed, ball-shaped structure consisting of one or more double layers of lipid molecules with aqueous interior; often called vesicle. |
| Lyotropic phase: | Structure with high degree of orientation formed by amphiphilic molecules and a solvent (especially water) (*e.g.* lamellar or rod-like structures). |
| Monoclonal antibodies: | Chemically homogeneous antibodies which can be prepared by cloning a single antibody-producing cell [166a]. Naturally occurring antibodies specific for a given antigen are heterogeneous. |
| Phase transition temperature: | In membrane systems, temperature at which a solid-analogous state is converted to a liquid-analogous state. |
| Pyrogens: | Substances, which, 1—2 h after injection into higher animals or men, cause fever and shivers. |
| RES (reticulo-endothelial system): | Collective term for cells of different morphology and origin which are capable of endocytosis, mainly occurring in bone marrow, liver, spleen, and lymphatic tissue. |
| Solid tumor: | Tumor which is localized. |
| Trypanosome: | Parasitic protozoon which is transferred to vertebrates by insects. *T. cruzi* is found in South America and causes Chagas' syndrome: lymph node swelling, swelling of spleen, liver and thyroid gland, myocardial defects; chronic or fatal. |
| Vesicle: | See liposome. |

---

[1] a) *J. Rutschmann,* Chimia *34,* 376 (1980); b) *A. S. Sartorelli, D. G. Johns:* Handbook of Experimental Pharmacology. Vol. 38, Part 1 und 2. Springer, Berlin 1974/1975.

[2] *S. K. Carter, M. Slavik,* Annu. Rev. Pharmacol. *14,* 157 (1974).

[3] a) *P. Ehrlich* in *L. Shuster:* Readings in Pharmacology. Little Brown, Boston 1962, p. 231; b) *T. Davies,* Nature *289,* 12 (1981).

[4] *E. J. Ariëns:* Drug Design. Vol. 1. Academic Press, New York 1971.

[5] *H. König,* Angew. Chem. *92,* 802 (1980); Angew. Chem. Int. Ed. Engl. *19,* 749 (1980).

[6] Cf. *V. T. de Vita, H. Busch:* Methods in Cancer Research. Vol. 16, Part A. Academic Press, New York 1979.

[7] *L. A. Smets,* Biochim. Biophys. Acta *605,* 93 (1980).

[8] *Smets* [7] has developed criteria for the description of differences between tumor and normal cells.

[9] *C. Cheng,* J. Pharm. Sci. *61,* 645 (1972).

[10] a) *G. Weber,* N. Engl. J. Med. *296,* 486, 541 (1977); b) *G. Weber,* Adv. Enzyme Regul. *11,* 79 (1973).

[11] a) *C. Tan,* Hosp. Pract. 7, 99 (1972); b) cf. also the contributions by *M. K. Patterson, Jr.* and *H. F. Oettgen* in [1b].

[12] *A. R. Poole* in *J. T. Dingle:* Lysosomes in Biology and Pathology. Vol. 3. Elsevier, North Holland, Amsterdam 1973, p. 303.

[13] a) *L. W. Oberley, G. R. Buettner,* Cancer Res. *39,* 1141 (1979); b) *G. M. Bartoli, S. Bartoli, T. Galeotti, E. Bertoli,* Biochim. Biophys. Acta *620,* 205 (1980).

[14] *C. P. Li:* Anticancer Agents Recently Developed in the People's Republic of China. D. H. E. W. Publication No. NIH 74, Washington D.C. 1974.

[15] *A. K. Brewer,* Am. Lab. *5,* 12 (1973).

[16] a) *C. H. Lo, V. J. Cristofalo, H. P. Morris, S. Weinhouse,* Cancer Res. *28,* 1 (1968); b) *Z. B. Papanastassiou, R. J. Bruni, E. White, P. L. Levins,* J. Med. Chem. 9, 725 (1966).

[17] a) *J. C. Robbins, G. L. Nicolson* in *F. F. Becker:* Biology of Tumors: Surfaces, Immunology and Comparative Pathology. Vol. 4. Plenum Press, New York 1975, p. 3; b) *G. L. Nicolson, G. Poste,* N. Engl. J. Med. *295,* 197, 253 (1976); c) *G. L. Nicolson,* Biochim. Biophys. Acta *457,* 57 (1976); *458,* 1 (1976); d) *D. F. H. Wallach:* Membrane Molecular Biology of Neoplastic Cells. Elsevier, Amsterdam 1975; e) *W. W. Franke* in *H. Koprowski:* Neoplastic Transformation: Mechanisms and Consequences. Dahlem Workshop Reports, Verlag Chemie, Weinheim 1977, p. 181; f) *G. Poste,* Biochem. Soc. Trans. *8,* 695 (1980).

[18] a) *H. Busch, E. Fujiwara, D. C. Firszt,* Cancer Res. *21,* 371 (1961); b) *C. H. Sutton, N. H. Becker,* Ann. N. Y. Acad. Sci. *159,* 497 (1969).

[19] a) *G. L. Nicolson,* Int. Rev. Cytol. *39,* 89 (1974); b) *M. M. Burger,* Fed. Proc. Fed. Am. Soc. Exp. Biol. *32,* 91 (1973); c) *M. E. Bramwell,* Biochem. Soc. Trans. *8,* 697 (1980).

[20] *D. A. Weiss,* Curr. Top. Microbiol. Immunol. *89,* 1 (1980).

[21] *K. W. Brunner, G. A. Nagel:* Internististische Krebstherapie. 2nd edit. Springer, Heidelberg 1979, p. 69.

[22] *R. Süss, V. Kinzel, J. D. Scribner:* Krebs – Experimente und Denkmodelle. Springer, Berlin 1970, p. 85.

[23] a) *G. Poste, J. J. Fidler,* Nature *283,* 139 (1980); b) *G. L. Nicolson,* Spektrum der Wissenschaft *1979* (5), 44.

[24] Cf. also the contributions by *M. K. Patterson, Jr.* and *H. F. Oettgen* in [1b].

[25] *L. N. Ferguson,* Chem. Soc. Rev. *4,* 289 (1975).

[26] a) *C. E. Tananis, M. G. McLoughlin, P. C. Walsh,* Cancer Treat. Rep. *61,* 265 (1977); b) *P. G. Riches, E. D. Gilby, S. M. Sellwood, R. Wilkinson, I. Konyves,* Eur. J. Cancer *13,* 873 (1977).

[27] *N. Brock,* Chem. Exp. Technol. *3,* 441 (1977).

[28] a) *D. S. Zaharko, M. Przybylski, V. T. Oliverio,* Methods Cancer Res. *16,* 347 (1979); b) *A. Trouet,* Eur. J. Cancer *14,* 105 (1978); c) *G. Gregoriadis:* Drug Carriers in Biology and Medicine. Academic Press, London 1979; d) *E. Goldberg, L. Donaruma, O. Vogl:* Targeted Drugs. Wiley, New York, in press.

[29] a) *H. K. Kimelberg, E. J. Mayhew,* CRC Crit. Rev. Toxicol. *6,* 25 (1978); b) *G. Gregoriadis, A. C. Allison:* Liposomes in Biological Systems. Wiley, New York 1980; c) *D. Papahadjopoulos:* Liposomes and Their Uses in Biology and Medicine. Ann. N. Y. Acad. Sci. *308* (1978); d) *R. E. Pagano* und *J. N. Weinstein* [Annu. Rev. Biophys. Bioeng. *7,* 435 (1978)] give a critical review of possible liposome-cell interactions, including experimental techniques.

[30] a) *U. Zimmermann, G. Pilwat,* Z. Naturforsch. *C 31,* 732 (1976); b) *U. Zimmermann, F. Riemann, G. Pilwat,* Biochim. Biophys. Acta *436,* 475 (1976); c) *M. Furusawa, M. Yamaizumi, T. Nishimura, T. Ushida, Y. Okada,* Methods Cell Biol. *14,* 73 (1976); d) *S. J. Updike, R. T. Wakamiya, E. N. Lightfood, Jr.,* Science *193,* 681 (1976); e) *D. A. Tyrell, B. E. Ryman,* Biochem. Soc. Trans. *4,* 677 (1976); f) *U. Zimmermann* in [28d].

[31] *H. F. Mark,* Pure Appl. Chem. *16,* 201 (1968).

[32] a) *D. J. Lyman,* Rev. Macromol. Chem. *1,* 355 (1966); b) *H. Lee, K. Neville:* Handbook for Surgery and Artificial Organs. Pasadena Technology Press, Pasadena 1971; c) *G. W. Hastings,* Angew. Chem. *82,* 367 (1970); Angew. Chem. Int. Ed. Engl. *9,* 332 (1970); d) cf. the papers presented at the 7th Biennial Manchester Polym. Symp. 1978, Br. Polym. J. *10,* 232–301 (1978); e) *O. Oest, K. Müller, W. Hupfauer:* Die Knochenzemente. Enke, Stuttgart 1975.

[33] *C. Schuerch,* Adv. Polym. Sci. *10,* 173 (1972).

[34] *V. Kabaivanov, M. Georgieva,* Plaste Kautsch. *19,* 886 (1972).

[35] *L. G. Donaruma,* Progr. Polym. Sci. *4,* 1 (1974).

[36] *H. Ringsdorf,* J. Polym. Sci. Polym. Symp. *51,* 135 (1975).

[37] *P. Ferruti,* Pharmacol. Res. Commun. *7,* 1 (1975).

[38] *H. G. Batz,* Adv. Polym. Sci. *23,* 25 (1977).

[39] *A. D. Virnik, V. A. Snieschko, K. P. Chomiakov,* Polim. Med. *6,* 197 (1976); *7,* 27 (1977).

[40] a) *R. J. Kostelnik:* Polymeric Delivery Systems. Midl. Macromol. Monogr., Vol. 5, Gordon & Breach, New York 1977; b) *B. Sedláček, C. G. Overberger, H. F. Mark:* Medical Polymers: Chemical Problems. J. Polym. Sci. Polym. Symp. *66* (1979).

[41] *J. Kopeček,* Polim. Med. *7,* 191 (1977).

[42] *L. G. Donaruma, O. Vogl:* Polymeric Drugs. Academic Press, New York 1978.

[43] *O. Vogl, D. Tirell,* J. Macromol. Sci. Chem. *13,* 415 (1979).

[44] *I. Iliev, M. Georgieva, V. Kabaivanov,* Russ. Chem. Rev. *43,* 69 (1974).

[45] *H. Busch,* Fed. Proc. Fed. Am. Soc. Exp. Biol. *38,* 94 (1979).

[46] a) *H. Jatzkewitz,* Hoppe-Seylers Z. Physiol. Chem. *297,* 149 (1954); b) Z. Naturforsch. *B 10,* 27 (1955); c) *K. P. Khomyakov, A. D. Virnik, Z. A. Rogovin,* Russ. Chem. Rev. *33,* 462 (1964); d) *C. G. Overberger, H. Ringsdorf, B. Avchen,* J. Med. Chem. *8,* 862 (1965); e) *H. Ringsdorf,* Strahlentherapie *132,* 627 (1967).

[47] *A. Gresser,* Dtsch. Med. Wochenschr. *88,* 2217 (1963).

[48] *C. G. Zubrod,* Cancer Res. *38,* 4377 (1978).

[49] *C. Abel, T. A. Connors, W. C. Ross, N. H. Nam, H. Hoellinger, L. Pichat,* Eur. J. Cancer *9,* 49 (1973).

[50] However, the corresponding sulfadiazine-containing polymer did not show the expected tumor specificity, cf. a) *V. Hofmann, H. Ringsdorf, E. Schaumlöffel,* Makromol. Chem. *180,* 595 (1979); b) *G. Abel, T. A. Connors, V. Hofmann, H. Ringsdorf, ibid. 177,* 2669 (1976).

[51] *T. A. Connors* [Top. Curr. Chem. *52,* 152 (1974)] reports on a sulfadiazine derivative with a triazene moiety as the active species; this compound is enriched in tumor tissues.

[52] Cf. *S. Neidle,* Nature *268,* 196 (1977).

[53] *H. Ringsdorf* in [40a], p. 197.

[54] Cf. *e. g.* a) *K. F. Mück, O. Christ, H. M. Kellner,* Makromol. Chem. *178,* 2785 (1977); b) *V. Hofmann, H. Ringsdorf, E. Schaumlöffel, ibid. 181,* 351 (1980); c) *L. Šprincl, J. Exner, V. Šterba, J. Kopeček,* J. Biomed. Mater. Res. *10,* 953 (1976); d) *G. Lindblad, J. Falk,* Infusionstherapie *3,* 301 (1976).

[55] *S. I. Rapoport:* Blood-Brain Barrier in Physiology and Medicine. Raven Press, New York 1976.

[56] Cf. *e. g. G. Hecht,* Ther. Ber. *10,* 264 (1956).

[57] Cf. *e. g. E. Grundmann,* Fortschr. Staublungenforsch. *2,* 223 (1967).

[58] *K. F. Mück, H. Rolly, K. H. Burg,* Makromol. Chem. *178,* 2773 (1977).

[59] *W. C. Shen, H. J. P. Ryser,* Mol. Pharmacol. *16,* 614 (1979).

[60] a) *H. Morawetz,* J. Macromol. Sci. Chem. *13,* 311 (1979); b) *M. A. Kraus, A. Patchornik,* J. Polym. Sci. Macromol. Rev. *15,* 55 (1980), especially p. 90 ff.

[61] *J. Heller, R. W. Baker, R. M. Gale, J. O. Rodin,* J. Appl. Polym. Sci. *22,* 1991 (1978).

[62] a) *K. J. Netter, H. Ringsdorf, H. C. Wilk,* Makromol. Chem. *177,* 3527 (1976); b) *J. Kálal, J. Drobnik, J. Kopeček, J. Exner,* Br. Polym. J. *10,* 111 (1978); c) *J. Kálal, J. Drobnik, J. Kopeček, J. Exner* in [42], p. 131.

[63] *E. Hurwitz, R. Maron, A. Bernstein, M. Wilchek, M. Sela, R. Arnon,* Int. J. Cancer *21,* 747 (1978).

[64] a) *J. Vidal-Gomez, L. Hammarstrøm, C. I. E. Smith,* Scand. J. Immunol. *8,* 313 (1978); *J. Vidal-Gomez, ibid. 8,* 323 (1978); b) *R. Schnee,* Dissertation, Universität Mainz 1980; c) *L. Gros, J. B. Lloyd, H. Ringsdorf, E. Rüde, R. Schnee, H. U. Schorlemmer, H. Stötter,* IUPAC Int. Symp. Macromol., Florenz 1980, Preprints *4,* 65 (1980).

[65] a) *C. E. Hall, O. Hall* [Experientia *18,* 38 (1962)] describe arterial hypertension ("macromolecular hypertension") and swelling of organs after subcutaneous injection of poly (vinyl alcohol) solutions. The biocompatibility of polymers is discussed by *e. g.* b) *J. Kálal,* Makromol. Chem. Suppl. *2,* 215 (1979); c) *S. D. Bruck,* Pure Appl. Chem. *46,* 221 (1976).

[66] Cf. *e. g.* a) [62c], p. 149; b) *P. Ferruti, M. C. Tanzi, F. Vaccaroni,* Makromol. Chem. *180,* 375 (1979).

[67] *E. D. Korn,* MTP Int. Rev. Sci. Biochem. Ser. I, *2,* 1 (1975).

[68] a) *H. J. P. Ryser,* Proc. Int. Congr. Pharmacol. 4th *3,* 96 (1970); b) Science *159,* 390 (1968).

[69] a) *Z. A. Cohn, E. Parks,* J. Exp. Med. *125,* 213 (1967); b) *H. J. P. Ryser,* Nature *215,* 934 (1967); c) *H. J. P. Ryser, M. P. Gabathuler, A. B. Roberts,* Biomembranes 2, 197 (1971); d) *C. J. van Oss, C. F. Gillman, A. W. Neumann:* Phagocytotic Engulfment and Cell Adhesiveness. Marcel Dekker, New York 1975; e) *T. Kooistra, A. M. Duursma, J. M. W. Bouma, M. Gruber,* Biochim. Biophys. Acta *587,* 282 (1980); f) *T. Kooistra, A. M. Duursma, M. K. Bijsterbosch, J. M. W. Bouma, M. Gruber, ibid. 587,* 298 (1980); g) *J. Quintart, M. A. Leroy-Houyet, A. Trouet, P. Baudhuin,* J. Cell Biol. *82,* 644 (1979).

[70] *A. J. Sbarra, W. Shirley, W. A. Bardawil,* Nature *194,* 255 (1962).

[71] *A. Trouet* in [40a], p. 157.

[72] a) *C. de Duve, Th. de Varsy, B. Poole, A. Trouet, P. Tulkens, F. van Hoof,* Biochem. Pharmacol. *23,* 2495 (1974); b) *P. Couvreur, B. Kante, M. Roland,* J. Pharm. Belg. *35,* 51 (1980).

[73] a) *D. S. Breslow,* Pure Appl. Chem. *46,* 102 (1976); b) *P. Pucetti, A. Giampetri,* Pharmacol. Res. Commun. *10,* 489 (1978).

[74] *T. C. Merigan, M. S. Finkelstein,* Nature *214,* 416 (1968).

[75] *L. G. Donaruma, R. M. Ottenbrite, O. Vogl:* Anionic Polymeric Drugs. Wiley, New York 1980.

[76] Cf. [28a], p. 370.

[77] a) *R. E. Falk, L. Makowka, N. Nossal, J. A. Falk, J. E. Fields, S. S. Asculai,* Br. J. Surg. *66,* 861 (1979); b) Br. Pat.-Anm. GB 2040951 A.

[78] *R. E. Falk, L. Makowka, L. E. Rotstein, J. A. Falk, N. Nossal, U. Ambus* in: *E. Mittersch, M. A. Chirigos, M. J. Mastrangelo* (eds.), Prog. Cancer Res. Ther. *16,* 295 (1981) .

[79] *R. Bierling, G. D. Wolf, B. Bömer,* Naturwissenschaften *67,* 366 (1980).

[80] *M. Przybylski, E. Fell, H. Ringsdorf, D. Zaharko,* Makromol. Chem. *179,* 1719 (1978).

[81] *M. Przybylski, D. S. Zaharko, M. A. Chirigos, R. H. Adamson, R. M. Schultz, H. Ringsdorf,* Cancer Treat. Rep. *62,* 1837 (1978).

[82] *M. Przybylski, W. P. Fung, H. Ringsdorf, R. H. Adamson, D. Zaharko,* 69th Annu. Meet. Am. Assoc. Cancer Res. 1978, Proc. Vol. 19, p. 2.

[83] *W. P. Fung, M. Przybylski, H. Ringsdorf, D. S. Zaharko,* J. Natl. Cancer Inst. *62,* 1261 (1979).

[84] a) Cf. [59]; b) cf. also *M. Szekerke, J. S. Driscoll,* Eur. J. Cancer *13,* 529 (1977).

[85] *D. L. Hill:* A Review of Cyclophosphamide. C. C. Thomas, Springfield 1975.

[86] *H. G. Batz, H. Ringsdorf, H. Ritter,* Makromol. Chem. *175,* 2229 (1974).

[87] a) *N. Brock, H. J. Hohorst,* Naturwissenschaften *49,* 610 (1962); b) for a comprehensive review see *N. Brock, H. J. Hohorst,* Z. Krebsforsch. *88,* 185 (1977).

[88] a) *T. A. Connors, P. J. Cox, P. B. Farmer, A. B. Foster, M. Jarmann,* Biochem. Pharmacol. *23,* 115 (1974); b) *P. J. Cox, B. J. Phillips, P. Thomas,* Cancer Res. *35,* 3755 (1975).

[89] *A. Takamizawa, S. Matsumoto, T. Iwata, K. Katagiri, Y. Tochino, K. Yamaguchi,* J. Am. Chem. Soc. *95,* 985 (1973).

[90] *G. Peter, T. Wagner, H. J. Hohorst,* Cancer Treat. Rep. *60,* 429 (1976).

[91] a) *T. Hirano, W. Klesse, H. Ringsdorf,* Makromol. Chem. *180,* 1125 (1979); b) *T. Hirano, W. Klesse, J. H. Heusinger, G. Lambert, H. Ringsdorf,* Tetrahedron Lett. *1979,* 883; c) *T. Hirano, H. Ringsdorf, D. S. Zaharko,* Cancer Res. *40,* 2263 (1980).

[92] *P. Molz, H. Ringsdorf, G. Abel, P. Cox,* Int. J. Biol. Macromol. *2,* 245 (1980).

[93] Review: *M. Wilchek,* Makromol. Chem. Suppl. *2,* 207 (1979).

[94] *C. F. Rowland, G. J. O'Neill, D. A. L. Davies,* Nature *255,* 487 (1975); cf. also in Chemotherapy *8,* 11 (1976).

[95] *G. F. Rowland,* Eur. J. Cancer *13,* 593 (1977).

[96] Cf. also *P. Franchimont, P. F. Zangerle,* Eur. J. Cancer *13,* 637 (1977).

[97] *F. M. Schabel, Jr., D. P. Griswold, Jr., W. R. Laster, Jr., T. H. Corbett, H. H. Lloyd,* Pharmacol. Ther. Part *A,* 1, 411 (1977).

[98] a) *D. A. Weiss,* Curr. Top. Microbiol. Immunol. *89,* 1 (1980); b) *R. B. Herberman,* Biochim. Biophys. Acta *473,* 93 (1977); c) *M. Herlyn, Z. Steplewski, D. Herlyn,* Proc. Natl. Acad. Sci. USA *76,* 1438 (1979); d) *J. Schlom, D. Wunderlich, Y. A. Tlramoto,* Proc. Natl. Acad. Sci. USA *77,* 6841 (1981).

[99] *L. J. Old,* Sci. Am. *236* (5), 62 (1977).

[100] a) *G. Poste, A. C. Allison,* Biochim. Biophys. Acta *300,* 421 (1973); b) *J. A. Lucy,* J. Reprod. Fertil. *44,* 193 (1975).

[101] *S. Sell:* Immunologie, Immunpathologie und Immunität. Verlag Chemie, Weinheim 1977, p. 199.

[102] a) *D. Papahadjopoulos, W. J. Vail, K. Jacobson, G. Poste,* Biochim. Biophys. Acta *394,* 483 (1975); b) *D. Papahadjopoulos, S. Hui, W. J. Vail, G. Poste, ibid. 448,* 245 (1976).

[103] a) *G. Poste* in [29b], p. 107; b) *F. Szoka, K. Jacobson, D. Papahadjopoulos,* Biochim. Biophys. Acta *551,* 295 (1979); c) *G. Gregoriadis* in [29b], p. 36.

[104] a) *Y. Okahata, F. Murayama, K. Yamada,* Virology *28,* 115 (1966); b) *G. Poste, C. A. Pasternak,* Cell Surf. Rev. *5,* 305 (1978).

[105] a) *J. Larsman, D. H. Haynes,* Biochim. Biophys. Acta *394,* 335 (1975); b) *D. Papahadjopoulos,* Cell Surf. Rev. *5,* 766 (1978).

[106] a) *U. Zimmermann, J. Vienken, G. Pilwat,* Bioelectrochem. Bioenerg. *7,* 332 (1980); b) *U. Zimmermann, B. Scheurich,* Planta *151,* 26 (1981); c) see *U. Zimmermann,* Angew. Chem. *93,* 332 (1980); Angew. Chem. Int. Ed. Engl. *20,* 325 (1980).

[107] a) *J. Ross McDougall* in [29b], p. 340; b) *G. Gregoriadis* in [29b], p. 34; c) *G. Poste* in [29b], p. 105.

[108] *D. A. Tyrrell, T. D. Heath, C. M. Colley, B. E. Ryman,* Biochim. Biophys. Acta *457,* 259 (1976).

[109] *F. Martin, R. MacDonald,* Nature *252,* 161 (1974).

[110] *G. Scherphof, F. Roerdink, D. Hoekstra, J. Zborowski, E. Wisse* in [29b], p. 179.

[111] *S. J. Singer, G. L. Nicolson,* Science *175,* 720 (1972).

[112] *F. S. Sjöstrand* in *S. Garattini, G. Franchi:* Chemotherapy of Cancer Dissemination and Metastatis. Raven Press, New York 1973, p. 4.

[113] *S. J. Singer* in *G. Weissmann, R. Clairborne:* Cell Membranes – Biochemistry, Cell Biology and Pathology. HP Publishing, New York 1975, p. 44.

[114] a) *B. Pearse,* Trends Biochem. Sci. Pers. Ed. *1980,* 131; b) *C. D. Ockleford, A. Whyte:* Coated Vesicles. Cambridge University Press, London 1980.

[115] *A. L. Lehninger,* Biochemistry, Worth, New York 1970, p. 232; Biochemie. 2nd edit. Verlag Chemie, Weinheim 1977.

[116] *J. Klein,* Kontakte (Merck) *3,* 29 (1980).

[117] *C. M. Gupta, C. E. Costello, H. G. Khorana,* Proc. Natl. Acad. Sci. USA *76,* 3139 (1979).

[118] *E. Sackmann,* Ber. Bunsenges. Phys. Chem. *78,* 929 (1974).

[119] *G. L. Gaines:* Insoluble Monolayers at Liquid-Gas Interfaces. Interscience, New York 1966.

[120] *H. C. Tien:* Bimolecular Lipid Membranes, Theory and Practice. Marcel Dekker, New York 1974.

[121] *H. C. Huang,* Biochemistry *8,* 344 (1969).

[122] *G. Nöll,* Biol. Unserer Zeit *6,* 65 (1976).

[123] *A. Akimoto, K. Dorn, L. Gros, H. Ringsdorf, H. Schupp,* Angew. Chem. *93,* 108 (1981); Angew. Chem. Int. Ed. Engl. *20,* 90 (1981).

[124] *J. H. Fendler,* Acc. Chem. Res. *13,* 7 (1980).

[125] a) *T. Kunitake, Y. Okahata,* Chem. Lett. *1977,* 1337; b) *T. Kunitake,* J. Macromol. Sci. Chem. *13,* 587 (1979).

[126] a) *J. Fuhrhop,* Nachr. Chem. Tech. Lab. *28,* 792 (1980); b) *E. Baumgartner, J. H. Fuhrhop,* Angew. Chem. *92,* 564 (1980); Angew. Chem. Int. Ed. Engl. *19,* 550 (1980).

[127] *Y. Okahata, T. Kunitake,* J. Am. Chem. Soc. *101,* 5231 (1979).

[128] *S. L. Regen, B. Czech, A. Singh,* J. Am. Chem. Soc. *102,* 6638 (1980).

[129] *H. Bader,* Diplom-Arbeit, Universität Mainz 1981.

[130] *B. Hupfer, H. Ringsdorf, H. Schupp,* Makromol. Chem. *182,* 247 (1981).

[131] *D. S. Johnston, S. Sanghera, M. Pons, D. Chapman,* Biochim. Biophys. Acta *602,* 57 (1980).

[132] *D. Day, H.-H. Hub, H. Ringsdorf,* Isr. J. Chem. *18,* 325 (1979).

[133] *K. Aliev,* unpublished.

[134] *H. Koch, H. Ringsdorf,* Makromol. Chem. *182,* 255 (1981).

[135] *D. Tabor,* J. Colloid Interface Sci. *75,* 240 (1980).

[136] *L. Langmuir,* J. Am. Chem. Soc. *39,* 1848 (1917).

[137] *H.-H. Hub, B. Hupfer, H. Koch, H. Ringsdorf,* J. Macromol. Sci. Chem. *A15,* 701 (1981).

[138] a) *M. C. Phillips, D. Chapman,* Biochim. Biophys. Acta *163,* 301 (1968); b) *R. E. Pagano, N. L. Gershfeld,* J. Colloid Interface Sci. *44,* 382 (1973); c) *H.-D. Dörfler, W. Rettig,* Colloid Polym. Sci. *258,* 839 (1980).

[139] a) *E. Gorter, F. Grendel,* J. Exp. Med. *41,* 439 (1925); b) Proc. Kon. Ned. Akad. Wetensch. *29,* 314 (1927).

[140] a) *T. Wiedmer, U. Brodbeck, P. Zahler, B. W. Fulpius,* Biochim. Biophys. Acta *506,* 161 (1978); b) *B. D. Read, R. A. Demel, H. Wiegandt, L. L. M. van Deenen, ibid. 470,* 325 (1977); c) *Y. London, R. A. Demel, W. S. M. Geurts van Kessel, P. Zahler, L. L. M. van Deenen, ibid. 332,* 69 (1974); d) *G. Colacicco, M. M. Rapport, D. Shapiro,* J. Colloid Interface Sci. *25,* 5 (1967); e) *D. Papahadjopoulos, M. Cowden, H. Kimelberg,* Biochim. Biophys. Acta *330,* 8 (1973).

[141] *R. A. Demel, W. S. M. Geurts van Kessel, R. F. A. Zwaal, B. Roelofsen, L. L. M. van Deenen,* Biochim. Biophys. Acta *406,* 97 (1975).

[142] a) [119], p. 281; b) *D. J. Crisp* in: Surf. Chem. Proc. Joint Meet. Faraday Soc. Chem. Phys., Butterworths, London 1967, p. 1944.

[143] a) *P. Schlieper, P. K. Medda,* Naunyn-Schmiedebergs Arch. Pharmakol. *310,* 195 (1980); b) *M. A. Singer,* Biochem. Pharmacol. *29,* 2651 (1980).

[144] *A. Blume,* Biochim. Biophys. Acta *557,* 32 (1979).

[145] *D. Naegele, H. Ringsdorf* in *H.-G. Elias:* Polymerization in Organized Systems. Midl. Macromol. Monogr. Vol. 3. Gordon and Breach, New York 1977, p. 79.

[146] *R. Ackermann, O. Inacker, H. Ringsdorf,* Kolloid Z. Z. Polym. *249,* 1118 (1971).

[147] a) *S. A. Letts, T. Fort, Jr., J. B. Lando,* J. Colloid Interface Sci. *56,* 64 (1976); b) *M. Hatada, M. Nishii,* J. Polym. Sci. *15,* 927 (1977); c) *D. Naegele, H. Ringsdorf, B. Tieke, G. Wegner, D. Day, J. B. Lando,* Chem.-Ztg. *100,* 426 (1976); d) *D. Day, H. Ringsdorf,* J. Polym. Sci. Polym. Lett. Ed. *16,* 205 (1978); e) *H. Ringsdorf, H. Schupp,* Coat. Plast. Repr. Pap. Meet. Am. Chem. Soc. Div. Org. Coat. Plast. Chem. *42,* 379 (1980).

[148] a) *D. Day, H. Ringsdorf,* Makromol. Chem. *180,* 1059 (1979); b) *H.-H. Hub,* Dissertation, Universität Mainz 1981.

[149] a) *G. Wegner,* Makromol. Chem. *154,* 35 (1972); b) *R. H. Baughman,* J. Appl. Phys. *43,* 4362 (1972).

[150] *B. Tieke, G. Lieser, G. Wegner,* J. Polym. Sci. Polym. Chem. Ed. *17,* 1631 (1979).

[151] *G. N. Patel, J. D. Witt, Y. P. Khanna,* J. Polym. Sci. Polym. Phys. Ed. *18,* 1383 (1980).

[152] *A. D. Bangham, M. M. Standish, J. C. Watkins,* J. Mol. Biol. *13,* 238 (1965).

[153] *H. Bodemann, H. Passow,* J. Membr. Biol. *8,* 1 (1972).

[154] a) *J. N. Weinstein, S. Yoshikami, L. Heukart, R. Blumenthal, W. A. Hagins,* Science *195,* 489 (1977); b) *H.-H. Hub, B. Hupfer, H. Koch, H. Ringsdorf,* Angew. Chem. *92,* 962 (1980); Angew. Chem. Int. Ed. Engl. *19,* 938 (1980).

[155] *J. M. Gebicki, M. Hicks,* Chem. Phys. Lipids *16,* 142 (1976).

[156] *H. Schupp,* Dissertation, Universität Mainz 1981.

[157] *W. Prass,* Staatsexamensarbeit, Universität Mainz 1981.

[158] *G. Gregoriadis* in [29b], p. 166.

[159] *C. M. Cohen, G. Weissmann, S. Hoffstein, Y. Awasthi, S. K. Srivastava,* Biochemistry *15,* 452 (1976).

[160] *G. Gregoriadis, E. D. Neerunjun,* Biochem. Biophys. Res. Commun. *65,* 537 (1975).

[161] *V. P. Torchilin, B. A. Khaw, V. N. Smirnov, E. Haber,* Biochem. Biophys. Res. Commun. *89,* 1114 (1979).

[162] *S. Roseman* in [113], p. 55.

[163] *I. J. Goldstein:* Carbohydrate-Protein Interaction. ACS Symp. Ser. *88* (1979).

[164] a) *G. A. Orr, R. R. Rando, F. W. Bangerter,* J. Biol. Chem. *254,* 4721 (1979); b) *R. Y. Hampton, R. W. Holz, I. J. Goldstein, ibid. 255,* 6766 (1980).

[165] *H. Bader, H. Ringsdorf, J. Skura,* Angew. Chem. *93,* 109 (1981); Angew. Chem. Int. Ed. Engl. *20,* 91 (1981).

[166] a) *C. Milstein,* Spektr. Wissensch. *1980* (12), 96; b) *A. Huang, L. Huang, S. J. Kennel,* J. Biol. Chem. *255,* 8015 (1980).

[167] *R. Andreesen, M. Modolell, H. U. Weitzien, H. J. Eibl, H. H. Common, G. W. Löhr, P. G. Munder,* Cancer Res. *38,* 3894 (1978); cf. also: *M. H. Runge et al.,* J. Natl. Cancer Inst. *64,* 1301 (1980).

[168] a) *G. Valet, W. Opferkuch,* J. Immunol. *115,* 1028 (1975); b) *E. R. Podack, G. Biesecker, H. J. Müller-Eberhard,* Proc. Natl. Acad. Sci. USA *76,* 897 (1979).

[169] *K. Kano, Y. Tanaka, T. Ogawa, M. Shimomura, J. Okahata, T. Kunitake,* Chem. Lett. *1980,* 421.

[170] *M. B. Yatvin, W. Kreutz, B. A. Horwitz, M. Shinitzky,* Science *210,* 1253 (1980).

[171] *J. N. Weinstein, R. L. Magin, M. B. Yatvin, D. S. Zaharko,* Science *204,* 188 (1979).

[172] *D. G. Whitten,* Angew. Chem. *91,* 472 (1979); Angew. Chem. Int. Ed. Engl. *18,* 440 (1979).

[173] Cf. *R. Breslow,* Acc. Chem. Res. *13,* 170 (1980).

[174] a) *M. Grätzel,* Ber. Bunsenges. Phys. Chem. *84,* 981 (1980); b) *K. Monserrat, M. Grätzel, P. Tundo,* J. Am. Chem. Soc. *102,* 5527 (1980); c) *H. Tien,* Sep. Sci. Technol. *15,* 1035 (1980).

[175] Cf. a) *T. Shimidzu,* Adv. Polym. Sci. *23,* 55 (1977); b) *H. J. Fendler, E. J. Fendler:* Catalysis in Micellar and Macromolecular Systems. Academic Press, New York 1975. c) *R. A. Moss, Y. S. Lee, K. W. Alwis,* J. Am. Chem. Soc. *102,* 6646 (1980).

[176] a) *T. S. Chang,* Science *146,* 524 (1964); b) *J. Kreuter,* Pharm. Acta Helv. *53,* 33 (1978); c) *Y. T. Yu, T. M. S. Chang,* Biomater., Med. Devices, Artif.

Organs *8*, 273 (1980); d) *M. F. Lim, A. M. Sun*, Science *210*, 908 (1980); e) *N. Sliwka*, Angew. Chem. *87*, 556 (1975); Angew. Chem. Int. Ed. Engl. *14*, 539 (1975).

[177] *G. Weissmann, R. Claiborne:* Cell Membranes – Biochemistry, Cell Biology and Pathology. H. P. Publishing, New York 1975.

[178] *H. Fischer, E. Rüde, D. Sellin*, Naturwissenschaften *57*, 507 (1970).

[179] *K. Dose, Th. Nawroth, N. Wagner*, private communication.

[180] *U. Zimmermann, J. Schultz, G. Pilwat*, Biophys. J. *13*, 1005 (1973).

[181] *P. Scheurich, U. Zimmermann, M. Mischel, J. Lamprecht*, Z. Naturforsch. *C 35*, 1081 (1980).

[182] *N. J. Harper*, J. Med. Pharm. Chem. *1*, 467 (1959).

[183] We are very much indebted to Professor *H. von Saalfeld* (Fachbereich Kunsterziehung der Universität Mainz) who gave us the original drawing.

# Cells with Manipulated Functions: New Perspectives for Cell Biology, Medicine, and Technology

**By Ulrich Zimmermann, Peter Scheurich, Günter Pilwat, and Roland Benz**[*]

Exposure to electrical fields can reversibly increase the electrical conductivity and permeability of a cell membrane, which regulates and directs the exchange of materials and information between the cell and its environment. If cell membranes (or artificial lipid membranes) are exposed to a field pulse of high intensity and short duration (ns to μs), local electrical breakdown occurs in them. This electrical breakdown is associated with a large permeability change in the membrane, which is such that substances or particles (up to the size of genes) which cannot normally permeate through the membrane, are able to traverse the membrane into the cell. The original properties of the membrane are restored within μs to min, depending on the experimental conditions and the membrane properties.

Electrical breakdown in the zone of contact between the membranes of cells (or lipid vesicles), which have been made to adhere to each other by the action of weak inhomogeneous alternating electrical fields, leads to fusion of these cells with formation of a single cell having new functional characteristics. The electrical fusion method is very mild, and the yield of fused cells is high.

The electrically induced fusion and entrapment of membrane-impermeable substances and genes in cells provide a new tool for the production of a wide range of cells with manipulated functions, which could be used (or are being used) for the solution of a number of problems in cell biology, medicine and technology.

The application of electrical membrane breakdown to clinical diagnostics, the development of cellular carrier systems for the selective transport of drugs to a site of action within the organism and the potential applications of electrically induced fusion for breeding salt-tolerant crop plants, for converting solar energy into ethanol, for synthesizing natural materials and manipulating genes, are described.

## 1. Introduction

Both the increasing demand for high-grade natural substances and pharmaceuticals for medical and technical applications, and the pressing problems of providing sufficient food and energy for the world population have led to the search for new technologies involving the use of biological systems. This interdisciplinary area of research, which comprises the disciplines of chemistry, physics, biology and medicine, is known as biotechnology. The use of microorganisms in industry for the production of medically and technically useful substances and pharmaceuticals has already proved highly successful, although this area is still at an early stage[1].

During the course of evolution, plant cells developed the ability to photosynthesize, *i. e.* of being capable to convert solar energy into chemical energy with a high degree of efficiency. This energy can, in turn, be converted by other cells and organisms into osmotic, mechanical and electrical work. Technologically, we are still far from being able to convert solar energy on a large scale and with a sufficient degree of efficiency.

Many organisms, such as algae and bacteria, have solved the problem of an optimum existence in a saline environment, *i. e.* they are able to grow and multiply. The ability of crop plants to adapt to saline conditions, coupled with irrigation of the soil with salt or brackish water in the arid zones of the earth (which occupy more than 40% of the land mass) could thus make an important contribution to the solution of the world's food shortage[2].

An alternative approach to the solution of this problem is to breed crop plants that will give high yields even under un-

---

[*] Prof. Dr. U. Zimmermann, Dr. P. Scheurich, Dr. G. Pilwat
Arbeitsgruppe Membranforschung am Institut für Medizin
der Kernforschungsanlage
Postfach 1913, D-5170 Jülich 1 (Germany)
Priv. Doz. Dr. R. Benz
Fakultät für Biologie der Universität
D-7750 Konstanz (Germany)

favorable conditions. Such high-yield varieties require a large amount of nitrogen fertilizer. Quite apart from the environmental problems caused by fertilization, the energy used world-wide for the production of mineral nitrogen fertilizers is, even today, quite considerable. A possible solution would be fixation of nitrogen by biological means, *i. e. via* cells of crop plants which have been manipulated in such a way that they are capable of binding and utilizing atmospheric nitrogen directly like some bacteria[3].

The technological application of biological systems for the amelioration of food and energy shortages, as well as for the production of medically valuable substances in general, thus requires the manipulation and modification of the spectrum of functions at the cellular level. The cell membrane, the plasmalemma, plays a central role in any considerations of this nature. This lipid-protein membrane, which is only 10 nm thick, regulates the exchange of substances between the cell and its environment. Its selectivity, its capacity to act as a filter and valve, as well as the presence of specific carrier systems for certain sugars, amino acids and ions, enables the cell to establish an intracellular environment which differs markedly from that of the external solution. In addition, intracellular compartmentalization with the aid of similarly constructed membranes (mitochondria, chloroplasts, nucleus *etc.*) fulfills the prerequisite of executing an enormous number of biochemical and biophysical reactions in a minimum of space[4,5].

In principle, it is possible to manipulate the spectrum of cellular functions, provided some means can be found of introducing genes or non-toxic substances through the plasma membrane, which is normally impermeable to these substances, without causing irreversible damage. Gene manipulation in microorganisms (procaryotes) has recently proved to be highly successful, although it has not been possible as yet to transfer the bacterial genes responsible for nitrogen fixation to higher plants[*].

Fusion of cells, organelles or cell nuclei with different properties and of different origin, which results in the formation of new cell systems, represents another type of gene manipulation which can be used to produce cells with the desired properties[6,7]. Even though there have been some quite remarkable results in this area using chemical and biological methods, we are certainly far from being able to satisfactorily manipulate cell function, particularly in more highly differentiated organisms (eucaryotes).

In this article a method is presented by means of which genes and substances which cannot normally permeate the membrane, appear in general able to cross the membrane of procaryotes and eucaryotes. In essence, this method entails subjecting the cell membranes, in which electrical fields of high intensity ($10^5$—$10^8$ V/cm) occur naturally, to a short external field pulse of comparable intensity[8]. Under these conditions, the membrane breaks down locally, so that it becomes permeable. This process is reversible, *i. e.* the membrane regenerates its original properties in time intervals which can be experimentally controlled.

The technique of electrical breakdown has been successfully employed for the entrapment of drugs in erythrocytes and lymphocytes[9-12]. Cells which have been modified in this manner can be used as carrier systems for organ- and tissue-specific transport of drugs or as storage systems in the blood stream, without eliciting any significant immunological reactions. With this type of carrier system (see also [12a]) it is possible to achieve an optimum concentration of the drug at the target site, while at the same time avoiding undesirable toxic side effects at other sites within the organism caused by high dosages and repeated administration.

In recent years it has been demonstrated that the technique of electrical breakdown can also be used for gene transfer and gene manipulation in eucaryotes. Furthermore, the fusion of cells by application of an electrical field puts a completely new perspective on the problems discussed above: problems which appear to be of a highly divergent nature[13]. In many areas we are still far removed from practical applications, but this article is designed to point out potential applications of this electrical method in medicine (therapeutics and diagnostics), gene technology, cell biology and plant physiology (crop science), by describing the processes which are induced in biological and artificial membranes in response to electrical fields, and by drawing attention to the current applications of manipulated cells.

## 2. Electrical Breakdown of Membranes

The currently accepted model of the biological membrane is depicted in Figure 1. Phospholipids are arranged in a planar bilayer into which peripheral or integral structural and carrier proteins are embedded in a mosaic-like fashion[4,5,14]. The lateral fluidity of the phospholipids is very high, while movement vertical to the membrane surface is severely limited. A 'flip-flop' movement of the lipids in this direction is therefore highly unlikely.

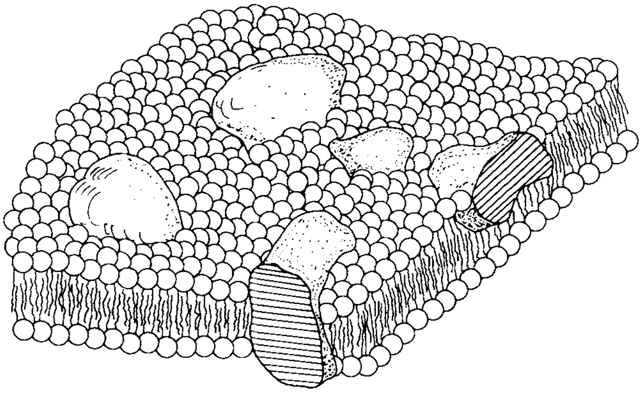


Fig. 1. Currently used model of cell membrane structure. Modified after [14].

In an equivalent electrical circuit, the membrane can be represented by a plate capacitor of specific capacitance $C_m$, and a resistor of specific resistance $R_m$, connected in parallel (Fig. 2). The aqueous external solution and the polar heads of the lipids represent the plates of the capacitor, while the membrane interior forms a dielectric with a relative dielectric constant of 2 to 3. The resistance of the aqueous external solution $R_E$ is in series with the membrane. The specific resistance of the cell membrane is in the order of $10^2$ to $10^4$ $\Omega$

---

[*] For a detailed discussion see Science *209*, 1317-1438 (1980).

$cm^2$, while that of artificial lipid bilayers is three to four orders of magnitude higher[15,16]. The specific capacitances of artificial and biological membranes, on the other hand, are comparable having values of 0.3 to 0.7 $\mu F\ cm^{-2}$ and 1 $\mu F\ cm^{-2}$, respectively[17,18].

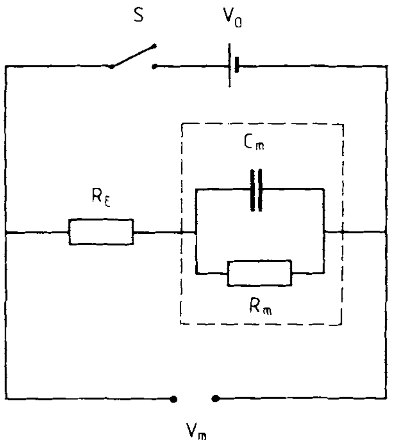


Fig. 2. Diagrammatic representation of the charge pulse technique and a model circuit diagram representing a biological or artificial membrane. The membrane can be regarded as a plate capacitor of specific capacitance, $C_m$, and a resistance connected in parallel (specific resistance, $R_m$). In charge pulse experiments the membrane capacitance, $C_m$, is connected to a voltage source ($V_0$ between 1 and 100 V) for ns to µs *via* a switch, S. After the pulse, the resistance of the outer circuit is increased, so that the charge on the membrane capacitance can only decay by ion transport through the membrane with a time constant of $\tau = R_m \cdot C_m$. The resolution is about 50 ns. See text and [28] for further details.

It is well known that capacitors can only be charged to a certain maximum voltage. Above this critical voltage level, which is dependent on the separation of the plates and on the dielectric, electrical (dielectric) breakdown is observed in the capacitor. Electrical breakdown is associated with an extreme increase in the electrical conductivity of the capacitor which is usually irreversible, *i.e.* the capacitor is destroyed. In "self-regenerating" capacitors, on the other hand, the original resistance and capacitance properties are restored. Under certain experimental conditions, biological membranes and artificial lipid bilayers behave in an analogous way to the electrical breakdown of the self-regenerating capacitors described above[8,19]. A prerequisite for reversible electrical breakdown in cell membranes is that the critical membrane voltage is reached in a matter of ns to µs. Reversible electrical breakdown is observed at membrane voltages ranging between 0.5 and 2.0 V, depending on temperature and charging time[12,20]. The increase in the electrical conductivity of the membrane and the associated increase in the permeability can be quite substantial. Proteins, deoxyribonucleic acids and even latex particles (diameter 0.2 µm) have been shown to permeate the membrane barrier of human red blood cells after field application[21-23]. If the polarization times of the membrane are relatively short, the electrically induced changes in membrane structure and permeability are reversible. The kinetics of the resealing process is a function of the temperature[24]. At high temperatures (37 °C) the resealing processes are completed within a few seconds or minutes, while at lower temperatures (4 °C) the permeability of the membrane remains high for many minutes to hours[12]. The degree of reversibility of the membrane breakdown phenomenon is largely dependent on the duration of the electrical field pulse. As far as biological membranes are concerned, the cells usually undergo irreversible changes if the field is applied for longer than 20 to 100 µs. When supercritical field pulses are applied, *i.e.* pulses whose intensity is 4—6 times higher than the intensity required to reach the breakdown voltage, the membrane and the cellular functions are irreversibly damaged, even after shorter application times[12]. Cells in which the volume of the nucleus occupies about 70 to 80% of the total cell volume (*e.g.* lymphocytes) are particularly sensitive to prolonged electrical field pulses of high intensity. In artificial planar lipid bilayer membranes, an irreversible mechanical destruction of the membrane is observed at pulse durations as short as 10 µs[25,26]. The latter phenomenon, which has been well known for artificial lipid bilayer membranes for more than 20 years, has been termed irreversible mechanical breakdown by *Benz* and *Zimmermann* (cf. [27]) in order to distinguish clearly the electrical and mechanical phenomenon in this pulse length range from that of reversible electrical breakdown.

### 2.1. Artificial Lipid Bilayer Membranes

Over the past two years, electrical charge pulse experiments on artificial lipid bilayer membranes have provided important insights into the processes involved in electrical and mechanical breakdown. These studies, which will be discussed in more detail, have paved the way both to the successful fusion of cells by using field pulses and to the entrapment of substances in cells to which the cell membrane is normally impermeable.

The schematic circuit diagram of the experimental set-up is shown in Figure 2[28]. The membrane is charged to a voltage, $V_m$, at a low resistance in a short time (ns to µs) using an external voltage source of high output voltage $V_0$. After application of the pulse, the outer circuit has a high resistance and the charge on the membrane capacitance (or the induced voltage $V_m$) can only decay by ion movement within the membrane.

From the exponentially decaying voltage it is possible to determine the relaxation time $\tau = R_m \cdot C_m$ of the membrane. Since the specific capacitance of the lipid bilayer membrane can be measured experimentally (see above), it is possible to determine the membrane resistance. The resolution of this charge pulse technique is in the order of 40 to 100 ns, if the planar lipid bilayer membranes are in contact with a 1 M KCl solution on both sides[27,28]. Figure 3 shows a charge pulse experiment on a planar lipid bilayer consisting of oxidized cholesterol/*n*-decane. This membrane was polarized to a voltage of 100 mV (relaxation 1) with a charge pulse of approximately 500 ns duration. Because of the high specific resistance, $10^7$—$10^8\ \Omega\ cm^2$, of the unmodified lipid bilayer, the membrane discharges within seconds. The same membrane was subsequently charged to 400 mV. At this voltage, mechanical breakdown of the membrane is observed, *i.e.* the membrane is irreversibly destroyed. Within about 300—400 µs, the membrane voltage drops to zero because of a widening hole (increasing permeability) (relaxation 2). *Chizmadzhev et al.*[29] have developed a theory for the mechanism of

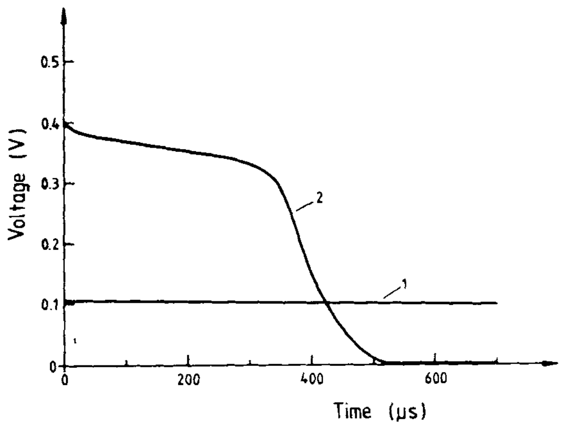


Fig. 3. Mechanical breakdown of artificial planar lipid bilayer membranes consisting of oxidized cholesterol (dissolved in *n*-decane). In the first charge pulse experiment (1) the membrane was charged to a voltage of 100 mV (pulse not shown; pulse duration 500 ns). Because of the long *RC*-time of the membrane the discharging process is very slow (almost parallel to the axis representing time). In the second experiment (2) the membrane was charged to 400 mV with a charge pulse of higher amplitude. After *ca.* 300 to 400 µs, the voltage declines to zero because of an irreversible mechanical breakdown [27]. Experimental conditions: solution 1 M KCl, temperature 17 °C.

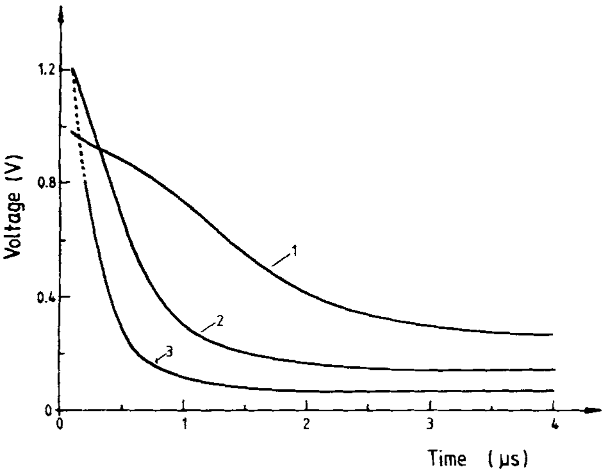


Fig. 4. Electrical (dielectric) breakdown of an artificial planar lipid bilayer membrane of oxidized cholesterol. The membrane was charged to 900 mV and 1.2 V with a charge pulse of high amplitude (pulse duration 500 ns) (experiment 1 and experiment 2, respectively). The rapid relaxation of the voltage after the end of the pulse is attributable to a large increase in the membrane conductance caused by reversible electrical breakdown. The voltage of about 1.2 V cannot be exceeded even if the amplitude of the charge pulse is increased (experiment 3). With supercritical charge pulses, electrical breakdown already occurs during the charging process, so that the initial voltage is apparently lower due to the limited time resolution between pulse application and the voltage measurement. The residual voltage across the membrane which remains after the electrical breakdown experiment, [1—3] is too low to induce mechanical, irreversible breakdown of the membrane. Experimental conditions: solution 1 M KCl, temperature 17 °C.

the mechanical breakdown in lipid bilayers based on pore fluctuation.

Figure 4 illustrates charge pulse experiments on an artificial lipid membrane in which the membrane was charged to substantially higher voltages within 500 ns. In the first experiment (relaxation 1) the membrane was polarized to about 900 mV. The charging process was followed by a very rapid discharge of the membrane, which was attributable to its electrical (dielectric) breakdown. Since electrical breakdown is reversible, the membrane remains mechanically stable, so that it can be recharged. In the second experiment (relaxation 2) the membrane was polarized to a voltage of about 1.2 V. The subsequent relaxation of the membrane voltage is considerably faster than that observed under the conditions of the first experiment. The rapid discharging of the membrane, as a result of electrical breakdown, is attributable to a transient resistance change in the membrane, which may be eight orders of magnitude (from $10^7$—$10^8$ Ω cm$^2$ to 0.1 Ω cm$^2$).

Because of the electrical breakdown of the membrane, the voltage level of about 1 V cannot be exceeded, not even when the amplitude of the charge pulse is raised several fold[25-27]. Rather, the use of supercritical charge pulses results in electrical breakdown during the charging process, so that the initial voltage drops as a result of the high conductivity of the membrane (relaxation 3). By extrapolating the relaxation curve to the end of the charge pulse, it is possible to estimate from this and similar experiments that reversible electrical breakdown occurs within 10 ns. Since breakdown is a very rapid event, longer charging times lead to current flow through the membrane which, in turn, can lead to secondary reactions. This result provides an explanation for the observation (see above) that, with longer pulse applications or higher field intensities, electrical breakdown causes increasingly irreversible changes in the cell and membrane. Studies on artificial lipid bilayers have shown that the currents flowing through the membrane can take on quite substantial values[27].

The electrical breakdown of the membrane can be explained in terms of local electro-mechanical compression. It can be shown theoretically[25-27] that the membrane becomes locally unstable above a certain level of compression and that it then breaks down, possibly resulting in the formation of pores filled with electrolyte. This concept of electrical breakdown in lipid membranes has been supported by extensive studies on cell membranes[19,20,30]. It has been shown that pressure gradients across the membrane or hydrostatic pressure can lead to transient conductivity phenomena equivalent to those observed during electrical field pulse applications[30-32].

The number of pores created during electrical breakdown in lipid bilayer membranes is estimated to be about $10^7$/cm$^2$, and the pore radius is calculated to be 4 nm[33]. During irreversible mechanical breakdown, on the other hand, the bilayer begins to tear from one point.

Compared to lipid protein membranes, the regeneration of lipid bilayer membranes is a very rapid process and is complete within a few µs. The regeneration of lipid bilayer membranes after electrical breakdown was examined in detail using a double-pulse method[33]. A current pulse of low amplitude is applied simultaneously with the pulse which is responsible for eliciting electrical breakdown. By measuring the current and voltage, it is possible to monitor the closure of the electrically induced pores as a function of time (Fig. 5). The reduction of the specific conductivity (reciprocal of the specific resistance) follows an exponential curve (cf. Fig. 6). At room temperature the time constants for the regenerative process are in the order of 2 µs, while at lower temperatures they increase to 10 µs[33].

Under certain assumptions it is possible to calculate the lateral diffusion coefficients of the lipid molecules within the

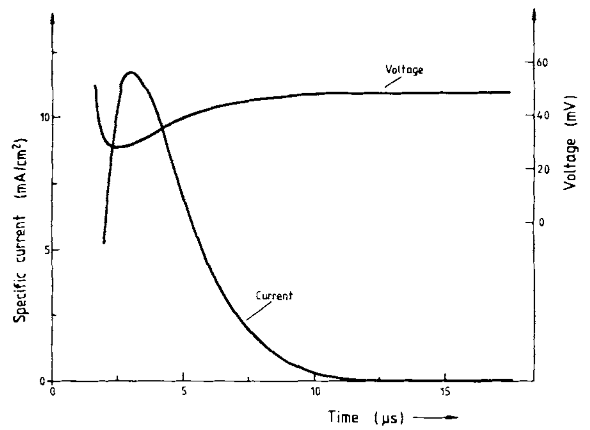


Fig. 5. Kinetics of the resealing process, after electrical breakdown, of an artificial lipid membrane consisting of oxidized cholesterol. Electrical breakdown is induced with a charge pulse of high amplitude and a duration of 500 ns (pulse not shown); a voltage pulse of low amplitude (48 mV) is simultaneously superimposed. The upper trace shows the course of the membrane voltage, the lower one the course of the current through the membrane during the process of regeneration [33]. During the resealing process the voltage increases to 48 mV while the current decreases correspondingly. Experimental conditions: solution 1 M KCl, temperature 20 °C.

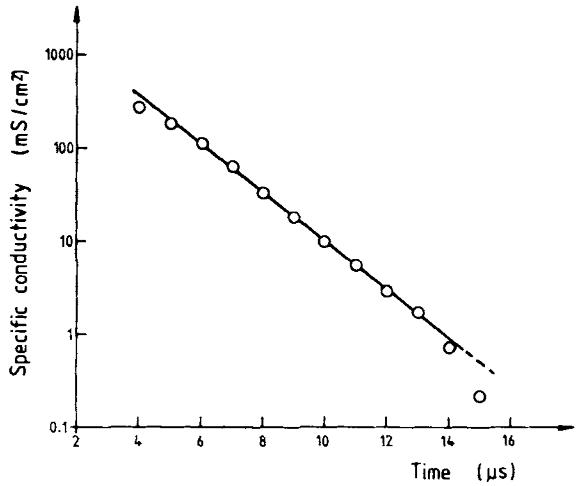


Fig. 6. Semi-logarithmic plot of the membrane conductivity during the resealing process, as a function of time. The corresponding current and voltage values are taken from Figure 5. The time constant of the exponential decline in conductivity with time is about 2 µs; the initial conductivity was about 4 S cm$^{-2}$.

membrane from the decline of the conductivity with time after electrical breakdown. The calculated value ($10^{-8}$ cm$^2$/s) is in the same range as that determined by optical means[33]. The time constants for the resealing processes in artificial lipid bilayer membranes are considerably lower than those normally calculated for cell membranes (s to min, see above)[12]. One can thus conclude that the reversal of field-induced changes in the proteins is much slower. In addition, enzymatic processes seem to play some part in the regeneration of the membrane.

Studies of cross-linked polymeric phospholipid membranes, such as those carried out by *Ringsdorf et al.*[34,35], can be expected to elucidate the mechanism of electrical breakdown and the subsequent resealing processes. The numerous variation possibilities in the production of such artificial membrane systems represent a fascinating future area of research.

## 2.2. Cell Membranes

In cells, which are large enough for the introduction of microelectrodes[2], electrical breakdown can be measured by determining the current-voltage characteristics or by charge pulse techniques, by analogy with the experiments on the planar lipid bilayers. Extensive studies of breakdown have been carried out in large algal cells, in eggs of *Fucus serratus* and, more recently, in the squid giant axon[36-39]. In marine algae, such as *Valonia utricularis* and *Halicystis parvula*, which can reach a cell diameter of up to 1 cm, the breakdown voltage exhibits the same dependence on pulse length[26,38], within a certain range, as in the planar lipid bilayers (Figs. 7 and 8). It is interesting to note that the range in which the breakdown voltage becomes dependent on the pulse length seems to be species-specific, an observation which is of great significance in the search for optimum conditions for electrically induced fusion and for the entrapment of impermeable substances in the cell.

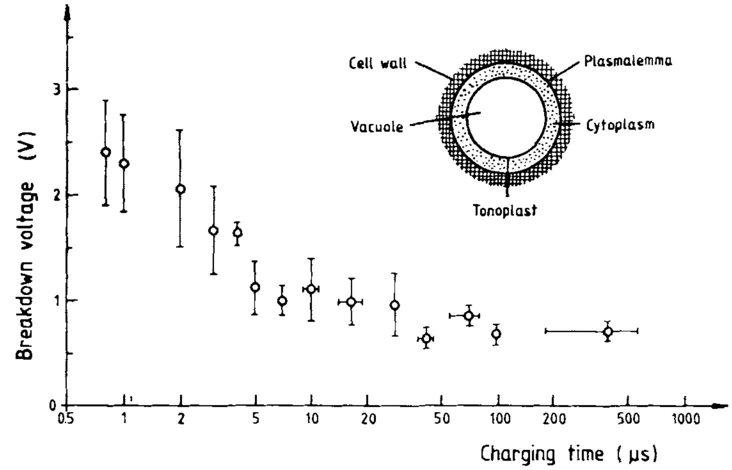


Fig. 7. Dependence of the electrical membrane breakdown voltage, $V_c$, on the charging time, t, for a cell of the giant alga *Valonia utricularis* (mean diameter: 0.5 cm). The electrical breakdown voltage is defined as the voltage which cannot be exceeded for a given charging time (pulse length). It should be noted that the dependence of the breakdown voltage on the pulse length over the range of 0.8—10 µs is different to that of *Halicystis parvula* (Fig. 8a). The inset shows the structure of a plant cell. Taking into account that there are two membranes in series in plant cells (tonoplast and plasmalemma membrane), the values for the electrical breakdown voltages are the same for very short and very long charging times, just as those measured in artificial lipid membranes (Fig. 8b); temperature 18 °C [38].

In plant cells, there are two membranes in series; the tonoplast and the plasmalemma (see Fig. 7). The tonoplast membrane separates the vacuole, a salt-containing compartment, from the cytoplasm, while the plasmalemma membrane protects the cytoplasm from the environment, as it does in animal cells. In addition, plant cells are stabilized by a cell wall which consists of cellulose, hemicellulose and pectin. This means that osmotic processes can set up a high hydrostatic pressure difference between the cell interior and environment under stationary conditions. The hydrostatic pressure difference is termed turgor pressure, and can assume values ranging between 1 and 40 bar[2,30]. If the plausible assumption that both membranes exhibit approximately the same breakdown voltage and *RC*-behavior is made, then the values for the electrical breakdown voltage, determined for very

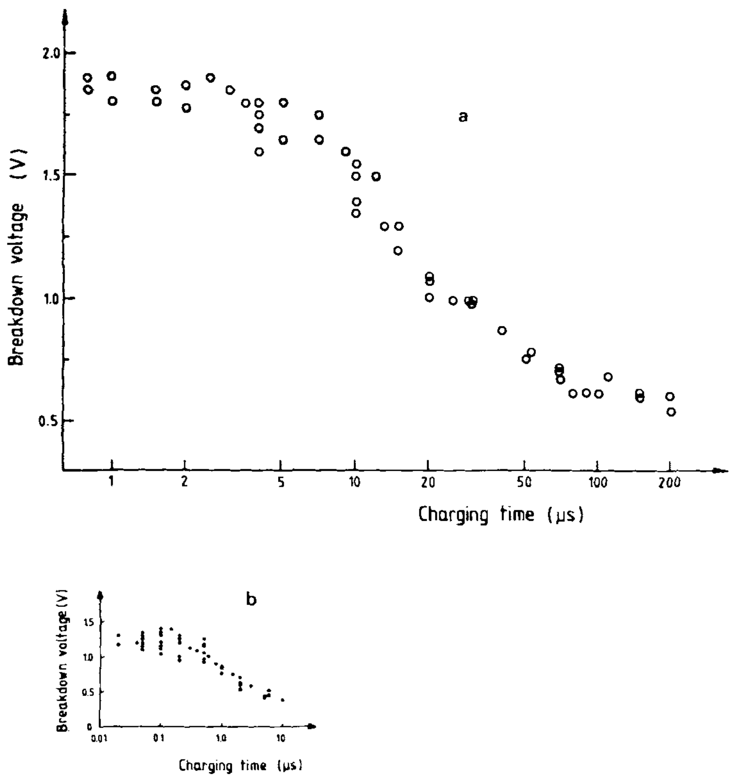


Fig. 8. Dependence of the breakdown voltage of the membrane on the charging time a) for a cell of the giant alga *Halicystis parvula* (mean diameter: 0.5 cm) and b) for artificial planar lipid membranes of oxidized cholesterol. In contrast to artificial lipid membranes and *Valonia utricularis*, the dependence of the breakdown voltage on the pulse duration in *H. parvula* is observed over the range 5 to 100 μs. Temperature 17 °C [25].

short or very long pulse durations, agree very well with those measured in artificial lipid bilayer membranes (Figs. 7 and 8).

For small cells, such as erythrocytes, lymphocytes, bacteria and plant cells (algae) it is necessary to demonstrate that reversible electrical breakdown has occurred by other means, since microelectrodes can no longer be used intracellularly without inflicting irreversible damage to the membrane. In general, the procedure with small cells is to either subject a cell suspension to an electrical field pulse of suitable intensity and duration or to move cells through a locally limited electrical field. Due to an external electrical field the membrane is polarized to a voltage, $V_m$, which is defined by the following equation (calculated for stationary conditions)[40]:

$$V_m = f \cdot a \cdot E \cdot \cos\theta, \qquad (1)$$

where $a$ is the radius of the spherical cell (or the semi-axis parallel to the direction of the field, in the case of elliptical cells) and $E$ is the field intensity. $\theta$ is the angle between the normal to the membrane surface and the field direction, *i.e.* with increasing field strength the breakdown voltage of the membrane is first reached at the poles (that is, in the direction of the field ($\cos 0° = 1$)) before other areas of the membrane break down: f is the shape factor which takes into account any distortions in the field brought about by the geometry of the cell. For spherical cells, $f = 1.5$, and for infinitely long cylinders, $f = 1$[41].

The breakdown of the membranes of suspended cells can be demonstrated, either by studying the exchange of substances across the membrane, or by measuring the resistance change in a particle analyzer, the latter being the more sensitive method.

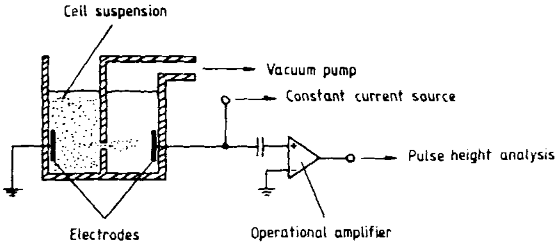


Fig. 9a. Diagrammatic representation of a particle volume analyzer. See text for further details [8].

The principle of the particle analyzer is illustrated in Figure 9a[42]. Two chambers, separated from each other by an electrically insulating wall, are filled with electrolyte. A small orifice in this wall forms a conducting connection between the two chambers, each of which contains an electrode. Because of the high conductivity of the electrolyte solution the voltage between the two electrodes drops almost completely across the measuring orifice. The field intensity in the orifice is thus in the range of $10^3$ to $10^4$ V/cm. The diameter of the orifice depends on the diameter of the cells to be investigated. It is usually 20 μm for bacteria and 40—60 μm for human red blood cells, tumor and other cells. The length of the orifice usually corresponds to the diameter. By creating a pressure difference across the measuring orifice, the cells, which are suspended in the electrolyte solution of one of the chambers, are drawn through the orifice. The nonconducting cells cause an increase in the electrical resistance of the orifice, which can be converted into a current or voltage signal by an operational amplifier.

The electrical field in the orifice is not homogeneous across its entire area. Furthermore, non-spherical cells may pass through the orifice with different orientations. The resistance change induced by a non-conducting particle (*e.g.* a cell surrounded by a membrane with a high electrical resistance) in the orifice, is thus not only dependent on the size of the particle in question but also on its orientation and path through the electrical field. After electrical amplification, the resistance change is analyzed by a pulse height analyzer. By calibrating the instrument with particles of known diameter, it is possible to determine the size distribution of the cells drawn through the orifice. Latex particles are normally used for calibration, since they exhibit a very distinct size distribution and because their diameter is known accurately.

Because of the field inhomogeneity and the random orientation during passage through the orifice, the size distribution of human red blood cells[*] is skewed to the right[43], even though it is known from other experiments (see below) that the distribution of these cells is normal. Particle analyzers of this sort, which are still in general use in clinics, are quite unsuitable for studies of electrical breakdown.

---

[*] Human red blood cells are biconcave and are deformed into ellipsoids because of the hydrodynamic focussing conditions in the orifice [44].

The inhomogeneity and the random orientation of cells passing through the orifice can be avoided if the cells are guided through the centre of the orifice by hydrodynamic focussing (Fig. 9b)[8]. This is achieved using a jet capillary whose diameter corresponds to that of the measuring orifice and whose tip is directed towards the orifice. The distance of the capillary tip from the latter is of the same order as the diameter of the orifice (see Fig. 9b).

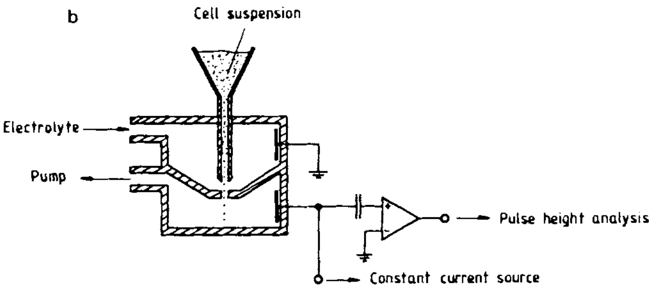


Fig. 9b. Diagrammatic representation of a particle volume analyzer with hydrodynamic focussing of the cells. Because of the focussing, the cells pass through the centre of the measuring orifice with the same orientations, an overestimation of the volume caused by peripheral disturbances (inhomogeneous field), such as occur in the apparatus illustrated in Figure 9a, can be avoided.

The hydrodynamic forces in the capillary tip (Bernoulli principle) force the cells to pass through the inhomogeneous field along the same pathway (*i.e.* along the central axis of the orifice). At the same time, non-spherical cells or cells which have been deformed by hydrodynamic forces are forced to enter the orifice under the same orientation, whereby the longitudinal axis of the particles is parallel to the central axis of the orifice. The cell-free electrolyte, which is drawn through the orifice along with the cell suspension, simultaneously cools the orifice. Under these conditions, the temperature increase in the capillary is less than 1 °C, and hence thermal effects on the cell membranes can be ruled out. The voltage signal induced by the passage of a cell through the orifice is dependent only on the resistance change caused by the cell and is therefore governed by the size of the cell. The volume of the cell can thus be accurately determined, provided that the deformation of the cells caused by the hydrodynamic focussing conditions in the orifice and, in turn, the shape factor have previously been determined by optical means[45].

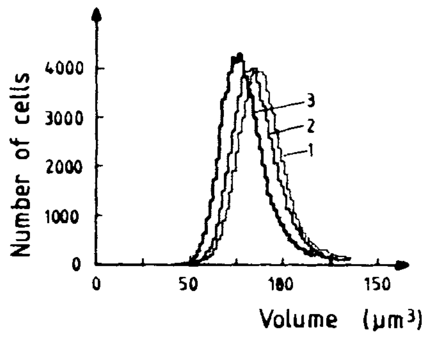


Fig. 9c. Volume distributions of human erythrocytes measured at different field intensities in the measuring arifice. The volume distribution (curve 1) was determined at subcritical field strength (0.6 kV/cm). The distribution is normal and exhibits a mean volume of 83 $\mu m^3$. Curves 2 and 3 show the increasing underestimation with increasing field strength in the orifice (2.5 or 3.5 kV/cm) due to electrical breakdown of the erythrocyte membrane [19].

Figure 9c shows a typical volume distribution for human red blood cells measured using this type of equipment[19]. Measurements were carried out at a field strength of 0.6 kV/cm in the orifice (curve 1). The distribution is normal and yields a mean volume of 83 $\mu m^3$. If the field strength in the orifice is raised (by a corresponding increase in the voltage between the two electrodes) a size distribution is obtained which, up to a certain critical value for the field strength (approximately 2.1 kV/cm), is identical with the distribution measured at low field strengths (provided that conditions of compensation gain were used[21]).

Above the critical field strength, which leads to the electrical breakdown of the cell membrane, the volumes are underestimated, resulting in an apparent shift of the volume distribution towards lower values (curves 2 and 3). The critical field strength at which underestimation occurs can usually only be accurately determined if the size distribution is not skewed at low field strengths (see above). The reason for this apparent underestimation of the volume at field strengths high enough to induce electrical breakdown is that the current (or field) lines partly pass through the cell interior which is considerably more conductive than the intact cell with its electrically insulating membrane. The change of resistance in the cell is correspondingly smaller and the volume of the cell apparently reduced. The underestimation of the cell volume is dependent on the field strength, on the one hand (Fig. 9c), and on the intracellular conductivity on the other. The more conductive the cell interior, the larger the underestimation (for a more detailed analysis see [40]). The intracellular conductivity of a cell is determined by the conductivity of the cytoplasm and the number and size of the compartments (organelles) in the cell. These compartments are also surrounded by an insulating membrane. Because of the smaller dimensions, the membranes of the compartments only break down at substantially higher field strengths [see eq. (1)]. In principle, the field strength can be raised to the level where the organelle membranes will also break down, so that the conductivity in these compartments and their breakdown voltage can be determined separately. Such studies yield information on the biochemical activity of the cell, since this is generally reflected by a change in the cell's conductivity spectrum.

The method described here for measuring the volume, the breakdown voltage and the internal conductivity of cells, has a few disadvantages. The number of cells to be studied must be relatively high ($10^5$ for each distribution), and measurement of the distribution as a function of the field strength is time-consuming and requires considerable effort. Furthermore, the values for the breakdown voltage and the internal conductivity cannot be assigned to the volume of an individual cell. It is therefore impossible, for example, to pick out cells with altered membrane or metabolic properties in the presence of a large number of cells with different properties. This is however, a prerequisite for broad diagnostic use in the laboratory.

In the procedure developed by *Pilwat* and *Zimmermann* (see *e.g.* [46–49]) these disadvantages have been elimated by modifying the experimental set-up (Fig. 9d). In this newly developed particle analyzer, the volume of the cell is measured as it enters the orifice. The cell is then subjected to a linearly increasing field during its passage along the central axis of the orifice. The level of the field strength is such that electrical breakdown of the membrane occurs when the cell is half-way through the orifice (Fig. 9d).

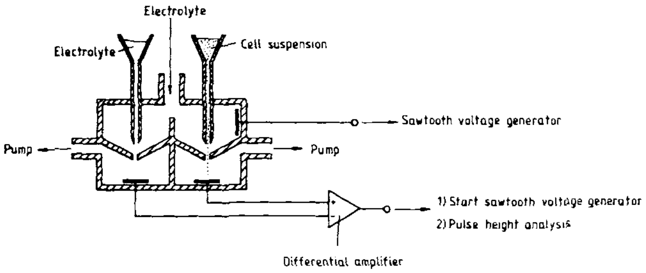


Fig. 9d. Multiparameter particle analyzer for electrical breakdown experiments on individual cells. During its passage through the orifice, every cell is first exposed to a constant field and then to a linearly increasing field. The increase in the field strength is chosen such that the membrane of the cell breaks down electrically about half-way through the orifice. This means that the cell volume, breakdown voltage of the membrane and the conductivity of the cell interior can be determined in one step. The increase in the field intensity in the measuring orifice induces an interference signal which is superimposed on the signal of the cell. The interference signal can be eliminated using a reference orifice in combination with a differential amplifier. See [46—49].

The increase in the field intensity is achieved by applying a saw-tooth voltage (range 10—40 V) to the orifice: the signal of the cell, which is of the order of 10 to 30 mV, is superimposed on the saw-tooth voltage. It is thus necessary to develop a method of registering this small signal. This can be achieved by arranging a second, geometrically almost identical orifice in parallel with the measuring orifice through which the cells are drawn. Cell-free electrolyte is drawn through this reference orifice, but the time-dependent field distribution in the reference orifice is the same as in the measuring orifice. By subtracting the voltage signals from the two orifices, using a differential amplifier, the voltage signal of the particle is obtained and is then amplified and analyzed electrically. Since it is technically not possible to produce orifices with exactly the same dimensions, the electric currents and resulting temperatures (however insignificantly small) are not identical in both. A temperature difference of only 0.01 °C can induce a voltage signal of the same order of magnitude as the voltage signal induced by the cell. This problem can be completely eliminated using the appropriate electric circuitry and experimental conditions (for a more detailed account see [46,47]).

Fig. 10 shows a typical measurement on a Friend cell. Friend cells are mouse erythroblasts which have been transformed by the Friend virus[50]. These cells represent a permanent cell line in which synthesis of hemoglobin can be induced by treatment with dimethyl sulfoxide. The first section of the Figure 10 corresponds to the constant field range where the signal height is proportional to the size of the cell. With increasing field strength the voltage signal of the cell increases linearly (Ohm's law), provided that the resistance of the cell membrane remains constant, and then continues to rise at a slower rate when breakdown of the membrane has occurred. From the ratio of the slope before breakdown to that after breakdown it is possible to calculate the degree of underestimation and, in principle, to determine the conductivity of the cell interior.

The histogram in Figure 11 summarizes more than 500 individual measurements described in Figure 10. The breakdown voltage varies between 0.7 and 1.25 V, with a peak value at 0.8 V. The range of volume of the cells, which was taken from the stationary growth phase, was between 500 and 1500 $\mu m^3$. In the stationary phase, one often observes (as in other permanent cell lines) a second, considerably smaller peak at a higher breakdown voltage, usually 1.1 V (see Fig. 11). The underestimation of the cell volumes after electrical breakdown of the membrane exhibits a distribution similar to that of the breakdown voltage. The main peak, with a breakdown voltage of 0.8 V, is correlated with an underestimation of 45%, while the subsidiary peak is correlated with an underestimation of only 30%.

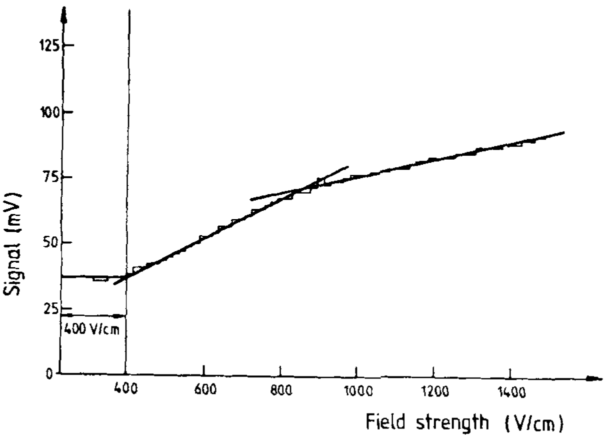


Fig. 10. The voltage signal of a Friend cell in the electrical field of the multi-parameter analyzer shown in Fig. 9d. When the cell enters the measuring orifice the voltage signal is first determined in a constant external field strength range (400 V/cm). In this range the signal of the cell is proportional to the volume and can thus be used for volume determinations. During its continuing passage through the orifice the cell is exposed to a linearly increasing field (see Fig. 9d). According to Ohm's law the signal of the cells thus initially increases linearly, because the membrane resistance and hence the resistance of the cell do not change in this field range. The volume can also be determined from the slope of this increase and used as a control. The membrane breakdown voltage is reached above a field strength of about 850 V/cm. Since the resistance of the cell decreases, the signal of the cell continues to rise at a slower rate after breakdown, with increasing external field intensity, than it did before breakdown of the membrane. From the ratio of the slope before and after breakdown conclusions about the intracellular conductivity of the cell can be drawn [46—49].

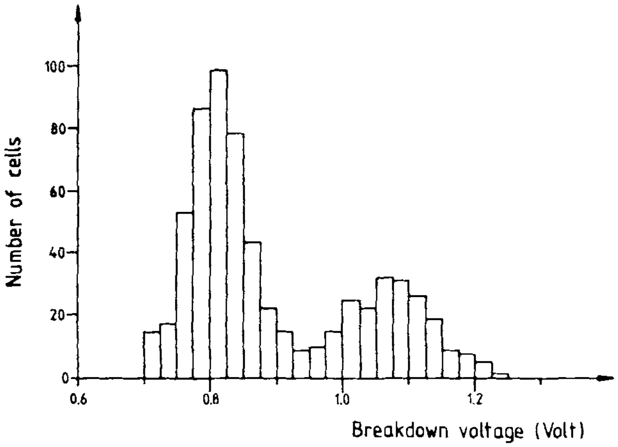


Fig. 11. Distribution of the electrical breakdown voltage in a population of Friend cells. The height of the second smaller maximum can vary considerably according to the culture conditions. The histogram represents 518 individual measurements as shown in Figure 10.

Studies of the sort, illustrated in Figures 10 and 11, provide information on the yield of electrically induced fusion of cells. To achieve an optimum yield in the fusion of cells by means of the electrical breakdown technique (see Section 4), the cells need to have a well-defined distribution for the breakdown voltage and volume. Under these conditions practically all the cells present in the field will fuse. Otherwise, only a proportion of cells exposed to the electrical field will normally fuse, because the membranes are not simultaneously polarized to the electrical breakdown voltage. A homogeneous distribution of the breakdown voltage for the whole population can be achieved by first subjecting the cells, in a discharge chamber, to a field pulse[19,51], the intensity of which is so high that some of the cells (about 20—40%) are irreversibly damaged. Irreversible damage occurs particularly in those cells which either have a low breakdown voltage or a large diameter, so that breakdown voltage is reached at very low field strengths [see equation (1)]. Those cells whose membranes have resealed can be separated by centrifugation. It is also advisable to remove large cells before application of a field pulse. This can be achieved by filtering the cell suspension using a filter of appropriate pore size. The discharge chamber[19,51] also permits the experimental study of solute exchange across the cell membrane induced by electrical breakdown and the entrapment of otherwise membrane-impermeable substances in the cells.

## 3. Electrically Induced Permeability Changes in the Membrane

Figure 12 shows a diagrammatic representation of the discharge chamber. Two electrodes, which are connected to a high-voltage capacitor *via* a high voltage switch, are submerged in a cell suspension. The capacitor is charged to the desired voltage by a high voltage source. The discharging process follows an exponential curve and the duration of the applied field pulse can thus be characterized by the *RC*-time, *i. e.* by the resistance of the solution and by the capacitance of the capacitor. Since the resistance of the solution can usually only be varied within certain small limits, the pulse duration must be varied by changing the capacitance of the capacitor. Pulse durations between 200 ns and 100 μs, which would be adequate for reversible electrical breakdown experiments, can thus be generated in this fashion.

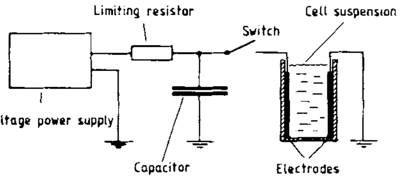


Fig. 12. Experimental set-up for the pulse apparatus and the discharge chamber. The capacitor is charged to the desired voltage by a high voltage source *via* a limiting resistance. By closing the switch the charge on the capacitor is discharged into the cell suspension *via* two platinum electrodes. The discharging of the capacitor follows an exponential course.

Figure 13 shows the results of experiments in which Friend cells (suspended in electrolyte solution buffered with phosphate buffer) were exposed to field pulses of varying intensity and duration at 4 °C. Following the application of the field, the cells were transferred to a nutrient medium and their growth followed at 37 °C. It is evident from Figure 13 that there is no observable influence on the growth of those cells exposed to an electrical field up to a pulse length of 1 μs and field intensity of *ca.* 10 kV/cm. On the other hand, above a pulse duration of 5 μs, or at higher field intensities, irreversible destruction of some cells (see above) and thus a reduced growth rate, or no growth at all occurs.

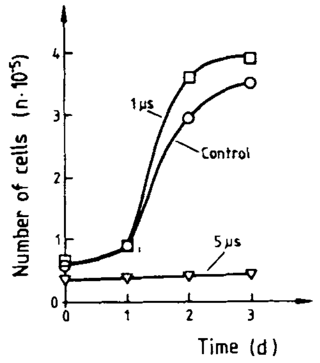


Fig. 13. The growth of Friend cells after pulse application in a discharge chamber (Fig. 12). The field intensity was 10 kV/cm. Up to a pulse length of 1 μs no influence on growth relative to the control is observed, whereas above a pulse length of 5 μs at the given field strength no growth at all occurs. For further details see text (*G. Pilwat, U. Rdest, W. Goebel* and *U. Zimmermann*, unpublished results).

Cells without a nucleus, such as human red blood cells, are considerably less sensitive to high field intensities and long application times. These cells can be exposed to field intensities of 12 kV/cm and pulse durations of 40 μs, without any observable effects on the resealing processes of the membrane at 37 °C[12].

With a pulse duration of 40 μs and a field strength of 2 kV/cm, a reversible $K^+/Na^+$ exchange is observed between the erythrocytes and the medium. This field intensity corresponds to a voltage of 1 V across the erythrocyte membrane, so that it may be concluded that reversible electrical breakdown is associated with an increase in the transport of ions across the membrane. At higher field intensities, incipient hemolysis is observed in the erythrocytes. The rate of hemolysis, *i. e.* the rate at which hemoglobin is lost from the cells, depends not only on the applied field intensity and the pulse duration, but also on the composition of the isotonic external medium. In isotonic electrolyte solutions hemolysis sets in at field intensities of 3—4 kV/cm (pulse duration 40 μs). To a first approximation, the kinetics of hemolysis follow an exponential course (first-order reaction), with a time constant of 1 minute. In isotonic solutions containing increasing concentrations of sucrose, hemolysis is correspondingly slower. At a concentration of 40 mM sucrose, for example, the time constant is about 2—3 h (see Fig. 14). In a theoretical study[51a] based on the phenomenological equations of the thermodynamics of irreversible processes[52], it has been possible to draw conclusions from these experiments about the diameter of the pores generated by the electric field.

These theoretical considerations are based on the assumption that the electrically induced permeability changes in the cell membrane are followed by osmotic processes. In the absence of an electric field there is an inwardly directed stationary concentration gradient for sodium ions across the intact erythrocyte membrane (20 mM intracellular, 85 mM extra-

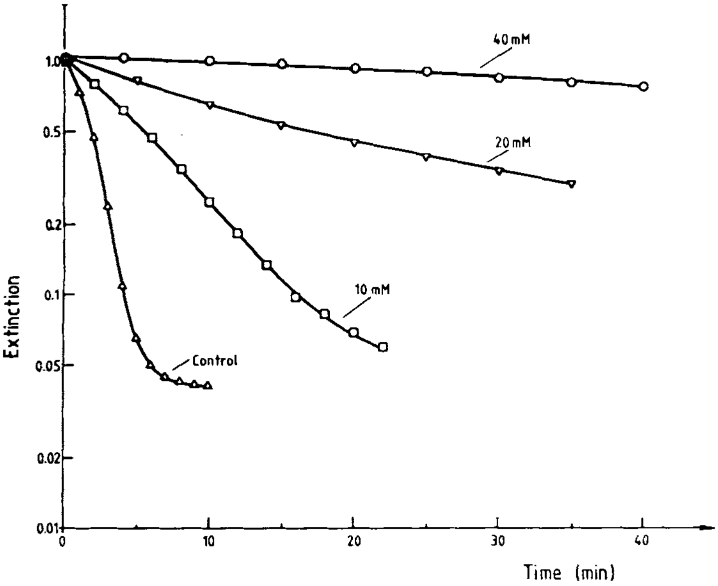


Fig. 14. Hemolysis of human erythrocytes after a field pulse application (field strength 8 kV/cm, pulse length 40 μs) in isotonic solutions containing different amounts of sucrose. After the pulse application in the discharge chamber at 4 °C, the rate of hemolysis was monitored by recording the decrease in intact cells by photometric measurement of the extinction at 700 nm. Hemolysis proceeds according to a first-order reaction and slows down with rising sucrose concentration.

cellular), which is osmotically compensated by an outwardly directed concentration gradient for potassium ions (95 mM or 40 mM respectively). Normally the membrane exhibits a certain permeability towards potassium and sodium ions, *i.e.* a passive transport (corresponding to the difference in the electrochemical potential of the ions concerned) is observed. The passive transport processes are compensated by active (dependent on the metabolism) transport processes in the opposite direction. A Donnan distribution is established for the main anion, the chloride ion, because the membrane is permeable to chloride ions[53]. The intact membrane is impermeable to sucrose. Under stationary conditions, the osmotic balance can thus be described by equations (2a) and (2b):

$$\sigma_{\text{Hb}}\pi_{\text{Hb}} + \sigma_{\text{KCl}}\Delta\pi_{\text{KCl}} + \sigma_{\text{NaCl}}\Delta\pi_{\text{NaCl}} = 0 \tag{2a}$$

for isotonic electrolyte solutions, and

$$\sigma_{\text{Hb}}\pi_{\text{Hb}} + \sigma_{\text{KCl}}\Delta\pi_{\text{KCl}} + \sigma_{\text{NaCl}}\Delta\pi_{\text{NaCl}} + \sigma_{\text{Sa}}\pi_{\text{Sa}} = 0 \tag{2b}$$

for isotonic electrolyte solutions with sucrose

where $\Delta\pi$ is the corresponding osmotic pressure difference for potassium and sodium ions, $\pi_{\text{Hb}}$ and $\pi_{\text{Sa}}$ the osmotic pressure of hemoglobin and sucrose respectively, and $\sigma$ the respective reflection coefficient which gives a measure of the permeability of the substance in question[52]. If $\sigma = 1$, the membrane is impermeable to that particular solute (ion). If the membrane becomes (or is) permeable to a given solute, the reflection coefficient decreases, as does the effective osmotic pressure, $\sigma\pi$, exerted on the membrane by the substance. $\sigma = 0$ means that the membrane has become completely permeable, so that the solute no longer contributes to the osmotic pressure balance[52]. $\sigma$ is a function of the field intensity and the pulse duration[24], *i.e.* a function of the field-induced permeability changes in the membrane. The decrease in $\sigma$ for a given solute with increasing permeability of the membrane is dependent on the size and charge of that particular solute. For monovalent ions (such as potassium and sodium ions) $\sigma$ becomes almost zero, even at electrical field intensities which are just sufficiently high to bring about electrical breakdown of the membrane. In the case of divalent ions (*e.g.* sulfate, hydrogen phosphate *etc.*) and non-electrolytes with a large radius (sucrose, 0.4 nm; inulin, 1.2 nm; and hemoglobin, 3.0 nm molecular radius)[54], considerably larger permeability changes have to be induced for the reflection coefficients to decrease significantly. The permeability of the membrane is markedly raised by electrical breakdown. The selectivity of the membrane, *i.e.* it's ability to discriminate between sodium and potassium ions is lost and the membrane becomes permeable to sucrose. The equilibration of potassium and sodium ions between the cell and the medium (Donnan equilibrium) thus proceeds very rapidly. According to equation (2a) the osmotic pressure of the hemoglobin can thus no longer be compensated for, and the cells hemolyze within a very short time. In the presence of sucrose hemolysis is retarded, because sucrose takes much longer to diffuse into the cell due to its larger molecular diameter and correspondingly higher reflection coefficient: this indicates, according to equation (2b), that the onset of hemolysis is reached considerably later. The amount of hemoglobin per cell is independent of age, while the volume decreases with age. Thus the hemoglobin exerts different osmotic pressures in the cells of the population of erythrocytes[55]. This is why not all cells reach the hemolytic point simultaneously, and hence hemolysis of the population as a whole extends over a longer time interval (see Fig. 14).

In principle, these considerations can be applied to other non-electrolytes or to electrolytes in the external solution.

From the slower rate of hemolysis, which is a function of the molecular diameter of the solute present in the external medium, it is thus possible to draw conclusions about the radius of the electrically induced pores[51a]. The radius of the pores was estimated to be 3 nm under these conditions, which is in excellent agreement with those estimated for artificial lipid membranes (see above).

At low temperatures the field induced permeability of the membrane remains high for prolonged periods of time, so that macromolecules are also able to equilibrate, provided that the appropriate field intensity and pulse length have been applied. If the temperature is raised to 37 °C, the original properties of the erythrocyte membrane are fully restored, including the active transport processes. Above 16 kV/cm (at pulse lengths of 40 μs), on the other hand, irreversible changes in the membrane are increasingly apparent. These may already have been observed at considerably lower field intensities under certain experimental conditions (*e.g.* isotonic sucrose solutions)[56]. As described above, the hemoglobin content of the resulting ghost cells can be varied to match the required experimental purpose. This is achieved by varying the field intensity and pulse length in combination with various compositions of the media[12,20,21,49].

Since the electrical field application is carried out in isotonic solutions, the described procedures can also be used en-trap membrane-impermeable substance into other cells. An example of this shown in Figure 15 for mouse lymphocytes[12]. Eosin, a dye which is irreversibly bound in the cytoplasm and which cannot normally permeate the intact membrane, was used as an indicator for electrically induced uptake across the membrane: it was added to the external solution at 4 °C before the pulse application. The pulse length was reduced to 500 ns, because the volume of the nucleus occupies 70% of the total volume in the lymphocytes, and hence irreversible secondary reactions in the cytoplasm, particularly in the nucleus after breakdown can occur (see above). It is evident from Figure 15 that the number of lymphocytes taking up eosin increases steadily with increasing field intensity. The reaction is reversible and this can be demonstrated by adding eosin at 37 °C just after the end of the resealing process in the membrane. Under these conditions, no uptake of dye is observed in the field-exposed and resealed cells up to field intensities of 16 kV/cm. It was possible to conclude from these experiments that the restoration of the cell membrane properties was complete in all cells within about 3 minutes[12].

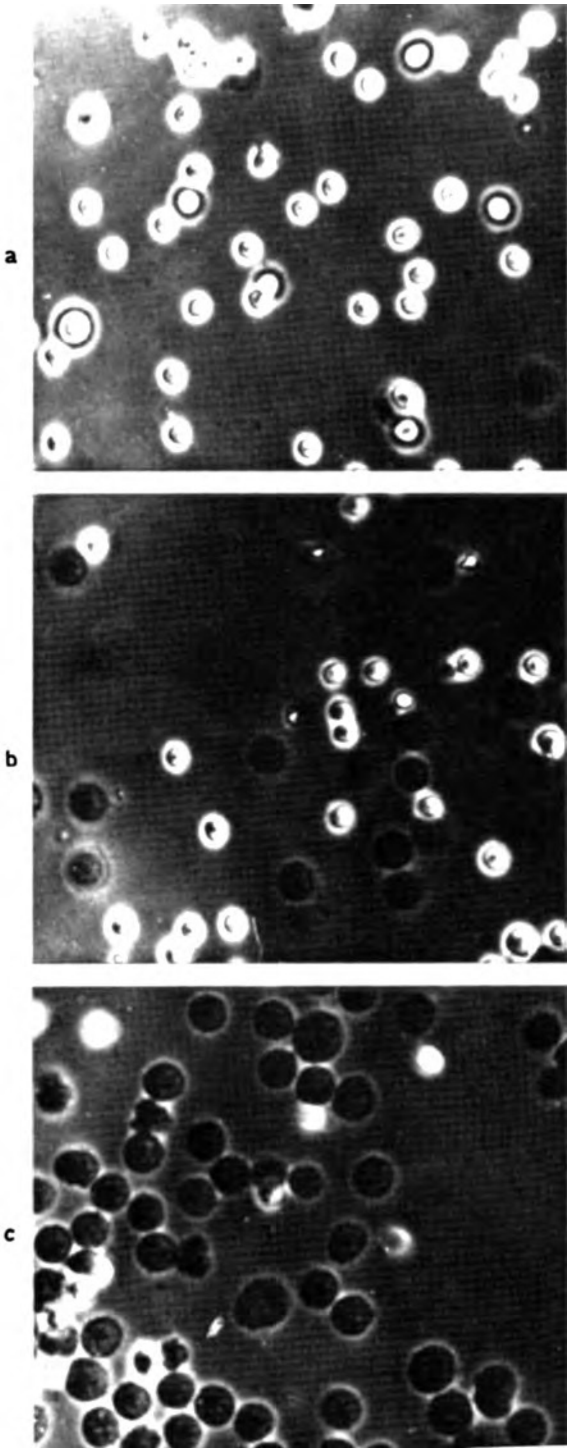


Fig. 15. The entrapment of eosin into mouse lymphocytes after the application of electrical field pulses (a, b or c resp. 6, 12 or 18 kV/cm, pulse duration 0.5 μs) at 4 °C. The dye was added to the isotonic solution before pulse application. The phase contrast pictures show that the number of lymphocytes taking up eosin steadily increases with increasing field strength [12].

## 4. Electrically Induced Fusion

The reversible electrical breakdown of the cell membrane leads to perturbation of the membrane structure, which permits an exchange of materials between the cell and its environment. In this section we shall consider field effects in two cells adhering to each other and orientated in the field direction (Fig. 16). In this case, electrical breakdown occurs at the poles of the cells and in the zone of contact between the two cells. As indicated diagrammatically, both an exchange of substances between the cells and their environment and an *intracellular* mass transport are possible under these conditions. If the membranes are in close enough contact (1—2 nm distance, say), it is also possible for lipid molecules (and possibly also protein molecules) to diffuse from one membrane into the other (Fig. 17). During the resealing process, lipid bridges may thus form between the membranes of the two cells; in other words, the two membranes do not reseal separately in the zone of contact. The bridges formed in this manner and illustrated in Figure 17, lead to very small radii of curvature and, in turn, to high surface tensions. The next step, *i. e.* the fusion of the cells into a sphere, is therefore energetically favored.

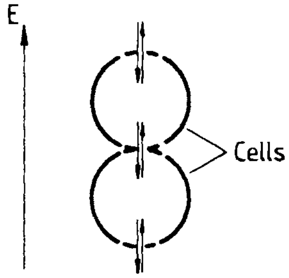


Fig. 16. Diagrammatic representation of electrical breakdown in two cells adhering to each other in the direction of the electrical field. Electrical breakdown occurs in the membrane areas in the zone of contact, which are orientated vertically with respect to the field lines [see arrows and equation (1)]. Under the given conditions electrical breakdown does not only induce exchange of substances between the cells and their medium but also intracellular exchange.

These qualitative considerations demonstrate that, in principle, electrical breakdown of the cell membranes can lead to fusion, provided that the membranes of two cells are in contact with each other and that the two cells are in the correct geometrical orientation. It has recently been observed that if

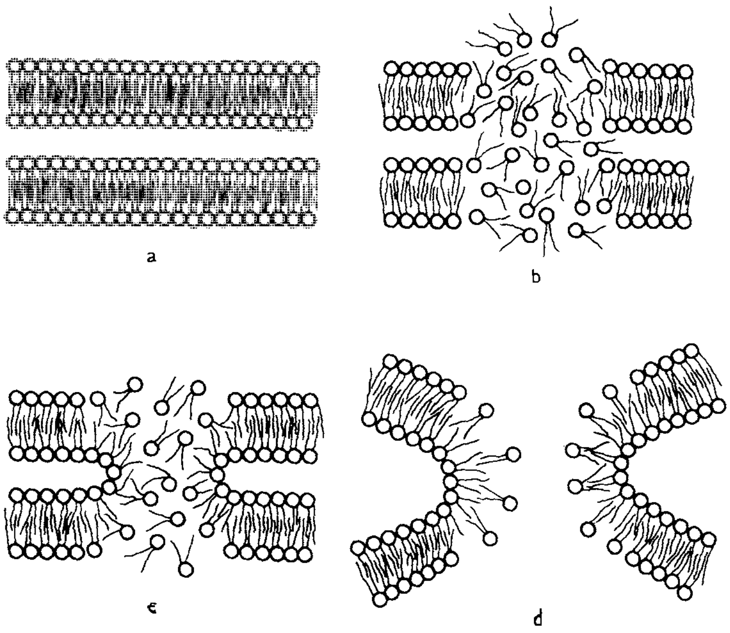


Fig. 17. Model of the molecular processes which are thought to occur during electrically induced fusion. The lipid bilayers of the two membranes are in close contact vertical to the field lines (a), whereby it is assumed that protein-free areas are formed by lateral diffusion of proteins. Electrical breakdown leads to a disruption of the membrane structure (b), so that bridges may be formed between the lipid bilayers of the two membranes during the reorganisation of the lipid molecules (c). The radius of curvature of the pores formed in this way is very small, so that formation of spherical "two-celled aggregates" is energetically favored (d).

an erythrocyte cell suspension of high density is subjected to field pulses by discharging a high voltage capacitor[57], some fused cells are formed. However, the yield was very low, since the necessary formation of two-celled aggregates is normally a rather improbable event. Brownian motion, the negative surface charge of the cell membranes, and the associated repellent forces prevent the necessary contact between membranes. This is also the reason why cells usually exhibit only a weak tendency towards spontaneous fusion under natural conditions. The current fusion methods are thus based on the use of "fusogenic" chemical substances or inactivated viruses having the same properties[6,7,58,59]. Fusogenic chemicals or viruses bring about "agglutination" of the cells and simultaneously disturb the membrane structure so that fusion is induced. However, as a rule, the cell suspensions have to be subjected to unphysiologically high or low pH-values or high calcium concentrations in order to bring about a sufficiently severe disturbance of the membrane[6,7,58,59]. The best-known and most effective fusogenic substance is polyethylene glycol (molecular weight about 6000). This substance has been used with great success for the fusion of protoplasts. For the fusion of mammalian cells, on the other hand, the *Sendai* viruses, which have a strongly agglutinative action, have proved to be particularly effective. The viruses are inactivated by UV irradiation before use, so that their effect is not associated with an infection of the cell[6,7]. Viruses whose fusogenic action depends on their replication in the cell, have not achieved any importance for the *in vitro* fusion of cells.

A number of disadvantages have to be accepted with these classic fusion methods. The unphysiological conditions influence the viability of the fused cells. The fusogenic substances or viruses can also elicit irreversible changes in the membranes, because they interact with the entire membrane surface for prolonged periods of time. Fusion is not synchronous and the yield is usually very low. Furthermore, the fusion methods are not understood mechanistically. They vary from one cell type to another and have to be optimized by trial and error. More recent fusion techniques suffer from similar disadvantages[60,61]. In this case, the cells are made to adhere to each other by chemical or viral means and the disturbance of the membrane necessary for the initiation of fusion is brought about by a field pulse exceeding the breakdown voltage of the membrane. Under these conditions, the yield is slightly higher, as demonstrated by *Berg et al.*[60] and *Neumann et al.*[61]. These studies demonstrate that fusion can be achieved by means of the electrical breakdown of the cell membranes. This conclusion is also supported by the observations of *Senda et al.*[62], who were able to show that two protoplasts held together with microcapillaries will fuse after the application of a field pulse. They, however, used dextran in the solution, which may have properties similar to polyethylene glycol. It is doubtful whether this method will find much practical application since the yield is *a priori* very low.

A generally applicable method with which different types of cells (or lipid vesicles) can be made to fuse with each other or with lipid vesicles has recently been developed by *Zimmermann* and *Scheurich*[13,63-66] (Fig. 18). The electrically induced fusion is based on the exclusive use of physical techniques and, in principle, consists of two stages. In the first stage, the membranes of the cells to be fused are brought into close contact by dielectrophoresis. In the second stage, fusion is induced in the resulting cell aggregates by electrical breakdown.

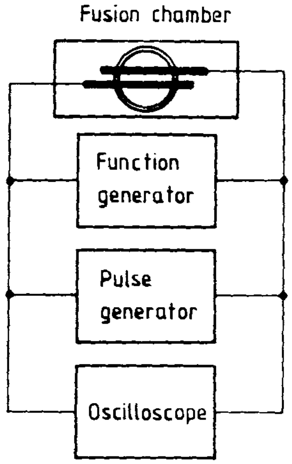


Fig. 18. Diagrammatic representation of the experimental set-up used for electrically induced fusion. Two electrodes, which can be observed under a microscope, are glued to a slide in parallel to each other. The frequency and amplitude of the dielectrophoretic voltage (see text) are controlled by a function generator; a pulse generator is connected in parallel and is used to elicit the breakdown pulse. The applied voltages are recorded on an oscilloscope. For further details see [13].

Dielectrophoresis, which was first applied to living cells by *Pohl* and *Crane*[67,68] has been known for a long time. It is used to render the distribution of the field lines in an electrostatic field visible with *e.g.* the aid of semolina particles suspended in oil. These particles orientate themselves along the field lines due to dielectric polarization.

In principle, the same applies to a cell present in an electrical field (Figs. 18 and 19). In a homogeneous electrical field (Fig. 19a) a force is exerted on the cells because of their net surface charge, and they begin to migrate towards the oppositely charged electrode. This phenomenon is known as electrophoresis. Since the surface charge is usually negative, the cells migrate towards the anode. In addition, a dipole moment is induced in the cells because of charge separation or because of orientation of dipoles in the membrane. However, this does not contribute to the movement of the cells since the field intensity in a homogeneous field acting on the generated dipole is equal on both sides of the cell; in other words, a neutral particle will not migrate in a homogeneous field (Fig. 19b). In an inhomogeneous electrical field, on the other hand, electrophoresis is observed as before, but the neutral particles are also seen to migrate, usually in the direction of greater field intensity (Fig. 19c). The reason for this migration is that the field intensities are different on the two sides of the dipole induced in the cell. The result is a net force which pulls the particle in the direction of greater field intensity. This effect is known as dielectrophoresis[67]. The direction of the net force exerted on a neutral particle in an inhomogeneous field does not change (cf. Fig. 19d) when the direction of the field is reversed by inverting the external voltage. The electrophoretic migration of a cell, on the other hand, which is determined only by its surface charge, proceeds in the opposite direction. In an inhomogeneous alternating electrical field, cells are no longer able to migrate because of their net charge. Instead, the cells oscillate around a certain position in the field and the surface charge is "masked". Only dielectrophoretically induced migration can occur, whereby the cells migrate towards the greater field intensity along the electrical field lines. The force exerted on the cell under dielectrophoretic conditions, is dependent on the square of the field intensity, on the field gradient, the particle volume, the difference between the dielectric constants of the cell and its environment (as well as the corresponding difference between their conductivities). As a rule, these differences are positive, so that cells are observed to migrate to the region of greater field intensity. Under certain conditions, however, the difference between the dielectric constants can become negative, so that negative dielectrophoresis is observed, *i.e.* migration into the region of lower field intensity. The reason for this is that the dielectric constant of a cell (or membrane) is a function of the frequency, since the membrane structure (including the boundary layers in contact with the solutions) is inhomogeneous[67,69]. The boundary layers become polarized, which is reflected macroscopically by a change in the dielectric constant (Maxwell-Wagner dispersion)[69]. At certain frequencies the dielectric constant of the cell may thus become smaller than that of the surrounding solution so that negative dielectrophoresis results. As a rule, positive dielectrophoresis is observed in the frequency range between 1 kHz and 10 MHz (for exceptions see [67]).

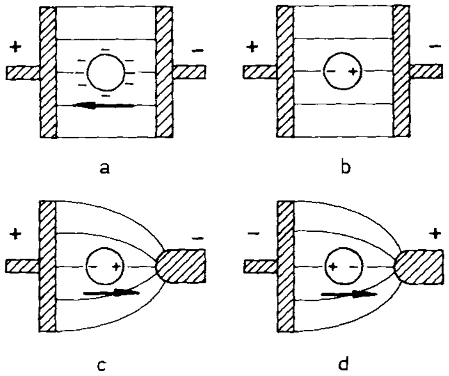


Fig. 19. Diagrammatic representation of electro- and dielectrophoresis. Because of the net charge on the outer surface of the membrane, cells or charged particles migrate in the direction of an electrode (electrophoresis) in a homogeneous electrical field (plate capacitor) (a). The direction of migration depends on the sign of the charge and on the direction of the external voltage. In general, cells have a negative surface charge. In addition, a dipole is induced in a dielectric particle or in a cell (regardless of whether these particles carry a net charge or not) (b). Since the electrical field intensity is equal on both sides of the particle or cell (b), this induced charge does not contribute to movement. Uncharged particles are thus unable to migrate in a homogeneous field. In an inhomogeneous electrical field, on the other hand, uncharged particles are also able to migrate, because the electrical field exerts a net force on the electrically induced dipole (c); the field intensity is not equal on both sides of the particle, resulting in a net force acting on the particle. This effect is known as dielectrophoresis. In contrast to the direction of migration during electrophoresis, the direction of the dielectrophoretic migration of the particles and cells is not reversed when the external electrical voltage between the two electrodes is reversed (d) (see [13, 67]).

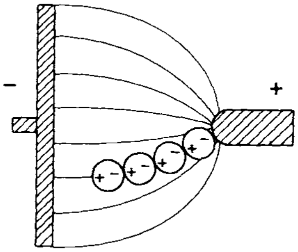


Fig. 20. Diagrammatic representation of the formation of cell chains during dielectrophoresis. The cells adhere to each other and form chains at the electrodes along the electrical field lines, because the dipoles induced in the cells attract each other.

When cells approach each other during their migration along the field lines towards regions of greater field intensity, they attract each other because of their dipole moments (Fig. 20) so that they move towards the electrode in the form of two-, three- or four-celled chains (depending on the suspension density), where they arrange themselves like "strings of pearls" along the field lines.

This configuration remains stable as long as the alternating external field is applied. If the field is removed, the chains break up, since the cells repel each other due to their net charge and Brownian motion. Dielectrophoresis is thus a reversible process (provided that the field intensity is not too high, see below), which allows membranes to come into close contact.

A limiting factor in the dielectrophoretic aggregation of cells is the electrical conductivity of the medium. If this is too high, too much current flows in the solution leading to heat production and associated turbulences which prevent the formation of chains. It is thus necessary to use non-ionic solutions if possible (specific conductivity $<10^{-4}$ S cm$^{-1}$). The osmolarity[*] of the solution must be established by addi-

---

[*] Where this term means the concentration of the osmotically active particles.

Table 1: Electrically induced fusion [a].

| Fusion between | | Medium | Minimum electrode-distance [μm] | Dielectrophoretic collection | | Electrical breakdown pulse | | Fusion time [min] | Remarks |
|---|---|---|---|---|---|---|---|---|---|
| Cell 1 | Cell 2 | | | Maximum field strength [V/cm] [a] | Frequency [MHz] | Field strength [V/cm] [a] | Duration [μs] | | |
| Mesophyll-protoplast, oats | as 1 | 0.5 M mannitol | 200 | 200 | 0.5 | 750 | 20 | 3–10 | cf. [63] |
| Mesophyll-protoplast, bean | as 1 | 0.5 M mannitol | 200 | 200 | 0.5 | 750 | 50 | 30–60 | cf. [13] |
| Mesophyll-protoplast, petunia | as 1 | 0.5 M mannitol | 200 | 200 | 0.5 | 750 | 50 | 30–60 | [c] |
| Guard cell-protoplast, bean | Mesophyll-protoplast, bean | 0.6 M mannitol | 200 | 200 | 0.5 | 2000 | 50 | 20–40 | cf. [64] |
| Mesophyll-protoplast, Kalanchoe | as 1 | 0.3 M sorbitol | 300 | 70 | 1 | 570 | 20 | 0.5 | [d] cf. [65] |
| Mesophyll-protoplast, Kalanchoe | Vacuole, Kalanchoe | 0.3 M sorbitol | 300 | 70 | 1 | 500 | 20 | 0.5 | [d] cf. [65] |
| Vacuole, Kalanchoe | as 1 | 0.4 M sorbitol | 300 | 50 | 1 | 500 | 20 | 0.1–0.2 | [d] cf. [65] |
| Mesophyll-protoplast, oats | as 1 [b] | 0.5 M mannitol | 200 | 200 | 0.5 | 750 | 20 | 3–10 | [d] cf. [65] |
| Mesophyll-protoplast, Kalanchoe | Mesophyll-protoplast, oats | 0.4 M sorbitol | 300 | 70 | 1 | 570 | 20 | 1 | [d] cf. [65] |
| Human. erythrocytes [e] | as 1 | 0.3 M glucose | 100 | 1000 | 2 | 2200 | 4 | 2–4 | cf. [66] |
| Friend-cells [f] | as 1 | 0.3 M glucose | 100 | 1000 | 2 | 2200 | 1–2 | 5–50 [g] | |
| Liposomes, diameter ~10 μm [h] | as 1 | 0.075 M sucrose | 300 | 330 | 2 | 660 | 20 | <0.1 | |

[a] Plants: oats (*Avena sativa*), beans (*Vicia faber*), petunia (*Petunia inflata*), Kalanchoe (*Kalanchoe daigremontiana*). [b] The field strength was calculated assuming an homogeneous electric field. [c] *P. Scheurich, U. Tisljar, U. Zimmermann*, unpublished results. [d] The density of the solutions was increased by addition of 45% Percoll and 5% Ficoll, resp. (pH 7.0). [e] Pretreatment with pronase (1 mg/cm$^3$) or neuramidase (4 μg/cm$^3$). [f] Pretreatment with pronase (1 mg/cm$^3$); *G. Pilwat, P. Scheurich, U. Zimmermann*, unpublished results. [g] The fusion time depends on the composition of the medium (cf. text and Fig. 23). [h] Unilamellar lipid vesicles; asolectin or egg-phosphatidylcholin were taken as lipids; *R. Benz, P. Scheurich, J. Vienken, U. Zimmermann*, unpublished results. [i] Protoplasts, which were grown under light and dark conditions, resp., were fused. Under light conditions chloroplasts are present, under dark conditions etioplasts, which are the precursors of the chloroplasts.

tion of non-electrolyte. Animal and plant cells have been shown to survive for long periods of time in solutions of mannitol, sucrose, glucose or neutral amino acids without any detectable irreversible deterioration of cell or membrane function[13,63–66].

In cells with high specific densities (*e.g.* mammalian cells with nuclei occupying up to 80% of the cell volume), the density of the external medium must be raised with Percoll, because otherwise the aggregated cells displace each other as a result of gravitational effects during and after the application of the electrical breakdown pulse.

Theory and experiment[13,63–66] have shown that the field intensity for the breakdown of the membranes of the dielectrophoretically aligned cells must be exceeded in order to induce fusion. The duration of the electrical field pulse, which leads to an optimum fusion of cells or cell organelles and lipid vesicles, depends on the properties of the respective biological system to be fused. It is evident from Table 1 that the optimum range for the pulse length is between 15 and 50 μs for plant protoplasts and isolated vacuoles, whereas for mammalian cells (*e.g.* Friend cells and human erythrocytes) the optimum range is between 1 and 4 μs. Outside these given ranges, fusion is observed only in a few cases or not at all. A possible explanation for this observation may be a cell- or membrane-specific dependence of the breakdown voltage on the pulse length (see Figs. 7 and 8). In the optimum range for the pulse length nearly all cells, both plant and animal, which have been exposed to the dielectric breakdown voltage, will fuse. Electrically induced fusion is shown in Figure 21 for mesophyll cell protoplasts of *Avena sativa* (oats), in Figure 22 for a vacuole and a mesophyll protoplast of *Kalanchoe daigremontiana*, in Figure 23 for Friend cells and in Fig-

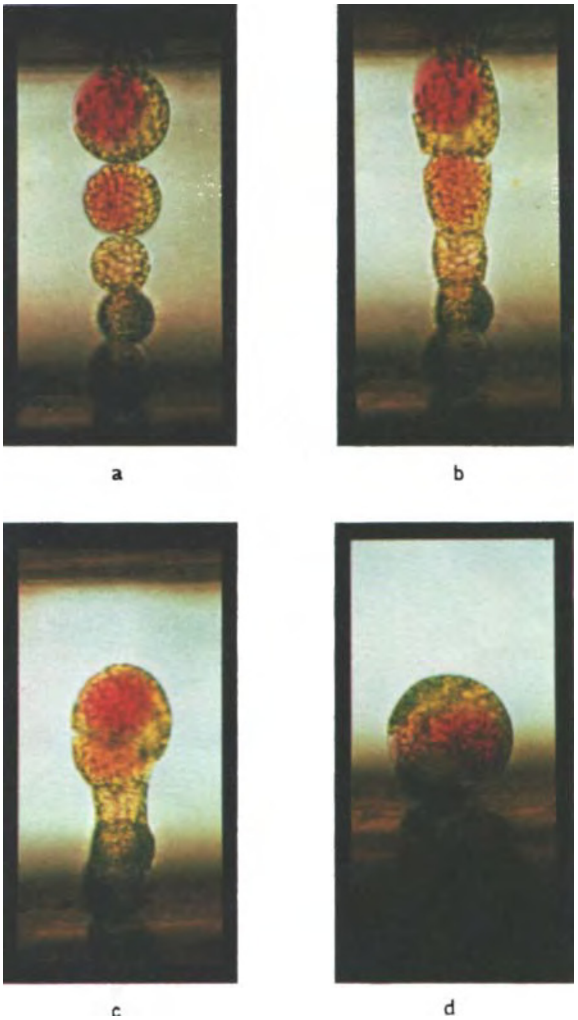


Fig. 21. Electrically induced cell fusion of mesophyll cell protoplasts of *Avena sativa*, some of which have been stained with neutral red, a vital dye which accumulates in the vacuole. The cells were suspended in a 0.5 M mannitol solution and collected by dielectrophoresis at the electrodes of the fusion chamber (a). Fusion was induced by an electrical field pulse of 20 μs duration, the intensity of which was so high that electrical breakdown occurred in the contact zone of the membranes. The photographs show the fusion process 10 s (b), 300 s (c) and 600 s (d) after the breakdown pulse [63]. 1 cm = 50 μm.

ure 24 for human erythrocytes. The relevant experimental conditions are given in Table 1. The time required for fusion following application of the pulse varies from seconds to 60 minutes (Table 1). The reason for this is not known but is probably related to different membrane fluidities in the various cell types and to different properties of the cytoskeleton (fibrillar system) within the cells. A determining factor for the duration of the fusion process is the extent to which the cell wall in plant cell protoplasts and the glycocalix layer on the outer membrane surface of animal cells has been enzymatically removed. The importance of the removal of these layers becomes apparent when erythrocytes, for example, are exposed to a critical alternating electrical field of long duration (a few seconds), after dielectrophoretic alignment[70]. Under these conditions, irreversible membrane fusion is observed with the formation of long tubes (corresponding to the length of the cell chain). Actual cell fusion, *i. e.* the formation of a single spherical cell, does not take place. It is not known whether intracellular transport of materials occurs in these erythrocyte tubes which can reach lengths of up to 200 μm or more and actually form bridges between the two electrodes.

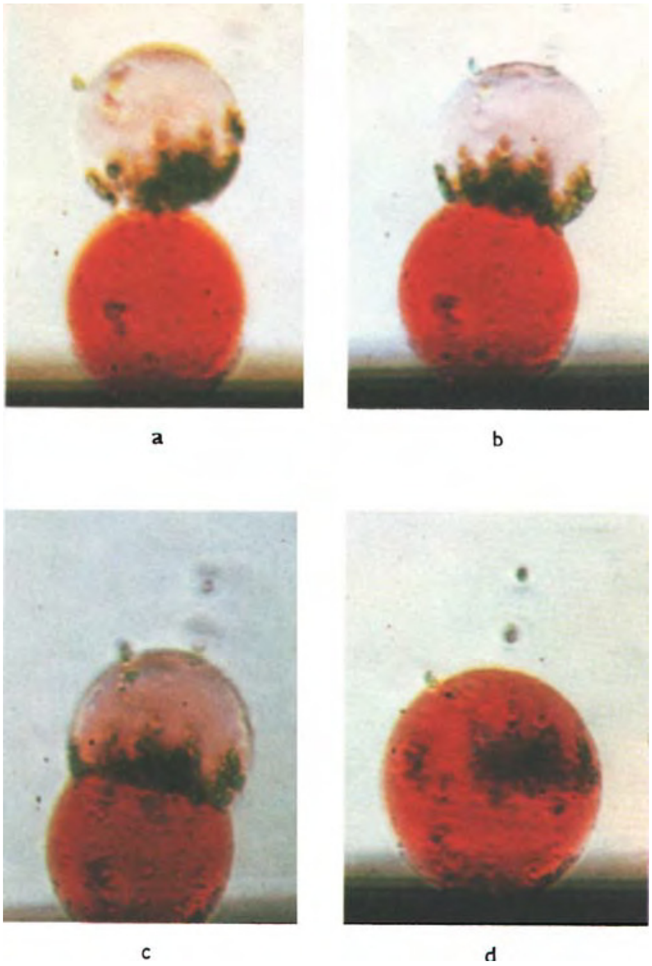


Fig. 22. Electrically induced fusion between a vacuole and a mesophyll cell protoplast of *Kalanchoe daigremontiana* (for conditions see Fig. 21). (a) Before the breakdown pulse, (b) 12 s, (c) 15 s and (d) 30 s after the breakdown pulse. For further details see text and Table 1. 1 cm = 35 μm [65].

For larger cells such as protoplasts and Friend cells it can be shown that the volume of the fused cells corresponds to the sum of the individual cell volumes, independent of the number of fused cells (see Figs. 21a, d and 22a, d). It has been observed that the tonoplast membranes, which surround the vacuoles, also fuse after fusion of the plasmalemma membranes. The fusion of the vacuoles was rendered visible with neutral red, a vital dye which does not lead to any irreversible changes and is exclusively accumulated in the vacuole.

The fusion of human erythrocytes offers particularly fascinating applications if it is carried out under the conditions described in Table 1. At high suspension densities, a large number of cell chains are obtained in which the cells are in very close contact (Fig. 24a). The breakdown pulse leads to the formation of a giant erythrocyte (Fig. 24b) which may have a diameter of up to 200 μm (the normal diameter is 7—8 μm). After fusion is complete, the glucose solution is replaced by an electrolyte solution and the individual giant erythrocytes may be isolated by a special technique using a pressure probe[2,30] and subsequently examined. At first sight, the formation of giant erythrocytes seems to contradict the mod-

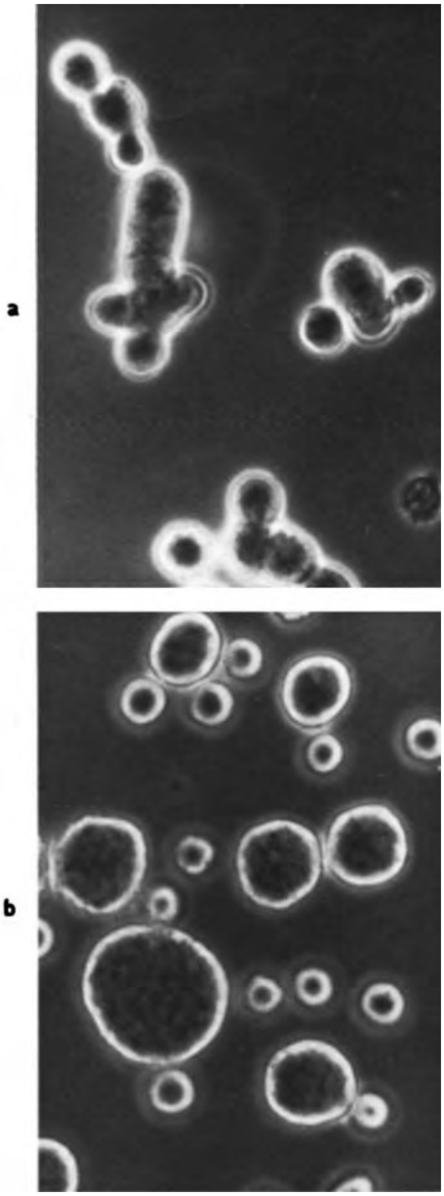


Fig. 23. Phase contrast photographs of electrically fused Friend cells. After brief pretreatment with pronase P (37 °C, 1 mg/cm$^3$, 5 min) designed to remove the glycocalix, the cells were suspended in the fusion chamber in a 0.3 M glucose solution and orientated dielectrophoretically. 1 min after application of the breakdown pulse (duration 2 μs), the cells were removed from the chamber with a specially constructed micropipette. The photograph (a) was taken 2 min after induction of electrical fusion. It also shows, in addition to fused aggregates individual cells which were not exposed to the field pulse (a). When the cells are transferred to a nutrient medium, the fusion aggregates become spherical within 10 min (b). 1 cm = 20 μm.

el developed for electrically induced fusion in Figure 17. According to the theory, breakdown should only occur in the polar regions, *i. e.* in the membrane areas in the zone of contact along the field lines. However, since electrical breakdown is an event lasting only 10 ns, as demonstrated by experiments on artificial lipid membranes, it does not seem improbable that the breakdown voltage is also reached in those membrane areas vertical to the electrodes given that the field lines pass through the cells and that the electrical field is distorted by the high suspension density of the cells.

It is interesting to note that in permanent cell lines, such as the Friend cells shown in Figure 23, the cells become more rapidly spherical after the fusion process when transferred from the glucose solution to a nutrient medium.

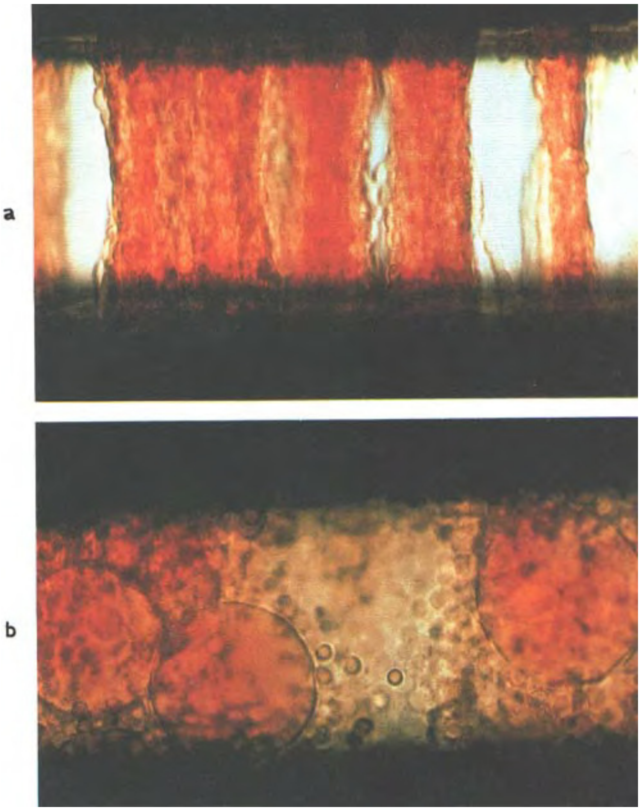


Fig. 24. Electrically induced fusion of human erythrocytes. The glycocalix layer was removed by treating the cells with neuramidase (37 °C, 4 μg/cm$^3$, 10 min). The cells were then suspended in 0.3 M glucose solution and collected dielectrophoretically between the electrodes (a). The suspension density chosen was high, so that many erythrocyte chains with membrane contact were formed in parallel to one another. Application of two breakdown pulses (duration 4 μs) leads to the formation of giant erythrocytes (diameter up to 100 μm) (b). There is no significant hemolysis during formation of giant erythrocytes. Under phase contrast they appear optically homogeneous [66]. 1 cm = 30 μm.

Furthermore, it is worth pointing out that it is also possible to fuse organelles, such as chloroplasts (the site of photosynthesis) and mitochondria (the site of energy production) by electrical means, even though these organelles have two membrane envelopes arranged in series. Artificial lipid vesicles can also be fused by electrical breakdown into giant vesicles with diameters exceeding 100 μm.

Fusion between cells of different types and between lipid vesicles and cells have also been demonstrated (see Table 1), so that one can conclude that electrical fusion is a generally applicable procedure for fusing different types of cells. Apart from the advantage of a high yield, fusion proceeds synchronously because it is triggered by a pulse. In future it should thus be possible to examine the molecular intermediate stages (still unknown), which occur during the process of fusion, by electron microscopy. It is quite conceivable that changes in the field in the membrane may also be important, even when the cells are fused by chemical or viral means.

Since the electrically induced fusion method causes only the minimum of damage (only small membrane zones are influenced for a very short time), the viability of the cells should be satisfactory. It has indeed been possible to demonstrate, for Friend cells, that growth continues after fusion and that hemoglobin synthesis can be induced by adding dimethyl sulfoxide to the suspension of fused cells[50]. There have been extensive studies on plant cell protoplasts of *Petu-*

*nia inflata*, and various authors[3] were able to show that individual mesophyll cell protoplasts of this species exhibit "totipotency": with this plant it is thus possible to observe formation of cell walls and subsequent cell division (and associated differentiation)[3] resulting in the development of a whole plant. Fusion experiments on protoplasts derived from this species are thus particularly tempting, since the viability of the fusion aggregates can be tested relatively quickly. Optimum conditions for the formation of cell walls and cell division can be achieved by immobilizing the fused protoplasts. It was first demonstrated in our laboratory[71-73] that plant protoplasts and animal cells can be immobilized in a cross-linked alginate matrix maintained in the appropriate nutrient medium. The alginate matrix is cross-linked by calcium ions. With the aid of this technique it has been possible to show that electrically fused protoplasts of *P. inflata* are capable of forming both cell walls and dividing. The immobilized cells can be released from the alginate matrix by adding a chelating agent (*e.g.* citrate) and then used for further breeding experiments. With citrate, nearly all the cells can be recovered without damage[71-73]. Experiments on sea urchin eggs (performed in collaboration with *H.-P. Richter*, Max-Planck-Institut für Biophysik, Frankfurt am Main) have revealed that fused eggs can still be fertilized by sperm.

## 5. Potential Applications of Electrical Membrane Breakdown

From the cell biological and medical point of view the breakdown voltage for the membrane can itself be used as a criterion for changes in membrane structure or composition. The variation in breakdown voltage during the growth cycle of a cell population (Fig. 11) indicates that there are changes in the electromechanical properties of the cell membrane during cell growth, which are reflected in changes in the breakdown voltage. *Escherichia coli* cells also exhibit an increase in the average breakdown voltage during the transition from logarithmic to stationary growth phase, as demonstrated in earlier studies with the particle analyzer as shown in Figure 9b[19]. These observations may indicate that specific growth phases can be characterized by the electrical breakdown voltage, a result which is very attractive from the medical and cell biological points of view, because the various stages of growth have until now normally only been identified by staining the cells with fluorescent dyes and by examination with an impulse cytophotometer[74]. Changes in the breakdown voltage as a result of processes of differentiation are also known. *Pilwat et al.*[75] were able to show that the breakdown voltage decreases significantly during the development of *Avena sativa* (oats) chloroplasts from the etioplast stage. The development of chloroplasts is induced within 48 hours by illuminating plants that have been grown in darkness. The decrease in the breakdown voltage as a function of the illumination time was interpreted in terms of an increase in the number of transport proteins incorporated into the membranes of the chloroplasts. The fact that certain local anaesthetics can change the electrical breakdown voltage of erythrocyte membranes may also be of clinical relevance. Increasing concentrations of benzyl alcohol decrease the breakdown voltage by more than 50%[76,77]. However, it should be pointed out that the breakdown voltage of planar artificial lipid membranes is apparently hardly influenced by the addition of various agents. Extensive studies, taking into account the recent finding that the breakdown voltage is dependent on the pulse length, will certainly be necessary to arrive at a more clear-cut statement. Furthermore, it is possible that the breakdown properties of the membranes are more sensitive to chemical changes in artificial lipid vesicles than in planar membranes. The interpretation of electrical breakdown in terms of local electromechanical compression with the formation of pores, indicates that elastic and mechanical forces in the membrane play a role (see above). The small radius of curvature of both lipid vesicles and cells and the tension forces in the membrane could considerably influence the value of the breakdown voltage, if the mechanical and elastic parameters of the membrane were influenced by the addition of certain substances. The development of a particle analyzer capable of making measurements on individual cells (Fig. 9d) will enable detailed studies of this nature to be carried out on phospholipid vesicles of varying chemical composition, different charge and degree of cross-linkage (see also [12a])[34,35,78-80].

In general, the present trend in medical technology is towards the development of multi-parameter analyzers, *i.e.* devices which enable measurements of a number of characteristic membrane and cell parameters in individual cells to be made simultaneously[81-83]. In the procedure described here (Fig. 9d), it is possible to measure the volume, breakdown voltage of the membrane and apparent underestimation of the cell volume after breakdown in individual cells, without any additional manipulation (*e.g.* staining *etc.*). As discussed above, the apparent underestimation of the cell volume is a direct measure of the intracellular conductivity pattern. The underestimation reflects the ratio of non-conducting to conducting space in the cell. This ratio depends, on the one hand, on the size and properties of the intracellular compartments within the cell, and, on the other hand, on the conductivity of the cytoplasm which itself is sensitively regulated by the biochemical activity in the cell. Measurements on human erythrocytes, which had been loaded with non-electrolytes or electrolytes by electrical breakdown in the discharge chamber, have shown that the degree of equilibration between the cell interior and the external solution can be monitored directly in the particle analyzer by measuring the apparent underestimation of the cell[10]. With appropriate calibration it is also possible to estimate the protein content of the cells. Studies of this type, which are of great clinical interest, are particularly simple to perform on human erythrocytes, since they have no nuclei or other intracellular compartments. *Pilwat* and *Zimmermann* (see *e.g.* [48]) were able to corroborate reports in the literature by showing that the hemoglobin content of erythrocytes of various ages, which were separated in a density gradient (Percoll), is independent of volume and hence age. With the aid of the new particle analyzer (Fig. 9d) it should be possible, in the future, to routinely detect early stages of pathological changes in the hemoglobin content of individual cells in an erythrocyte population (caused by anaemia, for example).

Field induced entrapment of membrane-impermeable substances in the cell interior and the associated possibility of manipulating the spectrum of cellular functions, offer a number of interesting prospects from the cell biological point of view. Two possible applications, both of which are at this moment being explored in different laboratories, will be mentioned in order to emphasize this aspect:

Specific reaction sites in carrier systems within the membrane or intermediate stages in biochemical and biophysical reaction chains, which are asymmetrically arranged in the membrane, can be located and identified by the entrapment of appropriate substances with a specific action (*e.g.* inhibitors). Since proteins and enzymes can be reversibly entrapped in cells by electrical breakdown[21], experiments in which the luciferin-luciferase system can be entrapped in cells to determine the ATP turnover in the cell, have become realizable. As a rule, since the turnover of ATP is determined using inhibitors and uncoupling agents, it is not always possible to exclude with any certainty side effects and non-specific interactions with the plasma membrane.

Cells whose functions have been manipulated, offer fascinating possibilities for clinical diagnostics and therapeutics. With a few exceptions, drugs (hormones, antibiotics, enzymes, radionuclides *etc.*) do not act in a cell-, tissue- or organ-specific way. The development of carrier systems which direct drugs to specific target sites and release them in a controlled manner, or which circulate in the blood for long periods of time acting as drug reservoirs, represents a very topical area of research in biomedical technology (see [10,79,84-87]).

So far, all work has concentrated on the development of artificial carrier systems (*e.g.* liposomes, microcapsules, binding to polymers, *etc.*). In spite of encouraging results, we are still far removed from the ultimate goal of clinical application. Compatibility with the organism, immunological reactions, lack of selectivity, and limitations in the life span of the carrier systems used at present are only some of the many problems which have still to be solved satisfactorily[10,79,84-86]. Cellular carrier systems have a number of intrinsic advantages, in particular, the lack of significant immunological reactions.

Experiments on mice, using erythrocytes which had been electrically loaded with a cytostaticum or other clinically relevant substances, confirm the satisfactory properties of the cellular carrier system[9,10,12,49,84]. A high percentage of the erythrocytes, which are loaded under the appropriate field conditions without any significant loss of hemoglobin and other cellular components, will circulate in the bloodstream after intravenous injection[10,88]. The life-span of these manipulated cells is of the same order as that of intact mouse erythrocytes. If, on the other hand, field conditions are chosen such that the hemoglobin content is very low after the resealing process (ghost cells) and the mean cell volume differs from that of the intact cells, the entrapped drug (*e.g.* methotrexate, a cytostatic agent which blocks an important step in the synthesis of purine) is targeted specifically to the liver[9,12,84]. Under these conditions, the manipulated erythrocytes are recognized as foreign bodies by the spleen and liver and degraded accordingly, so that the drug is specifically released in these organs. By the simultaneous field-induced entrapment of a drug and small magnetic particles (diameter about 10 nm) in erythrocytes, it is, in principle, possible to develop cellular carrier systems with other organ-specific properties. By external magnetic guidance, such "magnetic" erythrocytes can be directed to many specific sites within the organism. Experiments with mice have shown[10] that this procedure works in principle and that the magnetic particles can be eliminated by the body without any toxic reactions[10,89].

The fusion of cells by electric breakdown opens up a whole new range of possibilities for the development of drug carrier systems. Ghost cells loaded with a drug can be fused with intact erythrocytes, lymphocytes and other cells of an organism. Since there is apparently no significant loss of intracellular components, carrier systems with a long life span in the body and possibly with completely new organ-specific properties can be developed.

Carrier systems consisting of fused erythrocytes and liposomes could be of particularly interest, since liposomes can be loaded with proteins or DNA (genes) by simple chemical methods[85]. By incorporating liposomes into the erythrocyte membrane it should be possible to modify the membrane properties of the erythrocyte locally, depending on the chemical composition of the liposome membrane, so that the erythrocyte could release the entrapped substance in a controlled manner in space and time. The use of phospholipids, which can be polymerized under UV irradiation after the event of membrane fusion, is another promising tool for the development of an optimum drug carrier system[34,35,90].

Electrically induced fusion in general offers new possibilities for applications in other fields, since contrary to traditional methods it is universally applicable to all cells and artificial lipid vesicles. Both the lack of damage to the cells and the high yield indicate that fused cell systems are highly viable.

Nevertheless, we are still very much at the beginning of this development, but given our present knowledge, we can point out a number of potential applications for this fusion method.

Fusing plant protoplasts of different origins to produce crop plants with new properties such as improved yield or better salt tolerance is quite conceivable. Salt-tolerant mutants of the soya bean are well-known[91]. Several laboratories are thus attempting to fuse protoplasts of this mutant with protoplasts of other crop plants in order to produce a viable cell hybrid which can be used to breed plants having the combined properties of both.

The transfer of the gene responsible for nitrogen fixation from bacteria to plant protoplasts, with the aid of the electrical fusion method, is also coming into the realms of possibility. The fusion of protoplasts from yeast cells with plant cells is another fascinating area which could find technological application. Yeast cells are able to convert sugar into alcohol. By immobilizing yeast cells in cross-linked polymer matrices it is possible to produce alcohol in a continuous process [see [92-95]. Plant protoplasts on the other hand, are able to convert solar energy into sugar (and starch). A hybrid cell with the properties of both cells should thus be capable of converting solar energy directly into alcohol. If it were possible to operate such a cell system on a large scale, the implications for the solution of our current energy problems would be enormous. Undoubtedly the difficulties that would need to be overcome to achieve these goals technologically, are immense. In particular, it would be necessary to examine the compatibility of the cytoplasmic properties, the genetic material and other cellular factors when cells of different origins are fused. Even in the event of failure of the supposed technological applications, studies of this nature should at least provide fresh impetus for cell biology and for research into membrane structure and function, which may well result in the discovery of other applications which are not immediately obvious at present.

*The results reviewed here were partly supported by grants from the Bundesministerium für Forschung und Technologie and from the Deutsche Forschungsgemeinschaft. We are very grateful to Prof. Dr. Göbel, University of Würzburg, for supplying us with Friend cells, and to Mrs. S. Alexowsky for typewriting the manuscript.*

Received: January 20, 1981 [A 360 IE]
German version: Angew. Chem. *93*, 332 (1981)

---

[1] *G. B. Brown, G. Manecke, L. B. Wingard, Jr.:* Enzyme Engineering. Vol. 4. Plenum Press, New York 1978.
[2] *U. Zimmermann, E. Steudle,* Adv. Bot. Res. *6*, 45 (1978).
[3] *W. Klingmüller:* Genmanipulation und Gentherapie. Springer, Berlin 1976, p. 193.
[4] *M. H. Saier, Jr., C. D. Stiles:* Molecular Dynamics in Biological Membranes. Springer, Berlin 1975.
[5] *P. J. Quinn:* The Molecular Biology of Cell Membranes. Macmillan Press, London 1976.
[6] *G. Poste, G. L. Nicholson:* Cell Surface Reviews. Vol. 5. North Holland, Amsterdam 1976.
[7] *N. R. Ringertz, R. E. Savage:* Cell Hybrids. Academic Press, New York 1976.
[8] *U. Zimmermann, J. Schultz, G. Pilwat,* Biophys. J. *13*, 1005 (1973).
[9] *U. Zimmermann, G. Pilwat,* Z. Naturforsch. *C 31*, 732 (1976).
[10] *U. Zimmermann* in *E. Goldberg, L. Donaruma, O. Vogl:* Targeted Drugs. Wiley, New York, in press.
[11] *U. Zimmermann,* Chem. Labor Betr. *28*, 505 (1977).
[12] *U. Zimmermann, J. Vienken, G. Pilwat,* Bioelectrochem. Bioenerg. *7*, 554 (1980).
[12a] *L. Gros, H. Ringsdorf, H. Schupp,* Angew. Chem. *93*, 311 (1981); Angew. Chem. Int. Ed. Engl. *20*, 305 (1981).
[13] *U. Zimmermann, P. Scheurich,* Planta *151*, 26 (1981).
[14] *S. J. Singer, J. L. Nicolson,* Science *175*, 720 (1972).
[15] *N. Higinbotham,* Annu. Rev. Plant Physiol. *24*, 25 (1973).
[16] *U. V. Lassen, O. Sten-Knudsen,* J. Physiol. (London) *195*, 681 (1968).
[17] *G. Adam, P. Läuger, G. Stark:* Physikalische Chemie und Biophysik. Springer, Berlin 1977.
[18] *R. Benz:* Künstliche Lipidmembranen: Modelle für biologische Membranen? Konstanzer Universitätsreden, Universitätsverlag Konstanz 1980.
[19] *U. Zimmermann, G. Pilwat, F. Riemann,* Biophys. J. *14*, 881 (1974).
[20] *U. Zimmermann, G. Pilwat, F. Beckers, F. Riemann,* Bioelectrochem. Bioenerg. *3*, 58 (1976).
[21] *U. Zimmermann, F. Riemann, G. Pilwat,* Biochim. Biophys. Acta *436*, 460 (1976).
[22] *J. Vienken, E. Jeltsch, U. Zimmermann,* Cytobiologie Z. Exp. Zellforsch. *17*, 182 (1978).
[23] *D. Auer, G. Brandner, W. Bodemer,* Naturwissenschaften *63*, 391 (1976).
[24] *U. Zimmermann, G. Pilwat, C. Holzapfel, K. Rosenheck,* J. Membr. Biol. *30*, 135 (1976).
[25] *R. Benz, U. Zimmermann,* Biochim. Biophys. Acta *597*, 637 (1980).
[26] *R. Benz, U. Zimmermann,* Bioelectrochem. Bioenerg., *7*, 724 (1980).
[27] *R. Benz, F. Beckers, U. Zimmermann,* J. Membr. Biol. *48*, 181 (1979).
[28] *R. Benz, P. Läuger,* J. Membr. Biol. *27*, 171 (1976).
[29] *J. Y. Abidor, V. B. Arakelyan, L. V. Chernomordik, Yu. A. Chizmadzhev, V. F. Pastushenko, U. R. Tarasevich,* Bioelectrochem. Bioenerg. *6*, 63 (1979).
[30] *U. Zimmermann,* Annu. Rev. Plant Physiol. *29*, 121 (1978).
[31] *U. Zimmermann, G. Pilwat, A. Péqueux, R. Gilles,* J. Membr. Biol. *54*, 103 (1980).
[32] *A. Péqueux, R. Gilles, G. Pilwat, U. Zimmermann,* Experientia *36*, 565 (1980).
[33] *R. Benz, U. Zimmermann,* Biochim. Biophys. Acta *640*, 169 (1981).
[34] *H.-H. Hub, B. Hupfer, H. Koch, H. Ringsdorf,* Angew. Chem. *92*, 962 (1980); Angew. Chem. Int. Ed. Engl. *19*, 938 (1980).
[35] *A. Akimoto, K. Dorn, L. Gros, H. Ringsdorf, H. Schupp,* Angew. Chem., in press.
[36] *B. Gauger, F. W. Bentrup,* J. Membr. Biol. *48*, 249 (1979).
[37] *U. Zimmermann, F. Beckers, H. G. L. Coster,* Biochim. Biophys. Acta *464*, 399 (1977).
[38] *U. Zimmermann, R. Benz,* J. Membr. Biol. *53*, 33 (1980).
[39] *R. Benz, F. Conti,* Biochim. Biophys. Acta, in press.
[40] *E. Jeltsch, U. Zimmermann,* Bioelectrochem. Bioenerg. *6*, 349 (1979).
[41] *J. Hurley,* Biophys. J. *10*, 74 (1970).
[42] *H. E. Kubitschek* in *J. R. Noris, D. W. Ribbons:* Methods in Microbiology. Vol. 1. Academic Press, New York 1969, p. 593.
[43] *R. Thom,* Dtsch. Med. Wochenschr. *94*, 617 (1969).
[44] *R. Thom, A. Hampe, G. Sauerbrey,* Z. Gesamte Exp. Med. *151*, 331 (1969).
[45] *V. Kachel,* J. Histochem. Cytochem. *24*, 211 (1976).
[46] *G. Pilwat, U. Zimmermann, H. Schnabl* in *W. J. Lucas, J. Dainty:* Plant Membrane Transport: Current Conceptual Issues. Elsevier/North Holland, Amsterdam 1980, p. 475.
[47] *U. Zimmermann, M. Groves, H. Schnabl, G. Pilwat,* J. Membr. Biol. *52*, 37 (1980).
[48] *U. Zimmermann, G. Pilwat, M. R. Groves,* Deutsch. Pat.-Anm. P 2828232.8 (1978); US-Pat. 4220916, Sept. 1980.
[49] *U. Zimmermann, G. Pilwat, J. Vienken,* Recent Res. Cancer Res. *75*, 265 (1980).
[50] *C. Friend, W. Scher, J. G. Holland, T. Sato,* Proc. Natl. Acad. Sci. USA *68*, 378 (1971).
[51] *E. Neumann, K. Rosenheck,* J. Membr. Biol. *10*, 279 (1972).
[51a] *G. Pilwat, U. Zimmermann,* unpublished results.
[52] *A. Katchalsky, P. F. Curran:* Nonequilibrium Thermodynamics in Biophysics. Harvard University Press, Cambridge, Mass. 1965.
[53] *H. Passow* in *C. Bishop, D. M. Surgenor:* The Red Blood Cell. Academic Press, New York 1964, p. 71.
[54] *W. D. Stein:* The Movement of Molecules Across Cell Membranes. Academic Press, New York 1967.
[55] *D. Danon* in *R. Goldman, M. Rockstein:* The Physiology and Pathology of Human Aging. Academic Press, New York 1975, p. 95.
[56] *J. Teissie, T. Y. Tsong,* J. Membr. Biol. *55*, 133 (1980).
[57] *U. Zimmermann, G. Pilwat,* Sixth International Biophysics Congress, Kyoto 1978, Abstr. IV-19-(H), p. 140.
[58] *K. N. Kao, M. R. Michayluk,* Planta *115*, 355 (1974).
[59] *Z. Toister, A. Loyter,* J. Biol. Chem. *248*, 422 (1973).
[60] *H.-E. Jacob, W. Förster, H. Berg,* Z. Allg. Mikrobiol., in press.
[61] *E. Neumann, G. Gerisch, K. Opatz,* Naturwissenschaften *67*, 414 (1980).
[62] *M. Senda, J. Takeda, S. Abe, T. Nakamura,* Plant Cell Physiol. *20*, 1441 (1979).
[63] *U. Zimmermann, P. Scheurich,* Biochim. Biophys. Acta *641*, 160 (1981).
[64] *P. Scheurich, U. Zimmermann, H. Schnabl,* Plant Physiol., in press.
[65] *J. Vienken, M. Ganser, R. Hampp, U. Zimmermann,* Physiol. Plant, in press.
[66] *P. Scheurich, U. Zimmermann,* Naturwissenschaften *68*, 45 (1981).
[67] *H. A. Pohl:* Dielectrophoresis. Cambridge University Press, Cambridge 1978.
[68] *J. S. Crane, H. A. Pohl,* J. Electrochem. Soc. *115*, 584 (1968).
[69] *H. P. Schwan,* Adv. Biol. Med. Phys. *5*, 147 (1957).
[70] *P. Scheurich, U. Zimmermann, M. Mischel, I. Lamprecht,* Z. Naturforsch. *C 35*, 1081 (1980).
[71] *G. Pilwat, P. Washausen, J. Klein, U. Zimmermann,* Z. Naturforsch. *C 35*, 352 (1980).
[72] *P. Scheurich, H. Schnabl, U. Zimmermann,* Biochim. Biophys. Acta *598*, 645 (1980).
[73] *H. Schnabl, P. Scheurich, U. Zimmermann,* Planta *149*, 280 (1980).
[74] *W. Göhde, W. Dittrich,* Acta Histochem. *10*, 429 (1971).
[75] *G. Pilwat, R. Hampp, U. Zimmermann,* Planta *147*, 396 (1980).
[76] *U. Zimmermann, G. Pilwat, F. Riemann* in *U. Zimmermann, J. Dainty:* Membrane Transport in Plants. Springer, Berlin 1974, p. 146.
[77] *G. Pilwat, U. Zimmermann, F. Riemann,* Biochim. Biophys. Acta *406*, 424 (1975).
[78] *D. Day, H. H. Hub, H. Ringsdorf,* Isr. J. Chem. *18*, 325 (1979).
[79] *H. Ringsdorf* in *R. J. Kostelnick:* Midland Macromolecular Monographs. Vol. 5. Gordon and Breach, London 1978, p. 197.
[80] *H. Bader, H. Ringsdorf, J. Skura,* Angew. Chem. *93*, 109 (1981); Angew. Chem. Int. Ed. Engl. *20*, 91 (1981).
[81] *R. C. Leif* in *G. L. Wied, G. F. Bahr:* Automated Cell Identification and Sorting. Academic Press, New York 1970, p. 131.
[82] *D. J. Arndt-Jovin, T. M. Jovin,* J. Histochem. Cytochem. *22*, 622 (1974).
[83] *V. Kachel, E. Glossner, E. Kordwig, G. Ruhenstroth-Bauer,* J. Histochem. Cytochem. *25*, 804 (1977).
[84] *U. Zimmermann, G. Pilwat, B. Esser,* J. Clin. Chem. Clin. Biochem. *16*, 135 (1978).
[85] *G. Gregoriadis, A. C. Allison:* Liposomes in Biological Systems. Wiley, Chichester 1980.
[86] *T. Ming Swi Chang:* Biomedical Applications of Immobilized Enzymes and Proteins. Vol. 1. Plenum Press, New York 1971, p. 147.
[87] *G. M. Ihler* in *G. Gregoriadis:* Drug Carriers in Biology and Medicine. Academic Press, London 1979, p. 129.
[88] *K. Kinosita, Jr., T. Y. Tsong,* Nature *272*, 258 (1978).
[89] *T. Nakamura, K. Konno, T. Moronė, N. Tsuya, M. Hatano,* J. Appl. Phys. *42*, 1320 (1971).

[90] *D. S. Johnston, S. Saughera, M. Pons, D. Chapman,* Biochim. Biophys. Acta *602,* 57 (1980).
[91] *H. Greenway, R. Munns,* Annu. Rev. Plant Physiol. *31,* 149 (1980).
[92] *I. Chibata, T. Tosa, T. Sato, K. Yamamoto, I. Takato, F. Nishida* in [1], p. 335.
[93] *J. Klein,* Kontakte (Merck) *3,* 29 (1980).
[94] *P. Brodelius, B. Dens, K. Mosbach, M. H. Zack,* FEBS Lett. *103,* 93 (1979).
[95] *M. Wada, J. Kato, I. Chibata,* Eur. J. Appl. Microbiol. Biotechnol. *10,* 275 (1980).

# Half a Century of Polystyrene—A Survey of the Chemistry and Physics of a Pioneering Material

**By Adolf Echte, Franz Haaf, and Jürgen Hambrecht**[*]

*Hermann Staudinger,* the founder of polymer chemistry, would have been 100 years old this year. One of the key materials with which he elucidated the structure of high polymers was polystyrene.—Polystyrene, one of the most important thermoplastics, has now been manufactured industrially for some 50 years. Not only has it simplified our daily lives in a variety of ways, it has also been a model substance for the development and expansion of polymer chemistry and polymer physics, and it was the pioneering material for handling polymer solutions and melts. This article surveys the development and present state of knowledge of the polymerization of styrene and of the relationships between structure and properties.

## 1. Introduction

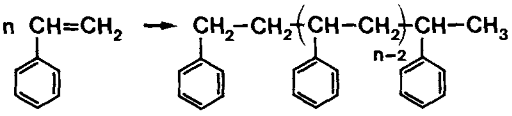
This year *Hermann Staudinger* would have celebrated his 100th birthday. It was *Staudinger* who founded polymer chemistry as a discipline; it was he who elucidated the structure of high molecular weight compounds and began to investigate their properties systematically[1]. For this fundamental work he was awarded the Nobel Prize for Chemistry in 1953.

*Staudinger*'s anniversary almost coincides with another milestone in the history of macromolecular chemistry: polystyrene had its 50th birthday in 1980. The pioneering material of high polymers was first manufactured on an industrial scale in 1930. In the autumn of 1930 I.G. Farbenindustrie AG's Ludwigshafen works—today BASF AG—became the first in the world to manufacture polystyrene industrially. Using this substance, *Staudinger* demonstrated that polymers are made up of fundamental units, the monomers, linked by primary valences.

### 1.1. Scientific Development

Polystyrene was first described by the Berlin pharmacist *E. Simon* in 1839[2]. In 1945, *J. Blyth* and *A. W. Hofmann* recognized that the polymerization of styrene was not accompanied by any change in chemical composition, and they called their glassy reaction product "Metastyrol", *i.e.* "metastyrene"[3]. This was followed by a period in which polystyrene only occasionally featured in the literature, as in a paper by *Berthelot*[4] and, later, *Stobbe* and *Posnjak*[5].

In 1920 *Staudinger* showed in his pioneering publication "Über Polymerisation"[6], that polystyrene is a high molecular weight substance, in which monomer units *(1)* are linked by covalent bonds to form macromolecular chains *(2)*. *Staudinger* also used polystyrene as a model substance in elucidating the radical chain mechanism of polymerization[7], and he resolved the long-standing controversy over the mechanism of formation of high polymers in favor of the radical chain concept, by hydrogenating polystyrene to polyvinylcyclohexane without changing its molecular weight[8]. This disproved[11] the low molecular weight synthesis principle of *Hess*[9] and the micelle theory of *K. H. Meyer*[10].



*(1)* *(2)*

Macromolecular substances require special techniques of investigation, because the methods suitable for low molecular weight substances are frequently inapplicable. As early as 1930, *Staudinger* first put forward a relationship between the viscosity of a polymer solution and the molecular weight of the polymer[12], and this was subsequently refined by *Mark et al.* and *Houwink*[13,14] and put on a theoretical basis by *W. Kuhn*[15]. Styrene also served as the principal compound in elucidating the reaction kinetics of radical chain polymerization. *Chalmers*[16], *Flory*[17], and *Breitenbach*[18] established

---

[*] Dr. A. Echte, Dr. F. Haaf, and Dr. J. Hambrecht
Plastics Laboratory, BASF Aktiengesellschaft
D-6700 Ludwigshafen (Germany)

0570-0833/81/0404-0344 $ 02.50/0

relationships between the rate of polymerization and the degree of polymerization, and finally *G. V. Schulz*[19] and *Flory*[20] also succeeded in providing a kinetic explanation of the molecular weight distribution.

In 1934, *Ziegler*[21] discovered that the polymerization of styrene could also be initiated by ions. His investigations on the effect of alkali metal-organic compounds on the polymerization of vinyl monomers followed earlier experiments by *Heumann et al.*[22] and *Schlenk et al.*[23], who in part envisaged a radical mechanism[23]. The first stereospecific polymerization of styrene was achieved by *Natta* in 1955, using Ziegler catalysts[24].

### 1.2. Technological Development

In 1911, *F. E. Matthews*[25] first described polystyrene as a construction material. However, it took until 1930 to develop the basic technology required for the industrial manufacture of polystyrene. After an unsuccessful attempt in the USA at the end of the 1920's, BASF set up a continuous manufacturing process, which also included manufacture of the monomer[26,27], and which, to this day, has remained the fundamental process in polystyrene manufacture.

The first polystyrene (PS) was a crystal-clear brittle material: crystal polystyrene[28]. 1934 saw the first attempt to produce polystyrene foam[29], but only in 1950 did this become an industrial reality[30]. The first copolymer (SAN) of styrene and acrylonitrile was produced industrially in 1936[31]. This was soon followed by the first rubber-modified polystyrene[32], which however only made a vital break-through in 1950 as a result of the development of a process for the continuous mass polymerization of styrene in the presence of rubber[33]. Styrene-butadiene (SBR) copolymer was first used as rubber component but this has now generally been replaced by polybutadiene.

It was a stroke of luck, and an essential factor in polystyrene development, that at the same time as the manufacturing process, a molding method was also developed to an industrially usable stage of perfection. This was injection molding, a joint achievement by Dynamit Nobel AG and IG Farbenindustrie AG, Ludwigshafen, again dating back to 1930[34]. This method first ensured the successful sales of polystyrene.

### 1.3. Commercial Development

After a modest start, polystyrene developed rapidly. In 1930, monthly production was only 6 tonnes; in 1936 the rate had risen to 500 tonnes per annum. Industrial production of polystyrene began in the USA in 1938[35] and Great Britain followed soon after. In 1939, polystyrene production was in excess of 6000 tonnes per annum[36]. The second world war interrupted this development, since styrene was needed for the manufacture of synthetic rubber. For this purpose, styrene monomer production capacity was greatly increased—in 1945, the USA alone had a styrene capacity of 270000 tonnes per annum—and this in turn stimulated rapid development of polystyrene in the post-war years. In 1950, the annual production of polystyrene had already reached 270000 tonnes. With the change in basic raw material in the 1950's—petroleum replacing coal—a substantial reduction in the price of styrene and hence also of polystyrene became possible. New fields of use were developed; in 1970, more than 2.1 million tonnes of polystyrene were used, and in 1980 the figure exceeded six million tonnes.

## 2. Synthesis

### 2.1. Polymerization Mechanisms

Polystyrene is one of the few polymers which can be produced by free radical, cationic, anionic, and coordinative polymerization. This behavior is due, not only to the extraordinary resonance stabilization of the reactive polystyryl species in the transition state, which lowers the activation barrier for the propagation reaction, but also to the low polarity of the styrene molecule, which facilitates attack by radicals and metal complexes and the addition of differently charged ions. Furthermore, side reactions similar to those occurring in the ionic polymerization of monomers with functional groups are excluded.

In industry, the free radical polymerization of styrene predominates by far[28]. Anionic polymerization is only employed for the production of block copolymers[37], whilst cationic and coordinative polymerization are not used on an industrial scale.

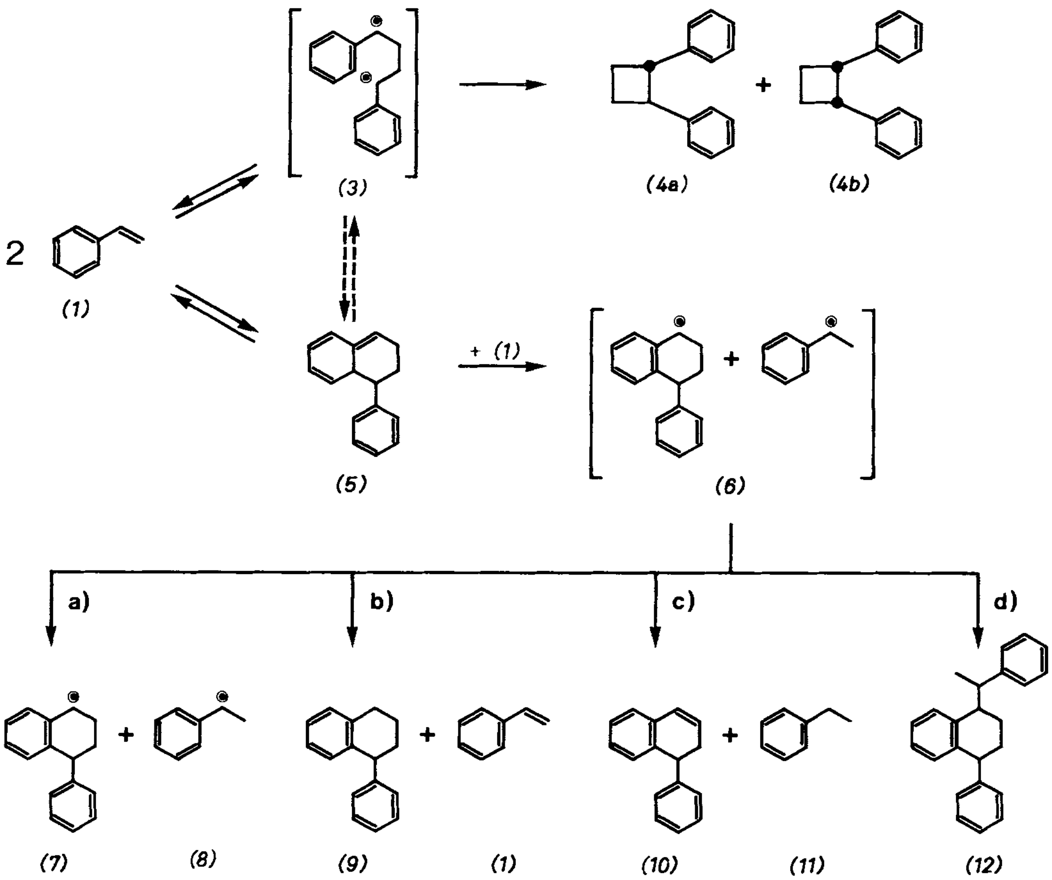
#### 2.1.1. Free Radical Polymerization

The *free radical* polymerization of polystyrene is one of the most extensively investigated reactions in polymer chemistry. It is started by free radicals (initiation), to which numerous monomer molecules then add successively (propagation). This produces a polymer radical which grows progressively until the process of growth is terminated. The polystyrene radical can also abstract a proton from a neutral molecule and thereby become saturated; this however produces a new radical, which in turn starts a new polymer chain (transfer). Finally, the polymer radical can react with another radical, by recombination or disproportionation, so that the existence of both radicals ceases (termination).

In styrene, the reaction chain can be initiated thermally or by addition of free radical initiators (peroxides or azo compounds). The mechanism of free radical-initiated polymerization was elucidated a number of years ago (see [38-41]). The mechanism of the initiation reaction in thermal polymerization of styrene is less well established (Scheme 1).

It is assumed that the Diels-Alder adduct *(5)*[42,43] eliminates the angular H atom and forms, with a further styrene molecule, a solvent cage *(6)* of two radicals[44]. These become stabilized either by recombination (route d) or disproportionation (routes b and c). The diffusion of the radicals from the cage (route a), which leads to initiation of the polymerization, is in fact only a side-reaction of oligomerization[17,45,46]. The extent to which the diradical *(3)*[47] participates in the initiation mechanism is unclear[48,49]. An analogous process has been proposed for the initiation of styrene-acrylonitrile copolymerization[50].

Chain termination was for many years thought to occur exclusively by recombination[51-53]. Investigations by *Olaj*[54] and by *Berger* and *Meyerhoff*[55,56] later indicated a contribution of disproportionation of 10—40%, which increases with



Scheme 1. a—d see text.

temperature. Studies on model radicals confirm these results[57,58].

Up to high conversions, the rate of polymerization can be satisfactorily represented as a 1st-order reaction[59]. Where more accuracy is required, the rate can be calculated from models given by *Hamielec et al.*[60,61] and *Bengough et al.*[49]. Though these models start from different initiation steps, they permit satisfactory predictions of the molecular weight and the polymolecularity index (Fig. 1).

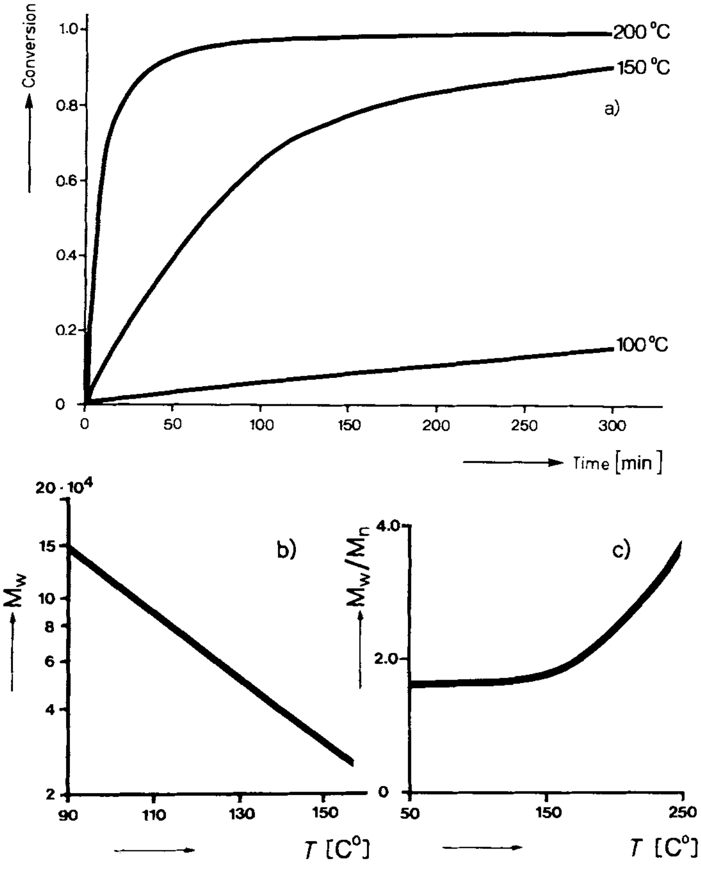
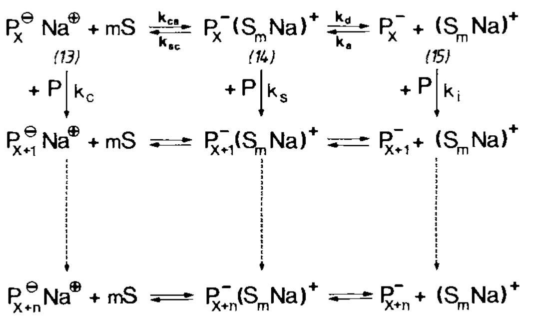


Fig. 1. a) Time-conversion curve for styrene polymerization at different temperatures [61]; b) dependence of molecular weight on polymerization temperature [28d] and c) polymolecularity index $M_w/M_n$ as a function of polymerization temperature [49].

### 2.1.2. Ionic Polymerization

The mechanism and kinetics of the *cationic* polymerization of styrene are inadequately known; the extremely rapid reaction makes a thorough investigation difficult (for our present state of knowledge see [62,63]). Hitherto, the cationic polymerization of styrene has not been utilized industrially, since the process can only be operated in a controlled manner under exotic conditions. The simultaneous use of Friedel-Crafts catalysts for the polymerization and for electrophilic substitution at the aromatic ring provides a starting point[64,65].

In contrast to the cationic polymerization, the *anionic* polymerization of styrene has been investigated comprehensively. The kinetics and reaction mechanism have been substantially clarified. Intermediate situations between a multi-route mechanism and a single-route mechanism are obtained, depending on the polarity of the solvent employed[66]. The multi-route mechanism of the extremely rapid polymerization in polar media has been elucidated, in particular, by the schools of *M. Szwarc*[67] and of *G. V. Schulz*[68] (see Scheme 2).



Scheme 2. $P_x$ = polymer, P = monomer, S = solvent.

Three forms of active carbanionic groups, namely the contact ion pair *(13)*, the solvate-separated ion pair *(14)*, and the free ions *(15)* are involved in the polymerization, thus explaining the great influence of solvent and of the temperature (Fig. 2[68]). The rate constants of the propagation reaction differ substantially and decrease in the sequence $k_i > k_s > k_c$[69,70].

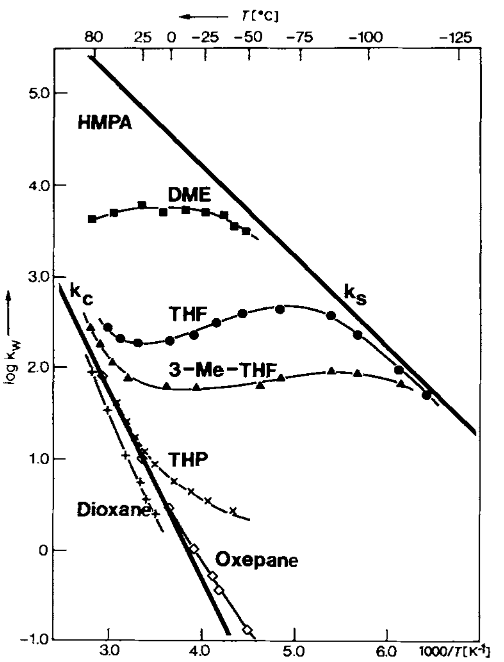
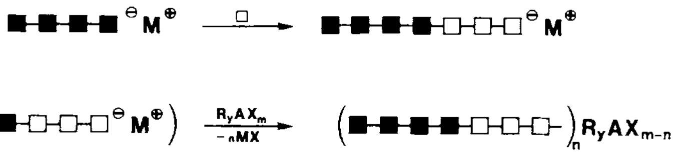


Fig. 2. Arrhenius plot of the rate constants of the ion-pairs of polystyrylsodium in different solvents [68c] (measurements in excess NaBPh$_4$). HMPA = hexamethylphosphoric triamide, DME = dimethoxyethane, THF = tetrahydrofuran, 3-Me-THF = 3-methyltetrahydrofuran, THP = tetrahydropyran.

Non-polar solvents, such as benzene, cyclohexane or monomeric styrene, are no longer capable of solvating the contact ion pair *(13)*. The growing chains form associates, and the polymerization accordingly takes place more slowly. Alkyllithium compounds, which are the preferred initiators because of their solubility, also form such associates; this additionally retards the polymerization[71-73].

In the absence of impurities, the anionic polymerization of styrene in polar and non-polar media takes place without chain termination and without chain transfer[67,68]. Hence, in contrast to the case of free radical polymerization, the molecular weight distribution of the product is very narrow and, in the extreme case, corresponds to a Poisson distribution[74].

If, after consumption of the monomeric styrene, the chain end is not deactivated by addition of a protonic substance, the chain continues to be active, giving so-called "living polymers". The polymer anion can continue to add further monomer, including other monomer types. This fact is used industrially for the synthesis of block copolymers of a defined structure[37]. Either polymerization is continued at the living chain end by addition of other monomers, resulting in linear block copolymers; or separately produced living polymers are coupled by means of bifunctional or multifunctional reagents, to give linear or radially branched block copolymers (Scheme 3). Both methods are employed industrially in the manufacture of thermoplastic styrene-butadiene copolymers having properties ranging from those of rubber through thermoplastic elastomers to impact-resistant thermoplastics[75,76]. Intensive work is being carried out in this sector. Certain combinations of properties can be obtained deliberately by means of novel coupling agents[77,78] and comonomers[79,80]. One example is the improvement in flow by increased branching or stellar arrangement of the molecule chains[81-83].

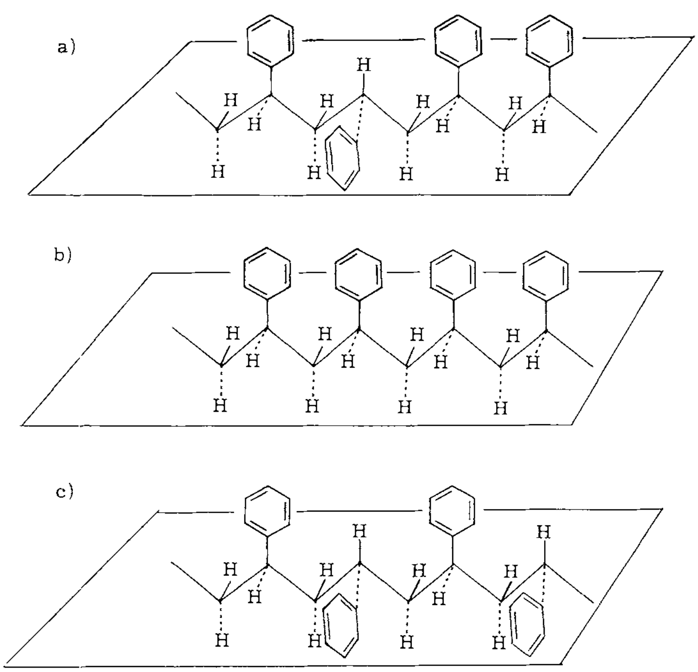


Scheme 3. ■, □ ≙ monomer units; *e.g.* ■ = butadiene, □ = styrene; y = 0—2, m = 1—4; X = halogen, COR, COOR, epoxide; R = H, alkyl, aryl, polymer residue; A = C, Si.

### 2.1.3. Coordinative Polymerization

The coordinative polymerization of styrene over complex Ziegler catalysts produces, alongside stereochemically irregular, atactic polystyrene, in particular isotactic polystyrene in which neighboring phenyl nuclei have sterically similar configuration (Scheme 4)[84-86]. Syndiotactic polystyrene, in which the phenyl nuclei are arranged in alternately opposite configurations, has hitherto not been discovered[87]. The catalysts used have a strong influence on the steric structure of the polymer[86]. The mechanism of coordinative polymerization of styrene is known only in outline; however, information[88] gathered from the analogous reaction of ethylene and propylene is largely applicable.

Coordinative polymerization of styrene has hitherto not achieved any practical importance, though isotactic polystyrene, because it has a substantially higher heat distortion temperature than atactic polystyrene[86], would appear to be of interest as a component of mixtures[89-91]. Development products[92] marketed towards the end of the 1960's were



Scheme 4. a) Atactic, b) isotactic, c) syndiotactic polystyrene.

however withdrawn, largely because of the low degree of crystallinity, the low rate of crystallization, processing difficulties, and the unsatisfactory mechanical properties of the isotactic polystyrene[86,93,94].

### 2.2. Copolymerization

Copolymerization of styrene is extremely important industrially, since it allows the pattern of properties of thermoplastic styrene polymers to be varied within wide limits[31]. In addition to random copolymerization (for reviews see [31,95-99]), it is above all graft copolymerization and anionic block copolymerization (see Section 2.1.2), which have acquired practical importance.

The random copolymerization of styrene can be initiated by free radicals or ionically. Differences from styrene homopolymerization are a result of the comonomers having different polarity and different reactivity from styrene. These factors especially affect chain propagation, since one of the monomers is preferred for addition to a particular chain end and for solvation of the growing chain[100-102]. However, the desired copolymer compositions can be achieved by making use of the copolymerization parameters derived from kinetic and quantum-chemical considerations. This approach is utilized industrially[31] in the manufacture of SAN, styrene/methyl methacrylate and styrene/maleic anhydride copolymers having various compositions.

The graft copolymerization of styrene with butadiene- or other rubbers is of vital importance in the manufacture of high-impact styrene polymers[103]. Such products consist of a polystyrene matrix with embedded rubber particles. In most cases, these particles are not compact but contain occluded matrix material ("cell particles", Fig. 3[104]). The heterogeneous rubber particles form a separate phase; they are also referred to as the soft component, in contrast to the hard component or matrix. The grafted rubber acts as an emulsifier in the polystyrene-rubber two-phase system and is responsible for the anchoring of the rubber in the polystyrene matrix[104-106,136]. Industrially, the graft copolymerization is carried out exclusively by free radical methods[107,108].

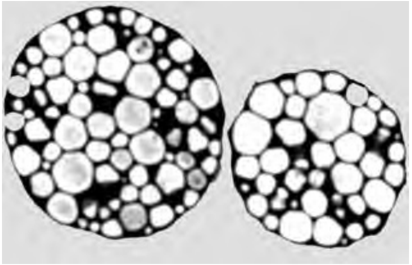
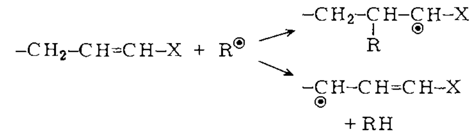


Fig. 3. Cell particles. Light phase: polystyrene, dark phase: polybutadiene.

The mechanism of the free radical grafting of styrene onto rubber has not been completely elucidated. The following initiation reactions have been discussed[109-113] (Scheme 5): An initiator radical or polymer radical $R^{\odot}$ can add onto the double bonds in the rubber or can, through chain transfer, abstract an activated hydrogen atom, in general from an allyl structure. In addition, homopolymer is also formed. All three reactions take place in parallel, and depending on the nature of the radical initiator and of any solvent used, as well as on the chosen temperature, addition or H abstraction dominates. For example, in polybutadiene rubbers addition increases with increasing 1,2-vinyl content[111,114], whilst in polyisoprene and EPDM rubbers[*] hydrogen abstraction predominates[115,116]. Polypropylene, polyethylene and polybutyl acrylate undergo grafting exclusively by H abstraction[117,118]. *tert*-Butoxy radicals released from initiators favor hydrogen abstraction, whilst alkyl radicals preferably undergo addition to double bonds[119]. In graft copolymerization using an added initiator, grafting occurs preferentially *via* the primary radicals, whilst thermal graft copolymerization is initiated by polymer radicals[111,120].



$$-CH_2-CH{=}CH-X + R^{\odot} \rightarrow \begin{cases} -CH_2-\underset{R}{CH}-\overset{\odot}{C}H-X \\ -\underset{\odot}{C}H-CH{=}CH-X + RH \end{cases}$$

Scheme 5. X = H, alkyl or polymer; $R^{\odot}$ = initiator or polymer radical.

The kinetics of graft copolymerization substantially correspond to those of styrene homopolymerization. Differences occur at low rubber concentrations and at high conversions, due to cross-linking reactions[108,121]. The molecular weight and polydispersity of the grafted polystyrene chains correspond, as a first approximation, to those of the matrix polystyrene[122]. At high conversions, the preferential solvation of the rubber, and the gel effect[**], cause an increase in the mo-

---

[*] EPDM rubbers are copolymers of *E*thylene *P*ropylene, and non-conjugated *D*iene *M*onomers.

[**] Gel effect: In highly viscous reaction solution the diffusion of the polymer molecules and hence also the chain termination are hindered. The diffusion of the monomer to the reaction site and thus the growth step of the chain reaction remain unaffected. This increases reaction rate and molecular weight equally (see also [38]).

lecular weight of the grafted polystyrene[123]. The proportion of grafted polystyrene depends on a large number of parameters; important amongst these are the polymerization process, the catalyst system, the chain transfer agent and the nature and amount of the rubber[111,124-126].

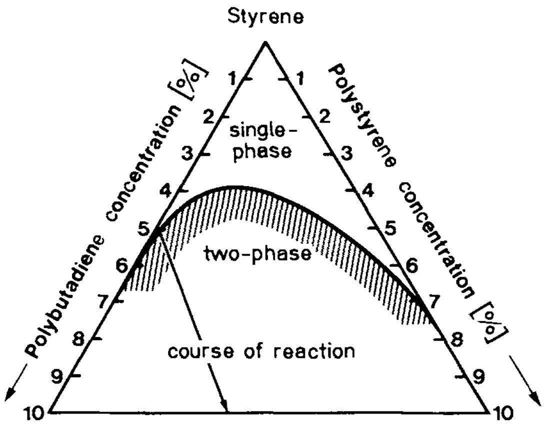


Fig. 4. Phase diagram of the styrene/polystyrene/polybutadiene system [132].

Most kinetic calculations do not allow for the fact that the styrene/polystyrene/rubber system is a two-phase system. The rate of polymerization is assumed to be the same in both phases[111]. *Rosen*[127] has, making allowance for the phase separation which starts even at very low conversions (Fig. 4), derived an equation for the maximum degree of grafting $f$.

$$f = \frac{\nu_R}{\nu_S}\ln\left(1+\frac{\nu_S}{\nu_R}\chi\right)$$

$\nu_R$, $\nu_S$ = phase volume of rubber and of polystyrene in styrene, respectively, $\chi$ = conversion

Experiments have confirmed the basic predictions of this equation.

### 2.3. Properties of the Polymer Solutions

The viscosity of polystyrene solutions increases sharply with molecular weight and concentration. Increases of more than 6 orders of magnitude during polymerization are not rare (Fig. 5)[128-130] and cause problems in mixing in the reactor, in heat removal, and in the gel effect[28,107]. The viscoelastic properties of the polystyrene solutions add to the difficulty of overcoming these problems[131]. Nevertheless, the styrene polymerization process is now well understood.

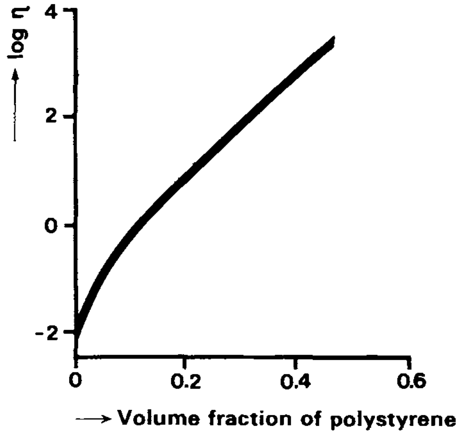


Fig. 5. Viscosity of polystyrene-styrene solutions as a function of the volume fraction of polystyrene [130].

The course of the two-phase grafting reaction can advantageously be represented in a phase diagram for ternary systems (see Fig. 4)[132-135]. If styrene is polymerized in the presence of dissolved rubber, the originally homogeneous solution undergoes phase separation even at very low conversion. The solution of polystyrene in monomer, and the solution of rubber in monomer, are incompatible and form an oil-in-oil emulsion[136]. When the volume of the polystyrene solution reaches, and exceeds, the volume of the rubber solution, phase inversion occurs. The cohesion barriers attributable to

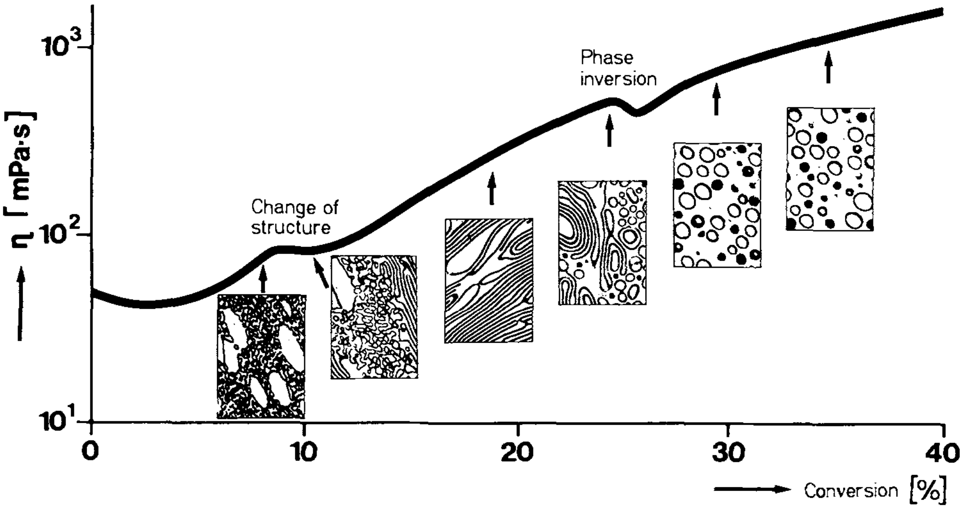


Fig. 6. Viscosity-conversion curve and structural change phenomena in the manufacture of high-impact polystyrene with capsule particle morphology.

the viscosity of the solution are overcome by the shearing action of the stirrer[137]. It is in this stage of the reaction that the particle size spectrum of the rubber phase (which is now the dispersed phase) is adjusted as required[104, 138-141]. The phase inversion can be detected from the fall and rise in the viscosity/conversion curve (Fig. 6)[142, 143].

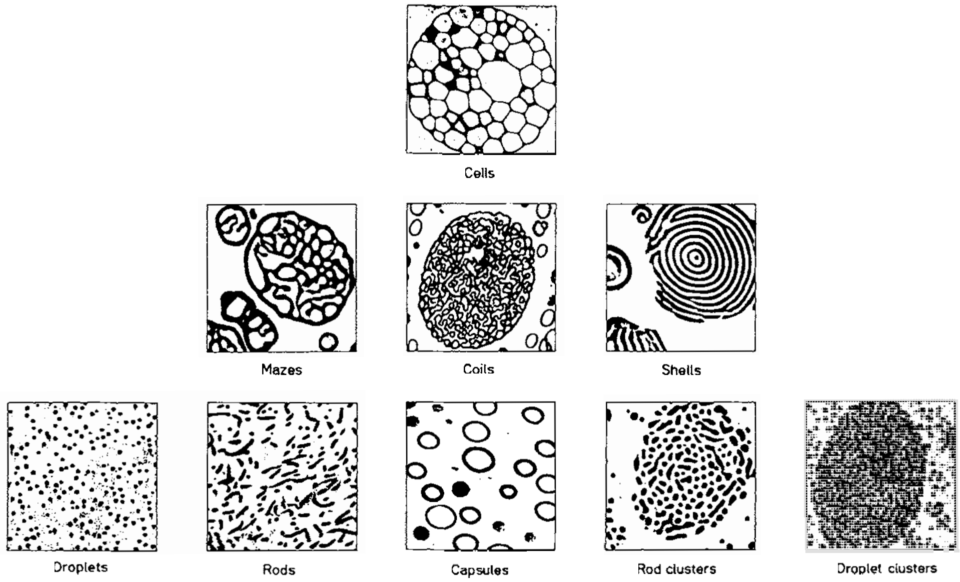


Fig. 7. Particle structures encountered in high-impact polystyrene

Styrene-butadiene block- and graft-copolymers form domain structures in styrene solution with various arrangements depending on their chemical structure[104, 109, 136, 144-149]. The ratio of polystyrene component to rubber component, which is a deciding factor in the particular structure, varies during polymerization, as a result of grafting and of embedding of low molecular weight polystyrene components[150]. When the limit of stability of the particular structural type is exceeded, complicated structural change processes start. Figure 6 shows a sequence of such structural changes during the polymerization of a styrene-butadiene block copolymer (impact resistant polystyrene), as well as the corresponding viscosity/conversion curve. The fall in the curve before phase inversion indicates the change in the domain structure of the rubber solution. The particle-formation process comes to an end even at relatively low conversions. The resulting morphology undergoes no further change up to high conversions, and is ultimately fixed by the cross-linking of the rubber phase[114, 142, 151]. The type of particle in the rubber-modified polystyrene accordingly depends on the domain structure of the rubber solution and on the grafting. If these parameters are varied, high-impact polystyrenes having very different particle structures are obtained (Fig. 7)[104, 149, 152-154].

### 2.4. Industrial Processes

For crystal polystyrene and high-impact polystyrene, and for styrene copolymers, continuous mass polymerization and solution polymerization processes have found acceptance. Expandable polystyrene is preferably produced by the suspension process, and high-impact styrene copolymers, such as ABS and ASA polymers[155], are preferably produced in emulsion. Gas phase polymerization is not used[156, 157]. Figures 8a and 8b illustrate the development of the industrially most important processes of manufacture, from the first process to be used industrially, namely the polystyrene III process of BASF[28], to today's mass polymerization process for the manufacture of modified and unmodified styrene homopolymers and copolymers[28] (for a detailed description of all the processes see [28, 31, 103, 107, 108, 156, 158-161]).

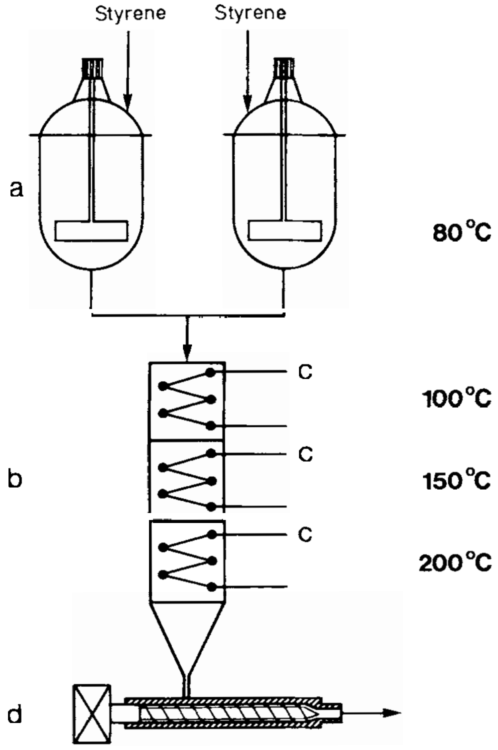


Fig. 8a. Polystyrene manufacturing process: polystyrene III process (BASF 1936 [36]); a = prepolymerization reactor, b = tower reactor, c = heating/cooling-system, d = extruder.

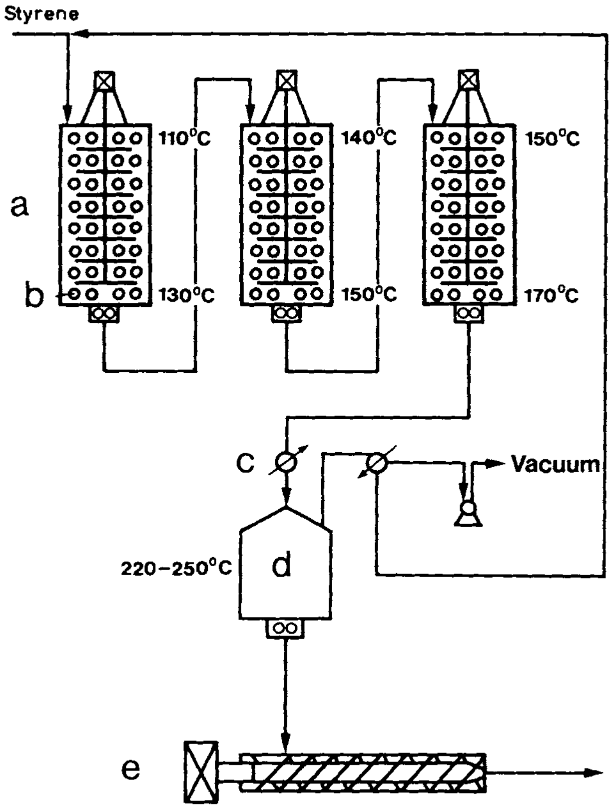


Fig. 8b. Polystyrene manufacturing process: Dow-process [159]. a = tower reactors, b = heating/cooling-system, c = heat exchanger, d = evaporator, e = extruder.

## 3. Structure and Properties

In this article, the "structure" of a styrene polymer means its molecular and morphological structure, whilst its "properties" are the processing properties and utility properties, in the broadest sense. The latter-mentioned properties determine the possible uses of the polymer as a material of construction; and it is these possibilities which provide the stimuli for development and improvement.

Amongst the large number of processing properties and utility properties, we have selected the following as being the most important:

- stiffness
- toughness
- heat distortion resistance
- flowability
- surface gloss and transparency

The structure the the styrene polymers is determined by the molecular parameters of molecular weight, molecular weight distribution, and content of low molecular weight materials, and, in the case of rubber-modified products, additionally by the following morphological parameters: rubber content, phase volume ratio, particle size and particle size distribution, degree of grafting and degree of cross-linking of the rubber. In order to relate structure to properties, parameters must be defined which enable quantitative comparisons to be made (for test methods see [103,162]).

### 3.1. Stiffness

The stiffness is the resistance of a body to elastic deformation by external forces. Polystyrene is a visco-elastic material. Its behavior under external load and at low deformations can be expressed in terms of the modulus of elasticity (or Young's modulus) $E$ or the shear modulus $G$. These moduli are time-dependent; under constant deformation, the stress relaxes, whilst under constant stress the material creeps. In order to be able to separate the viscous and elastic components, the moduli are generally measured by dynamic methods[162]. In the definition of the shear modulus $G^*$

$$G^* = G' + \mathrm{i}\,G''$$

$G'$ is the storage modulus and $G''$ is the loss modulus on shearing. $G'$ is the actual measure of stiffness at room temperature; it is one or two orders of magnitude greater than $G''$. Hence, the complex moduli can themselves be employed as a measure of the stiffness and, for example, Young's modulus $E$ easily derivable from tensile experiments can be employed. This, however, is only true at temperatures which are sufficiently below the glass transition temperature ($T_g$) that the temperature-dependence of $G'$ or $E'$ is small. At the glass transition temperature $T_g$, $G'$ and $E'$ decrease by several orders of magnitude (Fig. 9).

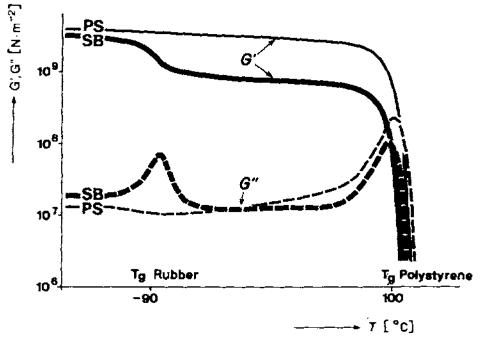


Fig. 9. Storage modulus $G'$ and loss modulus $G''$ of polystyrene (PS) and high-impact polystyrene (SB) as a function of temperature.

In isotropic test specimens of polystyrene, the moduli are independent of the direction of the external stress. In articles for practical use, this precondition in general does not apply, because the flow which occurs during the manufacturing process impresses preferred directions. Young's modulus is greatly increased in such directions and decreases in directions at right angles thereto. In polystyrene, use is made of this property, for example in biaxially oriented films.

Above a critical limit ($2\,M_c = 70000$), the moduli of polystyrene are independent of the molecular weight. This has been confirmed by *Fellers* and *Chapman*[163] in both tensile and compression experiments. $M_c$ is related to the critical entanglement length; this is the lowest molecular weight that allows the polystyrene chains to intertwine (cf. also [164]). According to *Fox* and *Loshak*[165] the exponent in the viscosity/molecular weight function $\eta \sim M^\alpha$ changes from $\alpha = 1$ to $\alpha = 3.4$ at molecular weight $M_c = 35000$. This molecular weight is equated with the critical entanglement length of the polystyrene molecule. *Fellers* and *Kee*[166] observed that the curves of the breaking stress and of the crazing stress (cf. Section 3.2 for crazes) plotted against molecular weight intersect at $2M_c = 70000$. *Wellinghoff* and *Baer*[167] found that crazing only becomes detectable by electron microscopy at molecular weights of about 30000; at lower molecular weights, the crazes show no fibrillation. This suggests that *Fox*'s interpretation is correct, though a more recent view holds that the exponent changes progressively from 1 to 3.4[168].

The addition of a few per cent of a low molecular weight lubricant also produces no change in the stiffness of polystyrene. On the other hand, the addition of compatible polymers alters the moduli which can be calculated by an almost linear function from the ratio in the mixture. This can be demonstrated, for example, for the case of mixtures of high-impact polystyrene and poly-2,6-dimethylphenylene oxide (PPO)[169,170].

The situation is different in the case of rubber-modified polystyrene. It is true that in this material the stiffness is substantially determined by the properties of the matrix, but the presence of the rubber particles causes a considerable decrease in the storage modulus $G'$ at temperatures above the glass transition temperature of the rubber (Fig. 9). $G'$ decreases noticeably at the glass transition temperature of the rubber, whilst $G''$ passes through a maximum at this point. It was in this way that *Buchdahl* and *Nielsen*[171] for the first time, in 1950, proved the two-phase nature of rubber-modified polystyrenes. Subsequently, *Cigna*[172] showed that the decrease in $G'$ was not dependent on the rubber content, but on the proportion by volume of the soft component phase; accordingly, the rubber particle acts as a unit. This has subsequently been repeatedly confirmed[139,173] (Fig. 10).

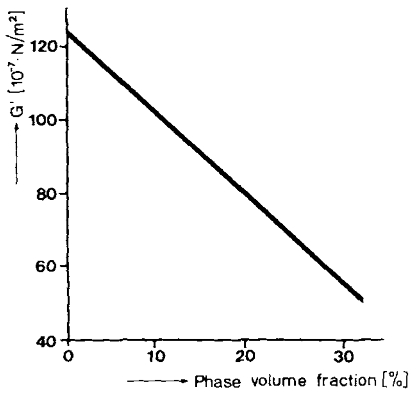


Fig. 10. Dependence of the storage modulus $G'$ of high-impact polystyrene on the proportion by volume of the soft component phase (after [172]).

In addition, the moduli depend, albeit to a lesser degree, on the size and degree of cross-linking of the particles. *M. Baer*[139] has described the decrease in modulus of elasticity with particle size (Fig. 11). We have found that the modulus of elasticity decreases with increasing swelling index[*] of the soft component. Since the degree of swelling is an indirect measure of the cross-linking of the rubber component, increasing cross-linking is associated with an increasing modulus of elasticity (Fig. 12).

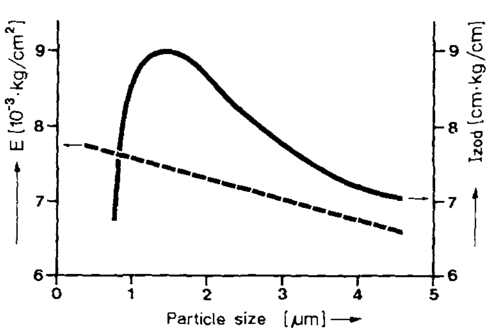


Fig. 11. Modulus of elasticity $E$ as a function of particle size (after [139]) and impact strength (Izod) of impact resistant polystyrene as a function of particle size (after [219]).

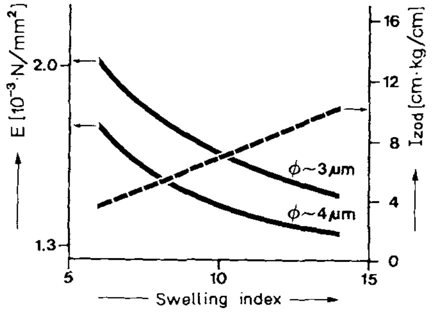


Fig. 12. Modulus of elasticity $E$ and impact strength (Izod) as a function of the swelling index (after [219]).

Many attempts have been made to calculate the modulus of a two-phase material from the moduli of the components, as a function of the phase ratio[174-176]. *Cigna* and *Bohn*[172,177] have compared the various approximations; none of the models proved capable of describing the experimental data quantitatively. They are, however, very good approximations. The reason for the deviations from the models may be that no account has been taken of the dependence of the moduli on the particle size and state of cross-linking.

### 3.2. Toughness

A material is described as tough if, under load, it undergoes not only elastic but also plastic deformation. Polystyrene becomes tough when modified with rubber. Such materials has been manufactured industrially since the end of the 1940's.

It was appreciated at a very early stage that mixtures of styrene and rubber have a two-phase structure[171]. These mixtures exhibit stress whitening when stretched to the yield point. Originally, this phenomenon was interpreted as being the formation of a large number of micro-cracks in the polystyrene matrix, bridged by the rubber particles[178]. However, this concept had to be abandoned because the rubber—according to this model—can at most absorb 10% of the fracture energy actually needed[179].

On the other hand, *Sauer et al.*[180,181] found, as early as 1949, that a sample of polystyrene was able to absorb considerable tensile stresses even though the sample was entirely pervaded by micro-cracks. On the basis of X-ray analyses, these authors postulated that the cracks had to be bridged by highly stretched matrix material. They called these cracks "craze cracks", which later come to be known just as "crazes" (Fig. 13). It took 13 years until this was confirmed

---

[*] The swelling index is defined as the ratio of the wet to dry weight of the gel centrifuged from toluene solution.

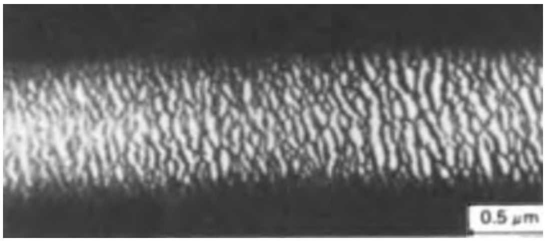


Fig. 13. Crazing in polystyrene.

by *Spurr* and *Niegisch*[182]. Subsequently, *Kambour* confirmed the structure of the crazes, determined the proportion of voids, and showed that crazes were also the preliminary stages of fracture[183]. *Bucknall* and *Smith*[184] then related crazing to stress whitening and to impact strength. Today, a craze is understood as a flat void which is spanned by fibrils of oriented polymer material (Fig. 13).

The mechanism which initiates the phenomenon of crazing is still under dispute, but it appears that the conception proposed by *Argon*[185,186] is gaining acceptance over the stress criterion of *Sternstein et al.*[187]. *Argon* interprets the formation of crazes as being due to a three-stage process: 1. Formation of stable micropores under stress; 2. formation of a craze nucleus by plastic extension of the pores; 3. expansion of the nucleus into a planar yield zone. Micropores generate predominately in zones of high stress, *i. e.* in the neighborhood of flaws or in the equatorial region of a rubber particle. The fact that crazes are formed at flaws has recently been shown once again[188]. The volume and number of micropores, on elongation of high-impact polystyrene, could be determined by means of small-angle X-ray scattering measurements.

In addition to crazing, there is a second deformation mechanism, namely shear flow. In polystyrene, it mostly manifests itself only in compression experiments[190], and in tensile experiments it is only observed with highly oriented samples[191]. During shear flow, there is no formation of voids in the material, as happens with crazing, and instead narrow plane zones inclined at roughly 45° to the stress direction are formed. The deformation of numerous thermoplastics takes place by this mechanism. There are also transitional cases between crazing and shear flow[170].

Crazes form at the interface between particles and matrix[192-195] or at the internal interfaces of the particles[196]. The particles themselves are stress concentrators; in their equatorial plane relative to the stress direction, a stress peak results[193], which initiates the craze. This effect is intensified by the overlap of the stress fields of adjacent particles[197-199]. Thermal stresses between the matrix and the particles also contribute to craze initiation[200-202].

After initiation, the crazes grow as a flat disk perpendicular to the stress direction. The spread of crazes can be hindered by the rubber particles and the crazes may stop, or branch, at such particles[203]. The agreement between theory and practice argues in favor of this mechanism: The impact strength, plotted as a function of the particle size, passes through a maximum[204,205] (Fig. 11).

The resistance of crazes to further deformation is also a factor in the impact strength. During such further deformation, the fibrillar crazed material is stretched further, becomes more highly oriented and consequently becomes strengthened (a phenomenon referred to as "strain hardening")[206]. The fibrils have an initial thickness of 250—500 Å, but a final thickness of only 100 Å[207].

"Toughness" is an all-embracing term. The resistance to failure at high deformation is important in selecting a material for a particular application, but cannot be expressed in terms of a single measured property. The toughness depends not only on the temperature but also on the rate of application of the stress, the dimensions and the internal state of the specimen (extent and direction of any orientation), and the type of stress.

In fracture mechanics, an attempt is made to express toughness in terms of a single constant for the material. According to *Griffith*[208] and *Irwin et al.*[209] a crack begins to extend if, in a material having a Young's modulus $E$ and a Poisson's ratio $\nu$, a critical stress $\sigma_c$ is reached at a sharp notch of length $a$. In that case, the following equation applies:

$$G_{IC} = \frac{\pi a(1-\nu^2)}{E}\sigma_c^2$$

$G_{IC}$ is the critical fracture energy. This equation applies to brittle fracture. Tough materials are more accurately described by a model proposed by *Dugdale*[210], in terms of the yield stress $\sigma_y$ and the corresponding critical strain $\delta_c$.

$$J_{IC} = \sigma_y\,\delta_c$$

*Plati* and *Williams*[211] have shown that the result of impact strength measurements can be described in terms of $G_{IC}$ or $J_{IC}$ independently of the geometry of the specimen. Nevertheless, these parameters have hitherto not found any acceptance in industrial practice. Instead, industry prefers to quote the results of standard tests. In the main, these are:

1. Impact test and notched impact test (Charpy test, Fig. 14a)[*].
2. Impact test or notched impact test (Izod test, Fig. 14b)[**].
3. Falling weight tests on round discs[***].

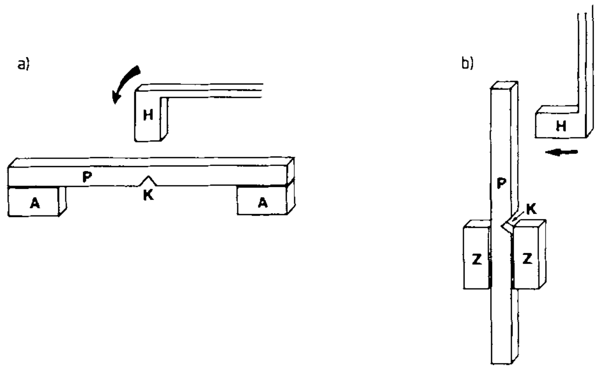


Fig. 14. Outline of the principles of two methods for measuring impact strength: a) Charpy test, b) Izod test. A = support, P = specimen, H = hammer, K = notch, Z = clamp.

The tests are mostly carried out on injection-molded test specimens. The ground state of the isotropic material and a certain amount of orientation are measured; this leads to

---

[*] DIN 53453, ISO 179 or ASTM-D 256, B [212].

[**] ASTM-D 256, A (cf. Fig. 11 and 12).

[***] DIN 53443 or ASTM-D 1709.

higher values in cases 1 and 2, and to lower values in case 3, than are obtained with isotropic material.

Form-annealed or compression-molded test specimens are isotropic[213,214]; they should be used for comparisons of materials. On the other hand, if a test simulating practical conditions and relating to a particular end use is intended, then the falling weight test (case 3) is more appropriate than cases 1 and 2[215].

Given a test method, the toughness can be related to the structure of the polymers.

The molecular weight is a significant factor only in the lower range. Low molecular weight polystyrene is extremely brittle. Using a special technique, ***Robertson***[216] succeeded in measuring $G_{IC}$ in crystal polystyrene down to a molecular weight of 3000. The measurements showed a jump of 2 orders of magnitude between $\bar{M}_n = 50000$ and $\bar{M}_n = 100000$. Similarly, ***Hauss***[217] found an abrupt increase in impact strength between $\bar{M}_w = 80000$ and $\bar{M}_w = 160000$, but no dependence on molecular weight above this value (Fig. 15). In the high-impact polystyrene, ***Wagner*** and ***Robeson***[151] showed that the addition of 5% of low molecular weight polystyrene dramatically reduces the impact strength, whilst the addition of an equal amount of high molecular weight polystyrene has virtually no effect.

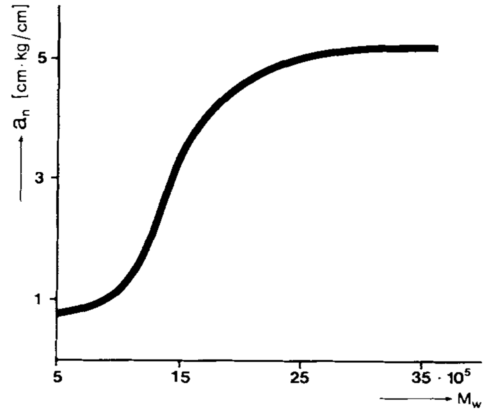


Fig. 15. Impact strength $a_n$ of crystalline polystyrene as a function of the molecular weight $M_w$ [217].

The molecular weight distribution has only little influence on the toughness of polystyrene[218], as long as the parts with $M_n < 10000$ remain negligible.

Low molecular weight lubricants such as paraffin oil or phthalic acid esters have hardly any effect on the toughness of crystal polystyrene. In high-impact polystyrene they slightly improve the toughness (Fig. 16).

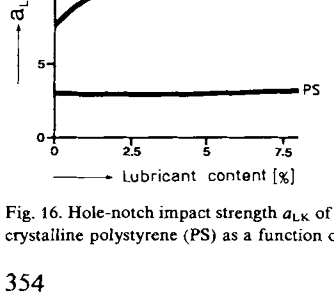


Fig. 16. Hole-notch impact strength $a_{LK}$ of impact resistant polystyrene (SB) and crystalline polystyrene (PS) as a function of the content of mineral oil.

The rubber content of high-impact polystyrenes has only an indirect effect on the toughness, the critical factor is the phase volume fraction of the soft component phase. Occluded matrix material must be regarded as part of this volume[139,172,219]. According to *Cigna et al.*[219] the impact strength increases linearly with gel content and with swelling index (Fig. 12, 17). Examined as a function of the rubber particle size, the impact strength goes through a maximum at particle sizes of from 1 to 2 μm (Fig. 11).

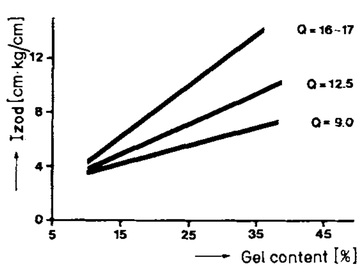


Fig. 17. Impact strength (Izod) of impact resistant polystyrene as a function of gel content (according to [219]). $Q$ = swelling index.

Finally, the anchoring of the particles in the matrix is also very important. The anchoring occurs *via* the grafted shell which forms during and after phase inversion. In thermal polymerization, anchoring can only be influenced by the temperatures used during the reaction. The use of grafting initiators increases grafting and also has an effect on the particle size[104].

### 3.3. Heat Distortion Temperature

The heat distortion temperature is the upper limit at which the material is serviceable. It is closely related to the glass transition temperature of the matrix polymer, the latter being the temperature at which rearrangements of sizable chain segments, with 50 or more chain units, become possible.

Within the range which is of practical interest, the molecular weight and molecular weight distribution have no effect on the glass transition temperature of crystal polystyrene. At low degrees of polymerization, the glass transition temperature decreases greatly; thermodynamic considerations lead to an entropy relationship between the glass transition temperature and the number-average degree of polymerization. *Überreiter* und *Kanig*[220,221] interpret the dependence in terms of the effect of the proportion of chain ends on the free volume (for a recent theoretical treatment see [222]).

However, it is only in homogeneous polymers that the glass transition temperature is a direct indication of the heat distortion temperature; in multi-phase systems, *i.e.* partially crystalline polymers or rubber modified polymers, a method which is a direct measure of stability of shape is required. The measurement of the Vicat softening temperature has found general acceptance for this purpose[*].

Low molecular weight additives have a great influence on the heat distortion temperature, the more so the greater their compatibility with the matrix. In practice, fatty acid esters, phthalic acid esters and, in the main, mineral oils are used as

---

[*] VST/B/50 according to DIN 53460 (ISO 306). The Vicat temperature is the temperature at which a needle, having a standard tip of 1 mm² area, penetrates, under a load of 50 N/mm², to a depth of 1 mm into the small test sheet of polymer, which is heated in a liquid bath at 50 °C/h [212].

auxiliaries to improve the flow of the polymers without adverse effect on the mechanical properties. The main disadvantage of such additives is that they reduce the heat distortion temperature. The degree of such influence, as a function of the concentration of the auxiliary, differs according to the auxiliary employed and is, *inter alia,* dependent on its solubility parameters (see also [223]).

Modification with rubber also influences the heat distortion temperature of the material; however, the glass transition temperatures of the components remain unaffected. The heat distortion temperature is largely determined by the glass transition temperature of the matrix. Accordingly, the Vicat softening temperature of high-impact polystyrenes is only a few degrees lower than that of unmodified polystyrene.

If a lubricant is incorporated into high-impact polystyrene, it distributes itself between the hard and the soft phase; accordingly, the distribution coefficient is a further parameter in the resulting heat distortion point. However, such factors are negligible in practice, since the changes in concentration are small.

### 3.4. Flowability

Polystyrene is processed virtually exclusively as a melt. Accordingly, the flow of the melt or, more precisely, its rheological character is the most important processing characteristic. If a polymer melt is exposed to shearing stress $\tau$, it undergoes elastic and plastic deformation simultaneously. To some extent, the melt can recover from impressed deformations $\gamma$, especially at temperatures only slightly above the glass transition temperature. The elastic component of the deformation $\gamma_r$ is described by the shear compliance

$$J_e^0 = \gamma_r/\tau$$

and the viscous component by the viscosity

$$\eta = \tau/\dot{\gamma}$$

The viscosity depends on the rate of deformation $\dot{\gamma}$; however, at low shearing rates many polymer melts exhibit Newtonian behavior. The viscosity tends to a constant value ("zero viscosity"), which is usually employed as a measure of the viscous behavior of a melt. $J_e^0$ and $\eta_0$ describe the behavior of a visco-elastic melt with time; if the shear stress is removed, the deformation recovers by the amount of the elastic deformation component (Fig. 18). Because they can be simply converted into shear, creep measurements are most suitable for determining $J_e^0$. The reversible shear deformation $\gamma_r$ has only to be replaced by the reversible elongation $\varepsilon_r$. The two parameters $J_e^0$ and $\eta_0$ together can be used to estimate the relaxation time $\bar{t}_r$, from the equation

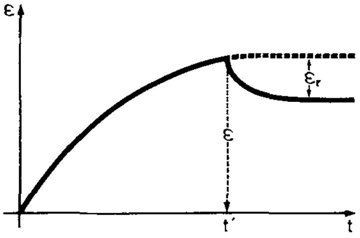


Fig. 18. Determination of the reversible elongation $\varepsilon_r$ of a polymer melt in a creep test (schematic). The sample is subjected to a constant stress $\sigma$ at constant temperature, and the stress is released at time $t'$.

$$\bar{t}_r = \eta_0 J_e^0$$

To obtain a rough estimate of the flow in general, and to compare products with one another, a single-point measurement is frequently employed, namely the apparent viscosity measured in a capillary viscometer under standard conditions[*]. However, it is well known that this measurement can, in practice, lead to considerable errors in forecasting properties. Hence, for a more precise assessment, the flow curve is employed. In this curve, the shear stress is plotted on a double logarithmic scale against the shear rate. Many polymer melts obey an exponential law:

$$\tau = C\dot{\gamma}^n$$

If they do, the flow curve in a double logarithmic scale gives the exponent $n$ as the slope of a straight line; given the value of $n$, the viscosity can be compared with that of a standard state, $\eta_s$, by eliminating the constant $C$:

$$\frac{\eta_1}{\eta_s} = \left(\frac{\dot{\gamma}_1}{\dot{\gamma}_s}\right)^{n-1}$$

*Han*[225] has found $n$ to be 0.29 for high-impact polystyrene.

The most important factor affecting the flow of polystyrene is the molecular weight. *Casale, Porter,* and *Johnson*[226] have derived the equation

$$\log \eta_0 = 3.38 \log \bar{M}_w - 13.08$$

from data in the literature, coupled with their own measurements. On the other hand, the zero viscosity does not depend on the molecular weight distribution. Only at relatively high shearing rates is a drop in viscosity observed (Fig. 19)[227].

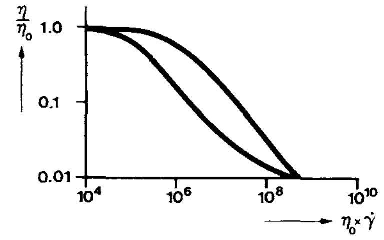


Fig. 19. Dependence of flow of polystyrene on molecular weight distribution (represented in the form of a master curve [227]).

In contrast to the zero viscosity, $J_e^0$ is independent of the molecular weight, but depends greatly on the molecular weight distribution. Polymers with a broad molecular weight distribution have a substantially higher $J_e^0$ than those with a narrow distribution. For this purpose the molecular weight distribution cannot, as is usually the case, be represented by the polymolecularity index $\bar{M}_w/\bar{M}_n$ or a higher moment of this type, since it is virtually exclusively the high molecular weight polystyrene component which affects the result (Fig-

---

[*] "Melt index" according to DIN 53735, ISO 1133 [224].

ure 20)[228]. In practice, this has the effect that the finished article from polystyrene with broader MWD contains more frozen-in elastic stresses; the article is more highly oriented and, when heated to above the glass transition temperature, shrinks more than an article made from polymer with a narrow distribution.

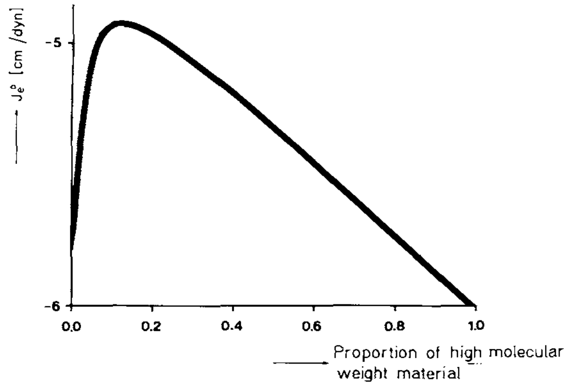


Fig. 20. Equilibrium yield $J_e^0$ as a function of the proportion of high molecular weight component in a mixture of two polystyrene samples of narrow molecular weight distribution (according to [228]).

An addition of rubber greatly increases the viscosity[225]. In the case of ABS[155], it is also dependent on the rubber particle size; small particles lead to higher viscosity. The thickness of the grafted shell also plays a part; plotted as a function of this thickness, the viscosity passes through a minimum[229]. The applicability of these results to high-impact polystyrene is subject to certain limitations, since in such a polystyrene grafting also affects the interior of the particles.

The addition of low molecular weight lubricants greatly reduces the viscosity of the polymers and is therefore a method generally employed to improve the flow. The effect is similar for crystal polystyrene and high-impact polystyrene and amounts to a shift of the viscosity/shear stress curve toward lower viscosity values. The amount of the shift is proportional to the concentration of lubricant; the effect is less pronounced at high shear rates than at lower rates.

For a given shear stress, the elastic deformation of the melt is less for high-impact polystyrene than for crystal polystyrene. Accordingly, melt fracture occurs in high-impact polystyrene at substantially higher shear rates than in crystal polystyrene[230]. "Die swell"[231] is also a measure of the elastic properties of a melt. As a strand of melt leaves a die, the imposed elastic stresses relax. The result is an increase in cross-section. Die swell decreases with increasing grafted rubber content[232].

### 3.5. Surface Structure and Transparency

The surface structure of injection-molded or thermoformed articles is critical for many applications. In some cases high gloss may be demanded, whilst in others matt surfaces may be preferred. On the other hand, transparency is a basic characteristic of unmodified polystyrene.

It is only in high-impact polystyrenes that gloss and transparency present a problem. The rubber particles remove the transparency and change the gloss for the worse. If the particles are made smaller, the gloss is improved but other properties may be adversely affected. In injection molding, it is possible to choose the process conditions (injection speed, mold temperature and follow-up pressure) so as to ensure that the gloss is preserved. In extrusion, the surface of high-impact polystyrene can be laminated with crystal polystyrene, but this has adverse effects on the mechanical strength[233]. A further alternative is a high rate of extrusion, since this tends to cause the rubber particles to migrate into the interior of the extruded sheet[234]. In recent times, attempts have been made to tackle the problem of gloss, both in injection molding and in extrusion, by changing the size and morphological structure of the particles. High-impact polystyrenes with capsule particles of ≈0.5 μm diameter (Fig. 7) give very glossy articles[104].

Approaching the problem through the morphology of the particles also gives improved transparency. Capsule-particle polystyrenes are translucent and can be used for clear-on-contact packaging. Full transparency is achievable by either matching the refractive index of the matrix and the disperse phase, for example by co-polymerization with methyl methacrylate, or by making the scattering centers small compared to the wavelength of the light and at the same time ensuring a uniform arrangement of these centers[109]. This may be achieved, for example, by anionic polymerization of styrene and butadiene to give block copolymers in which the styrene component predominates. Such polymers exhibit microscopic phase separation (Fig. 21). This provides a basis for synthesizing glass-clear transparent high-impact polystyrenes.

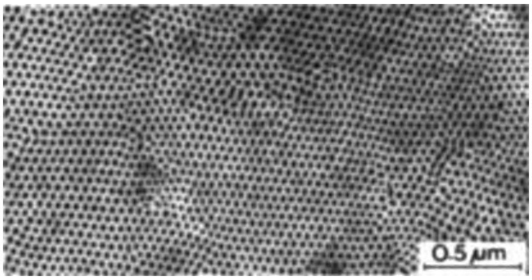


Fig. 21. Morphology of a styrene-butadiene-styrene ternary block copolymer (S/B/S proportions [%] = 37.5/25/37.5).

### 3.6. Property Combinations

We have shown that certain properties of polystyrene depend on the structure of the polymer. Figure 22 gives a diagrammatic survey of the various relationships. However, what matters in practical use of the material is a combination of properties, which must be appropriate to the particular application. A packaging material demands different combinations of properties than a material used for an electrical instrument housing, and a refrigerator door liner demands different properties from those of a yoghurt beaker. The appropriate combination of properties is, in most cases, a compromise. For example, the same step, say adding more of the soft component, has opposing effects on the toughness and on the stiffness; a gain in toughness is accompanied by a loss in stiffness. If flow is improved with lubricants, it adversely affects the heat distortion resistance, whilst if it is improved by lowering the molecular weight, it adversely affects the toughness. Smaller particles favor gloss in high-impact polystyrene, but improve toughness only down to an optimum value of the particle size. The know-how of the manufacturer amounts to his ability to offer the largest possible number of property combinations of maximum usefulness.

## 4. Processing and Use

### 4.1. Processing

Fabricators buy polystyrene in granular form. The material can be obtained without colorant (crystal, natural) or colored (opaque or transparent). The material is likely to be stored before processing and when it is used, care must be taken to remove moisture picked up from the atmosphere. In some factories, the material is separately pre-dried, whilst others use vented processing machines.

Polystyrene, as a construction material, is mainly injection-molded and extruded. Injection molding was used as long ago as 1930. The first machines were plunger injection-molding machines; today, exclusively screw injection-molding machines are used. Nowadays, there are large machines with clamping forces up to 25 MN, capable of producing moldings weighing up to 30 kg; there are also high-speed machines with multiple cavity molds, capable, for example, of producing 46 yoghurt beakers per minute[235].

Extrusion of polystyrene also dates back to the 1930's. One of the first cases of polystyrene extrusion was the production of biaxially oriented "Styroflex" polystyrene film, which from 1938 was employed for marine cable insulation. Nowadays, about 30% of the polystyrene is extruded to produce films or sheets; single-screw extruders with screw diameters of up to 200 mm and a driving power of 500 KW can process up to 2 tonnes of polystyrene per hour.

To produce shaped articles, the film or sheet is thermoformed. For this purpose, it is reheated to the thermoelastic state and is drawn into a mold by suction (see *e.g.* [161,236]; special versions see [237-240]; detailed description of the whole range of processing methods see [236,241,242]).

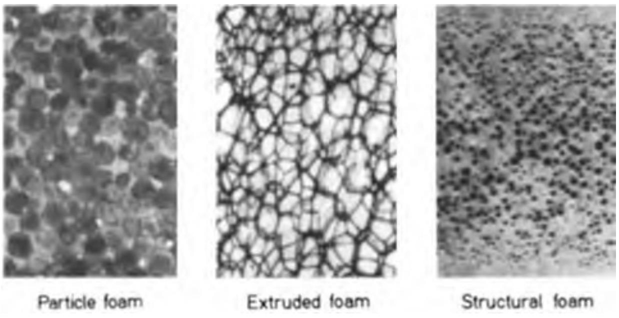


Fig. 23. Various structures of foamed polystyrene.

A detailed discussion of the processing of polystyrene to foamed articles is beyond the scope of this article (see [243]). The products are classifiable as particle foam, extruded foam, and structural foam (Fig. 23). The particle foam products are produced from expandable polystyrene beads or granules (EPS); the products may be either moldings or foam blocks which are subsequently split into boards. Extruded foam is obtained by extruding EPS or by direct gassing of polystyrene in an extruder; this results in foam boards and sheets. Structural foam has a higher density than the preceding products and is generally produced by injection molding of polystyrene containing chemical blowing agents. It is particularly employed for furniture components.

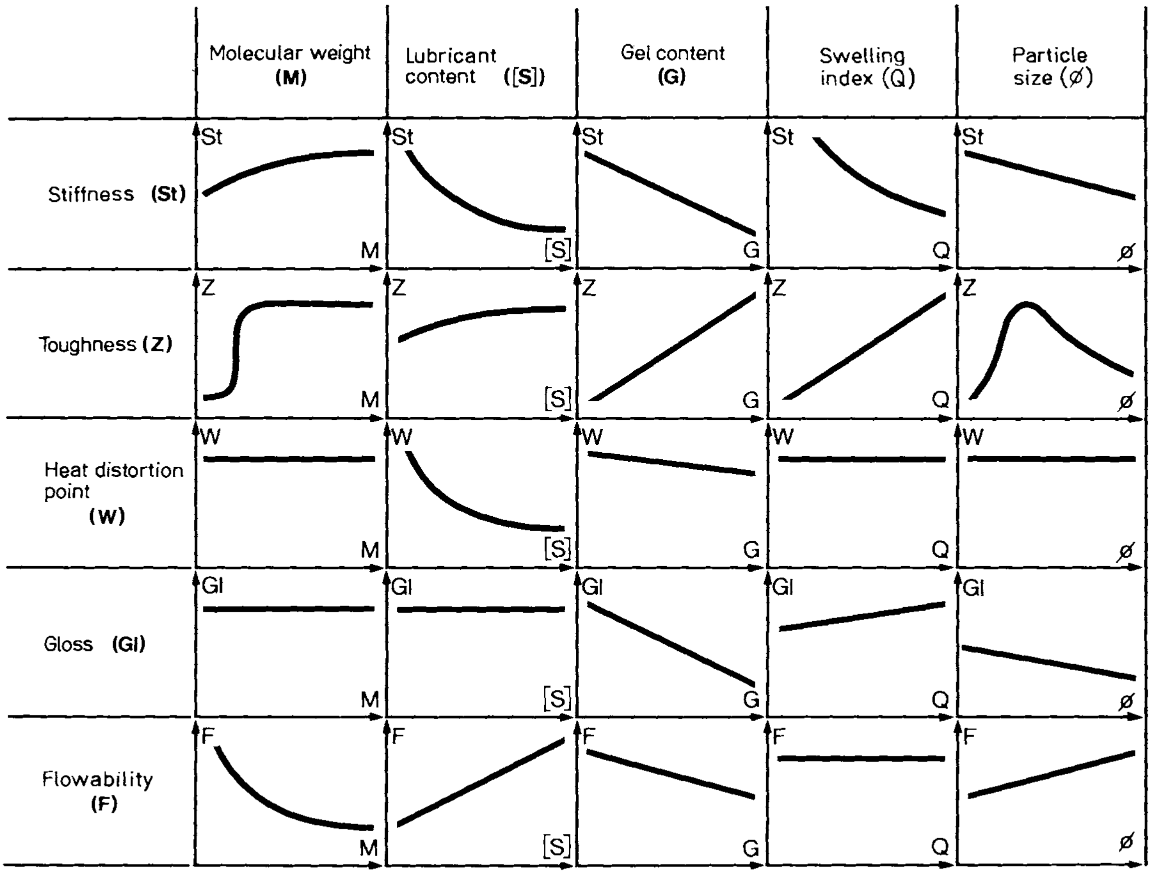


Fig. 22. Schematic representation of the interrelationships between structure and properties of polystyrenes.

Polystyrene articles can be processed further, and aftertreated, in a variety of ways, which include welding, glueing, surface-coating, printing, electroplating *etc.*

### 4.2. Uses

Because they have a good balance of properties, are easy and cheap to process, and have a low price per unit volume, thermoplastic styrene polymers have a wide range of uses, extending from high quality technical applications, for example as a material of construction in the electrical, automotive and office machine industries, to mass-production applications, for example for packaging and promotional articles, for domestic and camping items, for toys, for refrigerator and furniture components, for water pipes and for heat insulation[237,239,244-246]. The range of uses is constantly growing. Thermoplastic styrene polymers are replacing traditional materials, opening up new fields of application and finding entirely novel uses. Some recent examples are the new stress-crack-resistant polystyrenes in refrigerator construction, translucent high-impact polystyrenes in packaging, transparent super-high-impact styrene copolymers in the medical sector and flame-retardent polystyrene foams in the building trade[239,244,245].

## 5. Prospects

Since *Hermann Staudinger*'s basic work and the first industrial production of polystyrene in 1930, there has been a fundamental change in the situation. Macromolecular chemistry has become a discipline of its own, and the manufacture and processing of thermoplastics have developed into a widely diversified field with ramifications in chemical technology, mechanical engineering and process engineering.

There have also been changes in the tasks for the future and in development trends. Changes in the economic situation, particularly the fact that crude oil, as a raw material and source of energy, is becoming scarcer and more expensive, present other but not less fascinating challenges than in the pioneering period.

The theory of styrene polymerization has still not been fully elucidated. Not only the kinetics at high conversions, including the gel effect[50,61,62,247], but also the initiation of thermal polymerization are still a matter of dispute. Styrene polymerization has also become a model reaction for the behavior of commercial-scale reactors[157,248-250]. Copolymerization, too, offers numerous possibilities of modifying the properties of polymers. One example is the manufacture of purely organic ionomeric polystyrenes by incorporating cationic and anionic comonomers[251]. Ionomers open up new combinations of flow and mechanical properties. Considerable interest is also being shown in chemical modification of the polymers. Sulfonation, on the one hand, and chloromethylation, on the other, have long been used for the manufacture of ion exchangers from cross-linked polystyrene[258]; work is now proceeding more in the direction of polymer catalysts. Examples are the replacement of polystyrene by $-P(C_6H_5)_2$ as polymeric reagent for Wittig reactions[253] or the bonding of copper to aminated polystyrene as catalyst in the oxidative coupling of 2,6-dimethylphenol to give PPO[254]. Work is also being carried out on the bonding of biologically active enzymes to polymeric carriers[255-257]. In organic chemistry there are many applications for polymeric reagents (see [258-260]).

Increasing interest attaches to the graft reaction of styrene to synthetic or natural fibers, sheeting, boards and finished articles for improving the surface properties[261,262]. Attempts to polymerize natural materials such as wood flour and starch into polystyrene[263] are to be seen in the light of the increasing scarcity of raw materials.

Intensive efforts are being made in the field of polymer blends. The compatibility of polystyrene with PPO and the partial compatibility of ABS[155] with PVC, PMMA and polycarbonate have long been known[264]. More recently, still further polymer blends of industrial interest have been discovered, *e.g.* polystyrene with tetramethylbisphenol-A-polycarbonate[265] and ABS with polysulfones made compatible with polar pendant groups[266]. The object of this work is to unite the properties of the components to give a new combination. Particular attention is being paid to improving the heat distortion temperature of the blends; other main objectives are greater weathering resistance and better flame retardency.

Attempts are also currently being made to modify the property profile of impact-resistant polystyrene by morphological variation. Toughness, stiffness, flow and transparency can thus be varied within wide limits. The varied structures of rubber particles have been the subject of very recent, intensive investigation; their development offers very promising prospects[149,153].

Anionic polymerization may acquire greater interest as a process of manufacture. Block copolymers of very diverse structures (binary, ternary and multiblock products, radial block copolymers, comb structures and ABC-multicomponent systems) have already opened up a wide field of investigation and promise to yield further valuable results, since unusual combinations of properties, such as great toughness coupled with complete transparency, or great toughness coupled with good flow, can be achieved. Partially hydrogenated derivatives are also gaining in interest, not only as viscosity index improvers in mineral oils, but also as materials of construction.

In development work, priority is being given to measures which help to save energy. The manufacture of traditional materials requires more energy than does the manufacture of plastics[267,268]. In the USA, in 1977 alone, the use of plastics in building, packaging and household appliances saved 38 million barrels of crude oil[268].

All the stages of the polystyrene manufacturing process, from benzene and ethylene *via* ethylbenzene and styrene to polystyrene, up to its processing, must be scrutinized for further possible ways of saving energy. Thus, it has been proposed to utilize—by means of heat pumps—the heat of polymerization from the manufacture of polystyrene in order to degas the polymer melts, or to integrate the production of semi-finished and finished articles with the polymerization plant, since the latter in any case produces polymer melt[269]. Saving energy is also an important aspect in the development of equipment for injection molding[270], extrusion[271] and no-waste thermoforming[272].

These remarks will suffice to show that the development of polystyrene has not reached the end of the road. A number of scientific and technical innovations can still be expected for polystyrene, and its economic development can be viewed with optimism. The path which *Hermann Staudinger* trod in his pioneering work leads on.

*We thank our colleagues Drs. J. Stabenow, G. Wassmuth, and H. Breuer for their kind support of this work.*

Received: January 19, 1981 [A 358 IE]
German version: Angew. Chem. *93*, 372 (1981)

---

[1] *M. Staudinger, H. Hopff, W. Kern:* Das Wissenschaftliche Werk von Hermann Staudinger. Vol. 3/I. Hüthig & Wepf, Heidelberg 1975, p. 5; *H. Staudinger:* Arbeitserinnerungen. Hüthig, Heidelberg 1961.

[2] *E. Simon,* Justus Liebigs Ann. Chem. *31*, 265 (1839).

[3] *J. Blyth, A. W. Hofmann,* Justus Liebigs Ann. Chem. *53*, 311, 314 (1845).

[4] *M. Berthelot,* Bull. Soc. Chim. Fr. *6*, 294 (1866).

[5] *H. Stobbe, G. Posnjak,* Justus Liebigs Ann. Chem. *371*, 259 (1909).

[6] *H. Staudinger,* Ber. Dtsch. Chem. Ges. *53*, 1081 (1920).

[7] *H. Staudinger, M. Brunner, K. Frey, P. Garbsch, R. Signer, S. Wehrli,* Ber. Dtsch. Chem. Ges. *62*, 241 (1929); *H. Staudinger:* Die hochmolekularen organischen Verbindungen. Springer, Berlin 1932.

[8] *H. Staudinger, E. Geiger, E. Huber,* Ber. Dtsch. Chem. Ges. *62*, 263 (1929); *H. Staudinger, V. Wiedersheim, ibid. 62*, 2406 (1929).

[9] *K. Hess:* Chemie der Cellulose. Akad. Verlagsgesellschaft, Leipzig 1928, p. 590; cf. also *P. Karrer,* Helv. Chim. Acta *3*, 620 (1920); *P. Karrer,* Einführung in die Chemie der polymeren Kohlenhydrate. Akad. Verlagsgesellschaft, Leipzig 1925, p. 4ff.; *M. Bergmann,* Angew. Chem. *38*, 1141 (1925); Naturwissenschaften *14*, 1224 (1926); Ber. Dtsch. Chem. Ges. *59*, 2973 (1926); *P. Pummerer, ibid. 60*, 2167 (1927).

[10] *K. H. Meyer, H. Mark,* Ber. Dtsch. Chem. Ges. *61*, 593 (1928); *K. H. Meyer,* Angew. Chem. *41*, 935 (1928).

[11] For further information about intense scientific controversy between *H. Staudinger* and *K. H. Meyer* and *H. Mark* respectively, see the article by *C. Priesner* in Chemie in unserer Zeit *13*, 43 (1979), as well as in the summary thereof in *H. Staudinger, H. Mark, K. H. Meyer:* Thesen zur Größe und Struktur der Makromoleküle, Verlag Chemie, Weinheim-Deerfield Beach-Basel, 1980. Compare also the opinion of *B. Vollmert* in Nachr. Chem. Tech. Lab. *28*, 892 (1980).

[12] *H. Staudinger, W. Heuer,* Ber. Dtsch. Chem. Ges. *63*, 222 (1930).

[13] *T. Alfrey, A. Bartovics, H. Mark,* J. Am. Chem. Soc. *65*, 2319 (1943).

[14] *R. Houwink,* J. Prakt. Chem. *157*, 15 (1940); J. Chem. Phys. *18*, 837 (1950).

[15] *W. Kuhn,* Kolloid-Z. *68*, 2 (1934); Angew. Chem. *49*, 858 (1936).

[16] *W. J. Chalmers,* J. Am. Chem. Soc. *56*, 912 (1934).

[17] *P. J. Flory,* J. Am. Chem. Soc. *59*, 241 (1937).

[18] *J. W. Breitenbach,* Monatsh. Chem. *71*, 275 (1938).

[19] *G. V. Schulz,* Z. Phys. Chem. *B 30*, 379 (1935); *43*, 25 (1939); *46*, 137 (1940).

[20] *P. J. Flory,* J. Am. Chem. Soc. *58*, 1877 (1936).

[21] *K. Ziegler, L. Jakob, Justus Liebigs Ann. Chem. 511*, 45 (1934); *K. Ziegler,* Angew. Chem. *49*, 499 (1936).

[22] *P. Heumann, D. Vorländer,* Chem. Zentralbl. *70*, I, 730 (1899).

[23] *W. Schlenk, J. Appenrodt, A. Michael, A. Thal,* Ber. Dtsch. Chem. Ges. *47*, 473 (1914).

[24] *G. Natta,* Angew. Chem. *68*, 393 (1956); Makromol. Chem. *35*, 94 (1960).

[25] *F. E. Matthews,* Br. Pat. 16277, 16278 (1911).

[26] *H. Mark, C. Wulff,* DRP 550055 (1929), BASF.

[27] *C. Wulff, E. Dorrer,* DRP 634278 (1930), BASF.

[28] Vieweg/Daumiller: Kunststoffhandbuch. Vol. V: Polystyrol, Hanser-Verlag, München 1969; b) *D. J. Stein, H. W. Otto, P. Wittmer* in [28a], p. 118; c) Ullmanns Encyklopädie der technischen Chemie; d) *R. Fricker* in [28c], 2nd edit. Vol. 14. Urban & Schwarzenberg, München–Berlin, 1963, p. 187; *G. Simon* in [28c], 4th edit. Vol. 19. Verlag Chemie, Weinheim 1980, p. 266.

[29] *C. G. Munters, I. G. Tandberg,* Br. Pat. 406267 (1934).

[30] DBP 914322 (1949), BASF; US-Pat. 2515250 (1950), Dow.

[31] *J. Hambrecht* in [28c], 4th edit. Vol. 19. Verlag Chemie, Weinheim 1980, p. 272.

[32] *H. Mair,* Kunststoffe *43* (10), 397 (1953).

[33] US-Pat. 2694692 (1954), Dow.

[34] DRP 540552 (1929), Deutsche Legrit; DRP 858310 (1943), I.G. Farben.

[35] *R. Martino,* Mod. Plast. *1979*, March issue, p. 46.

[36] *H. Ohlinger:* Polystyrol. Springer, Berlin 1955.

[37] *S. L. Aggarwal,* Polymer *17*, 938 (1976); *T. Thorstad, J. Vandendael,* Kunststoffe *66*, 405 (1976).

[38] *G. Henrici-Olivé, S. Olivé:* Polymerisation, Katalyse-Kinetik-Mechanismen. Verlag Chemie, Weinheim 1969.

[39] *H. Schuller* in [28a], p. 87.

[40] *L. Küchler:* Polymerisationskinetik. Springer, Berlin 1951.

[41] *P. Flory:* Principles of Polymer Chemistry. Cornell Univ. Press, New York 1953.

[42] *F. R. Mayo,* J. Am. Chem. Soc. *75*, 6133 (1953).

[43] *R. R. Hiatt, P. D. Bartelt,* J. Am. Chem. Soc. *81*, 1149 (1959).

[44] *J. Kurze, D. J. Stein, P. Simak, R. Kaiser,* Angew. Makromol. Chem. *12*, 25 (1970).

[45] *F. R. Mayo,* Polymer Prepr. Am. Chem. Soc. Div. Polym. Chem. I 11, *2*, 55 (1961); J. Am. Chem. Soc. *90*, 1289 (1968).

[46] *J. Wiesner, P. Mehnert,* Makromol. Chem. *165*, 1 (1973); Chem.-Ing.-Tech. *45*, 1269 (1973).

[47] *W. A. Pryor,* Polymer. Prepr. Am. Chem. Soc. Div. Polym. Chem. *12*, 49 (1971).

[48] *W. A. Pryor, L. D. Lasswell,* Adv. Free-Radical Chem. *5*, 27 (1975).

[49] *N. J. Barr, W. I. Bengough, G. Beveridge, G. B. Park,* Eur. Polym. J. *14*, 245 (1978); *W. I. Bengough, G. B. Park, ibid. 14*, 889 (1978).

[50] *K. Kirchner, H. Schlapkohl,* Makromol. Chem. *177*, 2031 (1976).

[51] *J. C. Bevington, H. W. Melville, R. P. Taylor,* J. Polym. Sci. *12*, 440 (1954); *14*, 463 (1954).

[52] *G. Henrici-Olivé, S. Olivé,* Makromol. Chem. *68*, 120, 134 (1963).

[53] *G. V. Schulz, A. Scholz, R. V. Figini,* Makromol. Chem. *57*, 220 (1962).

[54] *F. Olaj, J. W. Breitenbach, B. Wolf,* Monatsh. Chem. *95*, 1646 (1964).

[55] *K. C. Berger, G. Meyerhoff,* Makromol. Chem. *176*, 1983 (1975).

[56] *K. C. Berger,* Makromol. Chem. *176*, 3575 (1975).

[57] *M. J. Gibian, R. C. Corley,* J. Am. Chem. Soc. *94*, 4278 (1972).

[58] *G. Gleixner, O. F. Olaj, J. W. Breitenbach,* Makromol. Chem. *180*, 2581 (1979).

[59] *P. Wittmer, T. Ankel, H. Gerrens, H. Romeis,* Chem.-Ing.-Tech. *37*, 392 (1967).

[60] *A. W. Hui, A. E. Hamielec,* J. Appl. Polym. Sci. *16*, 749 (1972).

[61] *A. Husain, A. E. Hamielec,* J. Appl. Polym. Sci. *22*, 1207 (1978).

[62] See [38], p. 124.

[63] *Z. Zlámal* in *G. E. Ham:* Vinylpolymerization. Pt. II. Marcel Dekker, New York 1969.

[64] DBP 2651435 (1976), BASF.

[65] US-Pat. 2713570 (1951), Eastman Kodak.

[66] *G. Henrici-Olivé* and *S. Olivé* differentiate in [38] between anionic polymerization in polar solvents, in which the dissociated ions can be present, and pseudo-ionic polymerization in an unpolar medium, in which no free ions occur.

[67] *D. N. Bhattacharyya, C. L. Lee, J. Smid, M. Szwarz,* Polymer. *5*, 54 (1964); *T. Shimomura, K. J. Tölle, J. Smid, M. Szwarz,* J. Am. Chem. Soc. *89*, 796 (1967); *T. Shimomura, J. Smid, M. Szwarz, ibid. 89*, 5743 (1967); *M. Szwarz:* Carbanions, Living Polymers and Elektron Transfer Processes. Interscience, New York 1968.

[68] a) *L. L. Böhm, M. Chmélir, G. Löhr, B. J. Schmitt, G. V. Schulz,* Adv. Polym. Sci. *9*, 1 (1972); b) *G. Löhr, B. J. Schmitt, G. V. Schulz,* Z. Phys. Chem. NF *78*, 177 (1972); c) *B. J. Schmitt, G. V. Schulz,* Eur. Polym. J. *11*, 119 (1975).

[69] *H. Hostalka, G. V. Schulz,* Z. Phys. Chem. NF *45*, 286 (1965).

[70] *W. K. H. Barnikol, G. V. Schulz,* Z. Phys. Chem. NF 47, 89 (1965).

[71] *D. Margerison, J. P. Newport,* Trans. Faraday Soc. *59*, 2058 (1963).

[72] *H. L. Hsieh, W. H. Glaze,* Rubber Chem. Technol. *43*, 22 (1970).

[73] *D. J. Worsfold, S. Bywater,* Can. J. Chem. *38*, 1891 (1960).

[74] *R. V. Figini, G. Löhr, G. V. Schulz,* J. Polym. Sci. *B* (Polym. Lett.) *3*, 985 (1965).

[75] US-Pat. 3265765 (1966), Shell Oil; *J. T. Bailey, E. T. Bishop, W. R. Hendricks, G. Holden, N. R. Legge,* Rubber Age *1966*, 98, 69.

[76] DAS 1520548 (1962), 1959922 (1969), Phillips.

[77] US-Pat. 4020258 (1977), 4120915 (1978), Phillips.

[78] US-Pat. 4167545 (1979), BASF.

[79] US-Pat. 4107227 (1979), Dow Corning.

[80] DOS 2855133 (1979), Anic.

[81] *L. K. Bi, L. J. Felters,* Macromolecules 9, 732 (1976).

[82] US-Pat. 3280084 (1966), Phillips.

[83] US-Pat. 4180530 (1979), Arco.

[84] *G. Natta, P. Pino, P. Corradini, F. Danusso, E. Mantica, G. Mazzanti, G. Moraglio,* J. Am. Chem. Soc. *77*, 1708 (1955); *G. Natta, F. Danusso, D. Sidanesi,* Belg. Pat. 555268 (1955), Montecatini.

[85] *R. J. Kern, H. G. Hurst, W. R. Richard,* J. Polym. Sci. *35*, 195 (1960).

[86] *V. A. Kargin, V. A. Kabanov, I. I. Mardenko,* Polym. Sci. USSR *1*, 41 (1960).

[87] *D. Y. Yoon, P. R. Sundararajan, P. J. Flory,* Macromolecules *8*, 776 (1975).

[88] *P. Pino, R. Mühlhaupt,* Angew. Chem. *92*, 869 (1980); Angew. Chem. Int. Ed. Engl. *19*, 857 (1980).

[89] US-Pat. 3337390 (1963), 3449268 (1966), Dow.

[90] Belg. Pat. 562220 (1956), Montecatini.

[91] Belg. Pat. 627377 (1962), 624253 (1961), BASF.

[92] *J. A. Currie, M. Dole,* J. Phys. Chem. *73*, 3384 (1969).

[93] *F. P. Warner, W. J. McKnight, R. S. Stein,* J. Polym. Sci. Polym. Phys. Ed. *15*, 2113 (1977).

[94] *A. M. Usmani, I. O. Salyer,* J. Elastomers Plast. *12*, 90 (1980).

[95] *T. J. Alfrey, J. J. Bohrer, H. Mark:* Copolymerization. Interscience, New York 1952.

[96] *G. E. Ham:* Copolymerization. Interscience, New York 1964.
[97] *F. R. Mayo, C. Walling,* Chem. Rev. *46,* 191 (1950).
[98] *R. H. Boundy, R. F. Boyer:* Styrene, Its Polymers, Copolymers and Derivatives. Reinhold, New York 1952.
[99] See [38], p. 57.
[100] *A. Guyot, J. Guillot,* J. Macromol. Sci. *A 1,* 779 (1958); *A 2, 5,* 889 (1968).
[101] *C. Pichot, A. Guyot, C. Strazielle,* J. Polym. Sci. Polym. Chem. Ed. *17,* 2269 (1979).
[102] *B. Sandner, E. Loth,* Faserforsch. Textiltech. *27,* 571, 633 (1976).
[103] *C. B. Bucknall:* Toughened Plastics. Applied Science Publ., London 1977.
[104] *A. Echte,* Angew. Makromol. Chem. *58/59,* 175 (1977).
[105] *G. E. Molau,* J. Polym. Sci. *A 3,* 4235 (1965).
[106] *H. Willersinn,* Makromol. Chem. *101,* 296 (1967).
[107] *A. Echte* in *Winnacker-Küchler:* Chemische Technologie. 4th edit. Hanser-Verlag, München 1981, in press.
[108] *K. H. Ott, H. Röhr* in [28c], 4th edit. Vol. 19. Verlag Chemie, Weinheim 1980, p. 277.
[109] *B. J. Schmitt,* Angew. Chem. *91,* 286 (1979); Angew. Chem. Int. Ed. Engl. *18,* 273 (1979).
[110] *K. Dinges, H. Schuster,* Makromol. Chem. *101,* 202 (1967).
[111] *J. P. Fischer,* Angew. Makromol. Chem. *33,* 35 (1973).
[112] *A. Brydon, G. M. Burnett, C. G. Cameron,* J. Polym. Sci. Polym. Chem. Ed. *12,* 1011 (1974).
[113] *D. J. Angier, E. M. Fettes,* Rubb. Chem. Technol. *1965,* 38.
[114] *D. J. Stein, G. Fahrbach, H. J. Adler,* Angew. Makromol. Chem. *38,* 67 (1974).
[115] *C. G. Cameron, M. Y. Qureshi,* J. Polym. Sci. Polym. Chem. Ed. *18,* 2143 (1980).
[116] *F. Severeni, A. Pagliari, C. Tavazzani, G. Vittadini,* Adv. Chem. Ser. *142,* 201 (1975).
[117] *E. Niki, N. Ohto, Y. Kanauchi, Y. Kamiya,* Eur. Polym. J. *16,* 559 (1980).
[118] *H. Alberts, H. Barth, R. Kuhn,* Adv. Chem. Ser. *142,* 214 (1975).
[119] *C. Walling,* Pure Appl. Chem. *15,* 69 (1967).
[120] *J. L. Locatelli, G. Riess,* Angew. Makromol. Chem. *35,* 57 (1974).
[121] *V. D. Yenalyev, N. A. Noskova, I. S. Popov,* Polym. Sci. USSR *16,* 2332 (1974); *V. D. Yenalyev, N. A. Noskova, V. I. Melnichenko, O. P. Bovkunenko, O. M. Mezentseva,* Am. Chem. Soc. Div. Org. Coat. Plast. Prepr. *37,* 639, 645 (1977).
[122] *L. H. Tung, R. M. Wiley,* J. Polym. Sci. Polym. Chem. Ed. *11,* 1413 (1973).
[123] *J. L. Réfregier, J. L. Locatelli, G. Riess,* Eur. Polym. J. *10,* 139 (1974).
[124] *A. Gasperowicz, W. Laskawski,* J. Polym. Sci. Polym. Chem. Ed. *14,* 2775 (1976).
[125] *P. Manaresi, V. Passalacqua, F. Pilati,* Polymer *16,* 520 (1975).
[126] *D. Kechajow,* Angew. Makromol. Chem. *81,* 1 (1979).
[127] *S. L. Rosen,* J. Appl. Polym. Sci. *17,* 1805 (1973).
[128] *R. S. Spencer, J. L. Williams,* J. Colloid. Sci. *2,* 117 (1947).
[129] *M. Hirose, E. O'Shima, H. Inoue,* J. Appl. Polym. Sci. *12,* 9 (1968).
[130] *N. Nishimura,* J. Polym. Sci. *A 3,* 237 (1965).
[131] *Y. Ide, J. L. White,* J. Appl. Polym. Sci. *18,* 2997 (1974).
[132] *W. A. Ludwico, S. L. Rosen,* J. Polym. Sci. Polym. Chem. Ed. *14,* 2121 (1976).
[133] *M. J. Moszkowicz, S. L. Rosen,* J. Polym. Sci. Polym. Phys. Ed. *17,* 715 (1979).
[134] *R. L. Kruse,* Adv. Chem. Ser. *142,* 141 (1975).
[135] *J. K. Rigler, L. Müller, B. A. Wolf,* Angew. Makromol. Chem. *74,* 113 (1978).
[136] *G. E. Molau,* J. Polym. Sci. *A 3,* 1267, 4235 (1965); *G. E. Molau, H. Keskkula,* J. Polym. Sci. *A-1, 4,* 1595 (1966); Appl. Polym. Symp. *7,* 35 (1968); *G. E. Molau, W. M. Wittbrodt, V. E. Meyer,* J. Appl. Polym. Sci. *13,* 2735 (1969).
[137] *G. F. Freeguard, M. Karmarkar,* J. Appl. Polym. Sci. *15,* 1657 (1971); *G. F. Freeguard,* Br. Polym. J. *6,* 205 (1974).
[138] *R. W. Flumerfelt,* Ind. Eng. Chem. Fundam. *11,* 312 (1972).
[139] *M. Baer,* J. Appl. Polym. Sci. *16,* 1109 (1972).
[140] *F. D. Rumscheidt, S. G. Mason,* J. Colloid Sci. *16,* 238 (1961).
[141] *H. J. Karam, J. C. Bellinger,* Ind. Eng. Chem. Fundam. *7,* 576 (1968).
[142] *H. Keskkula,* Int. Symp. on Polymer Compatibility and Incompatibility – Principles and Practice, Midland, Michigan 1980, Preprint.
[143] *B. W. Bender,* J. Appl. Polym. Sci. *9,* 2887 (1955).
[144] *B. Gallot,* Pure Appl. Chem. *38,* 1 (1974).
[145] *E. B. Bradford* in *G. E. Molau:* Colloidal and Morphological Behavior of Block and Graft Copolymers. Plenum Press, New York 1971, p. 21.
[146] *J. Vanzo,* J. Polym. Sci. *A-1, 4,* 1727 (1966).
[147] *M. Matsuo, T. Ueno, H. Horino, S. Chujyo, H. Asai,* Polymer *9,* 429 (1968).
[148] *J. Stölting,* Z. Phys. Chem. NF *120,* 177 (1980).
[149] *A. Echte, H. Gausepohl, H. Lütje,* Angew. Makromol. Chem. *90,* 95 (1980).
[150] *B. Ptaszynski, J. Terisse, A. Skoulios,* Makromol. Chem. *176,* 3483 (1975).
[151] *E. R. Wagner, L. M. Robeson,* Rubber Chem. Technol. *43,* 1129 (1970).
[152] *R. L. Kruse,* Polymer Prepr. Am. Chem. Soc. Div. Polym. Chem. *18,* 838 (1977).
[153] *G. Riess, M. Schlienger, S. Marti,* J. Macromol. Sci. Phys. *B 17,* 355 (1980).
[154] DOS 2613952 (1976), BASF.
[155] The name ABS-Polymer is derived from its monomer units, namely *A*crylonitrile, *B*utadiene and *S*tyrene. Similary the name ASA is derived from *A*crylonitrile, *S*tyrene and *A*crylate.
[156] *H. Gerrens,* Chem.-Ing.-Tech. *52,* 477 (1980).
[157] Cf. DDR-Pat. 135499 (1979).
[158] *R. H. Simon, D. C. Chappelear:* Technology of Styrenic Polymerization Reactors and Processes. Am. Chem. Soc. Symp. Ser. *104,* Washington D.C., 1976.
[159] *N. Platzer,* Ind. Eng. Chem. *62,* 11 (1970).
[160] *C. A. Brighton, G. Pritchard, G. A. Skinner:* Styrene Polymers: Technology and Environmental Aspects. Applied Science Publishers London 1979.
[161] *G. Daumiller,* Chem.-Ing.-Tech. *40,* 673 (1968).
[162] *M. Hoffmann, H. Krömer, R. Kuhn:* Polymeranalytik Vol. 1 and 2. Thieme, Stuttgart 1977.
[163] *J. F. Fellers, T. F. Chapman,* J. Appl. Polym. Sci. *22,* 1029 (1978).
[164] *J. F. Fellers, B. F. Kee,* J. Appl. Polym. Sci. *23,* 2463 (1979).
[165] *T. G. Fox, S. Loshak* in *R. F. Eirich:* Rheology. Vol. 1. Academic Press, New York 1956, p. 431.
[166] *J. F. Fellers, B. F. Kee,* J. Appl. Polym. Sci. *18,* 2355 (1974).
[167] *S. Wellinghoff, E. Baer,* J. Macromol. Sci. Phys. *B 11,* 367 (1975).
[168] *R. S. Lenk:* Polymer Rheology. Applied Science Publ., London 1978, p. 34ff.
[169] *L. R. Schmidt,* J. Appl. Polym. Sci. *23,* 2463 (1979).
[170] *C. B. Bucknall, D. Clayton, W. E. Keast,* J. Mater. Sci. *7,* 1443 (1972).
[171] *R. Buchdahl, L. E. Nielsen,* J. Appl. Phys. *21,* 482 (1950).
[172] *G. Cigna,* J. Appl. Polym. Sci. *14,* 1781 (1970).
[173] *S. G. Turley, H. Keskkula,* Polymer *21,* 466 (1980).
[174] *Z. Hashin,* J. Appl. Mech. *29,* 143 (1962).
[175] *M. Takayanagi,* J. Appl. Polym. Sci. *10,* 113 (1966).
[176] *E. H. Kerner,* Proc. Phys. Soc. (London) *B 69,* 808 (1956).
[177] *L. Bohn,* Adv. Chem. Ser. *142,* 66 (1975).
[178] *E. H. Merz, G. C. Claver, M. Baer,* J. Polym. Sci. *22,* 325 (1956).
[179] *S. Newman, S. Strella,* J. Appl. Polym. Sci. *9,* 2297 (1965).
[180] *J. A. Sauer, J. Martin, C. C. Hsiao,* J. Appl. Phys. *20,* 507 (1949).
[181] *C. C. Hsiao, J. Sauer,* J. Appl. Phys. *21,* 1071 (1950).
[182] *O. K. Spurr, W. D. Niegisch,* J. Appl. Polym. Sci. *6,* 23, 585 (1962).
[183] *R. Kambour,* J. Polym. Sci. *A 2,* 4159, 4165 (1964); *A-2, 4,* 17, 349 (1966).
[184] *C. B. Bucknall, R. R. Smith,* Polymer *6,* 437 (1965).
[185] *A. S. Argon,* Pure Appl. Chem. *43,* 247 (1975).
[186] *A. S. Argon,* J. Macromol. Chem. Phys. *B 8,* 573 (1973).
[187] *S. S. Sternstein, L. Ongchin,* Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem. *10,* 1117 (1969).
[188] *A. Moet, I. Palley, E. Baer,* Am. Chem. Soc. Div. Org. Coat. Plast. Chem. Prepr. *41/2,* 424 (1979).
[189] *T. R. Steger, L. E. Nielsen,* J. Polym. Sci. Phys. *B 14,* 387 (1977).
[190] *W. Whitney,* J. Appl. Phys. *34,* 3633 (1963).
[191] *L. S. Thomas, K. J. Cleereman,* SPE J. *28,* 6, 39, 61 (1972).
[192] *G. Pohl, K. Gruber, E. Taeger,* Plaste Kautsch. *19,* 255 (1972).
[193] *J. N. Goodier,* J. Appl. Mech. *55,* 39 (1933).
[194] *G. H. Michler,* Plaste Kautsch. *26,* 497 (1979).
[195] *A. N. Gent,* J. Mater. Sci. *15,* 2884 (1980).
[196] *T. Ricco, A. Pavan, F. Danusso,* Polymer *20,* 367 (1979).
[197] *T. T. Wang, M. Matsuo, T. K. Kwei,* J. Appl. Phys. *42,* 4188 (1971).
[198] *M. Matsuo, T. T. Wang, T. K. Kwei,* J. Polym. Sci. *A-2, 10,* 1085 (1972).
[199] *G. H. Michler, K. Gruber,* Plaste Kautsch. *23,* 346 (1976).
[200] *A. N. Gent,* J. Mater. Sci. *5,* 925 (1970).
[201] *L. Bohn,* Angew. Makromol. Chem. *20,* 129 (1971).
[202] *L. Morbitzer, K. H. Ott, H. Schuster, D. Kranz,* Angew. Makromol. Chem. *27,* 57 (1972).
[203] *C. G. Bragaw,* Adv. Chem. Ser. *99,* 86 (1971).
[204] *R. D. Sudduth,* J. Appl. Polym. Sci. *22,* 2427 (1978).
[205] *J. Silberberg, C. D. Han,* J. Appl. Polym. Sci. *22,* 599 (1978).
[206] *F. Ramsteiner,* Kunststoffe *67,* 517 (1977).
[207] *P. Beahan, M. Bevis, D. Hull,* J. Mater. Sci. *7,* 162 (1972).
[208] *A. A. Griffith,* Phil. Trans. R. Soc. *A 221,* 163 (1921).
[209] *G. R. Irwin, J. A. Kies, H. L. Smith,* ASTM Proc. *58,* 640 (1958).
[210] *D. S. Dugdale,* J. Mech. Phys. Solids *8,* 100 (1960).
[211] *E. Plati, J. G. Williams,* Polym. Eng. Sci. *15,* 470 (1975).
[212] Kunststoffe 1: Prüfnormen über mechanische, thermische und elektrische Eigenschaften, Vol. 18. Beuth-Vertrieb, Berlin 1980.
[213] *H. J. Orthmann,* Kunstst.-Rundsch. *14,* 221 (1967).
[214] *W. Retting,* Colloid Polym. Sci. *253,* 852 (1975).
[215] *H. Keskkula, J. W. Norton,* J. Appl. Polym. Sci. II, *6,* 289 (1959).
[216] *R. E. Robertson,* Am. Chem. Soc. Div. Org. Coat. Plast. Chem. Prepr. *34/2,* 229 (1974).
[217] *A. Hauss,* Angew. Makromol. Chem. *8,* 73 (1969).
[218] *S. Onoqi, T. Matsumoto, E. Kamei,* Polym. J. *3,* 531 (1972).
[219] *G. Cigna, S. Matarrese, G. F. Biglione,* J. Appl. Polym. Sci. *20,* 2285 (1976).
[220] *K. Überreiter, G. Kanig,* J. Colloid. Sci. *7,* 569 (1952).
[221] *G. Kanig,* Koll. Z. Z. f. Polym. *190,* 1 (1963).

[222] *P. R. Couchman,* J. Mater. Sci. *15,* 1680 (1980).
[223] *R. P. Kambour, C. I. Gruner, E. E. Ramagosa,* J. Polym. Sci. Polym. Phys. Ed. *11,* 1879 (1973).
[224] Kunststoffe 2: Prüfnormen über chemische, optische, Gebrauchs- und Verarbeitungseigenschaften. Vol. 48. Beuth-Vertrieb, Berlin 1980.
[225] *C. D. Han,* J. Appl. Polym. Sci. *15,* 2591 (1971).
[226] *A. Casale, R. S. Porter, J. F. Johnson,* J. Macromol. Sci. Rev. *C 5,* 387 (1971).
[227] *D. P. Thomas, A. Hagan,* Polym. Eng. Sci. *9/3,* 164 (1969).
[228] *W. M. Prest, R. S. Porter,* Polym. J. *4,* 154 (1973).
[229] *M. G. Huguet, T. R. Paxton* in *G. E. Molau:* Colloidal and Morphological Behavior of Block and Graft Copolymers. Plenum Press, New York 1971, p. 183.
[230] *Y. Saito, T. Sakita, T. Yuki,* Kobunshi Ronbunshu (Engl. Ed.) *3,* 1705 (1974).
[231] *H. Münstedt:* Praktische Rheologie der Kunststoffe. VDI-Verlag, Düsseldorf 1978, p. 63.
[232] *A. Casale, A. Moroni, C. Spreafico,* Adv. Chem. Ser. *142,* 16, 173 (1975).
[233] *R. O. Cahart, D. A. Davies, R. Giuffria,* SPE J. *18,* 440 (1962).
[234] *R. Giuffria, R. O. Cahart, D. A. Davies,* J. Appl. Polym. Sci. *7,* 551, 1731 (1963).
[235] *H. Sächtling:* Kunststoff-Taschenbuch. 21st edit. Hanser-Verlag, München 1979, p. 80.
[236] *J. Frados:* Plastics Engineering Handbook. 4th edit. Van Nostrand Reinhold, New York 1976.
[237] *H. Jenne,* Kunststoffe *66,* 581 (1976).
[238] Plastverarbeiter *27,* 355 (1976).
[239] *U. Reichert,* Kunststoffe *70,* 613 (1980).
[240] *E. Eckardt,* Kunststoffe *70,* 122 (1980).
[241] *H. Beck,* Plastverarbeiter 9, 441 (1958).
[242] *F. Förster, G. Wurl* in [28a], p. 230, 270, 315.
[243] *A. Echte* in *Winnacker-Küchler:* Chemische Technologie. 4th edit. Hanser-Verlag, München 1981, in press, and references cited therein.
[244] *A. Weber:* Polystyrol, ein technischer Werkstoff, in: 50 Jahre Formel für Erfolg, Polystyrol. BASF, Ludwigshafen.
[245] *K. Schneider,* Kunststoffe *70,* 617 (1980).
[246] *I. DeGrave,* Kunststoffe *70,* 625 (1980).
[247] *J. Dimisio, H. K. Mahabadi, K. E. O'Driskoll, E. Abuin, E. A. Lissi,* J. Polym. Sci. Polym. Chem. Ed. *17,* 1891 (1979).
[248] *L. L. van Dierendonk, J. A. de Leeuw den Bouter, K. H. Ostendorf,* Chem. Eng. Sci. *35,* 476 (1980).
[249] *G. Crone, A. Renken,* Chem.-Ing.-Tech. *51,* 42 (1979).
[250] *B. L. Bhatt, E. N. Ziegler,* AIChE J. *23,* 217 (1977).
[251] *J. C. Salamone, C. C. Tsai, A. P. Olson, A. C. Watterson,* J. Polym. Sci. Polym. Chem. Ed. *18,* 2983 (1980).
[252] US-Pat. 2366007 (1944), General Electric.
[253] *W. Heitz,* Adv. Polym. Sci. *23,* 1 (1977).
[254] *G. Challa, A. J. Schouten, G. ten Brinke, H. C. Meinders,* Am. Chem. Soc. Symp. Ser. *121,* 7 (1980).
[255] *G. Baum,* Biotechnol. Bioeng. *17,* 253 (1975).
[256] *J. Beitz, A. Schellenberger,* Acta Biol. Med. Pharm. *37,* 1309 (1978).
[257] DOS 2513412 (1975), Mitsubishi Chem.
[258] *G. Manecke, P. Reuter,* J. Polym. Sci. Symp. Ed. *62,* 227 (1978).
[259] *M. A. Kraus, A. Patchornik,* J. Polym. Sci. Rev. *15,* 55 (1980).
[260] *P. Hodge, D. C. Sherrington:* Polymer Supported Reactions in Organic Synthesis. Wiley, New York 1980.
[261] *P. L. Nayak,* J. Macromol. Sci. Rev. *17,* 267 (1979).
[262] *J. L. Gamett, N. T. Yen,* Am. Chem. Soc. Symp. Ser. *121,* 243 (1980).
[263] *T. A. Shaw, R. Antoine,* Fr. Pat. 2258398 (1974).
[264] *O. Olabisi, L. Robeson, M. T. Shaw:* Polymer Miscibility. Academic Press, New York 1979; *W. J. MacKnight, F. E. Karasz, J. R. Fried* in *D. R. Paul, S. Newman:* Polymer Blends. Vol. 1. Academic Press, New York 1978.
[265] *R. Casper, L. Morbitzer,* Angew. Makromol. Chem. *58/59,* 1 (1977).
[266] *O. Olabisi, A. G. Farnham,* Adv. Chem. Ser. *176,* 559 (1979).
[267] *H. Kindler, A. Nikles,* Chem.-Ing.-Tech. *51,* 1 (1979).
[268] *W. A. Axtell,* Polym. Plast. Technol. Eng. *14,* 1 (1980).
[269] *J. L. McCurdy,* Mod. Plast. Int. 9, 118 (1979).
[270] *N. R. Schott, H. Derby,* Am. Chem. Soc. Symp. Ser. *107,* 9 (1979).
[271] *C. I. Chung, E. M. Mount, D. E. McChalland,* Am. Chem. Soc. Symp. Ser. *107,* 21 (1979).
[272] Eur. Plast. News *4,* 21 (July 1977).

---

# Polymers with Metal-Like Conductivity—A Review of their Synthesis, Structure and Properties

## By Gerhard Wegner[*]

**Polymers such as polyacetylene, which have an extended π-electron system in their backbone, or like poly(*p*-phenylene) consist of a sequence of aromatic rings are excellent insulators in their native state and can be transformed by oxidation or reduction in the solid state into conductive CT-complexes which exhibit metal-like conduction characteristics. The chemical and physical processes involved and the reasons for the observed quasimetallic conductivity are not yet fully understood. The real structure of these materials in chemical and physical terms, *i. e.* their complicated morphology and texture, as well as the results available on the structure-property relationships of the "organic metals" must be considered when discussing their properties. In other words, a discussion of conductive polymers should be based on what is known of the highly conducting CT-complexes of low-molecular weight compounds. The discovery of the highly conducting polymer complexes has opened up a new interdisciplinary field of research which borders on polymer science, solid-state and semiconductor physics and on organic solid-state chemistry. It is hoped that this area will lead to numerous novel materials and technical applications.**

## 1. Introduction

### 1.1. Polymers as Materials

Strength, elasticity, plasticity, toughness and frictional resistance are properties which are described as typical of metals, but today are also characteristic of many polymers. Metals have therefore been replaced by plastics in many areas of application. This, however, is not the case with one of the most salient properties of metals—their electrical conductivity. Although the manufacture of electrical units would have been impossible without the development of polymers for insulation, the question of producing macromolecular materials which exhibit a conductivity similar to that of metals has long been posed. The importance of this question lies in the significance of being able to process such materials in the forms of films, foils or fibers according to the standard procedures of the plastics' industry so that they can act as a substitute for metals.

Despite numerous and concerted attempts, especially by preparative chemists, it was not until very recently that the

---

[*] Prof. Dr. Gerhard Wegner
Institut für Makromolekulare Chemie der Universität
Stefan-Meier-Strasse 31, D-7800 Freiburg (Germany)

production of macromolecular materials whose conductivity and conductivity characteristics were the same or closely similar to those of metals was possible. From monographs[1-4] and review articles[5-7] it can be gleaned that ideas concerning the relationships between the molecular structure, and the structure and electrical properties of macromolecular solids have neither been fully developed, nor have insights available from other fields been given sufficient consideration.

It comes as no surprise then, that the stimulus for the present research in this area of conducting polymers comes not from preparative organic or macromolecular chemistry, but rather from solid-state and semiconductor physics. Preparative chemists have long attempted to synthesize macromolecules with an extended $\pi$-electron system as a constituent part of the main chain. It was hoped that the delocalization of the electrons, assumed to take place in such systems, would necessarily lead to a high concentration of charge carriers in the transport of current. Within the framework of these model considerations, the low conductivity of polymer $\pi$-bonded systems observed experimentally was claimed to be due to impurities in the polymer, breaks in the $\pi$-bonding system by chain ends, and conformational and similar defects. It is known today, however, that polymers with polyconjugated structures in the main chain are insulators in the ground state; even irradiation by light only produces a limited number of charge carriers since the dominant absorption in the visible region of the spectrum of such polymers is due to the formation of an exciton and not to the transition of an electron from the valence into the conduction band.

New insights were introduced by *Heeger* and *MacDiarmid et al.* in 1977. In their work, they demonstrated for the first time that polyacetylene (PA), which is a semiconductor with a relatively large band gap, exhibits a dramatic increase in specific conductivity if it is treated with strong oxidizing or reducing agents[8-10]. When a thin film of *cis*-polyacetylene, obtained by polymerization of acetylene on the surface of a solution of suitable catalysts in an inert solvent, was treated with iodine, bromine, $AsF_5$ or sodium naphthalide, its conductivity increased from an initial value of approximately $10^{-9}\ \Omega^{-1}\ cm^{-1}$ to approximately $5\cdot10^{2}\ \Omega^{-1}\ cm^{-1}$. Data concerning the electrical and optical properties of the conductive polymer, *e.g.* the small dependence of the conductivity on the temperature and the dramatic increase in the absorption in the infrared with increasing degree of conversion, was interpreted within the framework of theories of phase transitions from semiconductors to metals. The behavior of the polymer was comparable to that of classical semiconductors[11], *e.g.* silicon, which upon doping with donors or acceptors, can be transformed into a conducting state. The reactions of the polymer with, for example, halides, pseudohalides, alkali metals or alkali metal derivatives was, therefore, using the language of semiconductor physics, termed "doping".

### 1.2. A Survey of Organic Metals and Polymeric Conductors

As shown in Figure 1, *Heeger* and *MacDiarmid et al.* observed an increase in the conductivity of PA when doped with typical dopants. Figure 2 presents a broad summary of the temperature dependence of the electrical conductivity of several materials compared to that of doped PA.

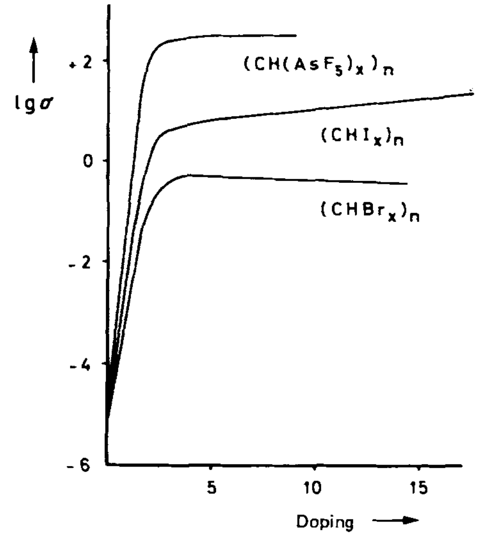


Fig. 1. Specific conductivity $\sigma[\Omega^{-1}\ cm^{-1}]$ of polyacetylene (PA) *versus* the concentration [mol% relative to —CH—] of the dopants $AsF_5$, $I_2$, $Br_2$ (after *Heeger et al.* [11]).

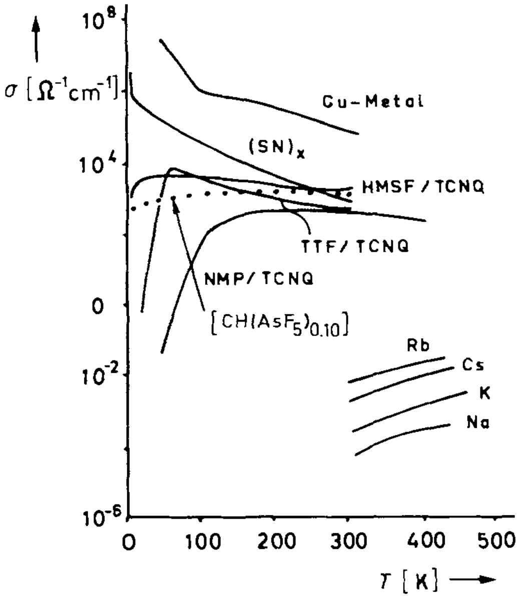
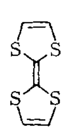


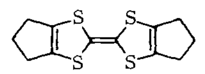
Fig. 2. Temperature dependence of the specific conductivity $\sigma$ of some organic CT-complexes and conductive polymers; all data from [13]. See text for abbreviations; the curves denoting Rb, Cs, K, Na refer to the alkali metal salts of TCNQ.

The discovery of conductive PA led to considerable research activity on "organic metals". This term indicates that materials, produced by methods of organic chemistry, can exhibit electrical properties which resemble those of metals[12-14].

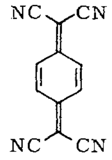
The most prominant example of such an organic metal is the charge-transfer-complex produced from tetrathiofulvalene (TTF) and tetracyanoquinodimethane (TCNQ). The electrical behavior of this material is also shown in Figure 2. In addition, two other salts of TCNQ with the *N*-methyl phenazinium cation (NMP) and hexamethylenetetraselenofulvalene (HMSF) are also mentioned.



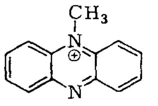
TTF



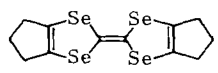
HMTTF



TCNQ



NMP



HMSF

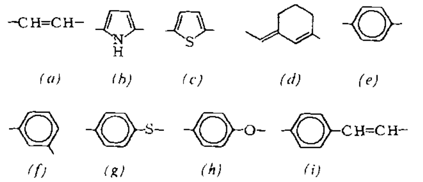
These CT-salts exhibit, just as doped PA, either a temperature independent or even increasing conductivity with decreasing temperatures. The latter is the behavior typical of metals such as copper.

In semiconductors, σ increases with temperature. The alkalimetal salts of TCNQ serve as an example of this phenomenon and are shown in Figure 2.

Polymeric sulfur nitride, $(SN)_x$, also possesses characteristic metallic properties and, in addition, at a temperature of *ca.* 0.5 K becomes superconducting. The chemical and physical properties of this interesting and unusual material have been discussed in detail in a recent review[15]. Since it seems to be a material with little or no analogies to other polymers or low molecular weight model compounds, it will not be discussed further.

Following the fundamental observations of *Heeger* and *MacDiarmid et al.*, further polymers which became conducting upon doping were quickly found (Table 1).

Table 1. Direct current conductivity of some doped polymers with the fundamental units *(a)*–*(i)* [a].



| Fundamental Unit | Doping material/ counterion | c [b] | σ [$\Omega^{-1}$ $cm^{-1}$] | Ref. |
|---|---|---|---|---|
| *(a)* [c] | $I_2$ | 0.25 | 360 | [10, 13] |
| | $Br_2$ [g] | 0.10 | 0.5 | [10, 11] |
| | $AsF_5$ | 0.28 | 560 | [10, 11] |
| | $AgClO_4$ | 0.036 [d] | 3.0 | [16] |
| | Sodium naphthalide | 0.28 [e] | 80 | [10, 11] |
| | $(n\text{-}C_4H_9)_4NClO_4$ [f] | 0.06 [d] | 970 | [17] |
| *(b)* | $BF_4^{\ominus}$ | 0.25 | 100 | [18] |
| *(c)* | $I_2$ | 0.10 | $3.4 \cdot 10^{-4}$ | [19] |
| *(d)* | $I_2$ | ca. 0.1 | ca. 0.1 | [20] |
| *(e)* | $AsF_5$ | 0.42 | 145 | [21, 22] |
| | Potassium naphthalide | 0.57 | 7 | [21, 22] |
| *(f)* | $AsF_5$ | 1.0 | $10^{-3}$ | [23, 24] |
| *(g)* | $AsF_5$ | ca. 1.0 | 1 | [24, 25] |
| *(h)* | $AsF_5$ | 0.4 | $10^{-3}$ | [26] |
| *(i)* [h] | $AsF_5$ | 0.75 | 3 | [27] |

[a] All values are valid at room temperature. [b] In mol/mol of the fundamental unit. [c] *cis*-Structure. [d] Concentration of $ClO_4^{\ominus}$. [e] Concentration of $Na^{\oplus}$. [f] Carrier electrolyte for anodic oxidation. [g] Starting from *trans*-PA. [h] Oligomers with $\bar{P}_n \sim 3$–5.

The significance of these polymeric conductors can be readily gathered from Table 2. If one considers the conductivity per unit weight, then conductive polymers are not far removed from the better conducting metals. This has, naturally, led to speculation concerning the possible technical applications for these polymers.

Table 2. Density ρ, conductivity σ, and σ/ρ of various materials.

| Material [a] | ρ [g $cm^{-3}$] | σ [$\Omega^{-1}$ $cm^{-1}$] | σ/ρ [$cm^2$ $g^{-1}$ $\Omega^{-1}$] |
|---|---|---|---|
| Cu | 8.92 | $6.5 \cdot 10^5$ | $7.6 \cdot 10^4$ |
| Au | 19.3 | $4.1 \cdot 10^5$ | $2.1 \cdot 10^4$ |
| Fe | 7.86 | $1.0 \cdot 10^5$ | $1.3 \cdot 10^4$ |
| $(SN)_n$ | 2.3 | $3.7 \cdot 10^3$ [b] | $1.6 \cdot 10^3$ |
| Hg | 13.6 | $1.0 \cdot 10^4$ | $7.4 \cdot 10^2$ |
| *cis* $[CH(AsF_5)_{0.14}]_n$ [c] | 0.8 | $5.6 \cdot 10^2$ | $7.0 \cdot 10^2$ |
| TTF·TCNQ | ≈1.0 | $7 \cdot 10^2$ [d] | $7 \cdot 10^2$ |
| TTF·TCNQ | ≈1.0 | 10 [e] | 10 |

[a] All values were determined at 300 K. [b] Measured in the chain direction [15]. [c] Polyacetylene, doped with $AsF_5$ (cf. Table 1). [d] Measured on a single crystal in the direction of greatest conductivity. [e] Measured on a polycrystalline sample.

The conductivity data presented in Table 1 has, however, by no means been optimized. Rather, it is merely the initial results of investigations in this field.

In this article the chemical and physical structure of the most important polymers, which become conductive through doping as well as the structure of these conductive polymer complexes will be discussed. Special emphasis will be placed on the chemistry of doping. Moreover, structural and functional features common to organic metals and conductive polymers will be indicated and discussed within the framework of present knowledge of the nature of charge carriers and transport processes in organic metals.

## 2. Polyacetylene PA

### 2.1. Synthesis

The method of preparation of PA described by *Shirakawa* and *Ikeda*[28,29] serves as the starting point for the majority of investigations into the structure, conductivity, optical and magnetic properties of pure and doped PA. Termed the "Shirakawa technique", this procedure involves blowing acetylene onto the quiescent surface of a concentrated solution of a Ziegler catalyst in an inert solvent: the most suitable Ziegler catalyst for this procedure consists of titanium tetrabutoxide and triethylaluminum. A thin layer of PA is immediately formed and floats on the surface. This black shiny film has a thickness of between 1 μm and several mm, depending upon the quantity of acetylene used, and can be removed intact from the reaction medium and, after purification and drying procedures made conductive through suitable doping. A widely employed variant of this technique involves wetting the interior of a glass vessel or the surface of a glass plate with a capillary film of the catalyst solution. Acetylene is then blown onto these surfaces to the desired amount, producing a thin layer of the polymer on an inert carrier[29]. The complex super-molecular structure of the films produced have the structural features of a hard foam and will be discussed in the following section. The layers of PA, which are erroneously called films in the literature[10,11], are inhomogeneous networks of low density. In short, the network itself is built up from clusters of morphological units consisting of individual compact particles of polyacetylene. The nature of these layers is shown in Figure 3. Macroscopically, however, these layers give the impression of a compact film with a silverish, almost metallic luster.

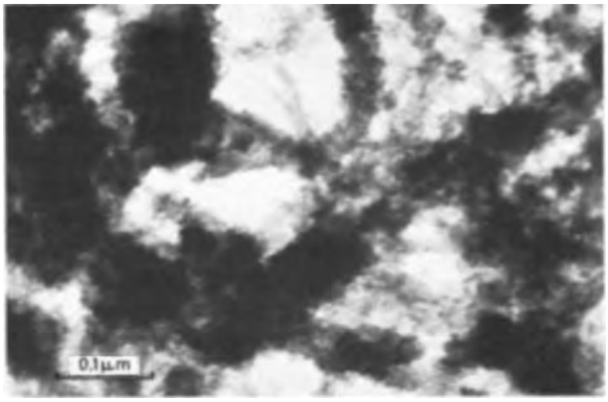


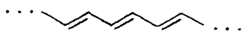
Fig. 3. Electron micrograph (TEM) of a layer of polyacetylene prepared by the Shirakawa-technique [29].

The catalysts used for the polymerization of acetylene in the Shirakawa technique were first described by *Natta et al.* in 1958[30]. Although *Natta* and co-workers conducted extensive investigations into the polymerization of acetylene using Ziegler catalysts, very little of this work was published[31]. They were able, however, to demonstrate that PA is formed as an insoluble, semicrystalline red powder if the monomer is bubbled into a solution of the catalyst system in a hydrocarbon solvent. X-ray diffraction studies led them to the correct conclusion that they had obtained *trans*-polyacetylene[30].

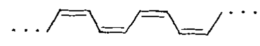
Due to the insolubility and oxidative instability of PA, they did not succeed in obtaining the polymer in the form required for measurements of its solid-state properties, or applicative purposes. Bearing these difficulties in mind, it is clear that the technique developed by *Shirakawa et al.*[28,29], involving the *in situ* production of free standing films of almost arbitrary dimension, was a noteable step forward. From these thin films, *Shirakawa* and *Ikeda* were able to obtain excellently resolved IR[28] and Raman spectra[32]. These allowed a comparison to be made between the experimentally obtained band positions and those calculated by normal coordinate analysis of the polymer vibrations. It was also shown that *cis*-PA *(1a)* was essentially formed at polymerization temperatures below 255 K and that *trans*-PA *(1b)* was produced exclusively at temperatures above 373 K.

At intermediate temperatures, polymers having, in part, the *trans*-structure are produced; the increase being proportional to the polymerization temperature. The spectroscopic data indicate, however, that block copolymers are formed between *cis*- and *trans*-PA with a temperature dependent block-length distribution[28] and not a random copolymer between individual units of either *cis*- or *trans*-configuration.

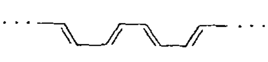
It seems probable that the triple bond of the monomer is always opened *via* a *cis*-insertion mechanism and that the *trans*-structure *(1a)* is only obtained through thermal isomerization of the initially formed polymer *(1b)*. This follows from the observation that *cis*-PA is thermally unstable and isomerizes slowly at 0 °C; at temperatures above 100 °C, however, the isomerization is rapid and irreversible and leads to the thermodynamically stable *trans*-isomer[32-35]. Although the *trans*-cisoid structure *(1c)* has not yet been experimentally detected, it has been discussed as an intermediate in the thermal *cis*-*trans*-isomerization[36].



*(1a)*



*(1b)*



*(1c)*

Polymerization of acetylene with Ziegler catalysts, as described by *Natta et al.*, has prompted numerous other investigations. These have resulted in the discovery of additional catalytically active systems, which however, are not true Ziegler catalysts.

Table 3. Some catalytically active systems for the polymerization of acetylene.

| Catalyst system | | | Ref. |
|---|---|---|---|
| $Ti(OR)_4$ | + $AlR_3$ | | [28, 30, 40, 41] |
| $Co(NO_3)_2$ | + $NaBH_4$ | (EtOH) | [37] |
| $NiX_2$ [a] | + $PPh_3$ | (pressure) | [42] |
| $NiX_2$ | + $PPh_3$ | + $NaBH_4$ | [43] |
| $CoX_2$ | + $PPh_3$ | + $NaBH_4$ | [44] |
| $Fe(dmg)_x 2py$ | + $AlEt_3$ | | [45] |
| Fe(acac) | + $AlR_3$ | | [46] |
| $FeCl_3$ | + PhMgBr | | [47] |
| $Ni(CO)_2$ | + $PPh_3$ | | [48] |

[a] X = Halogen.

The most important of these systems are shown in Table 3. *Luttinger*'s[37] account of a catalytically very active system, resulting from the reaction of cobalt and nickel salts with $NaBH_4$, deserves special mention. With this catalyst, acetylene can be polymerized at normal pressure in numerous solvents including water: polymerization is thus possible without the exclusion of moisture. The polymerization proceeds at temperatures between −80 and 20 °C in ethanol[38,39]: *cis*-PA is formed as a voluminous mass of very fine crystalline particles, when acetylene is passed into a cooled, stirred solution of the catalyst at −30 °C. Thin layers are obtained if the polymerization is carried out on the surface of capillary films of the catalyst solution on inert carriers. After appropriate purification and drying procedures, these do not differ from

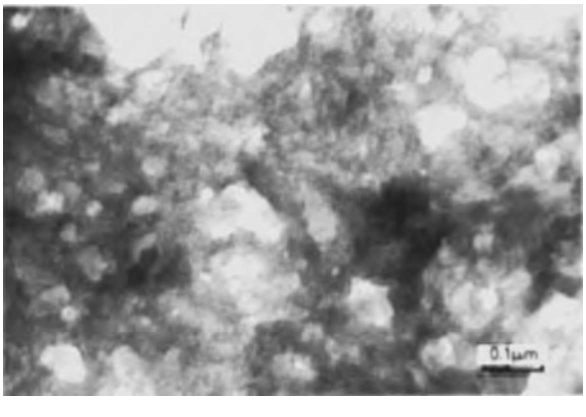


Fig. 4. Electron micrograph (TEM) of a thin layer of PA prepared with the aid of a Luttinger catalyst [37] in a procedure described in [39].

the "films" obtained through the Shirawaka technique, *i.e.*, they possess the same morphological structure, and within the framework of the reproducibility of the conductivity experiments, identical electrical properties to that of the Shirakawa material. Figure 4 shows an electron micrograph obtained from this type of thin layer.

*cis*-PA obtained by *Luttinger's* method may be thermally isomerized to *trans*-PA. Isomerization at room temperature clearly proceeds more slowly than with material produced by the *Shirakawa* method. It occurs, however, within minutes at temperatures of approximately 130 °C. In the following section, additional important distinctions between these two materials will be further discussed.

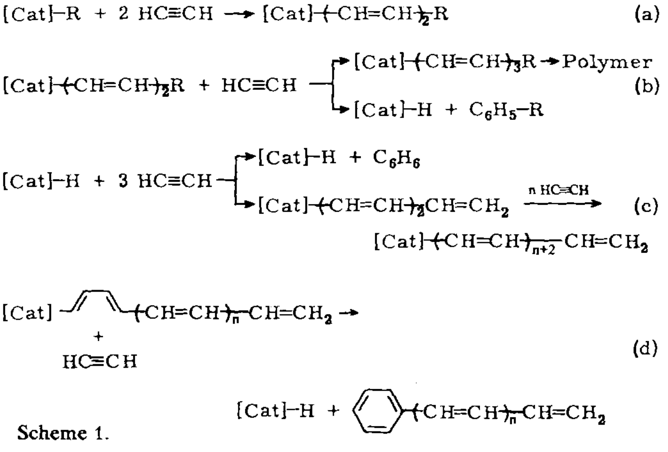
## 2.2. Polymerization Mechanism and Molecular Weight

Little is known concerning the mechanism of polymerization of acetylene. The majority of Ziegler catalysts cyclomerize acetylene to benzene, cyclooctatetraene, styrene and similar products[40,41,49-51]: PA is only produced as a by-product in small yields. Similar results are also found with other catalyst systems, specifically those based on nickel as the heavy metal component[50]. The catalyst discovered by *Natta*, which is used in the Shirakawa technique, as well as that found by *Luttinger*, have proven optimal for the maximum yield of PA. Nevertheless, cyclomerization also proceeds in these systems as a side reaction.

Consequently, a reaction mechanism should be able to explain the simultaneous formation of cyclic oligomers and linear polymers.

*Ikeda* and *Tamaki*[51] have demonstrated that ethylbenzene is produced in small quantities when the typical Ziegler catalyst TiCl$_4$/AlEt$_3$ is used and that the ethyl group originates from the catalyst.

Without speculating about the stereochemistry of the catalytically active complexes, the following simplified scheme shown in Scheme 1 is proposed:



Scheme 1.

In this scheme, the formation of benzene, styrene, cyclooctatetraene, *etc.* result from transfer reactions with the monomer at the degree of polymerization 3 and 4. In addition, the chain length of the polymer is limited by transfer reactions with the monomer, *e.g.* after eq. (d). This leads to formation of, vinyl and phenyl end groups, among others.

The insolubility of the polymer has until now prevented a direct determination of the end groups and the molecular weights. Recently, however, soluble derivatives of polyacetylene have been obtained by polymer analogous reactions, and this has enabled the molecular weights and their distribution to be determined for the first time. The information obtained from these investigations is of considerable significance to the discussion of the mechanisms of conductivity in the doped polymer.

Soluble derivatives of polyacetylenes can be prepared by chlorination or hydrogenation, provided that certain conditions are met. As was previously demonstrated by *Natta et al.*[30], PA takes up the calculated amount of chlorine quickly and almost quantitatively if it is reacted at 0—5 °C. However, a colorless and insoluble product is obtained, the properties of which somewhat resemble those of chlorinated polyvinyl chloride.

If, however, PA prepared following the method of *Luttinger*[37] at $T \leq 243$ K, is chlorinated *immediately* after the polymerization has been stopped, a completely soluble chlorinated PA is obtained[52,53]. When the polymer is stored for some time at −30 °C, however, an insoluble portion remains after chlorination, the amount of which increases with increasing storage time (Fig. 5). This increase in insoluble fraction can be considered as a crude measure of the spontaneous cross-linking which proceeds even at such low temperatures.

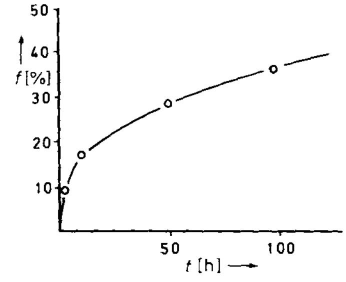


Fig. 5. Fraction *f* of PA which became insoluble by spontaneous cross-linking and could not be converted to a soluble, chlorinated product, as a function of the storage time *t* at −30 °C.

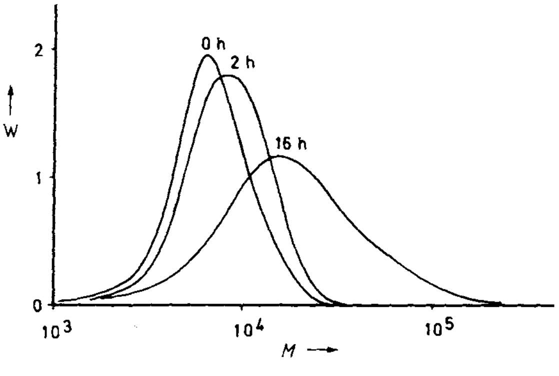
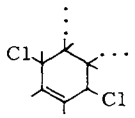


Fig. 6. Molecular weight distribution of the soluble chlorinated PA; chlorination immediately following the synthesis; 2 h and 16 h storage time at 0 °C, w is the logarithmic probability.

The presence and the formation of cross-links can be demonstrated more quantitatively by gel permeation chromatographic (GPC) analysis of the soluble portion isolated in each experiment. Figure 6 shows the molecular weight distributions determined by GPC for PA prepared over a Luttinger catalyst, worked-up at 0 °C, chlorinated immediately, and stored for periods of two and sixteen hours respectively prior to the chlorination. The chlorination was carried out at

0 °C. The average molecular weight, $\bar{M}_n$, increases from 5900 (corresponding to a degree of polymerization $\bar{P}_n \hat{=} 100$) for the native PA, to 9100 after 2 h and 12800 after 16 h. Simultaneously, the distribution broadens, as expected for cross-linking and the yield of the soluble product decreases.

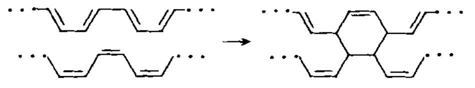
Only approximately 75% of the chlorine calculated if all double bonds had reacted is taken up. IR- and NMR-spectra indicate that structures of the type *(2)* may be responsible for

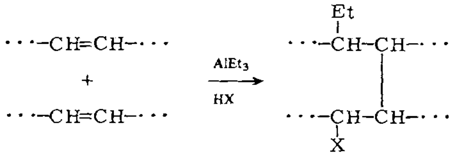

*(2)*

the deficit in chlorine up-take. Such structures can be formed by intramolecular cyclization during the course of the chlorination. PA prepared by the Shirakawa technique can never be entirely solubilized by chlorination; only when the polymerization was carried out in aliphatic hydrocarbons at $T \leq 243$ K, could a soluble fraction be extracted from the chlorinated product. The GPC elution curve of this fraction corresponded to a highly aged, *i.e.* strongly cross-linked, Luttinger-polymer.

It must be concluded from these results, that PA tends to undergo spontaneous cross-linking reactions and, moreover, that cross-linking even occurs during the polymerization if the Shirakawa technique is used. The cross-links may possibly be formed with assistance of components of the catalyst system.

Possible reactions leading to cross-links are cycloadditions of the Diels-Alder reaction type [eq. (e)], and additions assisted by fragments of the Ziegler catalyst [eq. (f)].


(e)

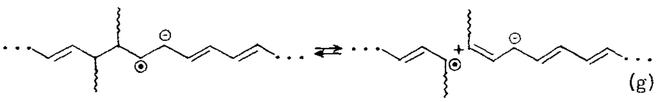

$$\begin{array}{c}\cdots\!-\!CH\!=\!CH\!-\!\cdots\\ +\\ \cdots\!-\!CH\!=\!CH\!-\!\cdots\end{array} \xrightarrow[HX]{AlEt_3} \begin{array}{c}Et\\ |\\ \cdots\!-\!CH\!-\!CH\!-\!\cdots\\ |\\ \cdots\!-\!CH\!-\!CH\!-\!\cdots\\ |\\ X\end{array} \quad (f)$$

X = OH, Cl etc.

Regarding the morphological structure of PA, it must be concluded that these cross-linking and branching reactions originate predominantly in the irregular boundary layers of the single polymer particles, and that they will be favored by the formation of packing and conformation defects during the *cis-trans*-isomerization[52]. For mechanistic considerations and certain material properties it is interesting to note that the degree of polymerization of the nascent polymers, as far as the Luttinger catalysts are concerned, is independent of the type and concentration of the metal salt. Moreover, it is also independent of the conversion and is little influenced by temperature[53].

Similar results are also noted in materials produced with Ziegler catalysts. *Shirakawa et al.*[54,55] have demonstrated that PA, which is initially reacted ("doped") with either sodium or potassium naphthalide, will be hydrogenated if kept for *ca.* 20 h under hydrogen pressure at temperatures ranging from 175 to 260 °C. Soluble polyethylene of average molecular weight $5700 < \bar{M}_n < 7900$ is obtained showing a heterogeneity $\overline{DP}_w/\overline{DP}_n = 2.4$. This corresponds to a $\overline{DP}_n \hat{=} 200$—300.

The reaction of PA with, for example potassium naphthalide, gives rise to polymeric structures with radical anion character. Their existence has been proven by further reaction with methanol by which partial hydrogenation is effected[56]. Hydrogenolysis of the branch-points, must be considered [eq. (g)], if branched or cross-linked polymers are hydrogenated under the aforementioned conditions[57].


(g)

The results of the hydrogenation, therefore, at best allow conclusions to be drawn concerning the average length of the branches and consequently, the original chain length *prior* to cross-linking. The nature of the partially branched and cross-linked system can, however, only be investigated using the method of chlorination, since rupture of the chain is not to be expected with this method.

The considerable mechanical strength observed[52] in PA layers ("films") can, therefore, only be explained through the additional cross-linking of the single morphological subunits over reactions between the individual surfaces and particle boundaries. It cannot be explained by invoking high molecular weight of the nascent polymers.

## 2.3. Morphology and Crystal Structure

The polymerization of acetylene proceeds with simultaneous crystallization of the polymer. In this manner, the same morphological structures are consistently produced, largely uninfluenced by the catalyst type and concentration ratio[38,39]. As Figures 3 and 4 demonstrate, the polymer reaction product consists of an aggregation of very small particles which assemble into network-like structures. Lamellae of irregularly shaped and ill-defined boundaries are identified as the smallest morphological units. These exhibit a thickness of 50—100 Å and an average diameter of up to 2000 Å. These units, aggregated to form a loose network, superficially give the impression of an irregular network of fibers. It is not difficult to arrive at this impression, given the poorly resolved SEM micrographs of the thin layers produced using the Shirakawa-technique[11,29,58]. Moreover, since very high catalyst concentrations are necessarily used in the Shirakawa-technique, gels of metal hydroxides are formed under the conditions used in the work-up of the nascent layers. These give rise to a number of artifacts in the course of the preparation of the micrographs which have been misinterpreted as structural features of PA[59].

Such textures are only defined as fibers or fibrils when the polymer chains within the crystallites are preferentially oriented parallel to a unique morphological direction. This direction is called the fiber-axis. These textures give rise to fiber diagrams on X-ray or electron diffraction. These, loosely speaking, contain a similar amount of information as the rotation photograph of a single crystal mounted along one of its main axes. Preparations with fiber-like textures, which are consequently oriented with regard to the chain direction, are usually obtained if partially crystalline films are stretched or if the solution or the melt of crystallizable polymers is spun. The latter can be considered as crystallization occurring in a shear gradient.

In the case of PA, which crystallizes *in statu nascendi,* it has not been possible thus far to obtain layers or films exhibiting a fiber texture, even if the layers initially obtained are subsequently stretched. Layers prepared by the Shirakawa-technique stretched threefold, immediately after synthesis, exhibit optical and electrical anisotropy[52]. These layers, however, are almost isotropic with respect to X-ray diffraction. The ratio of conductivity parallel and normal to the stretch direction ($\sigma_{\|}/\sigma_{\perp} \geq 10$; $\sigma_{\|} \geq 3000\ \Omega^{-1}\ \text{cm}^{-1}$), observed for PA doped with $AsF_5$[11], may also be explained as arising from an alteration in the percolation behavior (cf. Section 3.3). It is not necessary to assume a large scale orientation of the individual chains in order to account for these conductivity effects. Information concerning the crystal structure and chain direction and their relations to the sample morphology is best obtained by electron diffraction. The most important results from such investigations are as follows[39, 57].

The diffraction patterns from preparations of *cis*-PA, such as those shown in Figures 3 and 4, consist of Debye rings, even when the smallest diffraction aperture was selected and correspond to an area in the sample of approximately 1000 Å diameter. The majority of the sites in such a preparation produce Debye patterns in which all of the rings may be indexed as hk0 reflections. In only a few cases, patterns with 00k reflections are obtained. It must, therefore, be concluded that the morphological units are preferably unaxially oriented with respect to the geometry of the diffraction experiment such that the electron beam enters the morphological units parallel to the chain directions. Only rarely, when the electron beam meets an aggregation of lamellae such that it enters normal to their front end surfaces, may the 001 reflection appear.

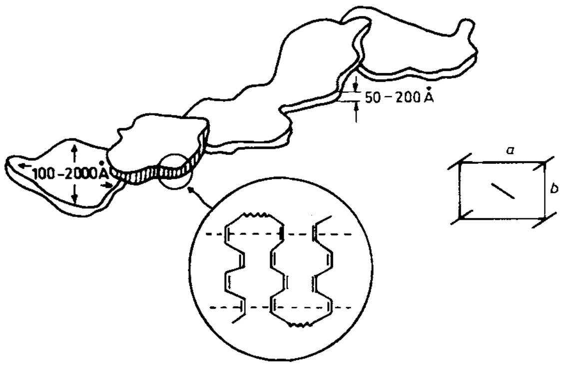


Fig. 7. Morphological units in pristine *cis*-PA and their aggregation to clusters [39]. The chain direction is normal to the surfaces of the lamellae. Chain folding is probable. The chain packing in the *a,b*-plane is indicated, the setting angle is, however, arbitarily chosen.

The model of the morphological structure and chain order in *cis*-PA thus obtained is sketched in Figure 7. Considering the results of the molecular weight determination it must be accepted (Section 2.2) that the chains present in a single lamella are folded several times, since the observed chain length far surpasses the thickness of the lamellae. It is probable that different lamellae are connected to each other *via* tie-molecules. However, at present, no definite assertion can be made regarding this point.

The unit cell parameters of *cis*-PA, based on sixteen observed reflections, have been derived and are compiled in Table 4. They agree well with the values estimated from X-ray data by *Baughman et al.*[60, 61], and uncertainty only exists over the space group. If the space group Pmna proposed by *Baughman* was correct, the 001 reflection observed by *Lieser et al.*[39] should not be observed. In addition, the setting angle (*i. e.* the angle between the plane of the chain and the *a*-axis) cannot yet be specified experimentally. *Bauthman et al.*[60, 61] have approached this problem using packing calculations: the results, however, depend strongly on the input data. Theoretical considerations regarding the interchain interaction require information about the setting angle. The experimental determination of this value is therefore an important goal.

Table 4. Data on the unit cells of *cis*- und *trans*-PA [63] at 120 K and. 300 K respectively.

| | *a* [Å] | *b* [Å] | *c* [Å] [a] | $\gamma$ | *Z* | $\rho$ [g cm$^{-3}$] |
|---|---|---|---|---|---|---|
| *cis*-PA<br>orthorhombic | 7.74 | 4.32 | 4.47 | 90 | 2 | 1.16 |
| *trans*-PA | | | | | | |
| Modification I<br>orthorhombic | 5.62 | 4.92 | 2.592 | 90 | 2 | 1.2 |
| Modification II<br>monoclinic | 3.73 | 3.63 | 2.44 | 98 | 1 | 1.27 |

[a] Chain-direction.

The quality of the available scattering data is not yet sufficient to allow a reasonable structural analysis from which bond lengths and angles can be derived. The numerous quantum chemical calculations so far published concerning the electronic structure and the nature of bonding in PA rely, consequently, on somewhat dubious assumptions on the distances between atoms and the bond angles.

*trans*-PA is produced by annealing *cis*-PA between 100—150 °C. The reaction proceeds as a phase transition without recognizable alteration of the morphology. In contrast to the situation prior to the phase transition, a Debye ring arising from a relatively strong 002 reflection is observed in the electron diffraction pattern. This indicates that the chains have tilted within the lamellae during the progress of the phase transition and that they now lie preferentially inclined to the lamellae surfaces.

A further modification of *trans*-PA was obtained by *W. H. Meyer* using polymerization under extreme shear conditions[62, 63]. *Meyer* has shown that fibrous PA is formed when acetylene is polymerized inside the gap of a Couette arrangement using the conventional Ziegler catalyst, *i. e.,* polymerization occurs inside a gap of approximately 1—2 mm in width between a cylinder rotating at 1000 r.p.m. and the wall of a cylindrical reaction vessel. *trans*-PA precipitates on the wall of the cylinder in the form of a thin, highly oriented layer. An electron micrograph of this layer is shown in Figure 8.

The electron diffraction pattern indicates a well-oriented aggregation of fibrous crystals of polymer. The unit cell data recorded in Table 4 under Modification I are evaluated from an analysis of this fiber diagram. The unit cell differs from that of *trans*-PA, obtained under normal conditions (Modification II) in that it exhibits higher symmetry but lower density. This is due to the surprisingly large value of the fiber peri-

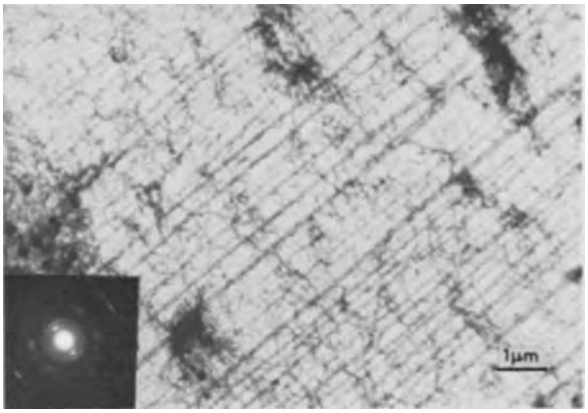


Fig. 8. Morphology of PA synthesized under application of a shear gradient.

od. The fiber period specifies the translational period in the chain direction. Assuming values of 1.35 Å and 1.46 Å for the lengths of the double and single bond, respectively, a bond angle of approximately 135° is calculated for *trans*-PA in Modification I; on the other hand, the expected value of 120° is derived from the data in Modification II.

Unambiguous crystallographic relationships exist between the unit cells of *cis*- and *trans*-PA. These enable the characterization of the phase transformation as a shear deformation and the prediction of twinned structures[63]. The twinning gives rise to phase boundaries or domain walls with components oblique to the chain direction, even in the well-oriented and fibrous preparations of *trans*-PA produced according to the method of *W. H. Meyer.* Modification II may be interpreted in terms of a strongly disturbed lattice of Modification I, insofar as the packing of the chains is concerned[63].

Due to the inconclusiveness of the existing data, assertions concerning bond angles and lengths can only be set forth with a large degree of uncertainty. X-ray crystallographic results clearly prove, however, that different bond lengths, *i. e.*, double and single bonds are present in the polymer. This is in agreement with spectroscopic data, especially with the resonance enhanced Raman spectra[32].

In the resonance Raman spectra of *trans*-PA, two strong bands at 1474 $cm^{-1}$ and 1080 $cm^{-1}$, as well as a weaker band at 1016 $cm^{-1}$ appear. In accordance with interpretations of the spectra of oligoenes, carotinoids and similar unsaturated compounds, the band at 1474 $cm^{-1}$ is ascribed to the double bond; the band at 1080 $cm^{-1}$ to the vibration of the single bond. The corresponding spectra of the pure *cis*-PA can not be obtained for practical reasons because *cis-trans*-isomerization readily occurs in the laser beam. If Raman spectra of *cis*-PA are recorded at $-78\,°C$, however, a strong band from the double bond vibration at 1552 $cm^{-1}$ and two bands from the single bonds at 1262 $cm^{-1}$ and 920 $cm^{-1}$ are observed. It can be concluded from this, in agreement with the IR data, that PA is present in the *cis*-transoid form *(1b)*[32].

A normal coordinate analysis of *cis*- and *trans*-PA has been presented, which enables identification of the IR active bands[28]. The IR spectrum of *trans*-PA only shows bands at 3013 $cm^{-1}$ (C—H valence vibration), 1292 $cm^{-1}$ (C—H in-plane deformation) and 1015 $cm^{-1}$ (C—H out-of-plane deformation). The 1015 $cm^{-1}$ band is reasonably strong and can be utilized as a diagnostic indicator. *cis*-PA shows, among others, strong bands at 1329 $cm^{-1}$ (C—H in-plane deformation), 740 $cm^{-1}$ (C—H out-of-plane deformation) and 446 $cm^{-1}$ (C—C—C deformational vibration). *Shirakawa* and *Ikeda*[28] have also investigated the spectra of fully and partially deuterated PA.

High resolution $^{13}C$-NMR spectra of solid *cis*- and *trans*-PA have been obtained using proton enhancement methods with magic angle sample rotation[64]. The chemical shift of the *trans*-C atoms is +139 ppm (relative to TMS), comparable to that of the central C atoms of butadiene (+137.2 ppm) and *trans*-hexatriene (+137.4 ppm). The chemical shift of the *cis*-polymer (+129 ppm) is close to that observed for the carbon atoms of benzene (+128 ppm). Besides these signals another small peak at higher field has been observed, which was attributed to $sp^3$-hybridized C-atoms. This may originate from the cross-linking reactions which proceed spontaneously.

The UV/VIS spectrum of *cis*-PA contains a very broad band with a peak at 594 nm and a shoulder at 560 nm; a continuous unstructured absorption of decreasing intensity extends into the UV range. A thin translucent layer of *cis*-PA appears wine-red on inspection. An exact value of the extinction coefficient cannot yet be determined due to the complex morphology of the samples. The value, however, should be of the order of $10^5$ to $10^6$ $cm^{-1}$ at the peak maximum[11]. In thin layer, *trans*-PA appears dark blue. The broad peak, with unstructured absorption lies at 700 nm.

So far, it has generally been assumed that these spectra arise from infinitely extended chains of *cis*- and *trans*-PA. Whether this view can still be held, in the light of recent information on the real structure of the samples, requires to be studied. In any case, it must be borne in mind that a single chain cannot be extended rectilinearly within the morphological units of the present samples over more than an average of 20 to 40 double bonds. The sequence of conjugated bonds then comes to an end, either by cross-linking or by extension of the chain into the disordered lamellar surface *via* conformational defects.

Moreover, investigations concerning what extent the width of the absorption peaks relate to the distribution of the lengths of effectively conjugated sequences and crystal size effects, respectively, should be undertaken. This follows from what is known about the structurally related poly(diacetylenes), which can be obtained in the form of perfect crystals without defects and which exhibit a much lower peak half-width[15].

### 2.4. Copolymers

Acetylene can be copolymerized with 1-alkynes using the technique described by *Shirakawa.* Possible comonomers are, for example, 1-propyne, 1-hexyne, phenylacetylene or propargyl alcohol[50]. Given the conditions of acetylene polymerization, these monomers by themselves only give rise to cyclic oligomers or linear polymers of limited degree of polymerization[40,48]. Mixtures of copolymers are formed, if acetylene is copolymerized with 1-hexyne[38] or 1-propyne[66]. With increasing feed of 1-hexyne, the fraction of a polymer or rather, oligomer, rich in comonomer and soluble in toluene increases. The soluble copolymers exhibit molecular weights of 500—1500. They tend to autoxidize rapidly.

The morphology of the acetylene/1-propyne copolymers is quite different from that of the pure polyacetylene produced by the Shirakawa technique and consists of thin layers of an accumulation of irregular clumps at higher comonomer content which amalgamate into smooth films. Nevertheless, as with pure PA, a similar increase in conductivity is observed upon treatment with gaseous $\mathrm{AsF_5}$. The final values which can be reached, decrease drastically with increasing comonomer content. *Chien et al.*[66] have explained this phenomenon as being due to an increasing disturbance of the planarity of the conjugated main chain.

## 2.5. Chemical Reactions Leading to Improvement in Conductivity

Despite numerous difficulties, which have so far prevented an exact characterization of PA, it is generally accepted that the rise in conductivity exhibited in Figure 1 originates from a chemical reaction between the polymer and the dopant[16,57,67,68]. This reaction is characterized by charge transfer from the dopant to the polymer. An ionic state of the polymer, delocalized along the backbone is formed, along with a counterion which is derived from the dopant. All reactions causing a marked increase in conductivity can be classified as redox reactions. The reactions of polymer chains with silver perchlorate[16].

$$(\mathrm{CH{=}CH})_n + \mathrm{AgClO_4} \longrightarrow (\mathrm{CH{=}CH})_n^{\oplus\odot} + \mathrm{ClO_4^{\ominus}} + \mathrm{Ag} \qquad \text{(h)}$$

or with iodine[10,60,61,68]

$$2\,(\mathrm{CH{=}CH})_n + 3\,\mathrm{I_2} \longrightarrow 2\,(\mathrm{CH{=}CH})_n^{\oplus\odot} + 2\,\mathrm{I_3^{\ominus}} \qquad \text{(i)}$$

serve as examples. In these reactions, segments of the polymer chain of length n are oxidized and structures are formed having the character of a delocalized radical cation. The length n can be identified, for example, with the length of the PA chain between the two surfaces of the fundamental morphological units. The idea that pure CT-complexes are formed between the chain and, for example, iodine, which was originally proposed by *Shirakawa et al.*[8], is no longer tenable. Raman spectroscopic studies indicate[16,69,70] that after having reacted, iodine is present as $\mathrm{I_3^{\ominus}}$ and probably as $\mathrm{I_5^{\ominus}}$ as well, bromine as $\mathrm{Br_3^{\ominus}}$. Microcrystalline, pure silver is one of the products of the reaction with $\mathrm{AgClO_4}$.

PA is usually doped by exposing the pristine layers of the polymer to the dopant, which may be either gaseous or dissolved in an inert solvent. Toluene, for example, is used as the solvent in the case of $\mathrm{AgClO_4}$; iodine as a dopant is usually applied from the gas phase at a predefined partial pressure.

Arsenic pentafluoride, which is a gas at room temperature, is often used as a dopant. It reacts with the polymer according to

$$2\,(\mathrm{CH{=}CH}) + 3\,\mathrm{AsF_5} \longrightarrow 2\,(\mathrm{CH{=}CH})^{\oplus\odot} + 2\,\mathrm{AsF_6^{\ominus}} + \mathrm{AsF_3} \qquad \text{(j)}$$

as was convincingly demonstrated by *Clarke et al.*[71,72] on the basis of IR-, Raman- and EXAFS-data. $\mathrm{AsF_3}$ can be sublimed *in vacuo* from the polymeric product. PA therefore reacts analogously to graphite, whose electrical conductivity increases markedly on reaction with $\mathrm{AsF_5}$[73]. $\mathrm{AsF_5}$ oxidizes the carbon layers of graphite[73–75] and the reaction products, $\mathrm{AsF_6^-}$ and $\mathrm{AsF_3}$ are thereby intercalated jointly with excess $\mathrm{AsF_5}$ between the carbon layers.

Side reactions, which lead to fluorination of the polymer, apparently occur in the course of doping. This is in part due to the fact that $\mathrm{AsF_5}$ hydrolyzes readily and an admixture of hydrogen fluoride can only be separated with difficulty.

The elemental analysis of PA doped with $\mathrm{AsF_5}$ can, therefore, not be brought easily into agreement with equation (j). This has prompted *MacDiarmid*[68] to propose other reactions as well, and to discuss other species, such as $\mathrm{As_2F_{10}^{2\ominus}}$. In the light of the results concerning the doping of graphite, poly(*p*-phenylene) and other polymers, and the electrochemical reaction behavior discussed below, it must be assumed that eq. (j) describes the principal reaction occurring which is of prime importance for the phenomenon of conductivity.

Numerous oxidizing agents have so far proven to be suitable dopants for PA. Among others, the salts[76] $\mathrm{NO_2^{\oplus}X^{\ominus}}$ and $\mathrm{NO^{\oplus}X^{\ominus}}$ with $\mathrm{X = SbF_6, SbCl_6, BF_4}$ have been used. However, the vapor of 98 percent $\mathrm{H_2SO_4}$ or 71 percent $\mathrm{HClO_4}$[76], as well as inorganic peroxides such as $\mathrm{FSO_2{-}O{-}O{-}SO_2F}$, have also been shown to work: The latter is applied as a solution in $\mathrm{SO_2F_2}$[77].

Undoubtably, the most elegant method of doping is accomplished by electrochemical oxidation of PA in the presence of a suitable supporting electrolyte. An electrolysis cell is set up for this purpose in which a thin layer of PA serves as the anode and a tetraalkylammonium salt of a not too nucleophilic anion, dissolved in an inert solvent, acts as the supporting electrolyte. Examples of suitable solvents are $\mathrm{CH_2Cl_2}$ or propylene carbonate. The polymer is oxidized at a working voltage of approximately 9 V at a current of 1—43 mA giving rise to a conductive structure. The anode reaction may be formulated:

$$(\mathrm{CH{=}CH})_n + \mathrm{R_4N^{\oplus}X^{\ominus}} \longrightarrow [(\mathrm{CH{=}CH})_n^{\odot\oplus}\mathrm{X^-}] + \mathrm{R_4N^{\oplus}} + e \qquad \text{(k)}$$

If a layer of PA is used as the cathode as well, cathodic reduction of the polymer takes place[68,79] as follows

$$(\mathrm{CH{=}CH})_n + \mathrm{R_4N^{\oplus}X^{\ominus}} + e \longrightarrow [(\mathrm{CH{=}CH})_n^{\odot\oplus}\mathrm{R_4N^{\oplus}}] + \mathrm{X^{\ominus}}$$

and the reduced polymer becomes conducting[89]. The negative charges on the polymer are compensated by tetraalkylammonium ions. Such an electrolysis cell functions after charging of the PA electrodes as a voltaic element in the reverse way. The entire reaction can then be described as an electrochemical equilibrium:

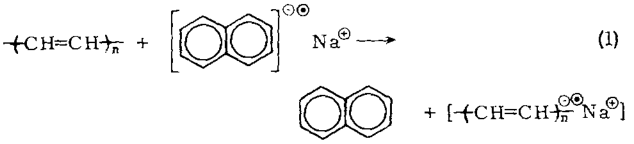
$$2\,(\mathrm{CH{=}CH})_n + \mathrm{R_4N^{\oplus}X^{\ominus}} \rightleftarrows [(\mathrm{CH{=}CH})_n^{\oplus\odot}\mathrm{X^{\ominus}}] + [(\mathrm{CH{=}CH})_n^{\ominus\odot}\mathrm{R_4N^{\oplus}}]$$

According to *MacDiarmid*[79], such a voltaic cell constructed from approximately 0.1 mm thick layers of PA exhibits a voltage of 2.5 V after charging (if no current is drawn) and delivers a current of up to 22 mA in a circuit of minimal resistance at an apparent electrode surface of only 1 cm$^2$.

All species, which are not so nucleophilic that they would react irreversibly with the radical cation sites formed upon oxidation on the polymer chain, may serve as anions $\mathrm{X^{\ominus}}$. So far, the species $\mathrm{BF_4^{\ominus}}$, $\mathrm{SbF_6^{\ominus}}$, $\mathrm{SbCl_6^{\ominus}}$, $\mathrm{AsF_6^{\ominus}}$, $\mathrm{PF_6^{\ominus}}$, $\mathrm{I_3^{\ominus}}$, $\mathrm{ClO_4^{\ominus}}$, $\mathrm{CF_3SO_3^{\ominus}}$ and similar anions, have proven to be suitable[76]. Similar considerations are appropriate for the cations which serve to compensate the anion radical sites delocalized on the polymer chain. So far, only tetraalkylammonium ions $R_4N^{\oplus}$ have been used. The substituents R (*e.g.* $CH_3$-, *n*-$C_4H_9$-, *etc.*) were selected according to the solubility characteristics of the salt used as the supporting electrolyte in the reaction medium.

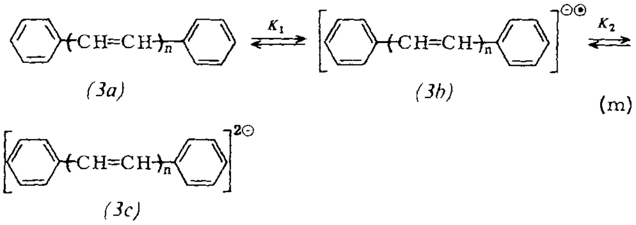
In this connection it is worth mentioning that the method of electrochemical oxidation or reduction is excellently suited for the production of radical ion salts of arenes[81-83] and heterocycles[84,85]. In part, this has already been known for some time. Under appropriate conditions of electrolysis, crystals of these salts precipitate and grow on the electrodes. These crystals, in general, exhibit high conductivity and can be classified as organic metals[83,85].

The reduction of PA to a conductive derivative can also be accomplished by treating the polymer with alkali metals or, even better, with sodium or potassium naphthalide in THF. This transformation is described in eq. (l) as a redox reaction, which is analogous to the well-characterized reactivity of the corresponding α,ω-diphenyloligoenes *(3)*[86].



(l)

*Hoijtink et al.*[86,87] have not only determined the optical and ESR spectra of the radical anions of the compounds *(3b)* $1<n<6$ but also the electrochemical redox potentials and values for the equilibrium constants $K_1$ and $K_2$ of the reactions described by eq. (m).



*(3a)* *(3b)* *(3c)*

(m)

It follows, that the reduction of the oligoene *(3a)* always leads to a mixture of the radical anion *(3b)* and the dianion *(3c)*, the partners of a dis- and syn-proportionation equilibrium, respectively.

$$2\,(3b) \overset{K}{\rightleftharpoons} (3a) + (3c) \qquad \text{(n)}$$

This fact, which can be formulated in an analogous manner for the radical cations produced according to eq. (h)—(k), must be taken into account when discussing, in detail, all reactions which play a role in the doping of PA.

In contrast to the reactions described by eq. (m) and (n), which take place under homogeneous conditions, the doping of PA in the solid state occurs at the surface of particles of complex morphology. Consequently, no exact assertion on the position of the equilibria may be formulated, by analogy to eq. (m) and (n), at present.

Finally, it should be mentioned that oxygen may act as a dopant if it acts upon pristine PA in small quantities[33,88,89]. At higher concentration, larger exposure times, and especially at higher temperatures, irreversible oxidation takes place and cuprene is formed[50] (cuprene, a material similar to cork, is formed by polymerization of acetylene at higher temperatures).

## 3. Electrical Conductivity and Mechanisms of Charge Transport

### 3.1. Definitions and Concepts

Investigation of the conductivity of organic metals requires a basic understanding of the electrical behavior of the solid state. Some of the most important definitions and relationships are summarized in the following short section, without claim to their completeness, in order to facilitate a discussion concerning the mechanisms of charge transport. For additional information, the reader is referred to the literature[1,13,14,90].

3.1.1. Electrical Conductivity of Metals

The electric behavior of metals is described by Ohm's Law, which states that at constant temperatures a current density, $j$, will adjust itself proportional to an external electrical field, $E$. The tensor $(\sigma)$ describing the electrical conductivity is independent of time and electrical field strength.

$$j = (\sigma) E$$

$j$ is maintained by a flux of charge carriers in the field direction. Assuming a conduction by $n$ electrons of charge $e$ per unit volume, $j$ corresponds to an average drift velocity, $\bar{v}_{\mathrm{dr}}$

$$\bar{v}_{\mathrm{dr}} = -j/en$$

For the case of direct current, $j$ and $\bar{v}_{\mathrm{dr}}$ are constant with time, and therefore

$$j = -e \cdot n \cdot \bar{v}_{\mathrm{dr}} = (\sigma) \cdot E.$$

The conductivity may hence be expressed as

$$\sigma = n \cdot e \cdot \mu \quad [\Omega^{-1}\,\mathrm{cm}^{-1}]$$

The constant $\mu$, termed mobility, is equivalent to $\sigma$ and is defined as

$$\mu = |\bar{v}_{\mathrm{dr}}|/|E| \quad [\mathrm{cm}^2\,\mathrm{V}^{-1}\,\mathrm{s}^{-1}]$$

$\mu$ can be experimentally determined by measuring $\sigma$, if $n$ is known. The electrons do not move freely in the field, rather they are scattered by phonons; that is, by the thermal density fluctuations of the lattice and by lattice defects. The phonon density increases with increasing temperature. Lattice defects may normally be considered as static and temperature independent scattering centers. Therefore, the temperature dependence of the resistivity $\rho = \sigma^{-1}$ follows Matthiesen's rule

$$\rho(T) = \rho_{\mathrm{R}} + \rho_{\mathrm{P}}(T)$$

where $\rho_{\mathrm{R}}$ is the portion of the total resistivity of an isotropic metal due to the scattering by defects and $\rho_{\mathrm{P}}$ is that portion caused by the phonons.

As a consequence $\rho$ increases with temperature for metals. $\rho_{\mathrm{P}}(T)$ increases proportionally to $T^5$ at $T \ll \theta$ and proportionally to $T$ at $T \gg \theta$ ($\theta$ is the Debye temperature). The residual resistivity $\rho_R$ is controlled by additives (creation of lattice defects).

If the dimensions of a metal sample decrease in comparison to the mean free path of the charge carriers between two scattering events, (*e.g.* in thin evaporation layers or fine threads) the resistivity may increase due to additional scattering events at the surfaces. Consequently, the resistivity calculated from the sample dimension is no longer a material constant in small samples.

This may be of importance when the conductivity data of doped PA are evaluated, since the charge transport takes place in this material inside very small particles, the dimensions of which are of the same order of magnitude as the expected value of the mean free path. Experimental data may serve to illustrate the above equations.

Using copper as an example, it is found that $\sigma(300\,\mathrm{K}) = 0.65 \times 10^6$ ($\Omega^{-1}$ cm$^{-1}$) with $n = 0.85 \times 10^{23}$ (conduction electrons cm$^{-3}$), the mobility $\mu(300\,\mathrm{K}) = 46$ (cm$^2$ V s$^{-1}$), and the mean free path $\bar{l}$ between two scattering events by phonons is $\bar{l}(300\,\mathrm{K}) = 420$ Å. These values increase by a factor of $10^3$ to $10^5$ at 4 K, the exact value depending on the purity of the sample.

### 3.1.2. Semiconductors

In semiconductors all valence electrons are situated in bound states at $T = 0$ (*i.e.* the valence band is filled and the conduction band is empty). The band gap may be interpreted to be the bonding energy of the valence electrons.

At finite temperatures, some of the atoms or molecules are thermally ionized, with the number of electrons in the conduction band being equal to the number of holes ("defect electrons") in the valence band. The electrons in the conduction band serve to maintain a current in an external electrical field, as described for metals. In addition, these holes move in the opposite direction.

This motion of electrons (holes) ceases when they recombine with the holes (electrons) and return to a bound state. In thermal equilibrium, these recombination events, along with the thermal excitation events, are in equilibrium. The equilibrium concentration of both the holes and the conduction electrons is equal and dependent of temperature. If the concentration of the conduction electrons is $n$ and that of the holes in the valence band $p$, then the expression for the electrical conductivity is (isotropic solid):

$$\sigma = e(n\,\mu_e + p\,\mu_p)$$

with $\mu_e$ and $\mu_p$ being the mobility of the electrons and holes, respectively. In other words, according to their mobility, the electrons and the holes contribute independently to the total conductivity. The magnitude of the conductivity depends on the number and the efficiency of the scattering processes occurring *via* phonons and defect sites, in the same way as has been previously discussed for metals.

In contrast to the behavior of metals, $n$ and $p$ are characteristically temperature dependent for individual semiconductors. In the simplest case, where the current is maintained by electron and hole pairs and all charge carriers have the same isotropic mobility, the concentration of the charge carriers at temperature $T$ is given by

$$n = p = (n_0 \cdot p_0)^{1/2} \cdot \exp(-E_A/(2kT))$$

and the temperature dependence of $\sigma$ by

$$\sigma(T) = e(\mu_e(T) + \mu_p(T))\, n_0 \cdot p_0^{1/2} \exp(-E_A/(2kT)) \tag{o}$$

$E_A$ represents the activation energy for the formation of the charge carriers (*i.e.* the electron-hole-pairs) and may be identified as the magnitude of the band gap; $k$ is the Boltzmann constant.

When $E_A \gg kT$, the behavior of a semiconductor is determined essentially by the exponential term of eq. (o); thus, $\sigma$ increases exponentially with temperature. If it is the case, however, that $E_A \leq 2kT$ or that the charge carriers are formed athermally, as for example by photoexcitation, the temperature dependence of the conductivity is determined by the pre-exponential factor of eq. (o).

By analogy to eq. (o), an equation has been formulated by *Epstein* and *Conwell*[91]

$$\sigma(T)/\sigma(T_R) = A\,T^{-\alpha} \exp(-E_A/(kT))$$

which describes the temperature dependence of the conductivity, normalized with regard to a reference temperature $T_R$. Experimentally[83,91,92], it has been found that $0.5 \leq \alpha \leq 2.5$ in organic metals.

The anisotropic mobility of the charge carriers in organic materials has seldom been experimentally determined. *Karl*[93] has impressively demonstrated, using anthracene, that the magnitude and temperature coefficient of the mobility does not only significantly depend on the purity of the molecular crystal, but also that both are extremely anisotropic. For the temperature interval 100 K $< T <$ 300 K, almost isotropic mobility of the holes $\mu_p \approx T^{-1.5}$ is found: the mobility of the electrons is, however, strongly anisotropic $\mu_{ea} \approx T^{-1.57}$, $\mu_{eb} \approx T^{-0.84}$ and $\mu_{ec} \approx T^{+0.16}$. The indices *a, b, c* refer to the axes of the anthracene unit cell.

For organic metals, (*e.g.* TFF-TCNQ) *Weger*[94] has developed a comprehensive, if not undisputed[95], theory by means of which the proportionality $\sigma \sim T^{-2}$ frequently found in this class of materials, can be interpreted by invoking special scattering processes. *Weger* correctly points out that one should differentiate between conductivity at constant pressure and constant volume. Because of the usually strong anisotropic temperature and pressure dependence of the lattice constants in organic materials, the conductivity should only be considered normalized for constant lattice dimensions.

## 3.2. Charge Transport and Structure

The electrical conductivity of doped PA and similar polymers must be discussed on the basis of available information pertaining to the charge transport and structure of organic metals. While it is not necessary to refer to the comprehensive theoretical background developed for organic metals, it must be noted that the high conductivity observed always accompanies certain packing modes of the molecules in the conductive crystals. All organic metals consist of molecular crystals of charge-transfer complexes. Almost all complexes of donors and acceptors crystallize in the form of mixed stacks, as indicated in Figure 9a; crystals which exhibit this type of packing are insulating. Only those crystals, in

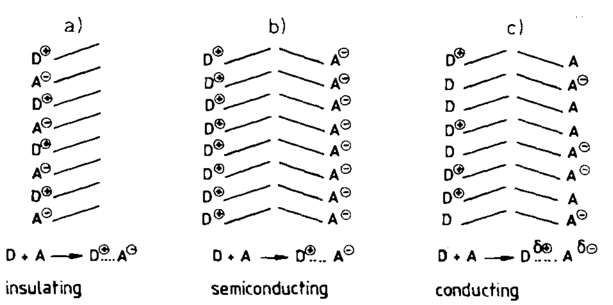


Fig. 9. Schematic view of the packing in organic CT-crystals. a) Insulating, b) semiconducting, and c) conducting CT-complex.

which the donating and accepting molecules after charge-transfer are found in segregated stacks, are conducting.

If, however, a full charge is transferred, as shown schematically in Figure 9b, a semiconductor results. An organic metal is only formed if there is a partial transfer of charge and, therefore, the stack of the acceptor molecules consists of a mixture of neutral and negatively charged units while the donor stack consists of a mixture of neutral and positive units (Fig. 9c). This is the pattern found in the conductive crystals of TTF-TCNQ. Such a crystal may also be described as an organic salt, consisting of two independent but interpenetrating lattices of stacks of TTF-cations and TCNQ-anions. It has, in fact, been demonstrated[13,14] that the charge transport proceeds independently in the two stacks; the TCNQ-stack supporting a current of electrons, the TTF-stack a current of holes.

The charge transport may be described, in a quasi-chemical formulation, as an exchange process. This is sketched in Figure 10b, which depicts the situation inside the TCNQ-stack. A partial charge transfer from the donor to the acceptor stack is understood as resulting in a random placement of neutral and negatively charged (radical anion) TCNQ molecules along a single stack. Electron transport is now described as a diffusive exchange of charge between free and occupied positions along a chain of such molecules.

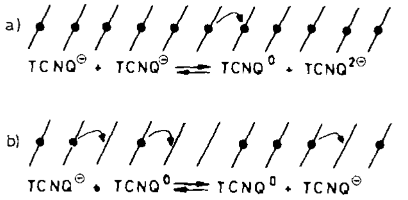


Fig. 10. Model of charge transport within a CT-complex using TCNQ as an example: a) at complete charge transfer from the donor to the acceptor (TCNQ); b) at only partial reduction of the acceptor.

If, however, complete charge transfer has taken place as depicted in Figures 9b and 10a (*i. e.* if each TCNQ-molecule carries a negative charge), the transport of charge must be described, in the present context, as a disproportionation. This requires considerable energy, since an electron has to travel to a lattice site already occupied by a negative charge; thus a large Coulomb potential has to be overcome, and hence, a semiconductor results (cf. in this context, the behavior of the alkali-salts of TCNQ exhibited in Fig. 2).

The bonding relationship within the stacks of an organic metal can be characterized from Figure 10b as a CT-interaction between neutral molecules and the radical ions formed from them. The numerous successful syntheses of salts exhibiting metallic conductivity[13,14,84,85] prove this description to be correct. Among others, mention must be made of the salts derived from TTF and its derivatives with simple anions X$^{\ominus}$ of low nucleophilicity exhibiting the general formula (TTF)$_y^{\oplus}$X$^{\ominus}$, as well as compounds of TCNQ with cations K$^{\oplus}$ of low electrophilicity of composition (TCNQ)$_y^{\ominus}$K$^{\oplus}$, with $1 < y < 3$.

According to this concept, the conductivity relates essentially to the structure of the lattice and to the packing of the molecules and not so much to structural pecularities of the individual molecules, as was previously often assumed[96]. In particular, the question of under what conditions the desired structure of stacks may be formed is principally a problem of the kinetics of crystallization and not a question of the electronic structure of the individual molecules[97].

The radical cation salts of simple aryls may serve as suitable examples to demonstrate some of these ideas. These materials exhibit conductivities of the order $1 < \sigma(300\,K) < 1000$ $\Omega^{-1}$ cm$^{-1}$. In addition, they may be considered as excellent models for doped PA and other conductive polymers. They are obtained by electrochemical oxidation (using a suitable supporting electrolyte, such as $n$Bu$_4$N$^{\oplus}$X$^{\ominus}$ with X = ClO$_4$, PF$_6$, ASF$_6$, SbCl$_6$, *etc.*) of, *e. g.*, naphthalene[81,82], fluoroanthene, perylene, pyrene[83,132], as single crystals having metallic luster, and exhibit the general formula (Aryl)$_2^{\cdot\oplus}$X$^{\ominus}$.

The desired packing shown in Figure 9c is realized in these crystals; the aryls are stacked with a distance of 3.2 Å between the planes of the rings. The projection of the crystal structure of [fluoroanthene]$_2^{\cdot\oplus}$PF$_6^{\ominus}$ onto and along the stacking axis is exhibited in Figure 11[83].

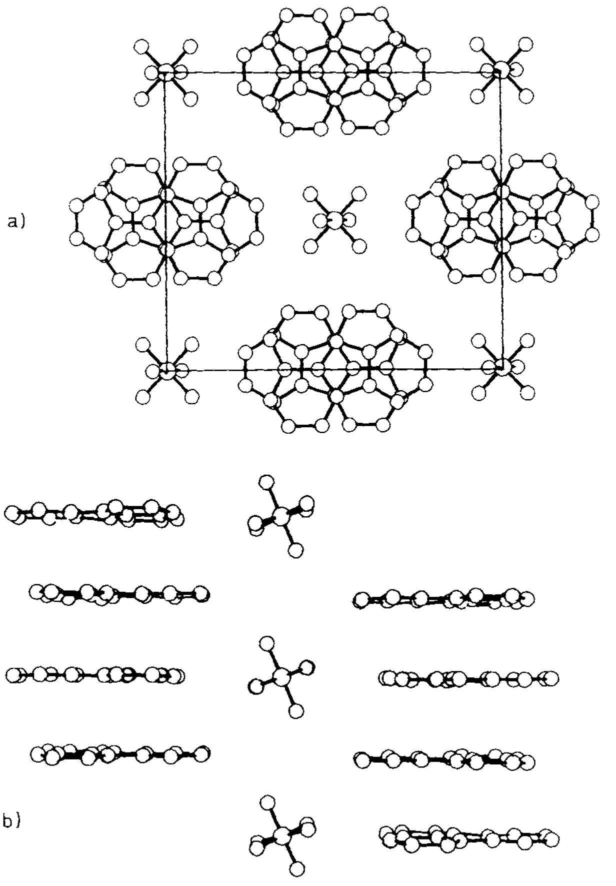


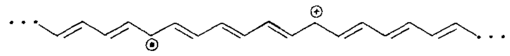
Fig. 11. Crystal structure [131] of the organic metal [Fluoroanthene]$_2^{\cdot\oplus}$PF$_6^{\ominus}$, projection a) on the stack-axis, and b) along the stack-axes.

With this background and considering the nature of the chemical reactions which proceed in the doping of PA (which have been previously discussed in Section 2.5), it is concluded that the conductivity in doped PA relies on the same type of interactions as are sketched in Figures 9c and 10b for the radical ion salts of simple aryls (cf. Fig. 1). Within the framework of these ideas, radical ions of individual polymer sequences consisting of n double bonds are formed when the doping agent reacts at, and with the surface of the morphological units of PA. These sequences extend between the surfaces of the lamellar structures and stabilize themselves by forming CT-complexes with adjacent and still neutral sequences. The doping proceeds to the extent at which, on the average, each conjugated chain sequence between conformative defects or cross-links has been transformed into the complex structure. The charge of the radical ions, which is situated on the sequences delocalized along the chains, is compensated by counter-ions. These are either intercalated in layers between the chains or deposited on the surfaces of the morphological units.

The original lattice breaks down in the course of doping PA. This is shown experimentally by the disappearance of the Bragg reflections. The latter remain, however, for some period of time during the doping, albeit with decreasing intensity. This is due to the fact that the doping proceeds inhomogeneously and individual morphological units become doped at different rates. Samples which have reached maximum conductivity are, however, amorphous as revealed by X-ray investigation. Hence, exact data on the packing of the chains and the counter-ions are not available at present and analogies have to be relied upon.

Presumably, charge transport takes place within a morphological unit normal to the chain direction as indicated by the exchange process sketched in Figure 10b. In other words, it is expected that a high mobility of the charge carriers exists normal to the chain direction, even in the absence of perfect crystalline order. It is another problem as to how the electric contact is made where the surfaces of the individual morphological units touch each other and where contact resistances are build up which have not thus far been characterized.

These ideas are contradictory to those proposed by, among others, *Heeger et al.*[11,80], *Chien et al.*[98], and *Rice et al.*[99,100]. These authors claim that the conductivity mainly arises from the transport of charge along individual chains. Apart from the fact that they incorrectly assumed that PA, as obtained by the Shirakawa procedure, consists of a network of extended fibers and fibrils of infinitely long extended chains, they did not take into account the expected interactions between neighboring chains. Rather, these authors believe that the charge carriers migrate along a single chain in a manner similar to delocalization of charge along an extended $\pi$-bonded system and that the constraints of strictly one-dimensional diffusion apply. Such a state of a charged $\pi$-bonded chain may be described mathematically as a soliton[99,100][*]. The chemical structure *(4)* envisaged in this context is the radical cation previously discussed in eq. (h)—(k). Any interactions with adjacent chains are, however, not allowed. The radical site in *(4)* is termed a "neutral" soliton and the site of the positive charge a "charged" soliton. It is only the latter which is able to transport a charge if an external electrical field is applied.



*(4)*

Unfortunately, until now, no successful measurements on samples in which the orientation of the chains with regard to the direction of the field was known have been reported (see Section 3.1). Hence, the question whether the charge transport occurs in a direction across the chains or along the individual chains, which is basic to the understanding of the electrical phenomena in doped polymers, cannot yet be answered experimentally.

### 3.3. Electrical Conductivity as a Percolation Problem

So far, the exponential increase in conductivity with increasing degree of conversion observed in the course of doping of PA has not been dealt with (see Fig. 1). Similar behavior is also found in other polymers. This is shown in Figure 12. It may therefore be asked whether the observed behavior may not be explained by a universal law.

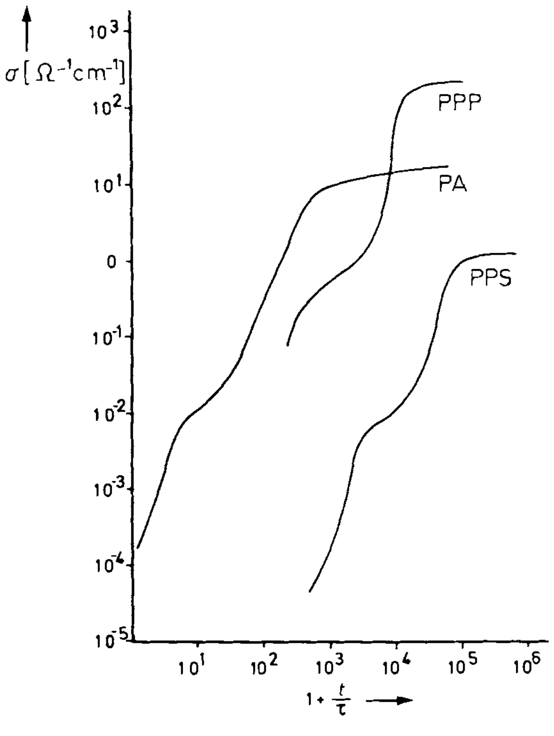


Fig. 12. Increase of the specific conductivity $\sigma$ with reaction time $t$ ($\tau = 1$ s) during doping of poly(*p*-phenylene) (PPP) [21, 22] [$\sigma_{max} = 145\ \Omega^{-1}\ cm^{-1}$, $AsF_5$, 455 torr] and poly(*p*-phenylene sulfide) (PPS) [$\sigma_{max} = 1\ \Omega^{-1}\ cm^{-1}$, $AsF_5$] [23, 24] as well as of polyacetylene (PA) [$\sigma_{max} = 15\ \Omega^{-1}\ cm^{-1}$, $I_2$, $2\cdot 10^{-2}$ torr] [89].

PA is semicrystalline, as are other polymers which may be made conductive by oxidation or reduction. The doping is inhomogeneous and occurs within and at the surfaces of the morphological subunits. It has been shown that polyacetylene is built-up from lamellar subunits of limited thickness with a lateral extension of approximately 1000 Å. Charge transport is only possible across the boundary of the particles at points of contact.

---

[*] In this context, the term soliton refers to the non-linear excited state of the chain; this operates in such a way that the $\pi$-electron wave function undergoes a 180° phase change at the site of the excited state. The excited state has free rotation along the chain. An analogues phenomenon is the well-known mobile replacement in single crystals.

The doping proceeds inhomogeneously, and in addition at low conversions, individual single particles are the first to react and become conductive[101]. Charge transport cannot yet take place since these particles remain isolated by the surrounding particles, which are still in their pristine insulating state. A macroscopic current may only begin to flow if sufficient particles have become conductive so that a path between the electrodes is formed. At this point, then, a jump in the conductivity and conductivity behavior must be experimentally observed if a critical concentration of the doping reagent has been applied. With increasing conversion, further paths and bridges will be formed until all of the morphological units have assumed the same conductive state. When this is the case, the saturation value of the conductivity will be reached. This process is illustrated in a two-dimensional model in Figures 13a—c.

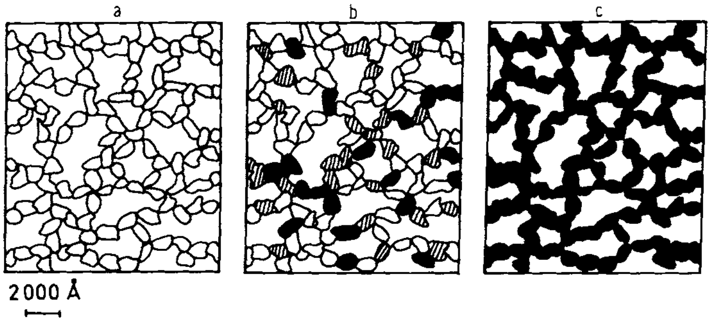


Fig. 13. Percolation model to explain the increase in conductivity during the doping of PA. a) All morphological structures are in their pristine, insulating state. b) State of the system at $\varphi_L < \varphi_L^c$; the black particles have already reached their maximum conductivity; the gray particles have not yet reached their final conductivity. c) State of the system whem maximum conductivity has been reached.

The electrical behavior of mixtures of two phases, each having a very different conductivity, has been investigated theoretically[102] as well as experimentally[103-105]. In the framework of percolation theory, the average conductivity $\sigma$ of a system undergoes a transition, termed "percolation", if the conductive phase attains a critical volume fraction $\varphi_L^c$.

The macroscopic properties of the system may be described, in a manner similar to thermal phase transitions, by universal "scaling laws". These are independent of the physical and chemical details of the system and depend only on their topology.

Above and in the vicinity of the critical volume fraction $\varphi_L^c$ at which percolation commences, the theory predicts that the conductivity should follow a simple exponential law

$$\sigma = \sigma_0(\varphi_L - \varphi_L^c)^t \qquad \varphi_L > \varphi_L^c$$

Below $\varphi_L^c$, it is predicted that

$$\sigma = \sigma_0'(\varphi_L^c - \varphi_L)^{-s}$$

The exponents t and s are constants, as are the pre-exponentials $\sigma_0$ and $\sigma_0'$. While the exponents are universal constants, the values of which have been predicted to be $|t| = 1.6$ and $|s| = 0.7$ for three-dimensional randomly placed particles, this is not true for the pre-exponential factors and $\varphi_L^c$ at which percolation occurs. The critical volume fraction $\varphi_L^c$ is dependent upon the dimensionality of the system, the arrangement of the particles, their degree of dispersion, and other morphological details of the system. Values of the pre-exponential factors $\sigma_0$ and $\sigma_0'$ may be calculated only when the conduction mechanism is known and specific models are assumed.

It is of considerable relevance when applying percolation theory, that all information concerning the dimensionality and topology of the system is contained in the terms $(\varphi_L - \varphi_L^c)^t$ and $(\varphi_L^c - \varphi_L)^{-s}$, respectively, while details of the mechanism of charge transport are contained in the pre-exponential factors. These can be determined experimentally.

In order to apply the theory to the doping of PA it is assumed that the individual particles are arranged in the form of a three-dimensional network, similar to that depicted in Fig. 13. It is further assumed that a single particle which has begun to react with the dopant, reacts to the saturation value much faster, due to kinetic or thermodynamic reasons, than an adjacent particle which is still in its pristine non-conductive state.

Since a partially converted particle may become conductive if the mechanism of conductivity—as discussed in Section 3.2—is dependent on charge transfer between adjacent chains, *via* a redox process, it would be expected that some conductivity would arise prior to the percolation between completely doped particles by percolation through partially reacted morphological units.

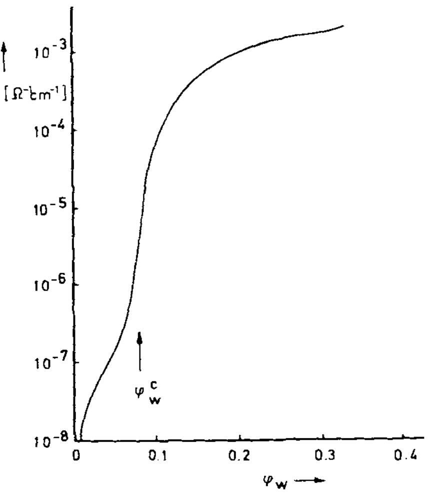


Fig. 14. Conductivity of a water-in-oil emulsion as a function of the volume fraction of the water droplets. This is a model case for percolation [105].

*Lagues* and *Sauteray*[105] have investigated a system, which serves as a model for the present discussion. For a water-in-oil emulsion of very fine droplets, having a diameter of approximately 100 Å, the conductivity increases in proportion to the volume fraction of the water phase $\varphi_W$, as shown in Figure 14. At $\varphi_W^c = 0.078$, percolation is observed. The conductivity above this value is proportional to $(\varphi_W - 0.078)^{1.55}$ and hence the theoretically expected behavior is observed. Below the critical concentration, the conductivity arises *via* Brownian motion of the electrically charged water droplets and is consequently proportional to the diffusion coefficient of the charge carriers. The authors mentioned above define this behavior as "stirred percolation", in contrast to the model, discussed initially, which is described as a "frozen" system.

The increase in conductivity as a function of the critical volume fraction of the aqueous phase, shown in Figure 14, exhibits a surprising similarity to the behavior of PA and other doped polymers as a function of time. In this comparison, it is assumed that the conversion of the sample is approximately proportional to the contact time with the dopant.

In fact, an evaluation of what is presently considered to be the best values for the dependence of the conductivity of PA from the concentration of iodine[89] results in the curve shown in Figure 15. In order to utilize the available published data in percolation theory, it is assumed that each morphological subunit accepts only a maximum number of iodine atoms and that the dimensions of these morphological subunits fluctuate very little around an average value, *i.e.*, it is assumed that they may be represented by an average particle volume. The unknown volume fraction $\varphi_L$, may then be replaced by the concentration of iodine $c$ consumed by the sample. Figure 15 shows the curve is that of $c > c^c$ calculated from

$$\sigma = 5(c-500)^{1.6}$$

and is in excellent agreement with the assumption of three-dimensional percolation. For $c < c^c$ it was found that $\sigma = 2.4 \cdot c^{1.0}$, *i.e.*, the conductivity is determined by the diffusion of the existing charge carriers between the still poorly conducting particles.

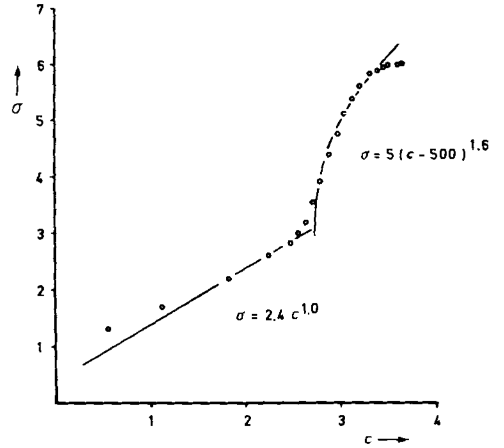


Fig. 15. Conductivity of PA as a function of the iodine concentration (arbitary units); o: data from [89]; solid curve calculated according to the equation in text.

The available data are not yet sufficiently extensive and precise to either sufficiently substantiate the behavior upon doping within the framework of percolation theory, or to attempt an evaluation and discussion of the magnitude of $c^c$ and $\sigma_0$. Nevertheless, it is certain that a more comprehensive alternative has been proposed, in which conductivity data is based on a physical model. This alternative accounts better than other theories for the real physical structure of the samples.

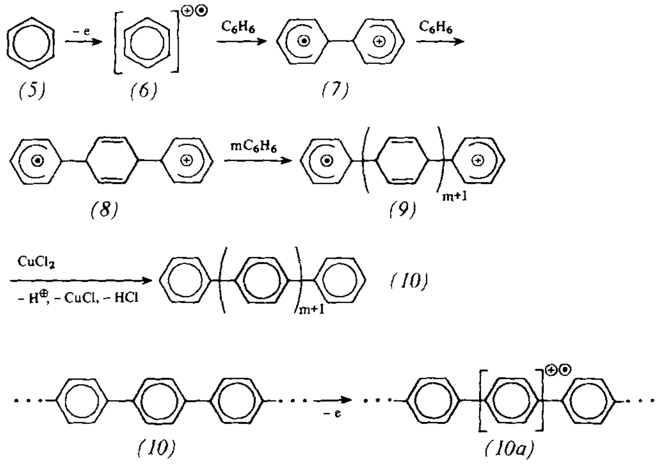
The explanations for the exponential increase of conductivity with increasing content of doping published in the literature, principally stem from the physics of semiconductors. In addition, they all rely on the assumption that PA is similar to semiconductors built up from rather large crystals and that the dopant enters lattice sites such as defects or is intercalated at interstitial sites[67,68,80].

As previously demonstrated, these assumptions are inappropriate. Further analysis of the conduction behavior and theoretical considerations can only be successful therefore, if the topological effects (which are described by percolation theory) are separated from other effects (which take place on the surface and within the single morphological subunits of the polymer).

## 4. Additional Polymers Exhibiting Conductivity

### 4.1. Poly-(*p*-phenylene) (PPP)

Poly-(*p*-phenylene) (PPP) *(10)* is obtained in quantitative yield as an insoluble and infusible powder when benzene is polymerized over $AlCl_3/CuCl_2$ (molar ratio 2:1) as a catalyst and reaction component[106]. Similarly, other reagents which act as both oxidants and Friedel-Crafts catalysts may be used for the polymerization, *e.g.*, $FeCl_3$, $MoCl_5$, *etc.* After *Kovacic*[106,107], the polymerization proceeds *via* radical cations such as *(6)*—*(9)* as the active intermediates according to a mechanism which explains the formation of branches and cross-links as well as by-products during the work-up procedures.

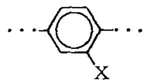


Benzene is initially oxidized to the cation radical *(6)* which dimerizes to the species *(7)* and rapidly adds further monomer *via* the cationically active chain end to form *(8)*. The oligomer or polymer with the quinoid structure *(9)* is subsequently oxidized by the oxidant present in the reaction medium to the polymer *(10)*.

Since the redox potential of the oligophenylenes decreases with increasing chain length, the polymer *(10)* itself is further oxidized to *(10a)*. Units of *(10a)* exhibiting the structure and reactivity of radical cations are thereby formed. These are the sites for branching, and in turn give rise to side reactions during the work-up. The ability of the radical cations derived from benzene or oligophenylenes to undergo electrophilic additions to aryls is well documented by cyclic voltammetry and the electrochemically induced oligomerization of arenes[108].

The structure *(10a)* explains why PPP is black immediately after its synthesis and prior to purification: purification is generally achieved by extracting the polymer with boiling hydrochloric acid. The spin density is reported to be $10^{21}$ spins·g$^{-1}$, *i.e.*, approximately one unpaired electron for every eight phenylene units.

After work-up, the brownish-red colored polymer still possesses a spin density[1,7,109] of *ca.* $10^{18}$ spins g$^{-1}$. Elemental analysis indicates that chlorine (1—4%), oxygen (<5%), copper (0.1—0.2%) and aluminum (0.3—0.6%) are present even in well purified PPP[106,107,110]. This indicates the presence of structures of type *(11)* in the polymer[107].


*(11)*, X = OH, Cl

The UV/VIS-spectrum of the purified polymer exhibits a broad absorption band with maximum at $\lambda = 385$—$395$ mm. The data may be interpreted by assuming that the constitutive units are essentially all linked to each other in *para*-positions. The presence of branching, however, is also highly probable[106]. The degree of polymerization of the polymers produced following *Kovacic*'s method are clearly smaller than was originally assumed[106]. More recent investigations by *Kovacic et al.*[111] seem to indicate that the polymer is, in part, cross-linked. Perhydrogenated oligomers of degree of polymerization 7.5 can be extracted from the polymer after hydrogenation, in a yield of approximately 5%. It seems reasonable to assume that the cross-linking occurs essentially *via* radical combination of the adjacent chains of structures such as *(10a)*.

Little is known about the morphological structure of the polymer[110,111], which consists of lamellar to grainy structures: it has a specific surface of approximately 50 m$^2$ g$^{-1}$. This value varies considerably, however, depending on the polymerization conditions. The discussion of the crystal structure and the chain packing is, therefore, limited to an analysis of the powder diagrams[111] and to comparisons with the known crystal structures of some oligophenylenes[21,22]. The orthorhombic unit cell most likely has the dimensions $a = 7.81$, $b = 5.53$, $c = 4.20$ Å (chain direction): it contains two chains. The density of the crystalline phase is reported to be $\rho_c = 1.39$ g cm$^{-3}$. Since the density of amorphous PPP is unknown, the crystallinity of the polymer samples cannot be evaluated.

PPP has a specific conductivity of $\sigma < 10^{-11}$ $\Omega^{-1}$ cm$^{-1}$ in purified from. *Baughman et al.*[21,22,112] have demonstrated that $\sigma$ increases exponentially if the polymer is treated with oxidants such as, $AsF_5$, $SbF_5$, $SbCl_5$ or reductants such as sodium, potassium, lithium or sodium naphthalide or similar reagents.

The increase in conductivity of PPP as a function of the contact time, *i.e.* with conversion on doping with $AsF_5$, is shown in Figure 12 as an example. A limiting value of the conductivity is reached at $\sigma = 145$ $\Omega^{-1}$ cm$^{-1}$ at a conversion of approximately 0.3 mol $AsF_5$ per mol of the constitutive units.

It is unclear how $AsF_5$ reacts. Elemental analysis produces a ratio As:F = 1:4 for the doped polymer[112]; in addition, HF seems to be split off in the course of the doping. The reaction behavior of oligomer model compounds as, for example terphenyl, suggests that fluorination may proceed as a side reaction. By taking into account what is known about the reaction behavior of PA, it is reasonable to assume that the radical cations of the structure *(10a)* formed by oxidation are compensated by $AsF_6^{\ominus}$ counterions. The As:F ratio found is then explained by assuming that part of the $AsF_3$ formed by disproportionation of $AsF_5$ fluorinates the polymer and gives rise to volatile by-products.

In contrast to PA, PPP cannot be made conductive by exposure to iodine or bromine. If PPP is reduced by, for example, potassium naphthalide dissolved in tetrahydrofuran, a conductivity of only $\sigma \leq 10$ $\Omega^{-1}$ cm$^{-1}$ is found despite the higher conversion (*ca.* 0.6 mol potassium per mol constitutive unit)[21,22].

Similar to PA, the activation energy of the conductivity decreases from 0.7 eV for the pure polymer to very small values for the doped material. If PPP is doped with $AsF_5$, the conductivity measured at 10 K is only smaller than that found at room temperature by a factor of 0.45[27].

The conductivity is electronic in nature. *Shaklette et al.*[112] report a charge carrier density of $2.2 \cdot 10^{27}$ m$^{-3}$ and a mobility of the charge carriers (holes) of 10 cm$^2$ V$^{-1}$ s$^{-1}$ for the polymer doped with $AsF_5$. The same authors found an electron mobility of $10^{-2}$ cm$^2$ V$^{-1}$ s$^{-1}$, when the polymer is doped with potassium naphthalide.

Considering the complex structure and morphology of the polymer, these data should not be used to come to premature conclusions on the relation between chemical and physical structure and conductivity behavior. An unexpectedly low value of the Pauli paramagnetism is, for example, obtained from the temperature dependence of the static susceptibility of PPP doped with $SbF_5$. The Pauli paramagnetism, $\chi_{Pauli}$, is defined as the susceptibility which arises from the spin of the charge-carriers. The value of $\chi_{Pauli} \leq 10^{-7}$ emu cm$^3$ mol$^{-1}$ $\pi$-bonded C-atoms determined for PPP·$SbF_5$ should be compared with that of a typical metal, for example, sodium ($\chi_{Pauli} = 2 \cdot 10^{-5}$ emu cm$^3$ mol$^{-1}$) and for HMTTF-TCNQ, a typical organic metal ($\chi_{Pauli} = 1.2 \cdot 10^{-5}$ emu cm$^3$ per mol of $\pi$-bonded C-atoms).

It is difficult to reconcile this result with the assumption that the conductivity arises according to a band model. Rather, it seems to suggest a "hopping process" and may be related to the previous discussion assuming that the equilibrium discussed by eq (n) is shifted to the side of disproportionation products in the solid doped polymers; hence the spin density, as determined experimentally for the samples made conductive by $SbF_5$, is smaller by a factor of at least $10^{-4}$ than the spin density calculated from the elemental analysis (content of antimony).

*Peo et al.*[109] propose, therefore, that the charge transport takes place by compensation of spins, since a high conductivity with metal-like temperature dependence is found and because in the case of PPP a charge transport *via* charged but spinless solitons cannot be reasonably assumed for structural grounds PPP[21,22].

Moreover, it is interesting to note that oligophenylenes such as terphenyl, quarterphenyl and sexiphenyl can be doped with $AsF_5$. Highly conducting complexes having a greenish-golden luster are formed by this reaction[112]. As may be expected from the work of *Kovacic*[106,111], combination of the initially formed radical cations gives rise to higher oligomers and polymers in the course of the doping of these compounds, in the form either of single crystals or polycrystalline powders[112]. The oligomers, as well as PPP, become X-ray-amorphous upon doping. It is therefore unreasonable to discuss possible intermolecular interactions or intercalation structures of the doped polymer on the basis of known packing of the polymer or of the oligomers, because the doping proceeds with destruction and/or reorganization of the packing.

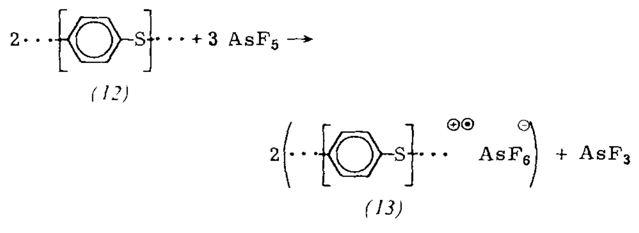
### 4.2. Poly(thio-1,4-phenylene) (PPS)

Poly(thio-1,4-phenylene) (poly-(phenylene sulfide), PPS) *(12)* becomes conductive when treated with AsF$_5$[24,25,113], although the maximum values of conductivity reached so far are only of the order of 1 $\Omega^{-1}$ cm$^{-1}$. This result is of great interest, however, since PPS is the first example of a polymer which can be doped, but which is moldable and soluble. It may, therefore, independent of the conditions of the synthesis, be produced in specifically selected forms such as fibers, films or threads.

PPS is obtained industrially by reaction of dichlorobenzene with sodium sulfide in *N*-methylpyrrolidone[114,115]. It precipitates as a white powder and is soluble in high boiling solvents. Presumably, the degree of polymerization is not very large; a determination of the number of end groups resulted in values of $40 < \bar{P}_n < 130$, for material prepared using pyridine as solvent[116].

The melting point of the commercially produced polymer of density $\rho = 1.35$ g cm$^{-3}$ is reported to be 288 °C; a brownish discoloration and cross-linking is observed if the polymer is melted in air. The glass temperature is reported to be 85 °C[114].

The lattice of PPS[117] is completely destroyed by reaction with AsF$_5$. The amorphous adduct of AsF$_5$ and the constitutive units of the polymer reaches the maximum conductivity[24,113] at a molar ratio of AsF$_5$ to the polymeric building units of 1:1. *Rabolt et al.*[25] assume that a reaction of *(12)* with AsF$_5$ occurs with formation of radical cations *(13)* as follows.

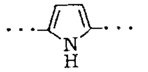


The presence of AsF$_6^{\ominus}$ ions is revealed by their characteristic IR absorption at 705 cm$^{-1}$[113].

Pure PPS is an excellent insulator ($\sigma \leq 10^{-16}$ $\Omega^{-1}$ cm$^{-1}$). Its conductivity rises exponentially in contact with AsF$_5$, as shown in Figure 12. The conductivity characteristics change in the course of the doping from that of a semiconductor to that of a semimetal. The activation energy of the conductivity is *ca.* 0.5 eV for the pure polymer and *ca.* 0.06 eV for the polymer doped to the maximum level. The colorless PPS assumes a dark blue to blue-black color in the course of reaction with AsF$_5$; a continuous absorption in the IR region, however, only develops at very large conversion. Such a continuous absorption would be expected for materials containing free and mobile charge carriers. The conductivity caused by reaction with AsF$_5$ can be destroyed by treating the doped polymers with ammonia or amines, whereby, however, the polymer seems to cross-link. The thermoelectric power (+40 μV K$^{-1}$) and the behavior in semiconductor contacts having a Schottky carrier configuration indicates that the current is maintained by positive charge carriers. There are literature reports that the structurally related polymers poly(thio-1,3-phenylene) and poly(1,4-phenylene oxide) can be reacted with AsF$_5$ and give conductive adducts as well (cf. Table 1).

### 4.3. Polypyrrole

*Kanazawa* and *Diaz et al.*[18,118,119] have described the electrochemical polymerization of pyrrole, which proceeds with simultaneous doping. When a solution of pyrrole (0.06 M) in 99% aqueous acetonitrile is electrolyzed in the presence of Et$_4$N$^{\oplus}$BF$_4^{\ominus}$ (0.1 M) as the supporting electrolyte, a blue-black film of an insoluble polymer precipitates on the anode. Its IR spectrum exhibits bands, which are characteristic of the pyrrole ring. The films contain BF$_4^{\ominus}$ ions in a molar ratio *ca.* 1:4 with respect to the pyrrole rings. The authors assume, following earlier literature data[120], that the constitutive units of the polymer are linked to each other *via* the α-C-atoms of the pyrrole rings. Consequently, the idealized structure *(14)* is proposed


*(14)*

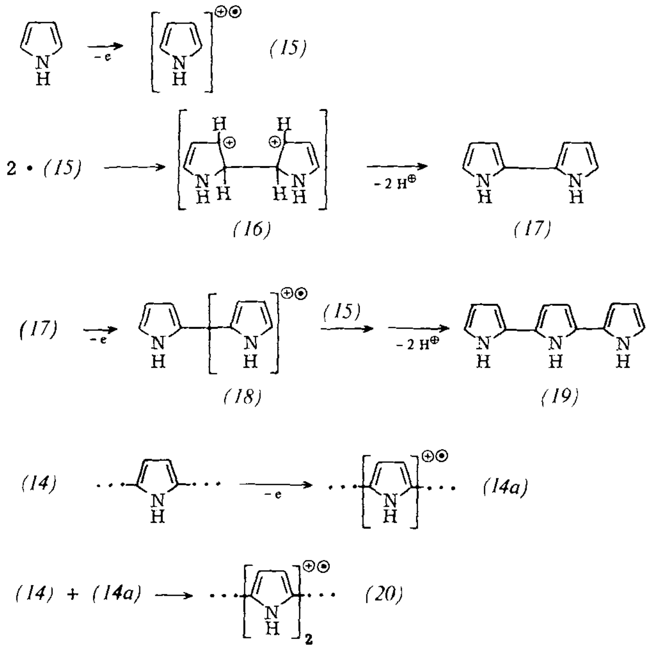
The films exhibit a conductivity of $\sigma = 100$ $\Omega^{-1}$ cm$^{-1}$, which is readily reproducible. $\sigma$ is weakly dependent on temperature and decreases from 100 $\Omega^{-1}$ cm$^{-1}$ at 300 K to 30 $\Omega^{-1}$ cm$^{-1}$ at 80 K; it is assumed that defect electrons (holes) act as the charge carriers. The conductive films of density 1.48 g cm$^{-3}$ are stable in air for long periods of time and, moreover, can be heated to temperatures approaching 100 °C without any essential alteration of their electrical properties. They are X-ray-amorphous. A diffuse halo, which is obtained by electron diffraction, corresponding to a *d*-value of 3.4 Å, is presumed to be caused by the characteristic distance between the ring planes of pyrrole rings in adjacent chains[18,118].

*N*-Methylpyrrole can be polymerized in a similar fashion, but results only in conductivities of the order of $\sigma \leq 10^{-3}$ $\Omega^{-1}$ cm$^{-1}$.

When pyrrole and *N*-methylpyrrole are copolymerized, films precipitate on the electrode whose conductivity is proportional to the composition of the copolymer between the limiting values of the two homopolymers.

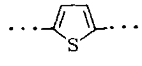
Unfortunately, little is known about the exact chemical structure of these interesting polymers or on the mechanism of their formation. One interesting observation concerns the polymerization mechanism. A polymer is not formed when Et$_4$N$^{\oplus}$Br$^{\ominus}$ is used as the supporting electrolyte. Considering the experimental results obtained in the electrocrystallization of the radical salts of simple arenes, TTF, TCNQ and similar compounds, the following reaction sequence is proposed to explain the formation of a conductive polymer film on the electrode:

Initially, the radical cation *(15)* is formed by a redox reaction; it dimerizes to the adduct *(16)* having the structure of a dication, which stabilizes itself by deprotonation to give the stable dimer of pyrrole *(17)*. This reaction may proceed with the help of excess monomer acting as a base. By subsequent oxidation of the dimer to *(18)*, combination with the radical ion of the monomer and deprotonation *(19)* is formed, and in this way the oligomer grows. Since the solubility of the oligomers decreases with increasing degree of polymerization, they finally precipitate on the electrode. There, further oxidation of the constitutive units of the polymer *(14)* to the radical cations *(14a)* takes place. These, in turn, may react with the constitutive units of an adjacent chain to form a conductive charge-transfer complex *(20)* of a similar nature to that previously discussed.



The inhibiting effect of $Et_4N^{\oplus}Br^{\ominus}$ is now explained by the trapping of the unstable dication *(16)* from which the dibromide is obtained. In contrast, $BF_4^{\ominus}$ is not sufficiently nucleophilic and, therefore, the intermediate stabilizes itself by rearomatization to *(17)*.

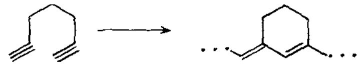
It would be unreasonable to assume that the dimerization of the radical cations occurs exclusively at the α-C-atom of the pyrrole ring. Consequently, isomeric structures, branching and cross-linking must be expected that would help to explain the insolubility and the lack of crystallinity.


*(21)*

The conductivity of poly(2,5-thienylene) *(21)*, which is structurally related to *(14)*, increases if treated with iodine[19]; the values so far measured, however, are only comparable to very poor semiconductors (cf. Table 1).

### 4.4. Additional Polyacetylenes

1,6-Heptadiyne *(22)* can be polymerized by Ziegler-catalysts[20,121]. A black film with silvery luster is obtained which, contrary to PA, does not consist of a network of individual morphological units but, rather, is presumed to be completely amorphous and homogeneous[20]. The chemical structure of the insoluble polymer is formulated in *(23)* on the basis of spectroscopic evidence. It is implicitly assumed that the monomer *(22)* reacts *via* a cyclopolymerization mechanism.


*(22)* *(23)*

The polymer *(23)* becomes conductive when doped with the reagents previously described for PA[20]; the conductivity is clearly below the values which may be reached in the case of PA (cf. Table 1) but the polymer should exhibit good thermal and oxidative stability.

Poly(phenylacetylene) (PPP) is a well known and relatively thoroughly investigated material. It is soluble, relatively stable and can be prepared as the mostly *cis*-, as well as, mostly *trans*-isomer.

The orange-red *cis*-isomer is obtained almost exclusively as an amorphous powder using $MoCl_5$ as the catalyst at reaction temperatures below 40 °C[122,123]. A polymer of mostly *trans*-structure and reddish-brown color is obtained when $WCl_6$ is used as the catalyst. Crystalline *cis*-PPA precipitates in the form of an insoluble orange-red powder in the course of polymerization with $Fe(acac)/Al(Bu)_3$ as catalyst and isomerizes at 120—130 °C to the soluble *trans*-isomer[124,125]. While a large number of other catalytically active systems have been reported[124,126,127], the mechanism of polymerization is still rather unclear. The polymers normally exhibit molecular weights of $\overline{M}_n \leq 10^4$.

Both amorphous and crystalline PPA rapidly take up halogens *e.g.* up to 50 mol% when exposed to gaseous iodine or bromine at room temperature. The conductivity rises, thereby, by 7 orders of magnitude from *ca.* $10^{-12}\ \Omega^{-1}\ cm^{-1}$ to *ca.* $10^{-5}\ \Omega^{-1}\ cm^{-1}$. The activation energy of the conductivity decreases steadily from approximately 0.8 eV to 0.2 eV with increasing iodine content[128]. The electrical behavior and the kinetics of the halogen uptake do not depend on the molecular weight.

Contrary to the behavior of PA and other conductive polymers, iodine and iodine-containing compounds separate at the anode when the d.c. conductivity is measured. All the results are in accord with the assumption that the conductivity arises *via* predominantly ionic mechanisms. It is believed that a charge-transfer complex is formed between the halogen and those segments of the polymer[129] in which mobile $I_3^{\ominus}$- or $I_5^{\ominus}$-ions provide the charge transport. The concentration dependence of σ is explained by a concentration dependent equilibrium in which the ionic charge carriers are formed[129].

It appears that the steric hindrance caused by the phenyl residues prevents the formation of stable CT-complexes between adjacent chains, in the case of PPA. Since a distance of 3.2 Å between the planes of the rings or double bonds of adjacent chains is a necessary requirement for complex formation (cf. Section 3.2 and Fig. 11), there is little hope in finding conductive complexes of unsaturated polymers with non-planar or freely rotating side groups. This may also be the reason why the production of conductive complexes by doping polydiacetylenes[130] has only recently been successful.

## 5. Future Developments

Research activities of the last three years, which have formed the main topic of the present discussion, have unambiguously demonstrated that polymers with metal-like conductivity can be realized. It is not necessary to prepare such polymers by lengthy synthesis or complicated procedures. Rather, they are obtained by extremely simple polymerizations, starting from easily prepared monomers which, in most cases, are already available on the industrial scale. Examples of such monomers are acetylene, benzene and pyrrole, among others. This fact is obviously of great importance for the further scientific and industrial development of the area.

The greatest obstacle still existing is to stabilize the level of conductivity of the doped polymers for periods of more than 24 hours. Most of the applications which might result from doped polymers require, however, the conductivity data to be constant and should approximately meet the durability of the usual plastic materials.

It should be remembered in this context, however, that many years of research and development were necessary to provide the plastics and synthetic fibers of current industrial importance with sufficient stability against autoxidation, hydrolysis and photochemical degradation. Further research in the area of conductive polymers will, therefore, primarily concentrate on how the radical ions, which have been found to be the chemical basis of the conductivity, can be stabilized. This problem cannot be solved without investigating the redox chemistry of polyunsaturated and polyaromatic compounds in much more detail; it is of major interest, as well, to investigate the influence of the counterions ("dopants") on the chemical reactivity of the conductive polymers. In this context, the relation between morphology, conductivity and chemical reactivity is of prime importance, because the doping, as well as the subsequent reactions leading to the decline of the conductivity, start as surface reactions. The future will, therefore, see many more attempts to prepare different polymer morphologies and textures which may be eventually doped and become conductive. A further interesting problem viewed from the chemical engineering point of view, is how the polymerization can proceed simultaneously with doping, by analogy with the electrochemical syntheses of polypyrrole.

Possible applications of the conductive polymers will result firstly from their rather low specific weight and secondly, from certain advantages they may have in production—provided that long term stability can be reached—compared to the current metallurgical methods. A prognosis as to what extent polymers may eventually replace metals seems unsubstantiated in the light of the presently available data. Nevertheless, one can imagine that doped polymers may soon find a limited application in certain areas of the aerospace and electronics industries.

A quite different area of application could develop from their possible usage as electrodes or components of batteries. This aspect has already been mentioned in Section 2.5. It is predominantly their low weight with high capacity and the unlimited specification with regard to possible designs which may lead to speculations or possible applications in the automobile industry.

Finally, mention should be made of the photophysics of the doped and partially doped polymers. Since the absorption bands of the conductive polymers cover a large portion of the visible spectrum, sunlight may be converted into electrical energy by photovoltaic cells composed of suitable combinations of p- and n-doped polymers. The feasibility of these ideas has been demonstrated, although the efficiency is as yet very low. As long as the problem of the long term stability of the polymers is not solved, too great an optimism is unwarranted at present. On the other hand, it should always be remembered when a prognosis is made, that very few people had the imagination and the courage to predict the current developments of, for example, semiconductor technology when the results of the first investigations into the behavior of silicon and germanium became known. In any case, further research on the electric and electronic properties of polymers with metal-like conductivity is a major and quite remarkable scientific challenge.

*For numerous discussions, suggestions and the permission to mention yet unpublished data and results, the following persons are greatly acknowledged: Dr. V. Enkelmann, Dr. C. H. Kröhnke, Dr. G. Lieser, Dr. B. Morra, Dr. W. Meyer (Zürich) and W. Müller. The Bundesministerium für Forschung und Technologie, the Stiftung Volkswagenwerk and the Fonds der Chemischen Industrie are also greatly acknowledged, for financial support of the work of the Freiburg Institute in the area of conductive polymers and organic metals.*

Received: February 19, 1981 [A 361 IE]
German version: Angew. Chem. *93*, 352 (1981)

---

[1] *H. Meier:* Organic Semiconductors. Verlag Chemie, Weinheim 1974.
[2] *Y. Okamoto, W. Brenner:* Organic Semiconductors. Reinhold Publ., New York 1964.
[3] *D. Fox, M. M. Labes, A. Weissberger:* Physics and Chemistry of the Organic Solid State. Interscience, New York 1963.
[4] *A. V. Patsis, D. A. Seanor:* Photoconductivity in Polymers – An Interdisciplinary Approach. Technomic Publ., Westport 1976.
[5] *M. Härtel, G. Kossmehl, G. Manecke, W. Wille, D. Wöhrle, D. Zerpner,* Angew. Makromol. Chem. *29/30*, 307 (1973).
[6] *E. P. Goodings,* Chem. Soc. Rev. *1977*, 95.
[7] *G. Koßmehl,* Ber. Bunsenges. Phys. Chem. *83*, 417 (1979).
[8] *H. Shirakawa, E. J. Louis, A. G. MacDiarmid, C. K. Chiang, A. J. Heeger,* J. Chem. Soc. Chem. Commun. *1977*, 578.
[9] *C. K. Chiang, Y. W. Park, A. J. Heeger, H. Shirakawa, E. J. Louis, A. G. MacDiarmid,* Phys. Rev. Lett. *39*, 1098 (1977).
[10] *C. K. Chiang, M. A. Druy, S. C. Gau, A. J. Heeger, E. J. Louis, A. G. MacDiarmid, Y. W. Park, H. Shirakawa,* J. Am. Chem. Soc. *100*, 1013 (1978).
[11] *A. G. MacDiarmid, A. J. Heeger* in *W. E. Hatfield:* Molecular Metals. Plenum Press, New York 1979, p. 161.
[12] *H. J. Keller:* Chemistry and Physics of One-Dimensional Metals. Plenum Press, New York 1977.
[13] *W. E. Hatfield:* Molecular Metals. Plenum Press, New York 1979.
[14] *L. Alcacer:* The Physics and Chemistry of Low Dimensional Solids. D. Reidel Publ., Dordrecht 1980.
[15] *M. M. Labes, P. Love, L. F. Nichols,* Chem. Rev. *79*, 1 (1979).
[16] *T. C. Clarke, R. H. Geiss, J. F. Kwak, G. B. Street,* J. Chem. Soc. Chem. Commun. *1978*, 489.
[17] *P. J. Nigrey, A. G. MacDiarmid, A. J. Heeger,* J. Chem. Soc. Chem. Commun. *1979*, 594.
[18] *K. K. Kanazawa, A. F. Diaz, R. H. Geiss, W. D. Gill, J. F. Kwak, J. A. Logan, J. F. Rabolt, G. B. Street,* J. Chem. Soc. Chem. Commun. *1979*, 854.
[19] *T. Yamamoto, K. Sanechika, A. Yamamoto,* J. Polym. Sci., Polym. Lett. Ed. *18*, 9 (1980).
[20] *H. W. Gibson, F. C. Bailey, A. J. Epstein, H. Rommelmann, J. M. Pochan,* J. Chem. Soc. Chem. Commun. *1980*, 426.
[21] *L. W. Shacklette, R. R. Chance, D. M. Ivory, G. G. Miller, R. H. Baughman,* Synth. Met. *1*, 307 (1979).
[22] *D. M. Ivory, G. G. Miller, J. M. Sowa, L. W. Shacklette, R. R. Chance, R. H. Baughman,* J. Chem. Phys. *71*, 1506 (1979).

[23] *R. H. Baughman, L. W. Shacklette, R. R. Chance, D. M. Ivory, G. G. Miller, A. F. Preziosi, M. Lahav,* Bull. Am. Phys. Soc. *25,* 314 (1980).

[24] *R. R. Chance, L. W. Shacklette, H. Eckhardt, J. M. Sowa, R. L. Elsenbaumer, D. M. Ivory, G. G. Miller, R. H. Baughman,* ACS-Meeting, San Francisco, August 1980.

[25] *J. F. Rabolt, T. C. Clarke, K. K. Kanazawa, J. R. Reynolds, G. B. Street,* J. Chem. Soc. Chem. Commun. *1980,* 347.

[26] *R. R. Chance, L. W. Shacklette, G. G. Miller, D. M. Ivory, J. M. Sowa, R. L. Elsenbaumer, R. H. Baughman,* J. Chem. Soc. Chem. Commun. *1980,* 349.

[27] *G. E. Wnek, J. C. W. Chien, F. E. Karasz, C. P. Lillya,* J. Polym. Sci. Polym. Lett. Ed. *20,* 1441 (1979).

[28] *H. Shirakawa, S. Ikeda,* Polym. J. *2,* 231 (1971).

[29] *T. Ito, H. Shirakawa, S. Ikeda,* J. Polym. Sci., Polym. Chem. Ed. *12,* 11 (1974).

[30] *G. Natta, G. Mazzanti, P. Corradini,* Atti Accad. Naz. Lincei, Cl. Sci. Fis. Mat. Nat. Rend. *25,* 2 (1958).

[31] *P. Pino,* personal communication.

[32] *H. Shirakawa, T. Ito, S. Ikeda,* Polym. J. *4,* 460 (1973).

[33] *H. Shirakawa, T. Ito, S. Ikeda,* Makromol. Chem. *179,* 1565 (1978).

[34] *T. Ito, H. Shirakawa, S. Ikeda,* J. Polym. Sci. Polym. Chem. Ed. *13,* 1943 (1975).

[35] *J. C. W. Chien, F. E. Karasz, G. E. Wnek, A. G. MacDiarmid, A. J. Heeger,* J. Polym. Sci. Polym. Lett. Ed. *18,* 45 (1980).

[36] *J. C. W. Chien, F. E. Karasz, G. E. Wnek,* Nature *285,* 390 (1980).

[37] *L. B. Luttinger,* J. Org. Chem. *27,* 1591 (1962); Chem. Ind. (London) *1960,* 1135.

[38] *V. Enkelmann, W. Müller, G. Wegner,* Synth. Met. *1,* 185 (1979/80).

[39] *G. Lieser, G. Wegner, W. Müller, V. Enkelmann,* Makromol. Chem. Rap. Commun. *1,* 621 (1980).

[40] *W. H. Watson, Jr., W. C. Mc Mordic, Jr., L. G. Lands,* J. Polym. Sci. *55,* 137 (1961).

[41] *S. Kambara, M. Hatano, T. Hosoe,* Kogyo Kagaku Zasshi *65,* 720 (1962).

[42] *M. L. H. Green, M. Nehmé, G. Wilkinson,* Chem. Ind. (London) *1960,* 1136.

[43] *W. E. Daniels,* J. Org. Chem. *29,* 2936 (1964).

[44] *H. Noguchi, S. Kambara,* J. Polym. Sci. Polym. Lett. Ed. *1,* 553 (1963).

[45] *F. Ciardelli, E. Benedetti, O. Pieroni,* Makromol. Chem. *103,* 1 (1967).

[46] *A. Job, G. Champetier,* C. R. Acad. Sci. *189,* 1089 (1929).

[47] *L. S. Merriwether,* J. Org. Chem. *26,* 5163 (1961).

[48] *P. S. Woon, M. F. Farona,* J. Polym. Sci. Polym. Chem. Ed. *12,* 1749 (1974).

[49] *A. F. Donda, G. Moretti,* J. Org. Chem. *31,* 985 (1966).

[50] *T. F. Rutledge:* Acetylenes and Allenes. Reinhold Book, New York 1969, Chapter 4–6, p. 327f.

[51] *S. Ikeda, A. Tamaki,* J. Polym. Sci. Polym. Lett. Ed. *4,* 605 (1966).

[52] *M. A. Druy, C.-H. Tsang, N. Brown, A. J. Heeger, A. G. MacDiarmid,* J. Polym. Sci. Polym. Phys. Ed. *18,* 429 (1980).

[53] *W. Müller, G. Wegner,* Makromol. Chem. Rap. Commun., in press.

[54] *H. Shirakawa, M. Sato, A. Hamano, S. Kawakami, K. Soga, S. Ikeda,* Macromolecules *13,* 457 (1980).

[55] *K. Soga, S. Kawakami, H. Shirakawa, S. Ikeda,* Makromol. Chem. Rap. Commun. *1,* 523 (1980).

[56] *K. Soga, S. Kawakami, H. Shirakawa, S. Ikeda,* Makromol. Chem. Rap. Commun. *1,* 643 (1980).

[57] *G. Wegner,* Makromol. Chem. Suppl. *4,* 155 (1981).

[58] *Y. W. Park, M. A. Druy, C. K. Chiang, A. J. Heeger, A. G. MacDiarmid, H. Shirakawa, S. Ikeda,* J. Polym. Sci. Polymer Lett. Ed. *17,* 195 (1979).

[59] *F. E. Karasz, J. C. W. Chien, R. Galkiewicz, G. E. Wnek, A. J. Heeger, A. G. MacDiarmid,* Nature *282,* 286 (1979).

[60] *R. H. Baughman, S. L. Hsu, G. P. Pez, A. J. Signorelli,* J. Chem. Phys. *68,* 5405 (1978).

[61] *R. H. Baughman, S. L. Hsu, L. R. Anderson, G. P. Pez, A. J. Signorelli,* in [13], p. 187.

[62] *W. H. Meyer,* Synth. Met., in press.

[63] *G. Lieser, G. Wegner, W. Müller, V. Enkelmann, W. H. Meyer,* Makromol. Chem. Rap. Commun. *1,* 627 (1980).

[64] *M. M. Maricq, J. S. Waugh, A. G. MacDiarmid, H. Shirakawa, A. J. Heeger,* J. Am. Chem. Soc. *100,* 7729 (1978).

[65] *G. Wegner* in [13], p. 209f.

[66] *J. C. W. Chien, G. E. Wnek, F. Karasz, J. A. Hirsch, A. G. MacDiarmid, A. J. Heeger,* J. Polym. Sci., in press.

[67] *A. G. MacDiarmid, A. J. Heeger,* Synth. Met. *1,* 101 (1980).

[68] *A. G. MacDiarmid, A. J. Heeger* in [14], p. 393f.

[69] *S. L. Hsu, A. J. Signorelli, G. P. Pez, R. H. Baughman,* J. Chem. Phys. *69,* 106 (1978).

[70] *S. Lefrant, L. S. Lichtmann, H. Temkin, D. B. Fitchen, D. C. Miller, G. E. Whitwell, J. H. Burlitch,* Solid State Commun. *29,* 191 (1979).

[71] *T. C. Clarke, G. B. Street,* Synth. Met. *1,* 119 (1980).

[72] *T. C. Clarke, R. H. Geiss, W. D. Gill, P. M. Grant, J. W. Macklin, H. Morawitz, J. F. Rabolt, D. Sayers, G. B. Street,* J. Chem. Soc. Chem. Commun. *1979,* 332.

[73] *N. Bartlett, B. Mc Quillan, A. S. Robertson,* Mater. Res. Bull. *13,* 1259 (1978).

[74] *R. S. Markiewicz, J. S. Kasper, L. V. Interrante,* Synth. Met. *2,* 363 (1980).

[75] *L. B. Ebert, J. C. Scanlon,* Ind. Eng. Chem. Prod. Res. Dev. *19,* 103 (1980).

[76] *Shek-Chung Gau, J. Milliken, A. Pron, A. G. MacDiarmid, A. J. Heeger,* J. Chem. Soc. Chem. Commun. *1979,* 662.

[77] *L. R. Anderson, G. P. Pez, S. L. Hsu,* J. Chem. Soc. Chem. Commun. *1978,* 1066.

[78] *P. J. Nigrey, A. G. MacDiarmid, A. J. Heeger,* J. Chem. Soc. Chem. Commun. *1979,* 594.

[79] *A. G. MacDiarmid,* cited in Chem. Eng. News *59* (4), 40 (1981).

[80] *A. J. Heeger, A. G. MacDiarmid* in [14], p. 353f.

[81] *H. P. Fritz, H. Gebauer, P. Friedrich, P. Ecker, R. Artes, U. Schubert,* Z. Naturforsch. *B 33,* 498 (1978).

[82] *H. P. Fritz, H. Gebauer,* Z. Naturforsch. *B 33,* 702 (1978).

[83] *Ch. Kröhnke, V. Enkelmann, G. Wegner,* Angew. Chem. *92,* 941 (1980); Angew. Chem. Int. Ed. Engl. *19,* 912 (1980).

[84] *P. Kathirgamanathan, S. A. Muckeljohn, D. R. Rosseinsky,* J. Chem. Soc. Chem. Commun. *1979,* 86; *1980,* 839.

[85] *D. Jerome, M. Ribault, K. Beechgaard,* New Sci. *1980,* 104.

[86] *G. J. Hoijtink, P. H. van der Meij,* Z. Phys. Chem. (Frankfurt) *20,* 1 (1959).

[87] *G. J. Hoijtink, E. De Boer, P. H. van der Meij, W. P. Weijland,* Recl. Trav. Chim. Pays-Bas *74,* 277 (1955); *75,* 487 (1956).

[88] *D. J. Berets, D. S. Smith,* Trans. Faraday Soc. *64,* 823 (1968).

[89a]*H. Kiess, W. Meyer, D. Baeriswyl, G. Harbecke,* J. Electron. Mater. *9,* 763 (1980); b) *J. M. Pochan, D. F. Pochan, H. Rommelmann, H. W. Gibson,* Macromolecules, *14,* 110 (1981).

[90] *K. H. Hellwege:* Einführung in die Festkörperphysik. Springer, Heidelberg 1976.

[91] *A. J. Epstein, E. M. Conwell,* Solid State Commun. *24,* 627 (1977).

[92] *T. E. Philipps, R. P. Scaringe, B. M. Hoffman, J. A. Ibers,* J. Am. Chem. Soc. *102,* 3435 (1980).

[93] *N. Karl:* Proc. 9th Mol. Cryst. Symp. Mittelberg 1980, p. 149f.

[94] *M. Weger* in [14], p. 77f.

[95] *E. M. Conwell* in [14], p. 213f.

[96] *R. C. Wheland, J. L. Gillson,* J. Am. Chem. Soc. *98,* 3916, 3926 (1976).

[97] *D. J. Sandman,* Mol. Cryst. Liqu. Cryst. *50,* 235 (1979).

[98] *J. C. W. Chien, F. E. Karasz, G. E. Wnek,* Nature *285,* 390 (1980).

[99] *M. J. Rice,* Phys. Lett. *71A,* 152 (1979).

[100] *M. J. Rice, J. Timonen,* Phys. Lett. *73A,* 368 (1979).

[101] *N. Mermilliod, L. Zuppiroli, B. François,* J. Phys. (Paris) *41,* 1453 (1980).

[102] *S. Kirkpatrick,* Rev. Mod. Phys. *45,* 574 (1973).

[103] *M. J. Stephen,* Phys. Rev. *B 17,* 4444 (1978).

[104] *P. S. Clarke, J. W. Orton, A. J. Guest,* Phys. Rev. *B 18,* 1813 (1978).

[105] *M. Lagues, C. Sauterey,* J. Phys. Chem. *84,* 3503 (1980).

[106] *J. G. Speight, P. Kovacic, F. W. Koch,* J. Macromol. Sci. *C 5,* 295 (1971).

[107] *M. B. Jones, P. Kovacic, R. F. Howe,* Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem. *21 (2),* 259 (1980).

[108] *T. Osa, A. Yildiz, T. Kuwana,* J. Am. Chem. Soc. *91,* 3994 (1969).

[109] *M. Peo, S. Roth, K. Dransfeld, B. Tieke, J. Hocker, H. Gross, A. Grupp, H. Sixl,* Solid State Commun. *35,* 119 (1980).

[110] *D. M. Gale,* J. Appl. Polym. Sci. *22,* 1955, 1971 (1978).

[111] *P. Kovacic, M. B. Feldmann, J. P. Kovacic, J. B. Lando,* J. Appl. Polym. Sci. *12,* 1735 (1968).

[112] *L. W. Shacklette, H. Eckhardt, R. R. Chance, G. G. Miller, D. M. Ivory, R. H. Baughman,* J. Chem. Phys. *73,* 4098 (1980).

[113] *R. R. Chance, L. W. Shacklette, G. G. Miller, D. M. Ivory, J. M. Sowa, R. L. Elsenbaumer, R. H. Baughman,* J. Chem. Soc. Chem. Commun. *1980,* 348.

[114] *J. N. Short, H. W. Hill, Jr.,* Chem. Technol. *2,* 481 (1972).

[115] *H. G. Elias:* Neue polymere Werkstoffe 1969–1973. Hanser, München 1975, p. 94f.

[116] *R. W. Lenz, C. E. Handlowits, H. A. Smith,* J. Polym. Sci. *58,* 351 (1962).

[117] *B. J. Tabor, E. P. Magré, J. Boon,* Eur. Polym. J. *7,* 1127 (1971).

[118] *A. F. Diaz, K. K. Kanazawa, G. P. Gardini,* J. Chem. Soc. Chem. Commun. *1979,* 635.

[119] *A. F. Diaz, J. I. Castillo,* J. Chem. Soc. Chem. Commun. *1980,* 397.

[120] *A. Dall'Olio, Y. Dascola, V. Varacca, V. Bocchi,* C. R. Acid. Sci. *C 267,* 433 (1968).

[121] *J. K. Stille, D. A. Frey,* J. Am. Chem. Soc. *83,* 1697 (1961).

[122] *T. Masuda, T. Higashimura,* Macromolecules *12,* 9 (1979).

[123] *T. Masuda, K. Hasegawa, T. Higashimura,* Macromolecules *7,* 728 (1974).

[124] *R. J. Kern,* J. Polym. Sci. Polym. Chem. Ed. *7,* 612 (1969).

[125] *C. I. Simionescu, V. Percec, S. Dumitresen,* J. Polym. Sci. Polym. Chem. Ed. *15,* 2497 (1977).

[126] *P. S. Woon, M. F. Farona,* J. Polym. Sci. Polym. Chem. Ed. *12,* 1749 (1974).

[127] *H. Noguchi, S. Kambara,* J. Polym. Sci., Polym. Lett. Ed. *1,* 553 (1963).

[128] *P. Cukor, J. I. Krugler, M. F. Rubner,* Makromol. Chem. *182,* 165 (1981).

[129] *P. S. Woon, M. F. Farona,* J. Polym. Sci. Polym. Lett. Ed. *13,* 567 (1975).

[130] *D. Bloor, C. L. Hubble, D. J. Ando* in [13], p. 249f.

[131] *V. Enkelmann*, unpublished results.
[132] *H. J. Keller, D. Nöthe, H. Pritzkow, D. Wehe, M. Werner, P. Koch, D. Schweitzer*, Mol. Cryst. Liq. Cryst. *62*, 181 (1980).
[133] A similar explanation has recently been forwarded to explain the conductivity and subsequent irreversible oxidation of PA upon treatment with oxygen: cf. [89b].

# COMMUNICATIONS

## Photochemical Hydroformylation[**]

By *Manfred J. Mirbach, Nicholaos Topalsavoglu, Tuyet Nhu Phu, Marlis F. Mirbach* and *Alfons Saus*[*]

Hydroformylation of olefins with molecular hydrogen and carbon monoxide to aldehydes is a reaction of industrial importance. We report here for the first time on the influence of light on high pressure hydroformylations catalyzed by cobalt and rhodium compounds[1]. We have found that UV irradiation leads, on the one hand, to reduction of metallic salts to catalytically active carbonyl metal compounds [eq. (a)], and, on the other, even to acceleration of the hydroformylation by increased formation of carbonyl(hydrido)metal derivatives when using carbonylmetal compounds [eq. (b)].

$$\mathrm{Co^{II}_{solv}} \xrightarrow[\mathrm{CO/H_2 + L}]{h\nu} \mathrm{HCo(CO)_3L} \qquad \text{(a)}$$

$$\mathrm{Co_2(CO)_8} + \mathrm{P}(n\mathrm{Bu})_3 \xrightarrow[\mathrm{CO/H_2}]{h\nu} \mathrm{HCo(CO)_3P}(n\mathrm{Bu})_3 \qquad \text{(b)}$$

$\mathrm{L} = \mathrm{CO}, \mathrm{P}(n\mathrm{Bu})_3$; 85 °C/80 bar; in MeOH

Infrared spectroscopy reveals that a carbonyl(hydrido)cobalt complex is formed photochemically in the presence of tri-*n*-butylphosphane and cobalt acetate, in methanol. This complex initiates the well-known catalytic cycle[2]. However, the hydrido complex, which is the active catalyst, is *not* formed in hydrocarbons (*e.g.* methylcyclohexane) where, consequently, no product is obtained[3].

Photochemically initiated hydroformylation of straight-chain 1-alkenes to the corresponding aldehydes (or acetals) features mild reaction conditions and high selectivity (Table 1). Propene, *e.g.*, can be hydroformylated to *n*-butyraldehyde with a selectivity ≥99%.

Table 1. Photochemical hydroformylation of olefins and dienes with $CO/H_2$ (1:1) at 80 bar [a].

| Entry | Starting material | Catalyst | $T$ [°C] | $t$ [h] | Product, rel. yield [%] (Conversion, %) |
|---|---|---|---|---|---|
| 1 | Propene [b] | $Co(OAc)_2/P(n\mathrm{Bu})_3$ (1:10) [d] | 85 | 30 | *n*-Butyraldehyde, 99 (20) |
| 2 | Propene [c] | $Co_2(CO)_8$ | 60 | 26 | *n*-Butyraldehyde + Acetal, 65 (25) |
| 3 | 1-Octene [b] | $Co_2(CO)_8/P(n\mathrm{Bu})_3$ (1:20) | 85 | 28 | $C_9$-Aldehydes, *n*-Nonanal, 87 (50) |
| 4 | 1-Octene [b] | $Co(OAc)_2/P(n\mathrm{Bu})_3$ (1:10) | 85 | 26 | $C_9$-Aldehydes, *n*-Nonanal, 90 (46) |
| 5 | 1-Octene [b] | $Co(OAc)_2$ | 85 | 6 | $C_9$-Aldehydes + Acetals, *n*-Isomer, 68 (80) |
| 6 | Styrene | $Co(OAc)_2/P(n\mathrm{Bu})_3$ (1:10) | 80 | — | Ethylbenzene [f] |
| 7 | Cyclohexene | $Co(OAc)_2$ | 85 | 12 | Cyclohexanecarbaldehyde + Acetal, 13 [g] |
| 8 | Norbornadiene [b, h] | $RhCl_3 \cdot 3H_2O$ | 25 | 18 | *A*, 10; *B*, 90 (99) |
| 9 | Norbornadiene [b, h] | $RhCl_3 \cdot 3H_2O + PPh_3$ [e] | 25 | 5.5 | *A*, 10; *B*, 90 (75) |
| 10 | Norbornadiene [b, h] | $HRh(CO)(PPh_3)_3$ | 25 | 4 | *A*, 20; *B*, 80 (80) |

[a] All experiments in methanol, irradiation with high pressure mercury lamp through Pyrex. [b] No reaction without irradiation. [c] Reaction rate is the same with or without irradiation. [d] 85 bar. [e] 100 bar. [f] Thermal reaction affords 3-phenylpropanal. [g] 30 h of thermal reaction affords 7% cyclohexanecarbaldehyde and acetal. [h] Products: *A* = 5-norbornene-2-carbaldehyde, *B* = bis-hydroformylation products.

No conversion is observed under the conditions of reaction 1, but without irradiation; even rhodium catalysts cannot achieve comparable preference of the straight-chain product under thermal conditions only[4]. Photochemically, 1-octene is also found to have high selectivity (≈90%) for the formation of the straight-chain product. The quantum yield $\Phi$ for the production of aldehyde using light with a wavelength of

---

[*] Dr. M. J. Mirbach [+], Dipl.-Chem. N. Topalsavoglu,
Dipl.-Chem. T. N. Phu, Dr. M. F. Mirbach, Prof. Dr. A. Saus
Fachbereich 6, Angewandte Chemie der Universität - GHS Duisburg
Lotharstrasse 55, D-4100 Duisburg (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was carried out in part at the Abteilung Strahlenchemie der Technischen Hochschule Aachen, and was supported by the Bundesministerium für Forschung und Technologie.

366 nm is 0.03 at 75 °C/80 bar $CO/H_2$. It rises with increasing synthesis gas pressure.

When using cobalt catalysts modified with phosphane the corresponding alkanes will also be obtained as by-products from 1-octene, propene and cyclohexene (10 to 15%); in the case of styrene, even hydrogenation to ethylbenzene becomes the main reaction.

It is of preparative interest that photochemical hydroformylation does not lead to formation of a deposit on the lamp shaft, which prevents practical application of many other photochemical reactions.

If $Co/PR_3$ complexes are used, the hydroformylation of 1-octene and propene is entirely photocatalytic, *i. e.* hydroformylated products are only obtained on irradiation; the reaction stops in the dark (see Fig. 1). A different behavior is observed in the absence of phosphane. Using cobalt acetate, the hydroformylation of 1-alkenes is photoinitiated, *i. e.* irradiation is required for the first two hours only, the reaction will then continue thermally. On using $Co_2(CO)_8$ as catalyst, the reaction procedes almost identically with or without irradiation.

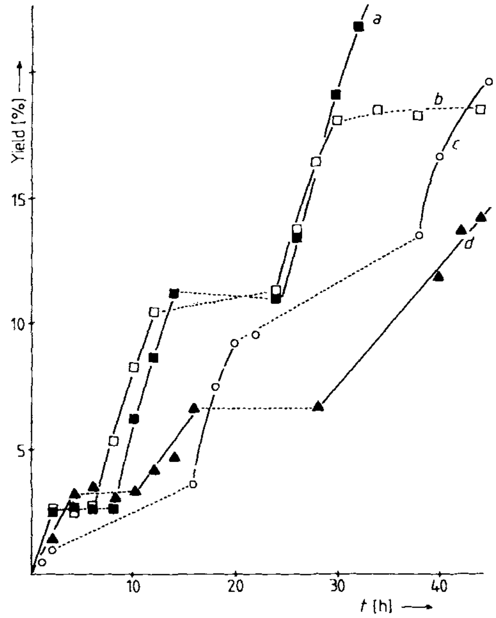
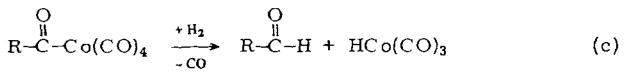


Fig. 1. Hydroformylation product yields over reaction time; (—) with UV irradiation, (···) without UV irradiation. *a:* 1-Octene/$Co_2(CO)_8/(nPBu)_3$; *b:* 1-Octene/$Co(OAc)_2/(nPBu)_3$; *c:* Cyclohexene/$Co(OAc)_2$; *d:* Propene/$Co(OAc)_2/P(nBu)_3$. Reaction conditions: 85 °C/80 bar $CO/H_2=(1:1)$, 0.017 mol/dm³ Co, 0.17 mol/dm³ $P(nBu)_3$ in methanol (500 cm³); lamp: TQ 718 (Hanau), Pyrex filter.

The different behavior depending on the kind of catalyst is explained in terms of the rate-determining step of the hydroformylation of reactive olefins with the relatively reactive catalyst $Co_2(CO)_8$ being at the end of the catalytic cycle: it is the reaction of the acyltetracarbonylcobalt complex to give aldehyde and $HCo(CO)_3$ [eq. (c)][5].



$$R-\overset{\displaystyle O}{\overset{\|}{C}}-Co(CO)_4 \xrightarrow[-CO]{+H_2} R-\overset{\displaystyle O}{\overset{\|}{C}}-H + HCo(CO)_3 \qquad (c)$$

If, on the other hand, less reactive olefins (*e.g.* cyclohexene) or less active phosphane-modified cobalt catalysts are used, the rate-determining step is at the beginning of the catalytic cycle [eq. (d)]. Apparently this step is thermally impossible under the mild conditions used.

$$Co_2(CO)_6L_2 \xrightarrow{+H_2} HCo(CO)_3L \qquad (d)$$

$$L = CO,\ P(nBu)_3$$

Without influencing the catalytic cycle itself, irradiation in the presence of CO and $H_2$ causes the reduction of cobalt acetate, which by itself is catalytically inactive, to $HCo(CO)_4$ or $HCo(CO)_3P(nBu)_3$, the real active species. The reaction continues only when sufficient hydrido complex has been formed.

Received: August 29, 1980 [Z 725 IE]
Revised: December 9, 1980
German version: Angew. Chem. *93*, 391 (1981)

CAS Registry numbers:
$HCo(CO)_4$, 16842-03-8; $HCo(CO)_3P(n\text{-}Bu)_3$, 20161-43-7; propene, 115-07-1; 1-octene, 111-66-0; styrene, 100-42-5; cyclohexene, 110-83-8; norbornadiene, 121-46-0

---

[1] The principle of the high pressure photochemical apparatus used is described in: *A. Saus*, CZ Chem. Tech. *2*, 19 (1973); *M. F. Mirbach, M. J. Mirbach, Th. Gascard*, Theses, Technische Hochschule Aachen 1976, 1976 and 1977, respectively.

[2] a) *I. Wender, H. W. Sternberg, M. Orchin*, J. Am. Chem. Soc. *75*, 3041 (1953); b) *R. F. Heck, D. S. Breslow*, Chem. Ind. *17*, 467 (1960); J. Am. Chem. Soc. *83*, 4023 (1961).

[3] For photochemical synthesis of $HCo(CO)_3PR_3$ from $Co_2(CO)_6(PR_3)_2$ in presence of silanes see *C. L. Reichel, M. S. Wrighton*, J. Am. Chem. Soc. *101*, 6769 (1979).

[4] *R. L. Pruett, J. A. Smith*, US-Pat. 3917661 (1975); *B. Cornils, R. Payer, K. C. Traenckner*, Hydrocarbon Process. *1975*, 83 (1975); *H. Siegel, W. Himmele*, Angew. Chem. *92*, 182 (1980); Angew. Chem. Int. Ed. Engl. *19*, 178 (1980).

[5] *R. Whyman*, J. Organomet. Chem. *66*, C23 (1974), *81*, 97 (1974).

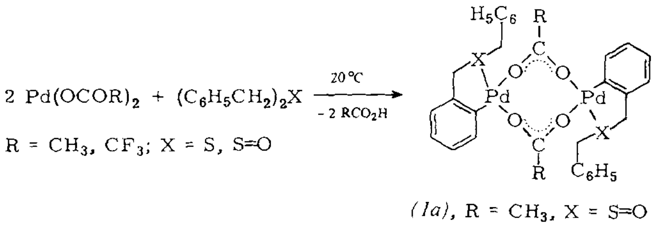
---

## *ortho*-Palladated Dibenzyl Sulfides and Sulfoxides from Palladium Carboxylates[**]

By *Reinhold Rüger, Walter Rittner* (deceased),
*Peter G. Jones, Wilhelm Isenberg*, and
*George M. Sheldrick*[*]

Organopalladium compounds, which are used in preparative chemistry and as catalysts, can often be prepared by using palladium(II) as an electrophilic reagent[1]. *ortho*-Metalation reactions can provide useful information as to the ligand dependence of the chemical reactivity of palladium(II) complexes[2].

*ortho*-Palladation reactions of amines, phosphanes and arsanes are well-known, whereas amongst sulfur compounds, they had only proved successful with arylthioketones[3,4].



*(1a)*, $R = CH_3$, $X = S{=}O$
*(1b)*, $R = CF_3$, $X = S{=}O$
*(1c)*, $R = CH_3$, $X = S$

---

[*] Prof. G. M. Sheldrick, Dr. R. Rüger, Dr. W. Rittner, Dr. P. G. Jones, W. Isenberg
Anorganisch-Chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

We have now achieved *ortho*-palladation of dibenzyl sulfoxide and dibenzyl sulfide by their reactions with palladium carboxylates.

These reactions demonstrate the advantage of palladium carboxylate complexes as metalation reagents[5]; the dimeric complexes *(1a)* and *(1b)* are obtained in good yield from dibenzyl sulfoxide and palladium(II) acetate or trifluoroacetate at room temperature. *(1c)* is obtained in an analogous manner from palladium(II) acetate and dibenzyl sulfide. The structures of *(1a)*—*(1c)* were deduced from elemental analysis, IR- and $^{1}$H-NMR-spectroscopy and confirmed by an X-ray structure determination of *(1b)* (Fig. 1).

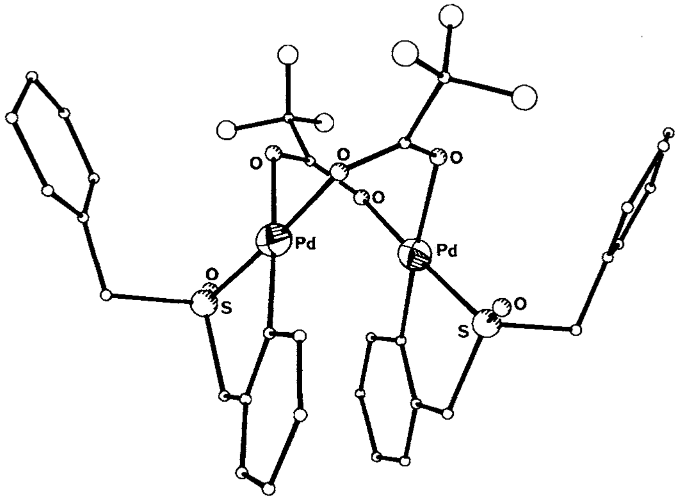


Fig. 1. Molecular structure of *(1b)* in the crystal. Monoclinic, C2/c, $a=2105(2)$, $b=1414(1)$, $c=1683(2)$ pm, $\beta=112.7(1)°$, $V=4.622$ μm$^3$, $Z=4$, $\mu=0.9$ mm$^{-1}$ (MoKα). Structure determined by heavy atom methods from 2087 diffractometer data with $F>4\sigma(F)$. Refinement (Pd, C, F, S and O anisotropic, fixed C—H bond lengths) to $R=0.14$. The high $R$ value is a result of disordered solvent and of the high thermal motion of $CF_3$ and phenyl groups.

*(1b)* crystallizes from dimethoxyethane as yellow prisms. The molecule possesses crystallographic twofold symmetry and contains two square-planar coordinated palladium atoms (Pd...Pd 289.8(3) pm). The dibenzyl sulfoxide is coordinated to the metal through the sulfur and *ortho*-carbon atom; the Pd—C bond length (194.5(2.2) pm) agrees with the sum of the covalent radii[1a]. The chelate ring angle at the metal atom is typical for this moiety (81.9(8)°)[6]. The *trans*-effect of the σ-bonded carbon is stronger than that of sulfur as is reflected in the Pd—O bond lengths. Both sulfur atoms are asymmetric centers; the structure contains the *R,R* and *S,S* forms, in which the benzyl groups are furthest apart.

The $^{1}$H-NMR spectrum of *(1a)* shows that a pair of diastereoisomers is present in solution; in the case of *(1c)* the inversion of configuration at sulfur is too fast[7] to allow this conclusion.

Received: April 22, 1980 [Z 726a IE]
German version: Angew. Chem. 93, 389 (1981)

CAS Registry numbers:
*(1a)*, 77097-07-5; *(1b)*, 77097-08-6; *(1c)*, 77123-38-7

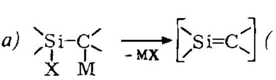
---

[1] a) *P. M. Maitlis:* The Organic Chemistry of Palladium. Vol. I and II. Academic Press, New York 1971; b) *F. R. Harley:* The Chemistry of Platinum and Palladium. Applied Science Publishers, London 1973.
[2] *M. I. Bruce,* Angew. Chem. *89*, 75 (1977); Angew. Chem. Int. Ed. Engl. *16*, 73 (1977).
[3] *J. Dehand, M. Pfeffer,* Coord. Chem. Rev. *18*, 327 (1976).
[4] a) *R. L. Bennett, M. I. Bruce, I. Matsuda,* Aust. J. Chem. *28*, 2307 (1975); b) *H. Alper,* J. Organomet. Chem. *61*, C62 (1973); c) *B. Bogdanović, C. Krüger, P. Locatelli,* Angew. Chem. *91*, 745 (1979); Angew. Chem. Int. Ed. Engl. *18*, 684 (1979).
[5] *R. Rüger,* Dissertation, Universität Göttingen 1980.
[6] Cf. [4c] and *A. J. Deeming, I. P. Rothwell, M. B. Hursthouse, L. New,* J. Chem. Soc. Dalton Trans. *1978*, 1480.
[7] *P. Haake, P. C. Turley,* J. Am. Chem. Soc. *89*, 4611, 4617 (1967).

## A 2,3,9,10-Tetraaza-1,6,8,12-tetrasila-dispiro[4.1.4.1]dodeca-3,10-diene *via* Dimerization of a Heterocycle with Exocyclic Si=C Double-Bond[**]

By *William Clegg, Uwe Klingebiel, Sabine Pohlmann, George M. Sheldrick,* and *Peter Werner*[*]

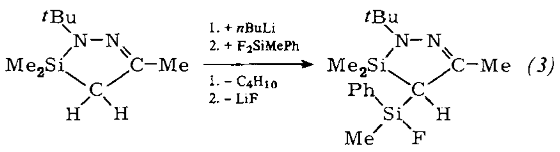
Silaethenes may be prepared in solution by elimination reactions of the type *(1a)*→*(1b)*, and identified as [2+2]-cycloadducts[1].

(1a)  (1b)

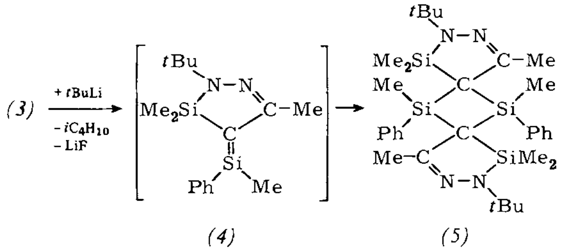
$$\underset{X}{\overset{\diagdown}{\underset{\diagup}{}}}\!\text{Si}-\underset{M}{\text{C}}\!\diagdown \xrightarrow[-MX]{} \left[\diagdown\text{Si}=\text{C}\diagdown\right]$$

X = electronegative substituent, M = alkali metal

We have obtained a novel type of compound involving the structural unit *(1b)*, by means of lithiation of the acidic methylene group of 1,2-diaza-3-sila-5-cyclopentene *(2)*[2] with *n*-butyllithium, followed by reaction with difluoro(methyl)phenylsilane to give *(3)*, and lithiation of *(3)* with subsequent elimination of LiF.

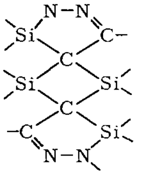


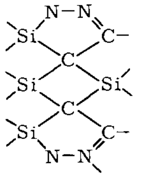
[2+2]-Cycloadducts of the intermediate 1,2-diaza-3-sila-3,5-cyclopentadienes are obtained in the reactions of fluorine-substituted 1,2-diaza-3-sila-5-cyclopentenes with organolithium reagents[3a]. However, *(3)* gives the spirocyclic product *(5)* with *tert*-butyllithium. By analogy to the formation of similar cycloadducts[3], *(5)* should be produced *via* the silanediyl-diazasilacyclopentene *(4)*.



Evidence for the existence of *(4)* comes from electron-impact (EI) and field-ionization (FI) mass spectra of *(5)*[3a]: in addition to the molecular-ion, the corresponding molecular-ion of *(4)* appeared.

(5a)





(5b)

---

[*] Prof. G. M. Sheldrick, Dr. W. Clegg, Priv.-Doz. Dr. U. Klingebiel, Dr. P. Werner, S. Pohlmann
Anorganisch-Chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Only by means of a crystal structure determination was it possible to show whether the dimer possessed the structure *(5a)* or *(5b)*, and how the substituents were arranged around the four-membered ring (Fig. 1). The two double-bonds are *trans* as in *(5a)*, but the phenyl groups on the central silicon atoms are *cis*. The middle ring is not planar (the angle between the two $Si_2C$-planes is 22.3°). In the two $SiN_2C_2$-rings the Si-atoms are displaced by 0.63 and 0.52 Å, respectively, from the plane of the other four atoms.

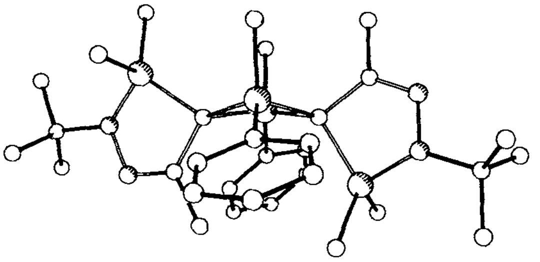


Fig. 1. Molecular structure of *(5)* in the crystal; Si- and N-atoms are shaded, H-atoms omitted. Monoclinic, $P2_1/n$, $a=11.101(2)$, $b=11.442(2)$, $c=27.806(6)$ Å, $\beta=97.56(2)°$, $Z=4$. Structure determined by direct methods from diffractometer data. Refined (Si, N, C anisotropic, H isotropic with fixed C—H bond-lengths) to $R=0.051$ for 3962 reflexions with $I>2\sigma(I)$.

*Experimental*

*(3):* A solution of 0.1 mol *(2)*[2b] in 100 $cm^3$ tetrahydrofuran is treated with 0.1 mol *n*-BuLi (15% solution in hexane) and heated for 2 h under reflux; the butane evolved is condensed in a cold trap. The resulting solution is added dropwise to 0.1 mol difluoro(methyl)phenylsilane in 100 $cm^3$ tetrahydrofuran. After evaporation of solvent, *(3)* is purified by distillation through a 30 cm Vigreux-column; yield 74%, b.p. = 112 °C/0.01 torr. A separation of the diastereoisomers (identified by NMR spectroscopy) was not successful[4].

*(5):* A solution of 0.1 mol *(3)* in 50 $cm^3$ petroleum ether is allowed to react with 0.1 mol *t*-BuLi (15% solution in pentane). After refluxing for 1 h, *(5)* is separated from solvent and LiF, and recrystallized from hexane; yield 28%, m.p. = 197 °C[5].

Received: April 10, 1980 [Z 726b IE]
German version: Angew. Chem. *93*, 390 (1981)

CAS Registry numbers:
*(2)*, 76616-34-7; *(3)*, 77080-54-7; *(5a)*, 77080-55-8; *(5b)*, 77080-56-9; difluor(methyl)phenylsilane, 328-57-4

---

[1] *N. Wiberg, G. Preiner*, Angew. Chem. *89*, 343 (1977); Angew. Chem. Int. Ed. Engl. *16*, 328 (1977).

[2] a) *U. Klingebiel, P. Werner*, Liebigs Ann. Chem. *1979*, 457; J. Organomet. Chem. *178*, 409 (1979); b) *U. Klingebiel, S. Pohlmann, P. Werner*, Liebigs Ann. Chem. 1898 (1980).

[3] a) *W. Clegg, U. Klingebiel, G. M. Sheldrick, P. Werner*, Angew. Chem. *93*, 391 (1981); Angew. Chem. Int. Ed. Engl. *20*, 384 (1981); b) *G. Märkl, P. Hofmeister, ibid. 91*, 863 (1979) and *18*, 789 (1979), resp.

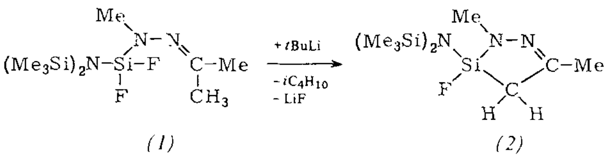
[4] *(3):* MS (70 eV): $m/e=322$ ($M^{\oplus}$, 18%); $^1H$-NMR (30% in $C_6H_6$, TMS int.): $\delta=0.07$ ($SiMe_2$), 0.14 (SiMe), 0.29 (SiMe), 0.40 (FSiMe, $J_{HF}=7.1$ Hz), 0.41 (FSiMe, $J_{HF}=7.6$ Hz, $J_{HH}=0.4$ Hz), 1.26 (*t*Bu), 1.28 (*t*-Bu), 1.67 (CH), 1.88 (CMe), 2.04 (CMe); $^{19}F$-NMR (30% in $CH_2Cl_2$, $C_6F_6$ int.): $\delta=8.3$, 9.4.

[5] *(5):* MS (70 eV): $m/e=604$ ($M^{\oplus}$, 72%), 302 ($1/2\,M^{\oplus}$, 48), 287 ($1/2\,M^{\oplus}-CH_3$, 100); $^1H$-NMR (30% solution in $C_6H_6$, TMS int.): $\delta=0.06$, 0.12 ($SiMe_2$), 0.37, 0.55 (SiMe), 1.43, 1.48 (*t*-Bu), 2.22, 2.30 (CMe).

## Synthesis and Crystal Structure of a Dimeric 1,2-Diaza-3-sila-3,5-cyclopentadiene[**]

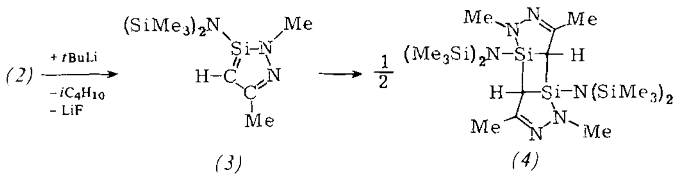
By *William Clegg, Uwe Klingebiel, George M. Sheldrick* and *Peter Werner*[*]

Substitution reactions[1] of *N*-lithiated hydrazones with fluorosilanes give products such as *(1)*. The reaction of *(1)* with organolithium derivatives leads to the substituted 1,2-diaza-3-sila-5-cyclopentene *(2)*[1]. 1,2,3-Phosphadiazoles are formed analogously from hydrazones and $PCl_3$[2]. We report here the extraction of HF from *(2)* by means of sterically hindered bases such as *tert*-butyllithium or lithium diisopropylamide (LDA).



*(1)* *(2)*

*(2)* reacts with *t*-BuLi, not with substitution of fluorine by a *tert*-butyl group, but instead with HF-elimination to give the colorless, crystalline tricyclic product *(4)*.



*(3)* *(4)*

The reaction *(2)*→*(4)* may be formulated as a dimerization of 1,2-diaza-3-sila-3,5-cyclopentadiene *(3)*, by analogy with the HCl-elimination from 1-chloro-1-sila-2,4-cyclohexadiene[3], which results in dimeric silabenzene. The electron-impact (EI) and field-ionization (FI) mass spectra of *(4)* provide evidence for the existence of *(3)*. The EI-spectrum of *(4)* shows a base-peak at $m/e=271$, corresponding to a fragment with the molecular weight of *(3)*. In the FI-spectrum of *(4)*

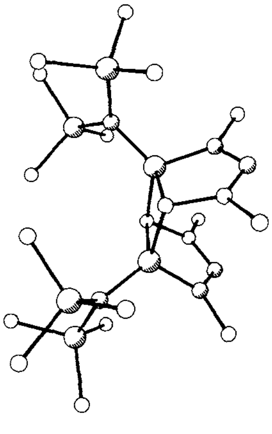


Fig. 1. Molecular structure of *(4)* in the crystal; Si- and N-atoms shaded, H-atoms omitted. Monoclinic, $P2_1/n$, $a=9.263(2)$, $b=15.960(3)$, $c=22.592(5)$ Å, $\beta=99.30(2)°$, $Z=4$. Structure determined by direct methods from diffractometer data. Refined (Si, N and C anisotropic, H isotropic, fixed C—H bond-lengths) to $R=0.051$ for 4191 reflexions with $I>2\sigma(I)$.

---

[*] Prof. G. M. Sheldrick, Dr. W. Clegg, Priv.-Doz. Dr. U. Klingebiel, Dr. P. Werner
Anorganisch-Chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

both $M^{\oplus}$ and *(3)*$^{\oplus}$ are observed. Attempts to stabilize a 1,2-diaza-3-sila-3,5-cyclopentadiene by means of bulkier substituents have so far been unsuccessful.

The crystal structure determination of *(4)* (Fig. 1) shows that the three rings are almost planar (largest deviation from the calculated plane: 0.051 Å). The $SiN_2C_2$-rings are attached to the same side of the central ring, and the interplanar angles are 114.4° and 114.8°, respectively.

## *Experimental*

*(1)*: 0.1 mol acetonemethylhydrazone in 100 $cm^3$ tetrahydrofuran (THF) is lithiated with the equimolar amount of *n*-BuLi (15% solution in hexane), and the resulting solution added dropwise to 0.1 mol trifluoro[bis(trimethylsilyl)amino]silane in 100 $cm^3$ petroleum ether. After heating for 2 h under reflux the product is separated from the LiF residue and distilled through a 20 cm Vigreux-column; yield 86%, b.p. = 104 °C/13 torr[4].

*(2)*: 0.05 mol *(1)* in 50 $cm^3$ is treated with an equimolar quantity of *t*-BuLi (15% solution in *n*-pentane); the isobutane evolved is condensed in a cold trap. After refluxing for 2 h and separation from the LiF residue the sample is fractionally distilled through a 20 cm Vigreux-column. *(4)* is already present as a by-product; unreacted *(1)* may be recovered. *(1)* and *(2)* (yield 24%, b.p. = 40 °C/0.05 torr)[5] were separated by gas-chromatography (SE 30, V2A steel column, 4 m, 3/8″, 195 °C, helium).

*(4)*: 0.05 mol *(2)* in 50 $cm^3$ tetrahydrofuran is treated with an equimolar amount of *t*-BuLi (15% solution in *n*-pentane) and refluxed for 2 h. The product is recrystallized from petroleum ether; yield *ca.* 30%, m.p. = 146 °C[6].

Received: April 10, 1980 [Z 726c IE]
German version: Angew. Chem. 93, 391 (1981)

CAS Registry numbers:
*(1)*, 77080-36-5; *(2)*, 77080-37-6; *(4)*, 77080-38-7; acetonemethylhydrazone, 5771-02-8; trifluoro[bis(trimethylsilyl)amino]silane, 2251-47-0

---

[1] a) *U. Klingebiel, P. Werner,* Liebigs Ann. Chem. *1979*, 457; J. Organomet. Chem. *178*, 409 (1979); b) *W. Clegg, M. Noltemeyer, G. M. Sheldrick,* Acta Crystallogr. *B 35*, 2243 (1979).

[2] a) *A. F. Vasilev, L. V. Vilkov, N. P. Ignatova, N. N. Mel'nikov, V. V. Negrebetskii, N. J. Shvetsov-Shilovskii, L. S. Khaikin,* Dokl. Akad. Nauk SSSR *183*, 945 (1968); b) *N. P. Ignatova, N. N. Mel'nikov, N. J. Shvetsov-Shilovskii,* Geterotsikl. Soedin. *4*, 753 (1967).

[3] *G. Märkl, P. Hofmeister,* Angew. Chem. *91*, 863 (1979); Angew. Chem. Int. Ed. Engl. *18*, 789 (1979) and references cited therein.

[4] *(1)*: MS (70 eV): $m/e = 311$ ($M^{\oplus}$, 85%); $^1$H-NMR ($CH_2Cl_2$, TMS int.): $\delta = 0.25$ ($SiMe_3$, $J_{HF} = 0.95$ Hz), 1.91 (CMe, $J_{HF} = 0.75$ Hz), 1.96 (CMe), 2.95 (NMe, $J_{HF} = 1.3$ Hz); $^{19}$F-NMR ($C_6F_6$ int.): $\delta = 29.88$; $^{29}$Si-NMR ($CH_2Cl_2$/$C_6F_6$, TMS int.): $\delta = -67.2$ ($SiF_2$, $J_{SiF_2} = 226.3$ Hz), 6.8 ($SiMe_3$, $J_{SiF} = 1.1$ Hz).

[5] *(2)*: MS (70 eV): $m/e = 291$ ($M^{\oplus}$, 100%); $^1$H-NMR ($CH_2Cl_2$, TMS int.): $\delta = 0.20$ ($SiMe_3$, $J_{HF} = 1.3$ Hz), 1.39 ($CH_2$, $J_{HF} = 10.5$ Hz), 1.91 (CMe), 2.97 (NMe, $J_{HF} = 1.9$ Hz); $^{19}$F-NMR ($C_6F_6$ int.): $\delta = 42.28$; $^{29}$Si-NMR ($CH_2Cl_2$/$C_6F_6$, TMS int.): $\delta = -13.23$ (SiF, $J_{SiF} = 279.88$ Hz), 5.64 ($SiMe_3$, $J_{SiF} = 4.22$ Hz).

[6] *(4)*: MS (70 eV): $m/e = 542$ ($M^{\oplus}$, 66%), 271 ($1/2\,M^{\oplus}$, 100%); $^1$H-NMR ($CH_2Cl_2$, TMS int.): $\delta = 0.25$ ($SiMe_3$), 1.92 (CMe), 2.19 (CH), 2.90 (NMe); $^{29}$Si-NMR ($CH_2Cl_2$, $C_6F_6$, TMS int.): $\delta = -9.48$ ($C_2SiN_2$), 5.83 ($SiMe_3$).

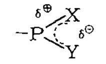
# 1,2λ$^3$,3λ$^3$-Azadiphosphiridines[**]

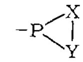
By *Edgar Niecke, Anke Nickloweit-Lüke,*
and *Reinhold Rüger*[*]

We recently demonstrated that phosphorus compounds of the ylidic type (*A*) and cyclic type (*B*) can be generated from isoelectronic precursors[1].

The possibility implied by this of a valence isomerization, which might occur by lowering the energy barrier of the conversion (*A*)→(*B*), stimulated investigations directed at the synthesis of the as yet unknown P—P—N system. Other than in the case of the previously described element-phosphorus-nitrogen compounds, for which the noncyclic dipolar structure (*A*), X = N—, proved to be energetically more favorable[2], a destabilization of the "homo-allyl-anion system" is to be expected for a derivative with X = N—, Y = P—.

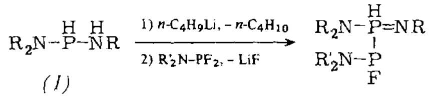
(*A*)





(*B*)

For elimination reactions, we obtained suitable precursors by metalation of the secondary aminophosphane *(1)*[3] and subsequent reaction with aminodifluorophosphanes. This reaction leads to P—P-bonding and formation of the phosphoranes *(2a)* and *(2b)*[4].



$$R_2N{-}\overset{H}{P}{-}\overset{H}{N}R \xrightarrow[2)\ R'_2N{-}PF_2,\ -LiF]{1)\ n\text{-}C_4H_9Li,\ -n\text{-}C_4H_{10}} \begin{array}{l} R_2N{-}\overset{H}{P}{=}NR \\ \quad\ \ | \\ R'_2N{-}\underset{F}{P} \end{array}$$

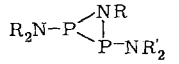
*(1)*

R = $SiMe_3$

*(2a)*, R' = $SiMe_3$
*(2b)*, R' = $CHMe_2$

Base-induced "HF"-elimination then affords *(3a)* and *(3b)* respectively, as could be demonstrated by elemental analysis and mass spectroscopy[5].

*(2a, b)* $\xrightarrow[-\,CH_4,\ -\,LiF]{CH_3Li}$



*(3a, b)*

From the NMR-data (Table 1) it is obvious that the products *(3a)* and *(3b)* are azaphosphiridines, *i. e.* compounds of type *(B)*.

Table 1. $^{31}$P-, $^1$H-, $^{13}$C-, and $^{29}$Si-NMR data of the 1,2λ$^3$,3λ$^3$-azadiphosphiridines *(3a)* and *(3b)* [a].

| | | *(3a)* | *(3b)* |
|---|---|---|---|
| $\delta(^{31}P)$ | ($^1J_{P_AP_B}$ [Hz]) | | |
| | | −67.2 | −71.1<br>−78.9 (215) |
| $\delta(^1H)$ | ($\lvert J_{HP}+J_{HP'}\rvert$ and $\lvert J_{HP_A}+J_{HP_B}\rvert$ [Hz]) | | |
| | $PPN(SiMe_3)_2$ | 0.22 (2.6) | 0.23 [c] |
| | $P_2NSiMe_3$ | 0.25 (0.5) | 0.25 [c] |
| | PPNCH | — | 2.87 (7) |
| | PPNCMe [b] | — | 1.13 [d] |
| | PPNCMe [b] | — | 1.05 [d] |
| $\delta(^{13}C)$ | ($\lvert J_{CP}+J_{CP'}\rvert$ and $\lvert J_{CP_A}+J_{CP_B}\rvert$ [Hz]) | | |
| | $PPN(SiC_3)_2$ | 4.6 (14.4) | 4.5 (12.5) |
| | $P_2NSiC_3$ | 2.4 (1.8) | 1.8 (3.1) |
| | PPNC | — | 43.3 (18.3) |
| | PPNCC [b] | — | 23.8 (4.1) |
| | PPNCC [b] | — | 24.2 (3.8) |
| $\delta(^{29}Si)$ | ($\lvert J_{SiP}+J_{SiP'}\rvert$ and $\lvert J_{SiP_A}+J_{SiP_B}\rvert$ [Hz]) | | |
| | $PPNSi_2$ | 4.0 (14.0) | 3.8 (9.6) |
| | $P_2NSi$ | 4.7 (1.4) | 4.8 (< 1.0) |

[a] 30% in $CDCl_3$, $H_3PO_4$ as external ($^{31}$P) or TMS as internal standard ($^1$H, $^{13}$C, $^{29}$Si), 28 °C. [b] Anisochronous methyl groups in a prochiral moiety. [c] Not resolved. [d] $^3J_{HH} = 6.7$ Hz.

In the $^{31}P\{^1H\}$-NMR-spectra, the cyclic arrangement of the phosphorus atoms follows from their chemical equivalence [*(3a)*], from the similar position of their signals [*(3b)*] ($\Delta\delta_{AB} = 7.8$ ppm), and from the typical high field shift of the signals. In the $^1$H-, $^{13}C\{^1H\}$-, and $^{29}Si\{^1H\}$-NMR spectra, the substituents give rise to pseudotriplets and pseudo-

---

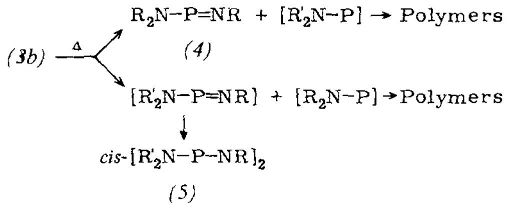
[*] Prof. Dr. E. Niecke, A. Nickloweit-Lüke, Dr. R. Rüger
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld 1 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie, the local government of NRW, and by gifts of chemicals from Bayer AG, Leverkusen.

doublets, respectively. In contrast to the correspondingly *(3a)* substituted diazadiphosphetidine $[R_2N—P—NR]_2$[6] the bis(trimethylsilyl)amino groups in *(3a, b)* can rotate freely, in accord with the steric relief on going from the four- to the three-membered ring.

The configuration of *(3a, b)* cannot be deduced from NMR-data, but the *trans* arrangement of the amino groups is favored by steric arguments.

The remarkably high kinetic stability of *(3a)* may be explained by the presence of two bis(trimethylsilyl)amino groups, which are sterically and electronically stabilizing, as well as by the high symmetry of the molecule[7]. Formal substitution of a $(Me_3Si)_2N$-group by a $(Me_2CH)_2N$-group leads to a perceptible destabilization, manifesting itself in a noticeable amount of [2 + 1]-cycloreversion of *(3b)* above 50 °C, the non-polymeric reaction products of the cycloreversion being [bis(trimethylsilyl)amino](trimethylsilylimino)phosphane *(4)* as well as the dimer *(5)* of diisopropylamino(trimethylsilylimino)phosphane[8].



In the series of three-membered ring systems of type *(B)*, X = P—[9], the 1,2λ$^3$,3λ$^3$-azadiphosphiridines are the first representatives with an electronegative element in the ring (Y = N—). In comparison with the open ylide arrangement, *(A)* (X = N—, Y = P—) such a ring system could be destabilized by "push pull" substituents at the phosphorus atoms in *(3)*.

*Experimental:*

*(1)* (8.5 g, 30 mmol) is metalated with an equivalent amount of *n*-butyllithium in *n*-hexane (50 ml) at −80 °C. After addition of 30 mmol [bis(trimethylsilyl)amino]-, or (diisopropylamino)difluorophosphane, the reaction mixture is allowed to warm up to room temperature with continuous stirring. Subsequently the mixture is metalated once again at 0 °C with 30 mmol of methyllithium, (5% in diethyl ether) and stirred for another 24 h. Evaporation of the mixture furnishes a crude product (*ca.* 70% yield), which is purified by repeated distillation[10]. 5.5 g of *(3a)* (40% yield, b.p. 112–115 °C/0.5 torr) or 3.7 g of *(3b)* (35% yield, b.p. 95—100 °C/0.5 torr) is obtained.

Received: September 22, 1980 [Z 727 IE]
German version: Angew. Chem. *93*, 406 (1981)

CAS Registry numbers:
*(1)*, 63104-54-1; *(2a)*, 77080-39-8; *(2b)*, 77080-40-1; *trans-(3a)*, 77080-41-2; *trans-(3b)*, 77080-42-3; *(4)*, 50732-21-3; *cis-(5)*, 66435-33-4; [bis(trimethylsilyl)amino]difluorophosphane, 50732-22-4; (diisopropylamino)difluorophosphane, 921-27-7

---

[1] *E. Niecke, W. Schoeller, D. A. Wildbredt*, Angew. Chem. *93*, 119 (1981); Angew. Chem. Int. Ed. Engl. *20*, 131 (1981).

[2] Reviews: *E. Niecke, O. J. Scherer*, Nachr. Chem. Tech. *23*, 395 (1975); *F. H. Westheimer*, Chem. Soc. Spec. Publ. *8*, 180 (1957); *E. Niecke, D. A. Wildbredt*, Angew. Chem. *90*, 209 (1978); Angew. Chem. Int. Ed. Engl. *17*, 199 (1978). Noted added in proof: In the imino(methylene)phosphorane system *(A)*, X = NR′, Y = CHR a valence isomerization to the 1,2λ$^3$-azaphosphiridine could recently be observed; *E. Niecke, A. Seyer, D. A. Wildbredt*, Angew. Chem., in press.

[3] *E. Niecke, G. Ringel*, Angew. Chem. *89*, 501 (1977); Angew. Chem. Int. Ed. Engl. *16*, 486 (1977).

[4] *(2a)*: $^{31}$P-NMR: $\delta = 172.9$ (*P*F—PH), $^1J_{PF} = 965$, $^1J_{PP} = 276.5$, $^2J_{PH} = 6.5$ Hz; −4.5 (PF—*P*H), $^1J_{PH} = 425.5$, $^2J_{PF} = 74.2$ Hz. *(2b)*: $^{31}$P-NMR: $\delta = 147.4$ (*P*F—PH), $^1J_{PF} = 941$, $^1J_{PP} = 199.5$, $^2J_{PH} = 5$ Hz; −11.3 (PF—*P*H), $^1J_{PH} = 429.5$, $^2J_{PF} = 103.3$ Hz.

[5] *(3a)*: MS (70 eV): $m/e = 469$ ($M^{\oplus}$, 11%), 263 ($M^{\oplus} - R'_2N - Me$, 100%).

[6] *E. Niecke, W. Flick, S. Pohl*, Angew. Chem. *88*, 305 (1976); Angew. Chem. Int. Ed. Engl. *15*, 309 (1976).

[7] The azadiphosphiridine $[(Me_2CH)_2N—P]_2NCMe_3$, available *via* another route, is likewise stable; *E. Niecke, A. Nickloweit-Lüke, R. Rüger, B. Krebs, H. Grewe*, unpublished results.

[8] *O. J. Scherer, W. Glässel*, Chem. Ber. *110*, 3874 (1977).

[9] *M. Baudler*, Pure and Applied Chemistry *52*, 755 (1980), and references cited therein.

[10] Because of its thermolability, *(3b)* is always contaminated with small amounts of *(4)* and *(5)*.

---

## Photochemical Formation of and Ligand Exchange in a Cationic Dithiolatonickel Complex[**]

By *Arnd Vogler* and *Horst Kunkely*[*]

Numerous anionic and neutral transition metal complexes containing 1,2-dithiolato ligands have already been synthesized and characterized[1]. They can be reduced and oxidized reversibly. In many cases only the dithiolato ligands and not the central metal take part in the redox reactions. Electrochemical investigations have shown that cationic complexes can be obtained reversibly for a brief period of time[2]. We now report on the photochemical formation of a cationic dithiolato complex which at low temperatures is stable and at room temperature immediately undergoes a unique ligand exchange.

*cis*-1,2-Diphenylethylene-1,2-dithiolato(1,10-phenanthroline)nickel(II) *(1)*[2] is virtually insensitive to light in most solvents, whereas in chlorinated solvents it is photolyzed by light of wavelength λ < 450 nm. The quantum yield for disappearance of *(1)* is Φ = 0.003 (λ = 366 nm). All previously investigated photoreactions of metal-complexes which exclusively take place in chlorinated solvents are photooxidations[3]. We have found that *(1)* also reacts in this way:

$$\underset{(1)}{[\mathrm{Ni^{II}(phen)(S_2C_2Ph_2)}]} + \mathrm{CHCl_3} \rightarrow \underset{(1)^{\oplus}}{[\mathrm{Ni^{II}(phen)(S_2C_2Ph_2)}]^{\oplus}} + \mathrm{Cl}^{\ominus} + {}^{\odot}\mathrm{CHCl_2}$$

The complex cation *(1)*$^{\oplus}$ is stable only at low temperatures. During the photolysis of *(1)* in toluene/$CHCl_3$-glass (50:50) at 77 K it could be characterized by its ESR spectrum. Regarding electron distribution *(1)* is best described as a nickel complex containing the neutral 1,10-phenanthroline and the readily oxidizable *cis*-1,2-diphenylethylene-1,2-dithiolate dianion as ligands[2]. Consistent with this concept, the ESR signal of *(1)*$^{\oplus}$, which with $g = 2.0093$ approximates the signal of a free electron, can only be assigned to the monoanion of the dithiolato ligand.

During the photolysis of *(1)* in $CHCl_3$ at room temperature, spectral changes were observed (Fig. 1) which indicate that *(1)*$^{\oplus}$ immediately and quantitatively undergoes a novel ligand exchange with formation of the symmetric complexes

---

[*] Prof. Dr. A. Vogler, Dr. H. Kunkely
Institut für Anorganische Chemie der Universität
Postfach, D-8400 Regensburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

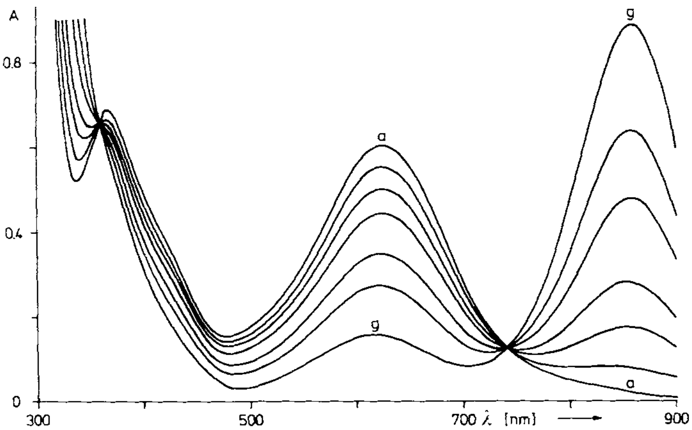


Fig. 1. Change in absorption spectrum during the photolysis of *(1)* ($1.02 \times 10^{-4}$ mol/dm$^3$) in $CHCl_3$ in a 1 cm cuvette. Excitation light: $\lambda > 350$ nm; duration of irradiation: $a = 0$, $g = 150$ min.

*(2)*[4] and *(3)*[5] in accordance with

$$\underset{(1)^{\oplus}}{2[Ni^{II}(phen)(S_2C_2Ph_2)]^{\oplus}} \rightarrow \underset{(2)}{[Ni^{II}(S_2C_2Ph_2)_2]} + \underset{(3)}{[Ni^{II}(phen)_2]^{2\oplus}}$$

Some unsymmetric, mixed dithiolato complexes have already been prepared from the symmetric complexes on reversal of this reaction[2,6]. These ligand-exchange reactions, however, proceed very slowly and require hours to days. Probably dinuclear complexes are formed as intermediates, as is often the case in solid dithiolato complexes[1].

Received: September 23, 1980 [Z 728 IE]
German version: Angew. Chem. *93*, 399 (1981)

CAS Registry numbers:
*(1)*, 42594-02-5; *(1)*$^{\oplus}$, 77097-47-3; *(2)*, 28984-20-5; *(3)*, 28293-66-5

---

[1] Review: *J. A. McCleverty*, Prog. Inorg. Chem. *10*, 49 (1968); *E. Hoyer, W. Dietzsch, W. Schroth*, Z. Chem. *11*, 41 (1971).
[2] *T. R. Miller, I. G. Dance*, J. Am. Chem. Soc. *95*, 6970 (1973).
[3] *K. R. Mann, H. B. Gray, G. S. Hammond*, J. Am. Chem. Soc. *99*, 306 (1977); *A. Vogler, W. Losse, H. Kunkely*, J. Chem. Soc. Chem. Commun. *1979*, 187; *A. Vogler, H. Kunkely*, Angew. Chem. *92*, 228 (1980); Angew. Chem. Int. Ed. Engl. *19*, 221 (1980).
[4] *G. N. Schrauzer, V. P. Mayweg*, J. Am. Chem. Soc. *87*, 1484 (1965).
[5] *C. M. Harris, E. D. McKenzie*, J. Inorg. Nucl. Chem. *29*, 1047 (1967).
[6] *A. Davison, J. A. McCleverty, E. T. Shawl, E. J. Wharton*, J. Am. Chem. Soc. *89*, 830 (1967).

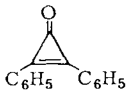
---

## Reaction of Dicarbonyl(cyclopentadienyl)(isobutene)iron Tetrafluoroborate with Diphenylcyclopropenone: Complexation without Ring Opening[**]

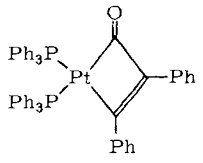
By *James B. Woell* and *Philip Boudjouk*[*]

Interest in organotransition metal complexes of cyclopropenones stems from suggestions[1] that they may be involved as intermediates in carbonylation reactions of acetylenes. Prior to this work however, isolation and characterization of such complexes have been unsuccessful[2] because the reactions of cyclopropenones with transition metal organometallic reagents typically lead to ring opening and/or the formation of complexes too unstable[2b] or too insoluble[2c] to obtain good data.

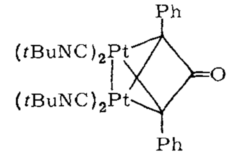
For example, tetracarbonylnickel and diphenylcyclopropenone *(1)* in benzene gave diphenylacetylene, tetracyclone and a novel π complex of tetracyclone[2a] while reactions with carbonyliron compounds produced derivatives of tetracarbonylferra-3-cyclopentene-2,5-dione in addition to tricarbonyliron complexes of diphenylacetylene and tetracyclone[2b]. Octacarbonyldicobalt and *(1)* formed an unstable salt formulated as $[(diphenylcyclopropenone)_6Co][Co(CO)_4]_2$ which generated hexacarbonyl(diphenylacetylene)dicobalt upon warming[2b]. The mode of bonding between *(1)* and cobalt was not determined.



*(1)*



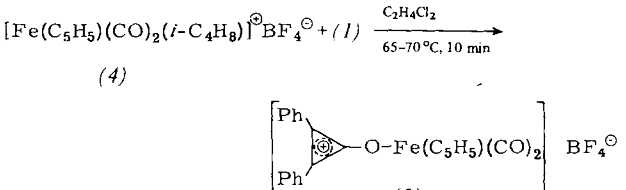
*(2)*



*(3)*

More recently, investigations of reactions of *(1)* with organoplatinum complexes have led to the synthesis of novel metallacycles; for example, *(2)* was obtained from *(1)* and $Pt(PPh_3)_4$ *via* insertion of platinum into the C—C bond of *(1)*[2d], while cleavage of the C=C linkage in *(1)*, accomplished by $Pt_3(tBuNC)_6$, gave the interesting dinuclear complex *(3)*[2e].

We have now been able to prepare dicarbonyl(cyclopentadienyl)(diphenylcyclopropenone)iron tetrafluoroborate *(5)* in 53% crude yield by treating dicarbonyl(cyclopentadienyl)(isobutene)iron tetrafluoroborate *(4)* with an excess of *(1)* in dichloroethane. Analytically pure samples of *(5)* were obtained as an air-stable red powder by recrystallization from $CH_2Cl_2$/ether.



The structural assignment is based mainly on spectroscopic data. The IR spectrum of *(5)* shows three carbonyl bands, two of which (at 2053 and 2004 cm$^{-1}$) are assigned to the carbon monoxide ligands at the iron, and one (at 1555 cm$^{-1}$) to the C=O group of the diphenylcyclopropenone. The corresponding band in free *(1)* appears at 1640 cm$^{-1}$[4]. This shift is larger than those observed for *(1)* upon its coordination to Lewis acids and hydrogen bonding solvents[2c,4b] but is similar to that in dicarbonyl(cyclopentadienyl)iron complexes of other organic carbonyl compounds[5]. The $^1$H-NMR spectrum is also consistent with structure *(5)* [($CD_3CN$, 0°): $\delta = 8.37$—8.03 (m, 4H), 8.03—7.63 (m, 6H), 5.50 (s, 5H)]. The UV-VIS spectrum [($CH_3CN$): $\lambda = 226$ ($\log\varepsilon = 4.77$), 286 (4.72), 296 (4.73), 312 cm$^{-1}$ sh] resembles that of *(1)*[6]. The diphenylcyclopropenone ligand in *(5)* is displaced by $CH_3CN$ ($t_{1/2} \approx 45$ min at 20 °C).

Received: September 8, 1980 [Z 729 IE]
German version: Angew. Chem. *93*, 412 (1981)

CAS Registry numbers:
*(1)*, 886-38-4; *(4)*, 41707-16-8; *(5)*, 77097-10-0

---

[*] Prof. Dr. P. Boudjouk, J. B. Woell
Department of Chemistry, North Dakota State University
Fargo, North Dakota 58105 (USA)

[**] The work was supported in part with funds provided by the Research Corporation and the U.S. Department of the Interior, Office of Water Research and Technology.

[1] *W. Reppe*, Justus Liebigs Ann. Chem. *582*, 1 (1953); *F. Basolo, R. G. Pearson:* Mechanisms of Inorganic Reactions. Wiley, New York 1958; *L. E. Orgel*, Chem. Soc. Spec. Publ. *13*, 93 (1959).

[2] a) *C. W. Bird, J. Hudec*, Chem. Ind. (London) *1959*, 570; *1964*, 1362; *C. W. Bird, E. M. Briggs*, J. Organomet. Chem. *69*, 311 (1974); b) *C. W. Bird, E. M. Briggs, J. Hudec*, J. Chem. Soc. *C 1967*, 1862; c) *C. W. Bird, E. M. Briggs*, J. Chem. Soc. *A 1967*, 1004; d) *W. Wong, S. J. Singer, W. D. Pitts, S. F. Watkins, W. H. Baddley*, J. Chem. Soc. Chem. Commun. *1972*, 672; e) *W. E. Carroll, M. Green, J. A. K. Howard, M. Pfeffer, F. G. A. Stone*, Angew. Chem. *89*, 838 (1977); Angew. Chem. Int. Ed. Engl. *16*, 793 (1977).

[3] *A. Cutter, D. Ehntholt, W. P. Giering, P. Lennon, S. Raghu, A. Rosan, M. Rosenblum*, J. Am. Chem. Soc. *98*, 3495 (1976).

[4] a) *S. Andreades*, J. Am. Chem. Soc. *87*, 3941 (1965); b) *A. Krebs, B. Schrader*, Z. Naturforsch. *B 21*, 194 (1966).

[5] *B. M. Foxman, P. T. Klemarczyk, R. E. Liptrot, M. Rosenblum*, J. Organomet. Chem. *187*, 253 (1980).

[6] *R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, J. Posner*, J. Am. Chem. Soc. *87*, 1320 (1965).

## A Novel Carbonyldiniobium Complex with Hydrogen Bridge[**]

By *Wolfgang A. Herrmann, Helmut Biersack, Manfred L. Ziegler*, and *Peter Wülknitz*[*]

Despite the wide variety of structural types of carbonylmetal compounds already known, only a vanishingly small number of polynuclear complexes of Group 5 elements have so far been reported[1]. The development of efficient methods for the synthesis of the half-sandwich complex *(1)*[2] has now enabled us to synthesize the first homodinuclear carbonylniobium compound having a hydrogen bridge.

Upon irradiation of *(1)* and bis($\eta^5$-cyclopentadienyl)trihydridoniobium *(2)* in tetrahydrofuran (THF) at −15 °C and subsequent column-chromatography of the crude product we obtained a crystalline, shiny-black, diamagnetic neutral complex *(3)*, which is thermally stable up to *ca.* 70 °C. This complex is air-stable in the solid state for a short period of time; in solution, however, it is extremely sensitive to oxygen.

$$\underset{(1)}{(\eta^5\text{-}C_5H_5)Nb(CO)_4} + \underset{(2)}{(\eta^5\text{-}C_5H_5)_2NbH_3} \xrightarrow[-H_2]{h\nu} \underset{(3)}{(\eta^5\text{-}C_5H_5)_3Nb_2(CO)_4H}$$

The composition of *(3)* is confirmed by elemental analysis, and by its IR and NMR spectra[7]. A conclusive elucidation of the structure, however, proved impossible from these data; therefore a single-crystal structure analysis was carried out.

Figure 1 shows that the dinuclear complex *(3)* consists of a ($\eta^5$-$C_5H_5$)Nb(CO)$_3$ fragment and a ($\eta^5$-$C_5H_5$)$_2$Nb(CO) unit, the latter formed by CO transfer, which are linked together by a bent hydrogen bond. Consistent with current opinions on metal-bridged hydrido functions the Nb—H—Nb unit might best be described, regarding the distribution of electrons, in terms of a three center bonding model[3,4]. The intermetal distance (373.8(3) pm) considerably exceeds the value to be expected on the basis of the atomic radii (294 pm[5]) and the bond lengths found in ($\eta^5$-$C_5H_5$)$_3$Nb$_3$(CO)$_7$ (304—332 pm[1b]); this is a further example of the well-documented bond lengthening effect which metal-to-metal bonds generally experience when bridged by hydrogen functionalities[4,6].

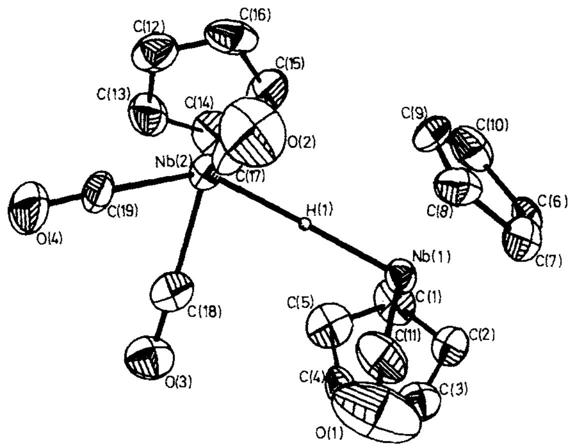


Fig. 1. ORTEP diagram of the μ-hydrido niobium complex *(3)*. The thermal vibration ellipsoids correspond to 50% probability. *(3)* crystallizes from $CH_2Cl_2$/ether in the space group $P\bar{1}(C_i^1)$ with $a = 1115.2(4)$, $b = 1341.9(6)$, $c = 1484.0(4)$ pm; $\alpha = 67.69(3)$, $\beta = 72.05(2)$, $\gamma = 69.10(3)°$; $Z = 4$ (two crystallographically independent molecules per unit cell). Triple measurement, θ-scan, P3 diffractometer program (Syntex) with absorption corrections, Mo$_{K\alpha}$ radiation, $60.0° \geq 2\theta \geq 3.0°$; 2449 independent non-zero reflections; $R_{isotropic} = 0.0828$, $R_{anisotropic} = 0.0459$. The data in Table 1 characterize one of the two crystallographically independent molecules; the bond parameters of the second molecule differ only slightly from the given data. The H-positions in *(3)* were determined from a model and the parameters were isotropically refined. The H-positions in the isomorphic compound ($\eta^5$-$C_5H_5$)(CO)$_3$V—H—Nb(CO)($\eta^5$-$C_5H_5$)$_2$[6] resulted from the difference Fourier synthesis ($R_{isotropic} = 0.067$, $R_{anisotropic} = 0.048$). *(3)* has approximate $C_s$-symmetry; the symmetry plane is defined by Nb(1) [−0.71], Nb(2) [0.01], C(19) [1.88], O(4) [−1.18], C(15) [6.34], C(11) [32.17], O(1) [53.77] (deviations from the best plane in square brackets). In the model the position of H(1) was postulated as being on this non-crystallographically determined mirror plane.

Table 1. Selected molecular parameters of *(3)*.

| Bond lengths [pm] | | Bond angles [°] | |
|---|---|---|---|
| Nb(1)—Nb(2) | 373.8(3) | Nb(1)—H(1)—Nb(2) | 167(12) |
| Nb(1)—H(1) | 186(25) | Nb(1)—C(11)—O(1) | 174.2(1.9) |
| Nb(2)—H(1) | 190(24) | Nb(2)—C(17)—O(2) | 178.4(1.6) |
| Nb(1)—C(11) | 205.1(18) | Nb(2)—C(18)—O(3) | 176.0(1.9) |
| Nb(2)—C(17) | 204.7(18) | Nb(2)—C(19)—O(4) | 177.3(1.2) |
| Nb(2)—C(18) | 205.5(14) | C(17)—Nb(2)—C(18) | 106.5(7) |
| Nb(2)—C(19) | 201.6(14) | C(18)—Nb(2)—C(19) | 69.5(6) |
| C(11)—O(1) | 116.4(24) | C(19)—Nb(2)—C(17) | 73.9(7) |
| C(17)—O(2) | 116.5(22) | | |
| C(18)—O(3) | 117.5(16) | | |
| C(19)—O(4) | 118.6(17) | | |
| Nb(1)—C(1—5) | 239.1 [a] | | |
| Nb(1)—C(6—10) | 238.9 [a] | | |
| Nb(2)—C(12—16) | 241.6 [a] | | |

[a] Mean values.

From the remarkable long-wave shift of the CO stretching frequencies of the ($\eta^5$-$C_5H_5$)Nb(CO)$_3$ fragment[7] compared to those in *(1)*[2] it appears that the coordination of the noble-gas configurated ($\eta^5$-$C_5H_5$)$_2$Nb(CO)H building block to the 16-electron species ($\eta^5$-$C_5H_5$)Nb(CO)$_3$ leads with donor sta-

---

[*] Prof. Dr. W. A. Herrmann, H. Biersack
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg 1 (Germany)
Prof. Dr. M. L. Ziegler, P. Wülknitz
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[**] Metalcarbonyl Syntheses, Part 7. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and by Hoechst AG.—Part 6: *J. Plank, D. Riedel, W. A. Herrmann*, Angew. Chem. *92*, 961 (1980); Angew. Chem. Int. Ed. Engl. *19*, 937 (1980).

bilization to extensive charge compensations of the two components. This interpretation is consistent with the fact that the Nb—CO bond lengths in *(3)* are significantly shorter and the C—O bond lengths longer than in *(1)*[8] (Table 1). Despite the presence of the hydrogen bridge the tetragonal-pyramidal stereochemistry of the metal center Nb(2) remains largely unchanged.

### *Procedure*

All preparations must be carried out with rigorous exclusion of $O_2$ and $H_2O$.—A solution of *(1)* (1.20 g, 4.4 mmol) and *(2)*[10] (990 mg, 4.4 mmol) in THF (230 cm$^3$) is irradiated (Hg high-pressure lamp 150 watt) at $-15\,^\circ C$ in an immersion-well photoreactor[9] for *ca.* 5 h; a total of *ca.* 170 cm$^3$ of gas (CO and $H_2$) is evolved. The resulting suspension is evaporated down in a vacuum ($+20\,^\circ C$) and chromatographed on silica (Merck 7734, 0.063—0.200 mm, Act. II—III; $+15\,^\circ C$; column: $l = 80$ cm, $\varnothing = 1.4$ cm). Unreacted *(1)* is eluted as an orange-colored zone (95—120 mg; 8—10%) with *n*-pentane/benzene (5:1); with diethyl ether, the by-product $(\eta^5\text{-}C_5H_5)_2Nb(CO)H$ (red-violet zone; *ca.* 110 mg) migrates, and with diethyl ether/acetone one finally obtains the dinuclear complex *(3)* (dark-green band). Crystallization from a minimum amount of $CH_2Cl_2$/diethyl ether ($\approx 3:1$; $-20\,^\circ C$) and drying under high-vacuum affords analytically pure *(3)*; yield 380—420 mg [20—22% based on consumed *(1)*].—The isomorphic vanadium derivative $(\eta^5\text{-}C_5H_5)(CO)_3V\text{—}H\text{—}Nb(CO)(\eta^5\text{-}C_5H_5)_2$[6] is synthesized analogously and has similar physical and spectroscopic properties.

Received: June 30, 1980 [Z 730 IE]
Publication delayed at authors' request
German version: Angew. Chem. *93*, 397 (1981)

CAS Registry numbers:
*(1)*, 12108-03-1; *(2)*, 11105-67-2; *(3)*, 77110-77-1; $(\eta^5\text{-}C_5H_5)_2Nb(CO)H$, 11105-68-3

---

[1] a) *M. Schneider, E. Weiss,* J. Organomet. Chem. *121*, 365 (1976); b) *W. A. Herrmann, M. L. Ziegler, K. Weidenhammer, H. Biersack,* Angew. Chem. *91*, 1026 (1979); Angew. Chem. Int. Ed. Engl. *18*, 960 (1979); J. Am. Chem. Soc., *103*, 1692 (1981); references cited therein.

[2] a) *W. A. Herrmann, H. Biersack,* Chem. Ber. *112*, 3942 (1979); b) J. Organomet. Chem. *191*, 397 (1980).

[3] Cf. *e.g. H. D. Kaesz, R. B. Saillant,* Chem. Rev. *72*, 231 (1972); *M. A. Andrews, S. W. Kirtley, H. D. Kaesz,* Adv. Chem. Ser. *167*, 215 (1978).

[4] *J. P. Olsen, T. F. Koetzle, S. W. Kirtley, M. Andrews, D. L. Tipton, R. Bau,* J. Am. Chem. Soc. *96*, 6621 (1974); cf. *J. L. Petersen, L. F. Dahl, J. M. Williams,* Adv. Chem. Ser. *167*, 11 (1978); *R. G. Teller, R. Bau,* Top. Curr. Chem. *44*, 1 (1981).

[5] *A. F. Wells:* Structural Inorganic Chemistry, 3rd Edit. Clarendon Press, Oxford 1962.

[6] Cf. [3]; recent examples: *K. S. Wong, W. R. Scheidt, J. A. Labinger,* Inorg. Chem. *18*, 136 (1979), and references cited therein.—The same effects were observed (X-ray structure analyses) for other complexes synthesized analogously to *(3)*: $(\eta^5\text{-}C_5H_5)(CO)_3V\text{—}H\text{—}Nb(CO)(\eta^5\text{-}C_5H_5)_2$ and $(CO)_5Cr\text{—}H\text{—}Nb(CO)(\eta^5\text{-}C_5H_5)_2$ [$d$(Nb—V) = 372.5(4) pm, ∢(Nb,H,V) = 172.7(80)° and $d$(Cr—Nb) = 345.3(2) pm, ∢(Cr,H,Nb) = 137.4(53)°, respectively]; *M. L. Ziegler, B. Balbach, H. Biersack, W. A. Herrmann, J. A. Labinger,* unpublished results, 1979.

[7] *(3)*: IR ($C_6H_6$): $\nu$CO = 2024 m, 1939 vs, 1872 s, 1856 s cm$^{-1}$; (KBr): $\nu$CO = 1935 s, 1923 vs, 1822 vs, 1800 vs cm$^{-1}$; $^1$H-NMR (90 MHz, [D$_6$]acetone, 29 °C, int. TMS): $\delta = 5.46$ (s, 5H), 5.34 (2×s, 10H; $\Delta\nu = 0.4$ Hz), $-19.8$ (br., 1H); $^{13}$C-NMR (22.63 MHz, [D$_8$]THF, 31 °C, int. TMS): $\delta = 85.6$, 91.5, 94.2 (all $C_5H_5$). For comparison: *(1)*: IR ($C_6H_6$): $\nu$CO = 2028 s, 1921 vs cm$^{-1}$.

[8] *W. A. Herrmann, W. Kalcher, H. Biersack, I. Bernal, M. Creswick,* Chem. Ber., in press; *(1)*: space group Pnma; $a = 780.0(3)$, $b = 1223.0(6)$, $c = 1061.9(5)$ pm; $Z = 4$; $d$(Nb—C,CO) = 208.1(7), 210.3(8) pm; $d$(C—O) = 111.8(11), 114.0(9) pm; ∢(*cis*-CO,Nb,CO) = 74.2(3)—75.0(4)°; ∢(*trans*-CO,Nb,CO) = 117.8(3)°.

[9] *W. A. Herrmann, I. Schweizer,* Z. Naturforsch. *B 33*, 1128 (1978).

[10] *J. A. Labinger,* Adv. Chem. Ser. *167*, 149 (1978).

---

# "Spin-Stabilization" *via* Complex Formation; ESR Investigation of some Catecholamine-Semiquinones[**]

By *Hartmut B. Stegmann, H. Ulrich Bergler,*
and *Klaus Scheffler*[*]

The lifetime of 1,2-benzosemiquinone radicals is chiefly determined by two reactions. The first is the nucleophilic substitution of the radical or its oxidation product 1,2-benzoquinone at the 4- and 5-positions[1]. The second, considerably slower reaction, which can lead to modification of the primary oxidation products, is the reaction with electrophiles causing substitution at the 3- or 6-positions[2]. The attacking reagent is normally the solvent, since benzosemiquinones are, on the whole, generated in reactive solvents[3a]. In inert solvents, in which these reactions either do not occur or occur only slowly, these radial anions can be generated *via* autoxidation in the presence of organometallic cations such as triorganotin[3b] or diorganothallium[4a]. In addition, the paramagnetic state is stabilized by complex formation. This method can also be applied to sensitive hydroquinones or enediols such as ascorbic acid[4b] and hence allows intermediate paramagnetic compounds of this type to be detected and studied at low concentrations.

We therefore reacted some catecholamines with organothallium hydroxides in pyridine in the presence of atmospheric oxygen. The ESR-spectra obtained, exhibit excellent signal to noise ratios and good resolution at a linewidth of *ca.* 300 mG compared to the spectra of the radical anions generated using a flow system[5], so that signals which, in addition to the proton HFS, show a thallium splitting (cf. *e.g.* Fig. 1, large coupling) can be readily interpreted. The radical half-life is of the order of days at room temperature, and even at $+100\,^\circ C$ no irreversible change in the spectrum can be observed.

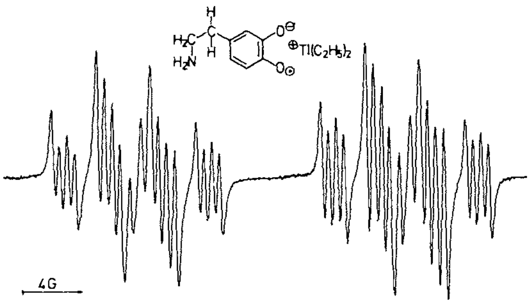


Fig. 1. ESR spectrum of the dopamine semiquinone-diethylthallium ion pair in pyridine at room temperature.

Assignment of the proton coupling constants, on the one hand, is made by comparison with variously substituted 1,2-semiquinones and, on the other, by investigation of the temperature dependence of the proton coupling constants. Values for the ESR-parameters obtained are shown in Table 1[6].

The proton coupling parameters are relatively insensitive to the variation of the organometallic cation, and similar to

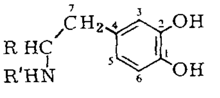
---

[*] Prof. Dr. H. B. Stegmann [+], Prof. Dr. K. Scheffler,
Dipl.-Chem. H. U. Bergler
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

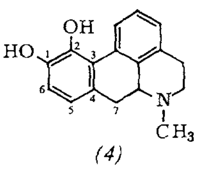
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft and from the Fonds der Chemischen Industrie.

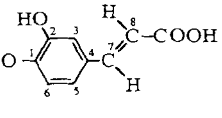
previously described values (dopamine *(1)*[5], caffeic acid *(5)*[7]); the spin density and radical geometry are not influence by the heavy metal atom. Statements concerning the conformation of substituents at C-7 in solution can be made from the magnitude of the proton coupling constants and their temperature dependence[8]. In radical anions derived from dopamine *(1)*, (see Fig. 1) both protons at C-7 are equivalent at room temperature (cf. Table 1), the mean hyperconjugation angle being 60°. This implies that there is no free rotation about the C-4—C-7 bond. If both C-7-protons are assigned positions below the plane of the benzene ring, the aminomethyl group lies above this plane. The molecule is, however, not rigid, and torsional vibration about the C-4—C-7 bond occurs. In the radical anions derived from methyl-L-dopa *(2)* and L-dopamethyl ester *(3)*, the protons on C-7 are diastereotopic and the mean angle of the protons recedes 2—3° from the symmetrical position.



*(1)*, R = R' = H
*(2)*, R = COOH, R' = $CH_3$
*(3)*, R = $COOCH_3$, R' = H



*(4)*



*(5)*

Table 1. Coupling constants [G], line widths [G] and g-factors of some catecholamine and semiquinone diorganothallium ion pairs and analogous system in pyridine at room temperature.

| Radical anion from | Cation $R_2Tl^+$ R = | $a_{Tl}$ [a] | $a_{3\text{-}H}$ | $a_{5\text{-}H}$ | $a_{6\text{-}H}$ | $a_{7\text{-}H}$ | $a_{7\text{-}H}$ | $\Delta H$ [b] | *g* |
|---|---|---|---|---|---|---|---|---|---|
| Dopamine *(1)* | $C_6H_5$ | 11.55 | 0.40 | 3.72 | 0.95 | 3.05 | 3.05 | 0.2 | 2.00370 |
| | Mesityl | 21.50 | 0.30 | 3.80 | 0.85 | 3.10 | 3.10 | 0.2 | 2.00328 |
| | $C_2H_5$ | 18.10 | 0.50 | 3.70 | 1.00 | 3.00 | 3.00 | 0.3 | 2.00397 |
| Methyl-L-dopa *(2)* | $C_2H_5$ | 18.40 | 0.59 | 3.45 | 0.97 | 2.90 | 2.05 | 0.3 | 2.00388 |
| L-Dopamethyl ester *(3)* | $C_6H_5$ | 11.90 | 0.50 | 3.65 | 1.00 | 2.95 | 2.45 | 0.3 | 2.00362 |
| Apomorphine *(4)* | $C_6H_5$ | 13.55 | — | 3.65 | 1.05 | 8.60 | 1.8 | 0.5 | 2.00357 |
| | Mesityl | 24.25 | — | 3.60 | 0.98 | 8.70 | 1.8 | 0.5 | — |
| | $C_2H_5$ | 19.60 | — | 3.60 | 1.13 | 8.50 | 1.65 | 0.4 | 2.00397 |
| | *n*-$C_4H_9$ | 22.60 | — | 3.60 | 1.12 | 8.45 | 1.65 | 0.4 | 2.00384 |
| Caffeic acid *(5)* | $C_6H_5$ | 11.25 | 0.35 | 3.00 | 1.13 | 2.31 | 1.24 [c] | 0.3 | 2.00372 |
| | $CH_3$ | 20.8 | 0.43 | 2.90 | 1.21 | 2.30 | 1.21 [c] | 0.3 | — |

[a] The splittings of both $^{205}$Tl- and $^{203}$Tl-isotopes could not be separately observed; the coupling constants given are average values. [b] The given values correspond to the low-field thallium term, the lines of the high-field term are *ca.* 50 mG smaller. [c] The value given is $a_{8\text{-}H}$.

The C-7 proton coupling constants of the radical derived from apomorphine *(4)* exhibit no temperature dependence, and hence the ESR results are consistent with a relatively rigid molecule. X-ray structural investigations on apomorphine hydrochloride[9a] indicate that the asymmetrical units of the unit cell contain two molecules having different conformations. From the atom coordination values, the hyperconjugation angles[9b] of conformer A can be calculated to be 4 and 64° and those of conformer B to be 17 and 77°. However, in solutions of the apomorphine semiquinone the conformation can be determined from the proton-HFS. The corresponding hyperconjugation angles, based on the proton coupling constants, are 3.7 and 63.7°, so that the geometry of apomorphine in solution corresponds to the solid state structure A.

Received: July 25, 1980 [Z 731 IE]
German version: Angew. Chem. 93, 398 (1981)

CAS Registry numbers:
*(1•)* $^-R_2Tl^+$, R = $C_6H_5$, 77152-78-4; *(1•)* $^-R_2Tl^+$, R = mesityl, 77152-79-5; *(1•)* $^-R_2Tl^+$, R = $C_2H_5$, 77152-80-8; *(2•)* $^-R_2Tl^+$, R = $C_2H_5$, 77153-81-2; *(3•)* $^-R_2Tl^+$, R = $C_6H_5$, 77152-81-9; *(4•)* $^-R_2Tl^+$, R = $C_6H_5$, 77152-82-0; *(4•)* $^-R_2Tl^+$, R = mesityl, 77152-83-1; *(4•)* $^-R_2Tl^+$, R = $C_2H_5$, 77152-84-2; *(4•)* $^-R_2Tl^+$, R = *n*-$C_4H_9$, 77152-85-3; *(5•)* $^-R_2Tl^+$, R = $C_6H_5$, 77153-82-3; *(5•)* $^-R_2Tl^+$, R = $CH_3$, 77153-83-4

---

[1] *K. B. Ulmschneider*, Dissertation, Universität Tübingen 1977.

[2] *L. H. Piette*, J. Phys. Chem. *71*, 29 (1967).

[3] a) *K. Scheffler, H. B. Stegmann:* Elektronenspinresonanz. Springer, Berlin 1970; b) *H. B. Stegmann, K. B. Ulmschneider, K. Scheffler*, J. Organomet. Chem. *101*, 145 (1975); *H. B. Stegmann, K. B. Ulmschneider, K. Hieke, K. Scheffler, ibid. 118*, 259 (1976).

[4] a) *H. B. Stegmann, W. Uber, K. Scheffler*, Tetrahedron Lett. *1977*, 2697; b) *H. B. Stegmann, K. Scheffler, P. Schuler*, Angew. Chem. *90*, 392 (1978); Angew. Chem. Int. Ed. Engl. *17*, 365 (1978).

[5] *M. Yoshioka, Y. Kirino, Z. Tamura, T. Kwan*, Chem. Pharm. Bull. *25*, 75 (1977).

[6] *H. U. Bergler*, Diplomarbeit, Universität Tübingen 1979; investigations on adrenaline, L-dopa and its derivatives: *H. B. Stegmann et al.*, unpublished results.

[7] *P. Ashworth*, J. Org. Chem. *41*, 2920 (1976).

[8] *K. Scheffler, K. Hieke, P. Schuler, H. B. Stegmann*, Z. Naturforsch. *A 31*, 1620 (1976).

[9] a) *J. Giesecke*, Acta Crystallogr. *B 29*, 1785 (1973); b) We thank Dr. habil. *W. Winter*, Tübingen for the interpretation of the coordinates given in [9a].

---

## σ-, π- and Mixed Electronic Structures in Radical Cations of Hydrazones[**]

By *Armin Berndt, Rudolf Bolze, Rainer Schnaut*, and *Helmut Woynar*[*]

*Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday*

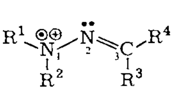
Depending on the type of substituents the radical cations *(1)* of hydrazones are present as σ-radicals in orthogonal conformation with delocalization corresponding to the resonance formulas *A*↔*B*[1], as π-radicals in planar conformation with delocalization corresponding to *C*↔*D*, or as radicals having a previously undescribed mixed σ- and π-electronic structure in twisted conformation *E* with delocalization involving participation of *F* and *G*.

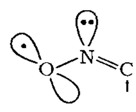
---

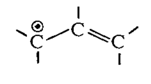
[*] Prof. Dr. A. Berndt, Dr. R. Bolze, Dipl.-Chem. R. Schnaut, Dr. H. Woynar
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

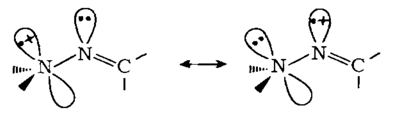
[**] This work was supported by the Fonds der Chemischen Industrie.

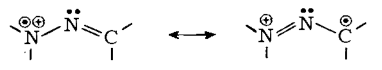
The related iminyl oxide radicals *(2)*[2] have σ-electronic structure, independent of the type of substituents, while allyl radicals *(3)* have π-electronic structure in all conformations.

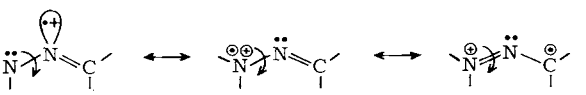

*(1)*


*(2)*


*(3)*


*A* *B*


*C* *D*


*F* *E* *G*

The radicals *(1)* can be obtained by oxidation of the corresponding hydrazones or pyrazolines in dichloromethane in a flow apparatus with tris(*p*-bromophenyl)ammoniumyl hexachloroantimonate and characterized (Table 1).

The distribution of the unpaired electron corresponding to formulas *A* and *B* is reflected in the large coupling constants of the two nitrogen atoms in *(1a)*—*(1c)*. The very small couplings of the protons of the methyl- and phenyl-substituents at $C_3$ in *(1a)* and *(1b)*, respectively, rule out participation of *D*. The large coupling of the proton bound to $C_3$ in *(1c)* is characteristic for protons in the *E*-position to the orbital of the unpaired electron in σ-radicals[3]. It must therefore have a positive sign.

Table 1. ESR coupling constants of the radical cations *(1a)*—*(1h)* [G] [a].

| *(1)* | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $a_1^N$ | $a_2^N$ | $a_3^H$ | $a_N^H$ CH₃ | Electronic structure | Conformation |
|---|---|---|---|---|---|---|---|---|---|---|
| *(a)* | *t*Bu | $CH_3$ | $CH_3$ | $CH_3$ | 18.8 [b] | 15.0 [b] | 0.9 (3H) | 17.4 | σ | orthogonal |
| *(b)* | —$(CH_3)_2C(CH_2)_3C(CH_3)_2$— | | $CH_3$ | $C_6H_5$ | 19.5 [b] | 14.8 [b] | < 1 [c] | — | σ | orthogonal |
| *(c)* | —$(CH_3)_2C(CH_2)_3C(CH_3)_2$— | | H | *t*Bu | 17.4 [b] | 15.7 [b] | +12.8 (1H) | — | σ | orthogonal |
| *(d)* | $CH_3$ | —$(CH_3)_2CCH_2$— | | *t*Bu | 15.6 | <0.8 [e] | 16.2 (2H) | 20.0 | π | planar |
| *(e)* | *t*Bu | $CH_3$ | H | Aryl [d] | 11.6 | <0.4 [c] | − 6.2 (1H) [e] | 11.0 | π | planar |
| *(f)* | *t*Bu | $CH_3$ | H | *t*Bu | 16.2 | 10.2 | 2.5 (1H) | 18.2 | σ + π | twisted |
| *(g)* | $CH_3$ | $CH_3$ | $CH_3$ | $C_6H_5$ | 13.7 | 11.8 | 3.9 (3H) | 15.0 | σ + π | twisted |
| *(h)* | $CH_3$ | $CH_3$ | $C_6H_5$ | $C_6H_5$ | 13.8 | 7.5 | — [c] | 13.8 | σ + π | twisted |

[a] Gauss = $10^{-4}$ Tesla. [b] Assignment possibly reversed. [c] Not resolved. [d] Aryl = 3,5-di-*tert*-butylphenyl. [e] $a_p^H = 4.2$, $a_o^H = 2.8$.

The large coupling constants for only *one* nitrogen and for the protons of the methylene or aryl substituents on $C_3$ in *(1d)* and *(1e)* evidence the distribution of the unpaired electron corresponding to the resonance formulas *C* and *D*. The very small coupling constants of the central nitrogen atom rule out participation of the resonance structure *B*. The coupling constant of the proton on $C_3$ in *(1e)* must thus have the negative sign characteristic for π-radicals.

In *(1f)*—*(1h)* $a_2^N$ lies ***between*** the characteristic values for orthogonal σ and planar π-structures. Here the values of $a_2^N$ are considerably greater than in the case of *(1d)* and *(1e)* and show delocalization corresponding to *F*; the coupling constant of the protons of the methyl group on $C_3$ is distinctly larger in *(1g)* than in *(1a)* and *(1b)*, indicating a delocalization corresponding to *G*. For *(1f)* the coupling constant of the proton bound to $C_3$, which lies ***between*** the values typical for σ- and for π-radicals, must be composed of components of opposite sign, as would result from the presence of σ- ***and*** π-electron structure.

The unusually strong influence of substituents on the conformation, and thus on the electronic structure, of the radicals *(1)* is supposed to be due to a compensation of the loss of π-π-delocalization (maximum effect in planar conformation) by gain of π-σ-delocalization (maximum effect in orthogonal conformation) during twisting. The competition between π-π- and π-σ-delocalization markedly manifests itself in the mixed electronic structure and twisted conformation of *(1f)*, in which steric hindrance (the third conformation-determining effect with maximum repulsion in planar conformation) can play only a small role. A slight increase in steric hindrance—*(1a)* or *(1c)* compared to *(1f)*—leads to orthogonality, while increased π-π-delocalization—*(1e)* compared to *(1f)*—leads to planarity. In the corresponding substituted allyl radicals these changes effect, ***in toto***, only twists of ***ca.*** 10°[4]: The loss of π-π-delocalization in such radicals is ***not*** compensated by a gain of π-σ-delocalization.

Received: July 2, 1980 [Z 732 IE]
German version: Angew. Chem. *93*, 400 (1981)

CAS Registry numbers:
*(1a)*, 77241-83-9; *(1b)*, 77286-38-5; *(1c)*, 77241-84-0; *(1d)*, 77241-85-1; *(1e)*, 77241-86-2; *(1f)*, 77241-87-3; *(1g)*, 77286-39-6; *(1h)*, 77241-88-4

---

[1] σ-Radicals are defined as radicals in which the unpaired electron resides in an orbital with s-character (in *(1)* and *(2)* the $sp^2$-orbital on the central nitrogen atom); cf. also *W. C. Danen, Ch. T. West*, J. Am. Chem. Soc. *95*, 6872 (1973).

[2] *R. O. C. Norman, B. C. Gilbert*, J. Phys. Chem. *71*, 14 (1967).

[3] In iminyl oxide radicals the corresponding coupling is 27 G, in the vinyl radical it is 68.5 G, see *K. Scheffler, H. B. Stegmann:* Elektronenspinresonanz. Springer, Berlin 1970, p. 306 and 332.

[4] *H. Regenstein, W. Ahrens, A. Berndt*, Tetrahedron *31*, 2837 (1975).

## ***trans*-15,16-Dimethyl-1,4:8,11-ethanediylidene[14]annulene**[**]

By *Walter Huber, Johann Lex, Thomas Meul,* and
*Klaus Müllen*[*]

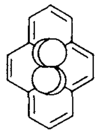
Efforts directed towards a verification of Hückel's rule for $(4n+2)\pi$-perimeter systems homologous to benzene have

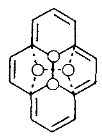
---

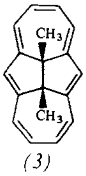
[*] Prof. Dr. K. Müllen, Dr. W. Huber, Dr. J. Lex, Dipl.-Chem. T. Meul
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

[**] This work has been supported by the Deutsche Forschungsgemeinschaft.

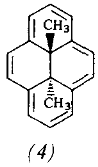
been particularly successful within the field of [14]annulenes[1]. Following the preparation of the parent [14]annulene *(1)*[1a] by *Sondheimer, Vogel*[1b] and *Boekelheide*[1c] prepared the bridged derivatives *(3)* and *(4)*, respectively, which, without the steric interaction of inner hydrogens, constitute essentially flattened rigid perimeters. From the strong interdependence of the π-bonding on the mode of bridging[2] it would appear to be a useful exercise to study the result of systematically varying the molecular geometry. We describe here the synthesis and properties of *trans*-15,16-dimethyl-1,4:8,11-ethanediylidene[14]annulene (*trans*-10b,10c-dihydro-10b,10c-dimethyldicyclopenta[*ef*,*kl*]heptalene) *(5a)*, which, in a formal sense, can be derived from *(4)* simply by rotating the bridge through 90° [see formula *(2)*].


*(1)*

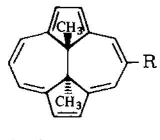

*(2)*



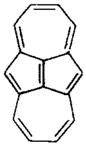
*(3)*

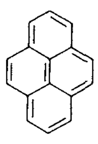


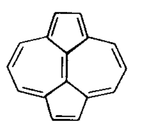
*(4)*



*(5a)*, R = H
*(5b)*, R = NO$_2$


*(6)*


*(7)*


*(8)*

On the basis of spectroscopic and theoretical findings[4] the pyrene systems *(6)*—*(8)*[3] can be adequately described as vinyl-bridged [14]annulenes and, thus, as precursors of the annulenes *(3)*, *(4)*, and *(5a)*. As simple MO-models clearly demonstrate, the lowest antibonding MO of *(6)* and *(7)* constitutes a pure perimeter-orbital (with a nodal plane through the bridge) whereas that of *(8)* possesses a pronounced contribution of the ethylene π*-orbital. This is reflected in the spectroscopic properties of the dianions *(6)*$^{2-}$, *(7)*$^{2-}$ and *(8)*$^{2-}$: one finds a vanishing probability for the excess charge to reside in the bridge centers of *(6)*$^{2-}$ and *(7)*$^{2-}$ and a high π-charge density within the bridge of *(8)*$^{2-}$[3]. Accordingly, *(8)*$^{2-}$[5], but not *(6)*$^{2-}$ and *(7)*$^{2-}$[6], could be attacked at the bridge positions by electrophiles and, thus, directly transformed into a bridged perimeter-π-system.

Indeed, *(8)*, which can be prepared according to the methods of *Jutz*[7a], *Anderson*[7b], and *Hafner*[7c] can be reduced with lithium in dry, oxygen-free tetrahydrofuran (0.025 M) quantitatively to the dianion *(8)*$^{2-}$. Treating the resulting green-brown solution at −78 °C with an excess of degassed dimethyl sulfate provides, after filtration over neutral aluminum oxide and recrystallization from methanol, compound *(5a)* in 35% yield (dark red needles, m.p. 186 °C).

The molecular weight indicates the incorporation of two methyl groups; moreover, the $^1$H-NMR (δ = 8.74 (H-2), 8.77 (H-5), 8.04 (H-6), −4.53 (H-15a)) and $^{13}$C-NMR spectra (δ = 143.7 (C-1), 119.2 (135.3) (C-2), 135.3 (119.2) (C-5), 152.6 (C-6), 43.1 (C-15), 15.0 (C-15a)) leave no doubt that the addition has taken place at the bridge centers C-15 and C-16 and that the effective $D_{2h}$-symmetry of the peripheral π-system is preserved. The extreme high-field resonance of the (methyl) bridge protons and the low-field absorption of the ring protons confirm the diatropism of the 14π-perimeter.

The absorption spectrum of *(5a)* [$\lambda_{max}$ ($C_6H_{12}$) = 335 nm (ε = 136280), 346 (101900), 377 (3500), 397 (4020), 420 (5430), 440 (6200), 445 (6870), 507 (69), 550 (127), 575 (163), 603 (277)], aside from a slight hypsochromic shift, closely resembles that of *(4)*. Compounds *(4)* and *(5a)*, therefore, constitute a most appropriate subject for comparative studies on the "bridging" of annulenes which is a necessary perturbation of the ideal bonding situation of a hypothetical $D_{14h}$-perimeter.

Model considerations indicate that only the *trans*- not the *cis*-configuration of the bridge will allow for a substantial flattening of the perimeter, thus, favoring the cyclic π-conjugation[1c]. An X-ray structure analysis of *(5a)* reveals not only the *trans*-arrangement of the methyl groups but also shows that the bond lengths in the flattened π-perimeter are essentially equalized (Fig. 1)[8].

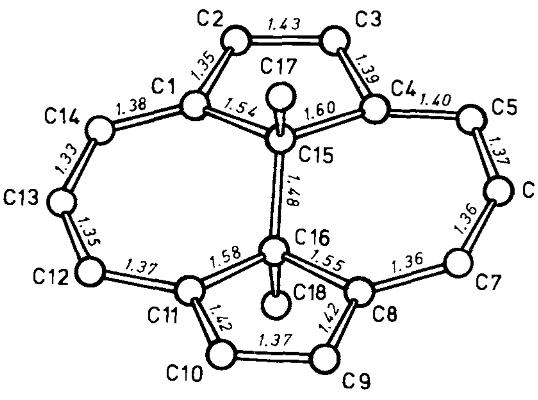


Fig. 1. Molecular structure of *(5a)*; bond lengths in Å [8].

The resulting well established description of the ground state of *(5a)* as that of a π-delocalized (aromatic) $(4n+2)\pi$-species compellingly raises the question of reactivity. Treating the annulene *(5a)* with copper nitrate in acetic anhydride affords the 6-nitro derivative *(5b)* in very good yields, thus providing a further indication of the benzene-type behavior of *(5a)*.

The protonation of *(8)*$^{2-}$ in THF does not yield the expected dihydro adduct, the 1,4:8,11-ethanediylidene[14]annulene. Methylation of *(8)*$^{2-}$ in liquid ammonia, however, does afford the parent annulene, in addition to *(5a)*, and a monomethyl adduct[9].

Received: September 1, 1980 [Z 733 IE]
Supplemented: February 24, 1981
German version: Angew. Chem. *93*, 401 (1981)

CAS Registry numbers:
*(5a)*, 77080-43-4; *(5b)*, 77080-44-5; *(8)*$^{2-}$, 69743-18-6

---

[1] a) *F. Sondheimer, Y. Gaoni*, J. Am. Chem. Soc. *82*, 5765 (1960); *Y. Gaoni, A. Melera, F. Sondheimer, R. Wolovsky*, Proc. Chem. Soc. *397* (1964); *F. Sondheimer, I. Calder, J. A. Elix, Y. Gaoni, P. J. Garratt, K. Grohmann, J. Mayer, M. V. Sargent, R. Wolovsky*, Chem. Soc. Spec. Publ. *21*, 75 (1967); b) *E. Vogel*, Chimia *22*, 21 (1968); Pure Appl. Chem. *28*, 355 (1971); Isr. J. Chem. *20*, 215 (1980); c) *V. Boekelheide, J. B. Phillips*, J. Am. Chem. Soc. *89*, 1695 (1967); *V. Boekelheide*, Pure Appl. Chem. *44*, 751 (1975); d) *U. E. Meissner, A. Gensler, H. A. Staab*, Angew. Chem. *88*, 374 (1976); Angew. Chem. Int.

Ed. Engl. *15*, 365 (1976); e) *H. Röttele, G. Schröder*, Angew. Chem. *92*, 204 (1980); Angew. Chem. Int. Ed. Engl. *19*, 207 (1980); f) *M. Nakagawa*, Pure Appl. Chem. *44*, 885 (1975).

[2] *R. H. Mitchell, V. Boekelheide*, J. Am. Chem. Soc. *96*, 1547 (1974); *E. Vogel, H. Reel, ibid. 94*, 4388 (1972).

[3] *K. Müllen*, Helv. Chim. Acta *61*, 2307 (1978); *B.-Ch. Becker, W. Huber, K. Müllen*, J. Am. Chem. Soc. *102*, 7803 (1980).

[4] *T. D. Alger, D. M. Grant, E. G. Paul*, J. Am. Chem. Soc. *88*, 5397 (1966); *H. Reel, E. Vogel*, Angew. Chem. *84*, 1064 (1972); Angew. Chem. Int. Ed. Engl. *11*, 1013 (1972); *M. Randić*, J. Am. Chem. Soc. *99*, 444 (1977).

[5] Although the spectroscopic data predict a high $\pi$-charge density at C-15 and C-16 of *(8)*$^{2-}$ neither the spectra nor MO-calculations (HMO, PPP, CNDO) could reliably predict whether or not the charge-controlled attack of electrophilic agents would primarily occur at these positions. In the present context we don't exclude that borderline structures with covalent C-15(C-16)—Li bonds contribute to the ground state of *(8)*$^{2-}$.

[6] In agreement with these arguments we find that reaction of *(7)*$^{2-}$ with dimethyl sulfate provides the 1,6-dimethyl-1,6-dihydropyrene as well as the analogous 1,8-diadduct.

[7] a) *Ch. Jutz, E. Schweiger*, Synthesis *1974*, 193; b) *A. G. Anderson, Jr., G. M. Masada, A. F. Montana*, J. Org. Chem. *38*, 1439 (1973); c) *K. Hafner, G. Knaup*, unpublished; we thank Prof. *Hafner* for making available unpublished results.

[8] Monoclinic, space group $P2_1/c$, $a = 13.819(3)$, $b = 11.646(2)$, $c = 12.853(3)$ Å, $\beta = 109.22(2)°$; $Z = 6$; $\rho_{calc} = 1.185$, $\rho_{obs} = 1.178$ g/cm$^3$. Nonius-CAD-4 diffractometer, 2044 symmetry-independent reflections ($I \geq 2\sigma(I)$); *(5a)* crystallizes in a distorted lattice! The molecular structure given in Figure 1 was determined after several successive FO-Fourier syntheses from the resulting electron density map.

[9] *W. Huber, W. Irmen, K. Müllen*, unpublished.

## Phenyl- and Biphenylylbicyclo[2.2.2]octane Derivatives—Two Novel Classes of Nematic Liquid Crystals[**]

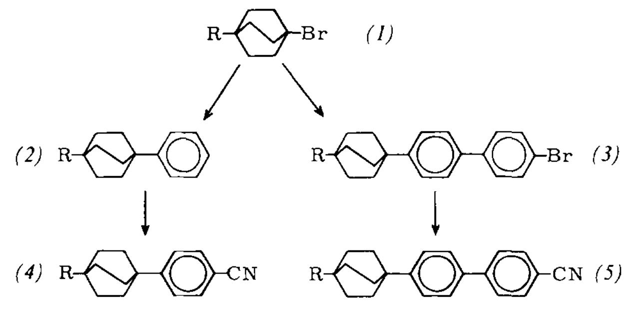
By *George W. Gray* and *Stephen M. Kelly*[*]

1-(4-cyanophenyl)bicyclo[2.2.2]octane derivatives *(4)* and 1-(4′-cyano-*p*-biphenylyl)bicyclo[2.2.2]octane derivatives *(5)* constitute two new and interesting classes of nematogens[1a]; the bicyclo[2.2.2]octane ring enhances nematic-isotropic transitions and suppresses the occurrence of smectic phases. The mesogens *(4)* and *(5)* exhibit wide-range nematic phases at significantly higher temperatures than analogous compounds containing a benzene-[1b] or cyclohexane-ring[2] in place of the bicyclo[2.2.2]octane moiety (Table 1).

Table 1. Transition temperatures [°C] of compounds *(4)* and *(5)* [a].

| | R | Crystalline→nematic or nematic→isotropic | | Nematic→isotropic | |
|---|---|---|---|---|---|
| | | *(4)* | *(5)* | *(4)* | *(5)* |
| *(a)* | $CH_3$ | 93 | 198 | (−35) [b] | (170) [b] |
| *(b)* | $C_2H_5$ | 62.5 | 188 | (−17) [b] | 221 |
| *(c)* | $n$-$C_3H_7$ | 66.5 | 180.5 | 88 | 276 |
| *(d)* | $n$-$C_4H_9$ | 75.5 | 173 | 85 | 271.5 |
| *(e)* | $n$-$C_5H_{11}$ | 62 | 159 | 100 | 269 |
| *(f)* | $n$-$C_6H_{13}$ | 72 | 133 | 86 | 259 |
| *(g)* | $n$-$C_7H_{15}$ | 61 | 141 | 95 | 250.5 |
| *(h)* | $n$-$C_8H_{17}$ | 52 | 126 [c] | 90 | 240.5 |
| *(i)* | $n$-$C_9H_{19}$ | 56 | | 90 | |

[a] The compounds gave correct elemental analyses, IR-, $^1$H-NMR- and mass spectra. The high degree of purity (≥99.9%) of *(4)* was established chromatographically. [b] Transformation into a monotropic phase. [c] Transformation of the smectic phase A into the nematic phase at 155 °C.



The mesogens *(4)* and *(5)* (Table 1) were prepared by Friedel-Crafts alkylation of either benzene or 4-bromobiphenyl with the appropriate 1-alkyl-4-bromobicyclo[2.2.2]octane derivatives *(1)* produced by the method of *Holtz* and *Stock*[3]. The nitrile group was introduced[4] in the usual way (Friedel-Crafts acetylation, haloform oxidation to yield the carboxylic acid, conversion into the amide and dehydration) into compound *(2)*, and into compound *(3)* using copper(I) cyanide[1b].

From the standpoint of their potential use in electro-optical displays, it is of interest to note here that the nematic phases *(4)* and *(5)* are similar in birefringence ($\Delta n = 0.14$) and dielectric properties ($\Delta\varepsilon = 13.3$) to the analogously substituted cyclohexane derivatives[2]. Furthermore, eutectic mixtures of the new compounds have comparably low melting points (*ca.* 0 °C), but the resulting nematic phases have much higher clearing points (90—95 °C), and this can be advantageous for certain display device requirements. In this connection, the new derivatives *(4)* and *(5)* share the excellent stability characteristics (photochemical, thermal, electrochemical) of the industrially important biphenyl and *p*-terphenyl analogues[1b], and the cyclohexane derivatives[2]. Their disadvantage lies in their relatively high viscosities (90 cP; 20 °C) compared with the analogous biphenyls (35 cP; 20 °C) and phenylcyclohexane derivatives (27 cP; 20 °C). This reflects in a low sharpness of the threshold in twisted nematic, electro-optical displays, particularly at low temperatures. However, the bicyclo[2.2.2]octane ring in *(4)* and *(5)* does give rise to much lower temperature dependencies of the splay elastic constant and the threshold voltage (0.9 and 0.22%/°C, respectively). These values are considerably lower than those for the corresponding biphenyls and cyclohexane derivatives.

Advantage has now been taken of these effects by incorporating the bicyclo[2.2.2]octane ring in various nematogenic esters. The new esters[5] show that they have considerable all-round advantages over the corresponding phenyl- or cyclohexyl-substituted esters for use in twisted nematic, electro-optical displays employing a multiplexed form of addressing.

Received: August 15, 1980 [Z 734 IE]
German version: Angew. Chem. *93*, 412 (1981)

CAS Registry numbers:
*(1a)*, 697-40-5; *(1b)*, 699-58-1; *(1c)*, 76921-50-1; *(1d)*, 73152-67-7; *(1e)*, 73152-68-8; *(1f)*, 73152-69-9; *(1g)*, 76921-49-8; *(1h)*, 77256-15-6; *(1i)*, 77256-16-7; *(4a)*, 74471-07-1; *(4b)*, 74471-08-2; *(4c)*, 74471-09-3; *(4d)*, 74471-10-6; *(4e)*, 74385-67-4; *(4f)*, 74471-11-7; *(4g)*, 74471-12-8; *(4h)*, 77256-17-8; *(4i)*, 77256-18-9; *(5a)*, 74471-13-9; *(5b)*, 74471-14-0; *(5c)*, 74471-15-1; *(5d)*, 74471-16-2; *(5e)*, 74385-66-3; *(5f)*, 74487-75-5; *(5g)*, 74487-76-6; *(5h)*, 77256-19-0; benzene, 71-43-2; 4-bromobiphenyl, 92-66-0

---

[*] Prof. G. W. Gray, S. M. Kelly, M. Sc.
Department of Chemistry, The University of Hull
Hull, HU6 7RX (England)

[**] This communication is published by permission of the Controller, HMSO, and the authors thank the UK Ministry of Defence for a research grant. They also thank Dr. *A. Mosley* and Mr. *D. G. McDonnell* for helpful discussions and constructive contributions in the formative stages of this work.

[1] a) *G. W. Gray, S. M. Kelly*, J. Chem. Soc. Perkin Trans. II, in press; b) *G. W. Gray, K. J. Harrison, J. A. Nash*, Pramana, Supply, *1*, 381 (1975); *G. W. Gray*, J. Phys. (Paris) *36*, 337 (1975); Liquid Crystal Catalogue. BDH Chemicals Limited, Poole, Dorset (England).

[2] *R. Eidenschink, D. Erdmann, J. Krause, L. Pohl,* Angew. Chem. *89,* 103 (1977); Angew. Chem. Int. Ed. Engl. *16,* 100 (1977); Phys. Lett. *60A,* 421 (1977).
[3] *H. D. Holtz, L. M. Stock,* J. Am. Chem. Soc. *86,* 5183 (1964).
[4] *S. M. Kelly,* MSc Thesis, Hull University 1979.
[5] *G. W. Gray, S. M. Kelly,* Mol. Cryst. Liq. Cryst., in press; *J. Constant, E. P. Raynes, ibid.,* in press.

## Separation and Determination of Sulfur Homocycles by High Pressure Liquid Chromatography—Detection of Novel Sulfur Rings[**]

By *Ralf Steudel, Hans-Joachim Mäusle, Doris Rosenbauer, Hermann Möckel,* and *Torsten Freyholdt*[*]

The known sulfur homocycles $S_n$ ($n=6$, 7, 8, 9, 10, 12, 18, 20) which have so far been prepared in pure form were identified and detected by vibrational spectroscopy in mixtures which usually are formed during preparative work-up. Attempts to separate such mixtures by thin-layer (TLC) or column chromatography (CC), led to complete decomposition (TLC), or incomplete separation with partial decomposition to $S_8$ (CC)[1]. We have now found that the homocycles $S_n$ with $n=6$—26 can be separated quantitatively without decomposition by high pressure liquid chromatography (HPLC) and thus detected and determined analytically alongside one another.

Since the thermally unstable rings $S_n$ ($n \neq 8$) rapidly decompose to $S_8$ on $SiO_2$ and $Al_2O_3$ the only potential method of separation is reversed-phase chromatography on $C_{18}$-phases (octadecylsilanes). For smaller rings ($n \leq 12$), methanol is suitable as eluting agent; for separation of the larger rings cyclohexane must be added up to 30 vol-% owing to their poorer solubility. On using a column of 25 cm length and 3.0 mm internal diameter and a flow rate of 1 $cm^3$/min, a pressure of 40—50 bar is built up[2]. Under these conditions (retention times $t_R=2$—25 min) no decomposition occurs at 26 °C, as has been established with the particularly unstable $S_7$ ($t_R \approx 3$ min) and with $S_{20}$ ($t_R \approx 13$ min) (Fig. 1a).

The retention times of the known pure rings unequivocally depend on the atomic number $n$ and so enable identification of the new compounds of the homologous series $S_n$ by inter- or extrapolation. The capacity factors $k'$ are linearly dependent on $n$ in a semilogarithmic plot, but give *two* straight lines which intercept at $n=9$ (Fig. 2). The straight lines obey the regressions $\log k' = -0.677+0.102n$ (correlation coefficient $r=0.994$) for $S_6$—$S_9$ and $\log k' = -0.319+0.064n$ ($r=0.999$) for $S_9$—$S_{20}$ (eluent: methanol/cyclohexane 80/20 vol-%).

Suitable for identification of the separated components are the seemingly intense UV absorptions of the sulfur rings at 254 nm, which enable a trace analysis [$\varepsilon_{254}(S_8)=5930$]. Using calibration solutions it could be established that the absorbance of $S_n$ ($n=7$, 8, 10, 12) in the range 0.3—1.8 mg $S_n$/100 $cm^3$ $CS_2$ is a linear function, in case of $S_6$ a non-linear function of the concentration. We ascribe the non-linearity in the case of $S_6$ to incomplete separation from the solvent $CS_2$, which can be improved by use of a $CH_3OH/H_2O$ mixture as eluent. This way a simultaneous quantitative determination of these compounds in admixture is possible. Such mixtures are formed, for example, on melting of $S_8$[3] or in the reaction of $SCl_2$ or $S_2Cl_2$ with potassium iodide[4]. From liquid sulfur which has been brought to equilibrium between 115 and 350 °C, $S_7$, $S_8$, $S_{12}$, $S_{18}$, and $S_{20}$ have been isolated after quenching, and $S_6$ has been detected spectroscopically. In addition, a species $S_x$ of high molecular weight ($\bar{x}=25$) but still soluble in $CS_2$ has been isolated as an orange-yellow resin-like mass and interpreted as a mixture of large rings. Figure 1c shows the chromatogram of $S_x$, which, as expected, contains rings with $n>18$. All other rings with $n=6$—17 have now been detected as components of liquid sulfur, some of them, howev-

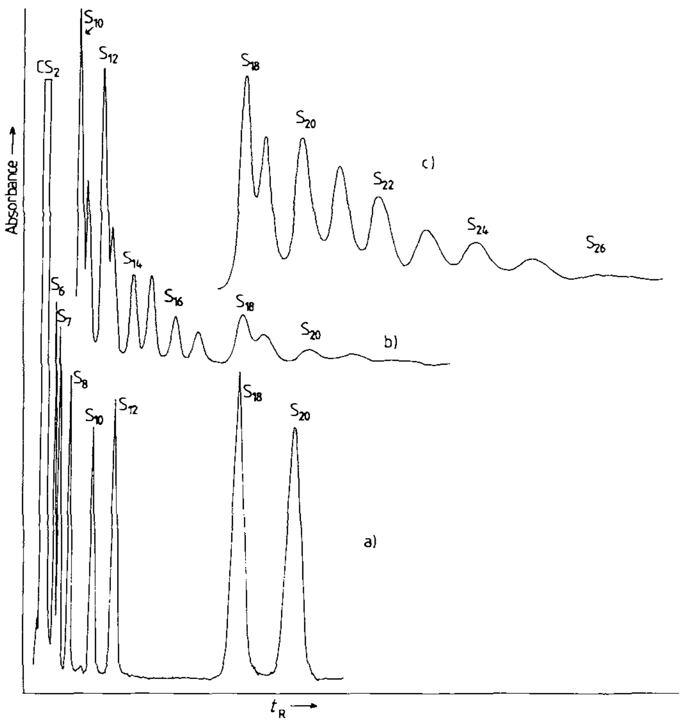


Fig. 1. a) Chromatogram of a mixture of $S_6$, $S_7$, $S_8$, $S_{10}$, $S_{12}$, $S_{18}$, and $S_{20}$ prepared from the pure components (eluent: methanol/cyclohexane 80/20 vol-%); b) chromatogram of the higher molecular weight species of sulfur formed from $SCl_2$ and KI (eluent: methanol/cyclohexane); c) chromatogram of the higher molecular weight $S_x$ from an equilibrium sulfur melt which is soluble in $CS_2$ (eluent methanol/cyclohexane 69/31 vol-%).

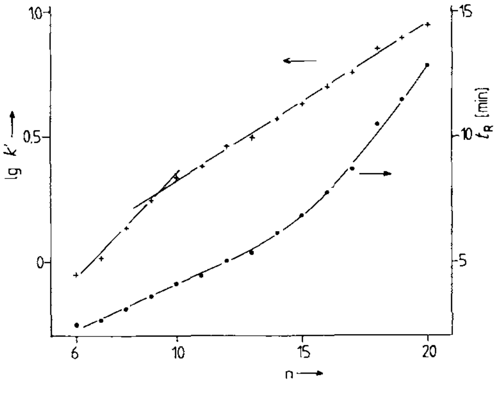


Fig. 2. Gross retention times $t_R$ and logarithm of the capacity factor $k' = (t_R - t_o)/t_o$ as a function of the atomic number $n$ of sulfur homocycles $S_n$ on elution with methanol/cyclohexane (80/20 vol-%); dead time $t_o = 1.3$ min.

---

[*] Prof. Dr. R. Steudel, Dr. H.-J. Mäusle, D. Rosenbauer
Institut für Anorganische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)
Dr. H. Möckel, Dipl.-Chem. T. Freyholdt
Hahn-Meitner-Institut für Kernforschung Berlin GmbH,
Bereich Strahlenchemie
Postfach 390128, D-1000 Berlin 39 (Germany)

[**] Sulfur Compounds, Part 74.—Part 73: *H.-J. Mäusle, R. Steudel,* Z. Anorg. Allg. Chem., in press.

*0570-0833/81/0404-0394 $ 02.50/0*

er, only in traces, especially $S_{11}$ and $S_{13}$. $S_5$ was not detectable.

In the reaction of $SCl_2$ or $S_2Cl_2$ with salt-like iodides at 25 °C, elemental sulfur is formed by decomposition of the unstable iodosulfanes according to

$$S_nCl_2 + 2\,KI \rightarrow S_nI_2 + 2\,KCl$$
$$n\,SI_2 \rightarrow S_n + n\,I_2$$
$$n\,S_2I_2 \rightarrow S_{2n} + n\,I_2$$

Chromatograms have now revealed that all rings with $n = 6$—21 are formed from $SI_2$, the relative concentrations decreasing with increasing ring size (Fig. 1b). As expected, almost only even-numbered rings are obtained from $S_2I_2$ (detected up to $n = 22$; of which the following have already been isolated previously: $S_6$, $S_{12}$, $S_{18}$, $S_{20}$ and $S_x$[4]). Hence, the existence of the homocycles $S_n$ with $n = 11$, 13—17, 19, and 21—26, for whose formation (from $S_2$) there was previously only mass spectroscopic evidence[5] has been unequivocally proven for the first time.

We have further found that the eight-membered rings $S_8$ and $Se_8$ can be quantitatively separated from each other and from heterocycles of the types $Se_nS_{8-n}$[6] and $Se_nS_{12-n}$[7]. From these results it can be expected that the composition of a large number of complex reaction mixtures of sulfur-rich compounds can be elucidated by HPLC.

Received: October 6, 1980 [Z 735 IE]
German version: Angew. Chem. 93, 402 (1981)

CAS Registry numbers:
$S_6$, 13798-23-7; $S_7$, 21459-04-1; $S_8$, 10544-50-0; $S_9$, 18808-47-4; $S_{10}$, 19269-86-4; $S_{11}$, 60349-28-2; $S_{12}$, 14999-38-3; $S_{13}$, 77152-68-2; $S_{14}$, 60349-29-3; $S_{15}$, 77152-69-3; $S_{16}$, 60349-30-6; $S_{17}$, 77152-70-6; $S_{18}$, 41371-12-4; $S_{19}$, 77152-71-7; $S_{20}$, 42817-30-1; $S_{21}$, 77152-72-8; $S_{22}$, 77152-73-9; $S_{23}$, 77152-74-0; $S_{24}$, 77152-75-1; $S_{25}$, 77152-76-2; $S_{26}$, 77152-77-3

[1] *R. Steudel, H.-J. Mäusle*, Z. Anorg. Allg. Chem., in press.

[2] High pressure liquid chromatograph 5000 with CDS 111-L data system (Varian GmbH, Darmstadt); UV detector (254 nm) (Waters GmbH, Königstein/Ts.); Nucleosil C-18 column (particle size 10 μm); sample addition (10 mm³) as $CS_2$-solution.

[3] *R. Steudel, H.-J. Mäusle*, Angew. Chem. *89*, 114 (1977); *90*, 54 (1978); *91*, 165 (1979); Angew. Chem. Int. Ed. Engl. *16*, 112 (1977); *17*, 56 (1978); *18*, 152 (1979); Chem. Unserer Zeit *14*, 73 (1980).

[4] *H.-J. Mäusle, R. Steudel*, Z. Anorg. Allg. Chem. *463*, 27 (1980).

[5] *D. L. Cocke, G. Abend, J. H. Block*, J. Phys. Chem. *80*, 524 (1976).

[6] *R. Laitinen, L. Niinistö, R. Steudel*, Acta Chem. Scand. *A 33*, 737 (1979); *J. Weiss*, Z. Anorg. Allg. Chem. *435*, 113 (1977); *R. Cooper, J. V. Culka*, J. Inorg. Nucl. Chem. *27*, 755 (1965); *29*, 1217 (1967); *32*, 1857 (1970); and references cited therein.

[7] *J. Weiss, W. Bachtler*, Z. Naturforsch. *B 28*, 523 (1973).

## Reductive Cleavage of 3-Oxazolin-5-ones; Application to the Synthesis of β,γ-Unsaturated Ketones from Allyl *N*-Acyl-2-phenylglycinates[**]

By *Ulrich Niewöhner* and *Wolfgang Steglich*[*]

*Dedicated to Professor Appel on the occasion of his 60th birthday*

An essential step in a recently described method for the synthesis of β,γ-unsaturated ketones[1] is the cyclization of an allyl *N*-acyl-2-phenylglycinate *(1)* with $PPh_3/C_2Cl_6/NEt_3$[2] to give the 2-allyl-3-oxazolin-5-one *(2)*[3,4], which is subsequently hydrolyzed with alkali to the ketone *(3)*. Since side-reactions frequently occur during the hydrolysis we have searched for a better method for isolating the ketone.

We have found that the 3-oxazolinones *(2)* can be reductively cleaved under mild conditions by treatment with chromium(II) acetate and aqueous $H_3PO_2$ in dimethylformamide (DMF) (Method *A*)[6]. The pure β,γ-unsaturated ketones are isolated in good yields from the organic phase (Table 1), while phenylglycine remains in the aqueous solution.

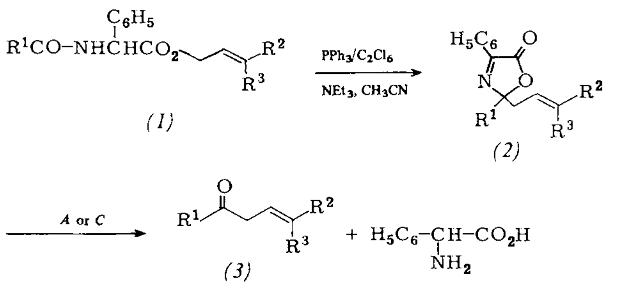
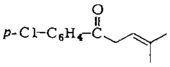
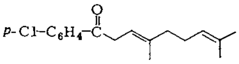
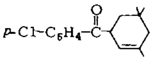
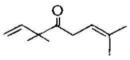
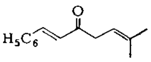
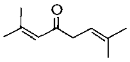
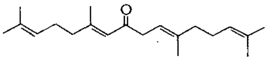
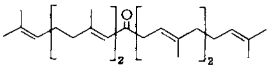


Table 1. β,γ-Unsaturated ketones *(3)* prepared from *(2)* [a].

| Compound | | Yield [%] | Method [b] | B.p. [°C/torr] [c] |
|---|---|---|---|---|
| *(3a)* |  | 94<br>85 | *A*<br>*B* | 130/0.1 [d] |
| *(3b)* |  | 97<br>47 | *A*<br>*B* | 180/0.25 |
| *(3c)* |  | 89 | *A* | |
| *(3d)* |  | 86 | *A* | 130/18 |
| *(3e)* |  | 59<br>77 | *B*<br>*C* [e] | 140/0.2 |
| *(3f)* |  | 54 | *B* | 135/14 |
| *(3g)* |  | 67 | *B* | 125/0.1 |
| *(3h)* |  | 64 | *B* | [f] |

[a] Structure and composition confirmed by NMR and IR data. [b] *A*: $Cr(OAc)_2$ reduction; *B*: $NaBH_4$ reduction and subsequent hydrolysis; *C*: $SnCl_2$ reduction. [c] Kugelrohr distillation at furnace temperature. [d] M.p. 43—45 °C (from $MeOH/H_2O$). [e] According to the ¹H-NMR spectrum contains 7% of the doubly conjugated dienone. [f] Undistilled, ¹H-NMR-pure 12-oxosqualene.

For reduction with tin(II) chloride the styrene derivative *(2e)* must be heated under reflux in citric acid, acetone, and water (method C), since the α,β-unsaturated ketone *(3e)* formed is further reduced by chromium(II) acetate to the dihydro compound[7].

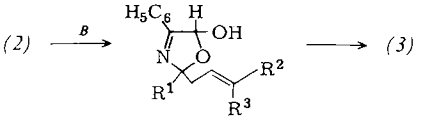
A further possible method for the isolation of the ketones *(3)* is the reduction of the oxazolinones *(2)* with $NaBH_4$ in tet-

---

[*] Prof. Dr. W. Steglich, Dipl.-Chem. U. Niewöhner
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[**] This work was supported by the Ministerium für Wissenschaft und Forschung des Landes Nordrhein-Westfalen and by BASF AG, Ludwigshafen.

rahydrofuran (THF) and anhydrous methanol (Method B). This leads almost quantitatively to the 3-oxazolin-5-oles *(4)*[8], which are cleaved with aqueous citric acid in presence of phloroglucinol at 100 °C to give *(3)*[9].



*(4)*

*Procedure*

*(3)* (Method A): A solution of *(2)* (5 mmol) and 50% $H_3PO_2$ (5.28 cm$^3$, 50 mmol) in oxygen-free DMF (50 cm$^3$) is treated in an inert atmosphere ($N_2$) with chromium(II) acetate (4.25 g, 25 mmol). The mixture is stirred for 45 min (TLC control), filtered and the precipitate carefully washed with 3.5 N HCl and ether. After separation of the ethereal phase, the filtrate is extracted with ether and the combined ether solutions are washed free of DMF. Subsequent drying and evaporation affords the NMR-pure ketones *(3)*.

*(3)* (Method B): Anhydrous methanol (5 cm$^3$) is poured directly into an ice-cooled solution of *(2)* (5 mmol) and $NaBH_4$ (0.57 g, 15 mmol) in THF (15 cm$^3$) (evolution of $H_2$!). The reaction solution is stirred for 2—3 h at 25 °C, evaporated down *in vacuo* rendered acidic with 20% citric acid, and extracted twice with ethyl acetate. The residue *(4)*, obtained on evaporation of the combined extracts is taken up in dioxane (15 cm$^3$), treated with 5 cm$^3$ 20% citric acid and 4.05 g (25 mmol) phloroglucinol dihydrate, and the mixture heated under reflux for 1—13 h. After hydrolysis is complete (TLC monitoring), water (30 cm$^3$) is added and the mixture extracted twice with petroleum ether (40—60 °C). The combined extracts are washed successively with a saturated $NaHCO_3$ solution and water, dried, and evaporated down *in vacuo* (in the case of readily volatile ketones, Vigreux column). *(3)* is purified by Kugelrohr distillation.

Received: December 10, 1980 [Z 737 IE]
German version: Angew. Chem. *93*, 411 (1981)

CAS Registry numbers:
*(1a)*, 62046-01-9; *(1b)*, 77080-14-9; *(1c)*, 77080-15-0; *(1d)*, 77080-16-1; *(1e)*, 77080-17-2; *(1f)*, 77080-18-3; *(1g)*, 77080-19-4; *(1h)*, 77080-20-7; *(2a)*, 62045-65-2; *(2b)*, 77097-68-8; *(2c)*, 77080-21-8; *(2d)*, 77080-22-9; *(2e)*, 77080-23-0; *(2f)*, 77080-24-1; *(2g)*, 77080-25-2; *(2h)*, 77080-26-3; *(3a)*, 62045-83-4; *(3b)*, 77080-27-4; *(3c)*, 77080-28-5; *(3d)*, 56663-68-4; *(3e)*, 77097-69-9; *(3f)*, 63426-15-3; *(3g)*, 77080-29-6; *(3h)*, 77080-30-9

---

[1] *N. Engel, B. Kübel, W. Steglich,* Angew. Chem. *89*, 408 (1977); Angew. Chem. Int. Ed. Engl. *16*, 394 (1977).

[2] *R. Appel, H. Schöler,* Chem. Ber. *110*, 2382 (1977); cf. also *R. Appel,* Angew. Chem. *87*, 863 (1975); Angew. Chem. Int. Ed. Engl. *14*, 801 (1975).

[3] *B. Kübel, G. Höfle, W. Steglich,* Angew. Chem. *87*, 64 (1975); Angew. Chem. Int. Ed. Engl. *14*, 58 (1975).

[4] When $R^2 = R^3 = H$ and $R^2$ or $R^3$ = alkyl, $R^2$ or $R^3 = H$, 4-allyl-2-oxazolin-5-ones are formed on cyclization; in the latter case they can be converted by heating in $CCl_4$ into 3-oxazolines *(2)* (Ref. [3] and *J. Fischer*, unpublished results).

[5] Double bond shift and subsequent dimerization, autoxidation (*N. Engel, W. Heitmann,* unpublished results).

[6] *D. H. R. Barton, N. K. Basu, R. H. Hesse, F. S. Morehouse, M. M. Pechet,* J. Am. Chem. Soc. *88*, 3016 (1966); cf. also *J. R. Hanson,* Synthesis *1974*, 1.

[7] *C. E. Castro, R. D. Stephens, S. Mojé,* J. Am. Chem. Soc. *88*, 4964 (1966); *J. B. Conant, H. B. Cutter, ibid. 48*, 1016 (1926).

[8] 1:1 Mixture of the diastereomers.

[9] For ease of cleavage by condensation with the phenylglyoxal moiety; cf. *G. H. A. Clowes,* Ber. Dtsch. Chem. Ges. *32*, 2841 (1899).

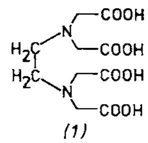
---

# The Stereology Concept: Novel Acidic Complexones and their Selectivity towards Cations[**]

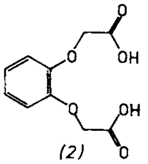
By *Reinhard Leppkes* and *Fritz Vögtle*[*]

*Dedicated to Professor Rolf Appel on the occasion of his 60th birthday*

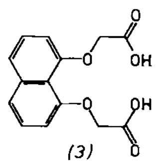
The stability constants and selectivity of ethylenediaminetetraacetic acid (ETDA) *(1)*, *O,O'*-pyrocatechol *(2)*[1] and analogous complexones in forming complexes can be varied if their donor functionalities are bonded to various anchor groups[2]. Although the anchor groups used until now have been recruited from the realms of classical chemistry with the donor functionalities separated only by a few bonds, novel possibilities exist today; for example donor centers can be attached to (proto-)[3a] phane skeletons[3b–d] at similar distances and disposition but separated by a greater number of bonds. Using these considerations as a starting point we firstly synthesized the acidic ligand systems *(4)* and *(5)*. We have characterized the ana*logy* between the *stereo*chemical disposition of the coordinating *donor* functions on going from *(3)*[4] to *(4)* and from *(1)* to *(5)* with the term *"donor-stereology"*[5].



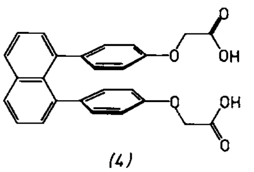
*(1)*



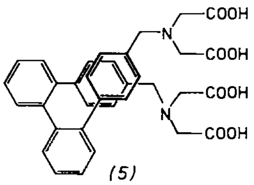
*(2)*



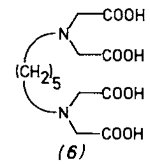
*(3)*



*(4)*



*(5)*



*(6)*

Example *(5)* illustrates that the application of this concept to the design of novel complexones meets with a high degree of success with regard to ligand efficiency.

According to *Schwarzenbach*[6a,b], EDTA forms stable monometallic complexes $[MY]^{2-}$[6c] with alkaline-earth metal ions by using both iminodiacetate groups cooperatively; the complex with hydrogen $[MHY]^-$ is only an intermediate of limited stability. In contrast, EDTA-homologues such as cadaverinetetraacetic acid *(6)* in which both donor groups are separated by a pentamethylene chain, can form complexes in which each of the iminodiacetate groups is bound to a metal ion [MY]. Among other reasons, this can be attributed to the reduction in stability caused by formation of a large chelate ring.

p$K_s$-values of the free ligand *(5)* and the stability constants of its complexes were determined by potentiometric titration[6a,b]. The stability constants of *(5)* (Table 1), which were determined in ethanol/water (1:1), are not quite as high as those of EDTA, but show structural singularities.

The stability constants found, indicate that *(5)* preferentially forms binuclear (dimetallic)[6b] complexes with the

---

[*] Prof. Dr. F. Vögtle, Dipl.-Chem. R. Leppkes
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

smaller alkaline-earth metal ions $Mg^{2+}$ and $Ca^{2+}$; in contrast, $Sr^{2+}$ and $Ba^{2+}$ ions appear to be preferably bound as monometallic complexes (cf. $\lg K_{k_2}$ in Table 1 and Fig. 1), because one-sided complexation of a metal ion by *one* iminodiacetate—as opposed to formation of monometallic complexes by cooperative bonding of both—leads to a reduction in the magnitude of the stability of the complexes with increasing cationic radius[2]. Intramolecular cooperation of all four carboxy groups satisfactorily explains the increase in $K_{k_2}$.

Table 1. Logarithms of the stability constants [a] of *(5)* as well as (for comparison) of EDTA *(1)* and *(6)*.

| Acid | $\lg K_{k_i}$ | $Mg^{2+}$ | $Ca^{2+}$ | $Sr^{2+}$ | $Ba^{2+}$ |
|---|---|---|---|---|---|
| *(1)* | i = 1 | 2.2(8) | 3.5(1) | 2.3(0) | 2.0(7) |
| | i = 2 | 8.6(9) | 10.5(9) | 8.6(3) | 7.7(6) |
| | i = 3 | — | < 0.7 | — | — |
| *(6)* | i = 1 | 3.63 | 3.50 | 2.72 | 2.38 |
| | i = 2 | — | 4.60 | — | — |
| | i = 3 | — | 2.60 | — | — |
| *(5)* | i = 1 | 4.0 | 4.2 | 3.6 | 3.7 |
| | i = 2 | 3.6 | 4.0 | 4.3 | 4.6 |
| | i = 3 | 4.4 | 4.4 | 3.0 | 2.8 |

[a] The constants $K_{k_i}$ are defined by the following complexation equilibria:

(1) $HY^{3-} + M^{2+} \rightleftharpoons MHY^{-}$
(2) $Y^{4-} + M^{2+} \rightleftharpoons MY^{2-}$
(3) $MY^{2-} + M^{2+} \rightleftharpoons M_2Y$

They are valid at 20 °C in 0.1 N KCl [*(1)* and *(6)*] or in ethanol/water (1:1) [*(5)*] as solvent. Standard deviation ±0.1.

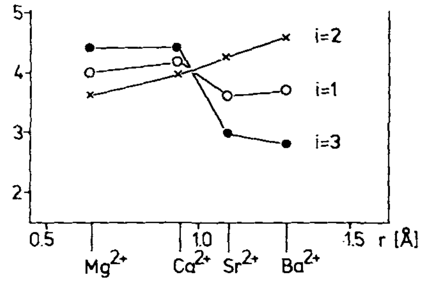
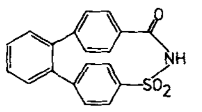


Fig. 1. Stability constants ($\lg K_{k_i}$) of *(5)* as a function of the cation radius.

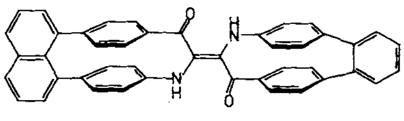
In complexation of larger cations, a phane-ring closure-like macrocyclization of the framework can apparently occur, which with *(5)* should lead to chiral (helical) structures[3b]. In this connection it would first have to be established that *cations as ring building blocks* can be incorporated ionically into large rings.

Discrimination, on the basis of ionic size, can accordingly be attributed to the spacer effect of the hydrocarbon-framework in *(5)* which is stereologous to the ethano group in EDTA, and which unlike the model compound *(1)* does not lead to the formation of complexes with small cations *via* both iminodiacetic functionalities.

Since a closely similar stereologous molecular structure does not necessarily lead to closely similar chemical behaviour, it follows that *(4)*, unlike *(2)*, does not form a crystalline potassium complex[1] under analogous conditions, but only a hemihydrate of the free carboxylic acid (elemental analysis). In consequence, the scope of application and limits of the stereology concept must be studied, especially to determine whether it is restricted to ligands ("donor-stereology") or cooperating functional groups. The examples *(7)* and *(8)* illustrate further applications.



*(7)* *"stereologous saccharin"*



*(8)* *"stereologous indigo"*

### *Procedure*

*(5)*[7]: Reaction of 4,4'''-bis(bromomethyl)-*o*-quaterphenyl[8] with dimethyl iminoacetate[9] and saponification, leads to formation of *(5)* in 72% yield; m.p. = 200—201 °C ($H_2O$) (decomp.); $^1H$-NMR ([$D_6$]DMSO, TMS int.): $\delta = 3.45$ (s, 8H, $NCH_2$), 3.75 (s, benzyl, $CH_2$).

*(4)*[7]: 1,8-diiodonaphthalene was coupled with 4-methoxyphenylmagnesium iodide to form 1,8-bis(4-methoxyphenyl)naphthalene (m.p. = 144—146 °C)[10]. Cleavage of the ether by $BBr_3$ produced 4,4'-(1,8-naphthylene)diphenol (m.p. = 253—254 °C) and reaction of this species with bromoethyl acetate in acetone followed by alkaline hydrolysis gave *(4)*$\cdot 1/2\,H_2O$, m.p. = 275—276 °C; $^1H$-NMR ([$D_6$]DMSO, TMS, int.): $\delta = 4.50$ (s, 4H, $CH_2$).

Received: October 2, 1980 [Z 738 IE]
German version: Angew. Chem. *20*, 404 (1981)

CAS Registry numbers:
*(1)*, 60-00-4; *(4)*, 77256-09-8; *(5)*, 77256-10-1; *(6)*, 1798-14-7; 4,4'''-bis(bromomethyl)-*o*-quaterphenyl, 61846-71-7; dimethyliminodiacetate, 6096-81-7; 1,8-diiodonaphthalene, 1730-04-7; 4-methoxyphenyl iodide, 696-62-8; 1,8-bis(4-methoxyphenyl)naphthalene, 77256-11-2; 4,4'-(1,8-naphthylene)diphenol, 77256-12-3; Mg, 7439-95-4; Ca, 7440-70-2; Sr, 7440-24-6; Ba, 7440-39-3

---

[1] *E. A. Green, W. L. Duax, G. M. Smith, F. Wudl,* J. Am. Chem. Soc. *97*, 6689 (1975).

[2] a) *G. Schwarzenbach, H. Flaschka:* Die komplexometrische Titration. Enke, Stuttgart 1965; b) *R. Pribil:* Die Komplexone in der chemischen Analyse. VEB Deutscher Verlag der Wissenschaften, Berlin 1961.

[3] a) *Th. Kauffmann,* Tetrahedron *28*, 5183 (1972); *Th. Kauffmann, G. Beißner, R. Maibaum,* Angew. Chem. *83*, 795 (1971); Angew. Chem. Int. Ed. Engl. *10*, 740 (1971); b) *F. Vögtle, M. Atzmüller, W. Wehner, J. Grütze, ibid. 89*, 338 (1977); *16*, 325 (1977); c) *E. Hammerschmidt, F. Vögtle,* Chem. Ber. *112*, 1785 (1979); d) *R. Leppkes,* Diplomarbeit, Universität Bonn 1979.

[4] Cf. *E. Blasius, G. Kynast,* J. Radioanal. Chem. *2*, 55 (1969).

[5] Cf. in this connection the "Isokonformations-Konzept": *H. Lehner,* Monatsh. Chem. *105*, 895 (1974) and *D. K. Johnson, P. S. Pregosin, L. M. Venanzi,* Helv. Chim. Acta *59*, 2691 (1976).

[6] a) *G. Schwarzenbach, H. Ackermann,* Helv. Chim. Acta *30*, 1798 (1947); b) *ibid. 31*, 1029 (1948); c) $H_{4-n}Y^{n-}$ is normally used to symbolize a tetrabasic acid or its anions.

[7] Satisfactory elemental analyses were obtained for the new compounds, and the mass spectra are consient with the given structures.

[8] *M. Atzmüller,* Dissertation, Universität Bonn 1978.

[9] *G. Shtacher, W. Taub,* J. Med. Chem. *9*, 197 (1966).

[10] After the method of *R. L. Cough, P. Mison, J. D. Roberts,* J. Org. Chem. *41*, 2252 (1976).

---

## Diastereoselective Synthesis of β-Nitro- and β-Aminoalcohols

By *Dieter Seebach, Albert K. Beck, Friedrich Lehr, Thomas Weller* and *Ernest Colvin*[*]

The nitro-aldol or Henry reaction[1] is an important process for the formation of C—C bonds. As shown in path *(a)*[1a], starting from aldehydes and nitroalkanes, β-nitroalco-

---

[*] Prof. Dr. D. Seebach, A. K. Beck, Dr. F. Lehr, Dipl.-Chem. Th. Weller, Dr. E. W. Colvin
Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

hols *(1)* are formed, which—with the exception of cyclization methods[2]—are obtained as mixtures of the two possible diastereomeric pairs of enantiomers (*RR/SS* and *RS/SR*). Usually, the diastereomer *A* is predominant; the ratio *A*:*B* (up to 3:1) remains unchanged if the mixture is treated with *tert*-butyl(dimethyl)silyl (TBDMS) chloride/imidazole in dimethylformamide[3] to give *(2)*.

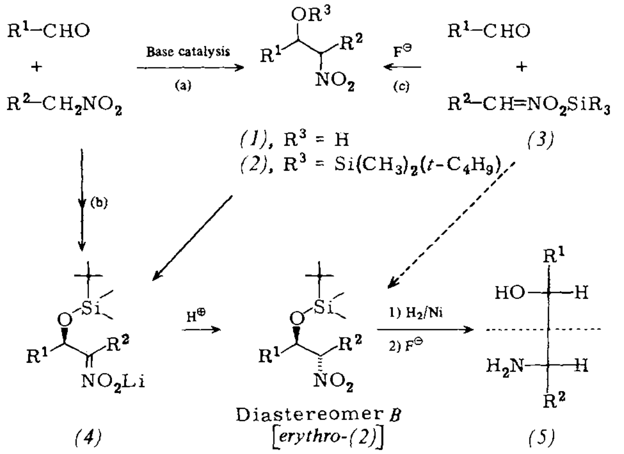


Table 1. Enrichment of the diastereomer *(B)* (probably the *erythro*-form, see text) of the classically prepared [1 a] isomeric mixtures *(2)* by deprotonation of the *O*-silyl nitroalcohols to *(4)* and low temperature protonation, and examples of the fluoride-catalyzed silylnitroaldol reaction leading to diastereomer B. The given product ratios were determined by quantitative $^{13}C$-NMR spectroscopy. The signals for the α-nitro-C-atoms are situated at $\delta = 85$—98, and those of the 2-silyloxy-C-atoms at $\delta = 70$—78; the α-nitro signals in the diastereomers *B* appear at higher field, and the α-silyloxy signals at lower field than in the corresponding diastereomers *A*. In contrast to *B*, the methyl groups of the TBDMS-function in *A* are isochronic. All compounds gave satisfactory elemental analyses. $Bu_4NF$, which had been dried over a molecular sieve, was used in path (c) [cf. *H. Gerlach, P. Kunzler*, Helv. Chim. Acta *61*, 2503 (1978)].

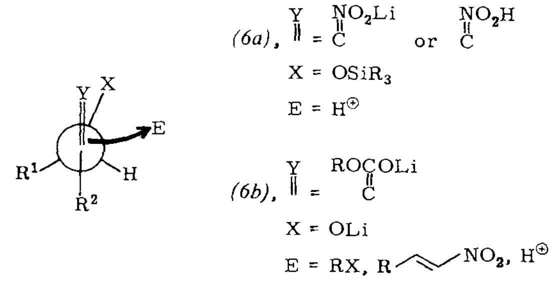
| Substituents | | Ratio of the diastereomers *B*:*A* (% B) in *(2)* | | | | | |
|---|---|---|---|---|---|---|---|
| | | before deprotonation to *(4)* | | after protonation from *(4)* | | from *(3)* path (c) | |
| *R*¹ | *R*² | | | | | | |
| $C_3H_7$ | $C_2H_5$ | 1:2.5 | (29) | 9:1 | (90) | >20:1 | (>95) |
| $CH(CH_3)_2$ | $C_2H_5$ | 1:1 | (50) | >20:1 | (>95) | | |
| $C_3H_7$ | $CH(CH_3)_2$ | 2:1 | (66) | >20:1 | (>95) | | |
| $C_5H_{11}$ | $CH_3$ | 1:1 | (50) | >20:1 | (>95) | >20:1 | (>95) |
| $C_5H_{11}$ | $C_2H_5$ | 1:2 | (34) | >20:1 | (>95) | >20:1 | (>95) |
| $C_3H_7$ | $C_7H_{15}$ | 1:2 | (34) | 4.5:1 | (82) | >20:1 | (>95) |
| $C_{10}H_{21}$ | $CH_3$ | 1:1 | (50) | >20:1 | (>95) | | |
| $C_5H_{11}$ | $C_9H_{19}$ | 1:2 | (34) | 2:1 | (66) | | |
| $C_6H_5$ | $C_2H_5$ | 1:3 | (25) | 4.5:1 | (82) | 3.5:1 | (78) |

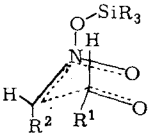
As a contribution to the diastereoselective synthesis of *open chain* compounds[4], we report a simple trick, by which *one* diastereomer-*B*- of the TBDMS-protected nitroalcohols *(2)* can be prepared, in some instances in more than 97% selectivity: Deprotonation of *(2)*, as an *A/B* mixture, (see Table 1, column 3) by lithium diisopropylamide in tetrahydrofuran at dry ice temperature afforded the enantiomeric pair *(4)*. When the resulting solution was treated with glacial acetic acid at low temperature[5] (1:1 mixture with THF, fivefold excess of acid), *(2)* was reisolated in *ca.* 80% yield. The product, in which B was previously the minor component now contained *B* as the major component [see Table 1, column 4; exceptions: $R^1 = C_3H_7$, $R^2 = CH(CH_3)_2$]. Solutions of the *aci*-nitro salts *(4)* required for diastereoselective protonation, can also be prepared by silylation of the primary adducts[6] obtained from reaction of doubly deprotonated nitroalkanes[7] and aldehydes with TBDMSCl (see path (b)).

We have now found that the direct synthesis of silyl nitroalcohols *(2)* *via* C—C bond formation, *i.e.* addition of silylated *aci*-nitro derivatives *(3)* catalyzed by fluoride ions as shown in path (c)[1c], can also be carried out diastereoselectively: The compounds *(2)* synthesized *via* this novel variation of the Henry reaction[1c] are obtained—with the exception of the benzaldehyde adduct—as practically pure diastereomers of type *B* (see Table 1, column 5), as shown by comparison of their $^1H$-NMR spectra with the spectra of compounds obtained by protonation of *(4)*.

*Preliminary* assignment of the configuration of *A* and *B* was carried out as follows: Catalytic hydrogenation of the nitro group over completely neutral, washed Raney nickel and desilylation ($Bu_4NF$/THF)[3b] gave—without loss of diastereomeric purity—the aminoalcohols *(5)*, whose *erythro*-form, according to the literature[8], should have the smaller (3—4 Hz) and whose *threo*-form the larger (*ca.* 6 Hz) vicinal [$C\underline{H}(NH_2)$—$C\underline{H}(OH)$]—coupling constant in the $^1H$-NMR spectrum.

We do not wish to speculate at present about the reasons for the diastereoselective protonation of *(4)*[9]; the result can be accounted for *via* the same model *(6)* used to describe the reactions of doubly deprotonated β-hydroxyesters[10] [cf. *(6a)* with *(6b)*].





*(7)*

The preferential formation of one diastereomer in the silyl nitro-aldol reaction [path (c)] is consistent with the mechanism suggested for the normal aldol reaction[4, 11] [see formula *(7)*].

The results described indicate firstly that nitroalcohol derivatives can be prepared diastereoselectively and also that the β-aminoalcohols *(5)*, which cannot be obtained by the opening of epoxide rings with $NH_3$ or by $HO/H_2N$-addition to alkenes (oxyamination)[12] are now accessible.

Received: September 1, 1980 [Z 739 IE]
Supplemented: November 6, 1980
German version: Angew. Chem. *93*, 422 (1981)

---

[1] a) *L. Henry*, C. R. Acad. Sci. *120*, 1265 (1895); review of the nitro-aldol reaction: Houben-Weyl-Müller, Methoden der Organischen Chemie. Bd. 10/1. Thieme, Stuttgart 1971, p. 246 ff.; b) Review of nitroalkanes in organic synthesis: *D. Seebach, E. W. Colvin, F. Lehr, Th. Weller*, Chimia *33*, 1 (1979). c) *E. W. Colvin, D. Seebach*, J. Chem. Soc. Chem. Commun. *1978*, 689; *E. W. Colvin, A. K. Beck, B. Bastani, D. Seebach, Y. Kai, J. D. Dunitz*, Helv. Chim. Acta *63*, 697 (1980).

[2] See *e. g.: V. Ehrig, D. Seebach*, Chem. Ber. *108*, 1961 (1975); *D. Seebach, M. S. Hoekstra, G. Protschuk*, Angew. Chem. *89*, 334 (1977); Angew. Chem. Int. Ed. Engl. *16*, 321 (1977); *Th. Weller, D. Seebach, R. E. Davis, B. B. Laird*, Helv. Chim. Acta *64*, 736 (1981).

*0570-0833/81/0404-0398 $ 02.50/0*

[3] a) *G. Stork, P. F. Hudrlik*, J. Am. Chem. Soc. *90*, 4462 (1968); b) *E. J. Corey, A. Venkateswarlu, ibid. 94*, 6190 (1972); *H. Gerlach, K. Oertle, A. Thalmann*, Helv. Chim. Acta *60*, 2860 (1977).

[4] Review: *P. A. Bartlett*, Tetrahedron *36*, 3 (1980), and literature cited therein.

[5] Internal temperature; to permit rapid addition of acid, a bath at a temperature of between −90 to −100 °C was used.

[6] In certain cases it is possible to increase the fraction of *A* in *(1)* by protonating the doubly deprotonated nitroalkohols, $R^1—CH(OLi)—C(NO_2Li)R^2$ [7].

[7] *D. Seebach, F. Lehr*, Helv. Chim. Acta *62*, 2239 (1979); *F. Lehr, J. Gonnermann, D. Seebach, ibid. 62*, 2258 (1979).

[8] *B. Renger, D. Seebach*, Chem. Ber. *110*, 2334 (1977), and literature cited therein.

[9] Cf. diastereoselective protonation in the Wittig reaction. *E. J. Corey, H. Yamamoto*, J. Am. Chem. Soc. *92*, 226 (1970); *M. Schlosser, K. F. Christmann*, Justus Liebigs Ann. Chem. *708*, 1 (1967); *M. Schlosser, K. F. Christmann, A. Piskala, D. Coffinet*, Synthesis *1971*, 29; as well as enantioselective protonation of enamines: *H. Matsushita, M. Noguchi, M. Saburi, S. Yoshikawa*, Bull. Chem. Soc. Jpn. *48*, 3715 (1975); *H. Matsushita, Y. Tsujino, M. Noguchi, S. Yoshikawa, ibid. 49*, 3629 (1976); *H. Matsushita, Y. Tsujino, M. Noguchi, M. Saburi, S. Yoshikawa, ibid. 51*, 862 (1978); *L. Duhamel, J.-C. Plaquevent*, Tetrahedron Lett. *1977*, 2285; J. Am. Chem. Soc. *100*, 7415 (1978); Tetrahedron Lett. *1980*, 2521.

[10] *Th. Weller, M. Züger, D. Seebach*, Helv. Chim. Acta *63*, 2005 (1980), and literature cited therein.

[11] *J. Mulzer, G. Brüntrup, J. Finke, M. Zippel*, J. Am. Chem. Soc. *101*, 7723 (1979).

[12] *J.-E. Bäckvall, K. Oshima, R. E. Palermo, K. B. Sharpless*, J. Org. Chem. *44*, 1953 (1979), and literature cited therein.

---

# Epimeric Equilibration and Substituent Interaction in 2-Oxetanones (β-Lactones)

By *Johann Mulzer* and *Matthias Zippel*[*]

*cis-trans*-Equilibria of *cis-trans* disubstituted four-membered rings[1] have apparently been studied to only a limited extent so far[2]. We wish to report—to our knowledge the first—successful equilibration of β-lactones (2-oxetaneones)[3] of type *(1)/(2)*.

*(1)*

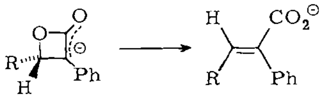
*(2)*

Table 1. Position of equilibrium and ΔG′ values for the equilibration of *(1)* to *(2)*. K = [*(1)*]/[*(2)*].

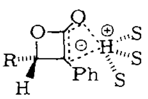
| | R | *K* [a] | Δ*G* [kcal/mol] | Δ*G* [kcal/mol] [kJ/mol] |
|---|---|---|---|---|
| *a* | $CH_3$ | 0.36 | 0.73 | 3.1 |
| *b* | $C_2H_5$ | 0.22 | 1.1 | 4.6 |
| *c* | $CH(CH_3)_2$ | 0.20 | 1.2 | 5.0 |
| *d* | $C(CH_3)_3$ | <0.02 | >2.8 | >11.7 |

[a] Determined by ¹H-NMR (precision ±2%).

The equilibration (Table 1), which is complete after 2 hours in triethylamine at 89 °C, proceeds *via* deprotonation/reprotonation at C-3; addition of $D_2O$ to the reaction mixture results in complete H/D-exchange at this center. Astonishingly, ring-opening does not occur. A free enolate ion of type *(3)* therefore cannot be an intermediate in the epimerization, since *(3)* under the reaction conditions would spontaneously isomerize to the acrylate ion *(4)*[4]. Instead, we postulate a contact ion-pair *(5)* in which the proton, enolate and solvent (S) are tightly associated.



*(3)* *(4)*

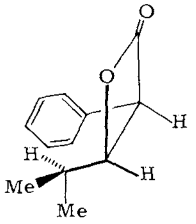


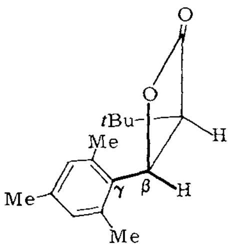
*(5)*

Although the ring substituents in *(1a—c)* are held in a rigid, almost eclipsed arrangement, the resulting van der Waals compression is insufficient for shifting the equilibrium totally to the side of *(2)*. This is only observed for *(1d)*, which possesses a bulky substituent R. In *(1a—c)*, the substituents R are always able to adopt an unhindered conformation, whereas large repulsions between the *tert*-butyl group and phenyl group cannot be avoided in *(1d)*.

The interaction of the *cis*-eclipsed substituents in β-lactones of type *(1)* manifests itself not only in the rearrangement to *(2)*, but also in the ¹H-NMR spectra. In consequence, the $CH_3$-signals in *(1c)* are clearly anisochronic ($\delta_1 = 0.47$, $\delta_2 = 1.00$ in $CCl_4$) whereas they are almost concordant in *(2c)* ($\delta_1 = 0.97$, $\delta_2 = 1.07$ in $CCl_4$). This may be due to the preferred conformation of the isopropyl group in *(1c)*; in contrast, the isopropyl group in *(2c)* enjoys almost unrestricted rotational freedom.

*(1c)*





*(1e)*

The exceedingly bulky substituents in the *cis*-lactone *(1c)* lead to a "frozen" conformation about the β—γ bond: at 37 °C the two *o*-methyl groups of the mesityl moiety have considerably different ¹H-NMR chemical shifts ($\delta_1 = 2.02$, $\delta_2 = 2.40$ in 1,2-dichlorobenzene). Coalescence of the two singlets occurs at 124 ± 1 °C, from which an energy barrier to rotation about the β,γ-bond of 23.6 kcal/mol (98.6 kJ/mol) can be estimated[5]; the value being unusually high compared to similar systems[5]. In contrast, the *o*-methyl groups of the mesityl moiety in the *trans*-isomer *(2e)* absorb isochronically at $\delta = 2.34$ (in 1,2-dichlorobenzene).

Received: October 28, 1980 [Z 740 IE]
German version: Angew. Chem. *93*, 405 (1981)

CAS Registry numbers:
*(1a)*, 70982-83-1; *(1b)*, 70982-84-2; *(1c)*, 71647-90-0; *(1d)*, 71647-84-2; *(1e)*, 77241-92-0; *(2a)*, 74686-88-7; *(2b)*, 74686-87-6; *(2c)*, 70982-88-6; *(2d)*, 69974-12-5; *(2e)*, 77241-93-1

---

[*] Dr. J. Mulzer, Dipl.-Chem. M. Zippel
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München (Germany)

[1] See *e.g.* a) *E. Eliel*: Conformational Analysis. Wiley, New York 1965, p. 58ff.

[2] For the equilibration of 2-thietanones, see *S. D. Carter, R. J. Stoodley*, J. Chem. Soc. Chem. Commun. *1977*, 92.

[3] Stereospecific synthesis of *(1)* and *(2)*: *J. Mulzer et al.*, unpublished results.

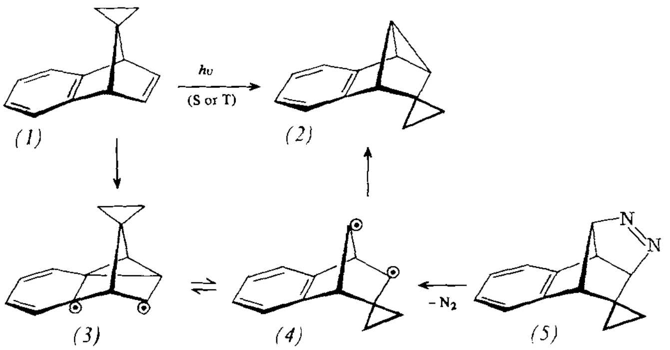
[4] Cf. *J. Mulzer, Th. Kerkmann*, J. Am. Chem. Soc. *102*, 3620 (1980).

[5] *H. Kessler*, Angew. Chem. *82*, 237 (1970); Angew. Chem. Int. Ed. Engl. *9*, 219 (1970).

# Thermal and Photochemical Denitrogenation of a Polycyclic Azoalkane as Mechanistic Probe for the Di-π-Methane Rearrangement of 7,7-Dimethylenebenzonorbornadiene[**]

By *Waldemar Adam* and *Ottorino De Lucchi*[*]

One of the most intriguing photorearrangements to have been intensively investigated for mechanistic as well as synthetic purposes, is the ubiquitous di-π-methane rearrangement[1]. For example, 7,7-dimethylenebenzonorbornadiene *(1)* rearranges into the polycycle *(2)* on direct and sensitized photolysis[2], presumably *via* the diradicals *(3)* and *(4)*. It was recently demonstrated[3] that denitrogenation of polycyclic azoalkanes constitutes an effective route for the independent generation of such diradical intermediates and thereby substantiates experimentally the mechanism of such di-π-methane rearrangements.



*Via* the novel dipolar cycloaddition[4] of *N*-phenyl-1,2,4-triazoline-3,5-dione (PTAD) to *(1)* we prepared the polycyclic azoalkane *(5)*[5], which provides a convenient entry to the diradical manifold postulated for the di-π-methane rearrangement of *(1)*. Presently we communicate our findings on the thermal and photochemical denitrogenation of azoalkane *(5)*. Our results, *i.e.*

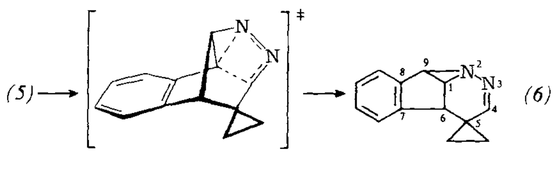
a) thermolysis of *(5)* at *ca.* 400 °C affords only *(2)*,
b) direct photolysis of *(5)* at 350 nm ($n_- \rightarrow \pi^*$ transition of the azo-chromophore) and at 254 nm ($\pi \rightarrow \pi^*$ excitation of the benzene ring) gives mainly (99.5 ± 0.3%) *(2)* and traces (*ca.* 0.5 ± 0.1%) of *(1)*,
c) benzophenone-sensitized photolysis of *(5)* at 300—330 nm results in the unusual rearrangement product *(6)*,

have important mechanistic implications on the di-π-methane rearrangement of *(1)*.

Vacuum flash pyrolysis of azoalkane *(5)* (*ca.* 400 °C/0.3 torr, substrate at 60 °C) afforded *(2)* quantitatively, which was characterized by comparison of its IR and $^1$H-NMR spectra with authentic material. By VPC analysis it was established that no *(1)* was produced in the thermal denitrogenation of *(5)*. Control experiments confirmed that the VPC detection limit was *ca.* 0.01%. Consequently, the singlet bicyclo[2.2.1]heptenediyl diradical *(4)* that is generated in the thermal denitrogenation of azoalkane *(5)* does not revert to the cyclopropanedimethyl diradical *(3)*.

Under the conditions of direct photolysis (0.01 M solution of *(5)* in pentane, Rayonet Photoreactor) the educt *(1)* was converted, as control experiments showed, into the di-π-methane product *(2)*. To suppress this menacing rearrangement, the photo-extrusion of nitrogen from *(5)* was carried out to less than 5% conversion. Product yields were established by quantitative VPC. The di-π-methane reaction *(1)*→*(2)* was negligible under these photolysis conditions. Therefore, the small amount (*ca.* 0.5%) of *(1)* formed in the photodenitrogenation of azoalkane *(5)* is an authentic primary photoproduct. We conclude again that the singlet bicyclo[2.2.1]heptenediyl diradical *(4)*, formed in the direct photolysis of azoalkane *(5)* by nitrogen loss, prefers to cyclize into *(2)*; but a small fraction rearranges *via* the diradical *(3)* into *(1)*. Clearly, the excited state energy surfaces for the di-π-methane reaction of bicycloalkadiene *(1)* and for the photodenitrogenation of azoalkane *(5)* are connected, albeit inefficiently, through the interconverting respective diradicals *(3)* and *(4)*.

Analogously to the corresponding polycycle without spirocyclopropane ring[6], the benzophenone-sensitized photolysis of azoalkane *(5)* (irradiation of a pentane solution 0.1 M in *(5)* and 1.0 M in benzophenone in a Rayonet photoreactor equipped with 300 nm lamps, using a Pyrex vessel and an aqueous $K_2Cr_2O_7$—$K_2CO_3$ filter to allow only 300—330 nm radiation to pass[3a]) gave exclusively ($^1$H-NMR) the novel rearrangement product *(6)*[7]. Unfortunately, this unexpected product *(6)* of the triplet sensitization of *(5)* did not permit us to populate the diradical manifold which connects the triplet excited state energy surfaces of the di-π-methane reaction of bicycloalkadiene *(1)* with the photodenitrogenation of azoalkane *(5)*. Consequently, no mechanistic conclusions can be drawn from our results about the behavior of the triplet diradicals *(3)* and *(4)*.



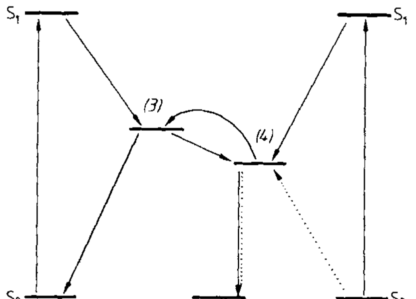


Fig. 1. Qualitative energy diagram for the pyrolytic (····) and direct photolytic (—) denitrogenation of azoalkane *(5)* and di-π-methane rearrangement of bicycloalkadiene *(1)*.

The pyrolytic and direct photolytic denitrogenations of *(5)* are mechanistically rationalized in the qualitative energy diagram shown in Figure 1. The rearrangements between the cyclopropanedimethyl diradical *(3)* and the bicyclo[2.2.1]heptenediyl diradical *(4)* interconnect the di-π-methane rearrangement of the bicycloalkadiene *(1)* and the de-

---

[*] Prof. Dr. W. Adam (NIH Career Awardee, 1975—1980),
Dr. O. De Lucchi
Department of Chemistry, University of Puerto Rico
Rio Piedras, Puerto Rico 00931 (USA)
and Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (address for correspondence)

[**] Acknowledgements are made to the Donors of the Petroleum Research Fund administered by the American Chemical Society (Grant No. 11022-AC1), the National Science Foundation (Grant No. 78-12621), the National Institutes of Health (Grant Nos. GM-00141-04 and RR-8102-07), the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie for financial support.

0570-0833/81/0404-0400 $ 02.50/0

nitrogenation of azoalkane *(5)*. The energy gap between the singlet state diradicals *(3)* and *(4)* is apparently quite large so that the thermal denitrogenation of *(5)* leads exclusively to the polycycle *(2)* *via* diradical *(4)*. However, in the direct photolysis the denitrogenation of *(5)* generates a sufficiently "hot" diradical *(4)* that a small fraction suffers *retro*-di-π-methane rearrangement into bicycloalkadiene *(1)* *via* diradical *(3)*. Therefore, the diradical *(4)* constitutes an effective funnel[8] on the interconnecting singlet excited state energy surfaces for the di-π-methane rearrangement of bicycloalkadiene *(1)* and the denitrogenation of azoalkane *(5)*.

Received: December 5, 1980 [Z 741 IE]
German version: Angew. Chem. *93*, 408 (1981)

CAS Registry numbers:
*(1)*, 22003-58-3; *(2)*, 22003-59-4; *(3)*, 77241-94-2; *(4)*, 77241-95-3; *(5)*, 74045-84-4; *(6)*, 77241-96-4

---

[1] *S. S. Hixson, P. S. Mariano, H. E. Zimmerman*, Chem. Rev. *73*, 531 (1973).

[2] a) *B. M. Trost*, J. Org. Chem. *34*, 3644 (1969); b) *W. Eberbach, P. Würsch, H. Prinzbach*, Helv. Chim. Acta *53*, 1235 (1970).

[3] a) *H. E. Zimmerman, R. J. Boettcher, N. E. Buehler, G. E. Keck, M. G. Steinmetz*, J. Am. Chem. Soc. *98*, 7680 (1976); b) *W. Adam, N. Carballeira, O. De Lucchi, ibid. 102*, 2107 (1980).

[4] *W. Adam, O. De Lucchi*, Angew. Chem. *92*, 815 (1980); Angew. Chem. Int. Ed. Engl. *19*, 762 (1980).

[5] *(5)*, 72% yield, m.p. 85—86 °C, colorless needles from hexane; $^1$H-NMR ($CCl_4$, ext. TMS): $\delta = 0.0—1.37$ (4H, m, spirocyclopropane), 2.30 (1H, narrow m), 3.33 (1H, narrow m), 4.00 (1H, narrow m), 5.45 (1H, narrow m), 6.95 (4H, m, $C_6H_4$); IR ($CCl_4$): $\nu = 3080$, 3010, 1495, 1470, 1450, 1430, 1260, 1210, 1175, 1150, 1140, 1022, 940, 905 $cm^{-1}$; UV (hexane): $\lambda_{max}(\varepsilon) = 220—253$ (802), 263 (661), 272 (801), 278 (784), 350 (sh, 385), 360 nm (543).

[6] *W. Adam, O. De Lucchi*, J. Am. Chem. Soc. *102*, 2109 (1980).

[7] *(6)*, 41% yield (isolated from acetone-sensitized photolysis), m.p. 133—135 °C (acetone/pentane 1:1); $^1$H-NMR ($CDCl_3$, TMS): $\delta = 0.6—1.3$ (4H, m, spirocyclopropane), 2.65 (1H, d, $J_{1,6} = 5.83$ Hz, 6-H), 3.62 (1H, dd, 1-H), 3.88 (1H, d, $J_{1,9} = 3.67$ Hz, 9-H), 6.90 (1H, s, 4-H), 6.90—7.40 (4H, m, $C_6H_4$); IR (KBr): $\nu = 3075$, 3060, 3005, 1630, 1600, 1475, 1460, 1322, 1310, 1230, 1163, 1040, 990, 962, 770, 760, 700 $cm^{-1}$. Decoupling experiments were decisive in establishing this structure assignment.

[8] *J. Michl*, Photochem. Photobiol. *2*, 27 (1970).

---

## A Novel Organometallic Cluster with $Ir_4C_2$-framework and Fluxional Hydrido Bridges

By *Jörn Müller, Helmuth Menig*, and *Joachim Pickardt*[*]

Dimeric ($\eta^4$-cyclodiene)chloroiridium complexes react with isopropylmagnesium halides in the presence of cyclodienes to form bis($\eta^4$-cyclodiene)hydridoiridium compounds[1], while in the presence of cyclotrienes, ($\eta^4$-cyclodiene)($\eta^5$-cyclodienyl)iridium complexes are produced[2]. As an example, the reaction of $[Ir(COD)Cl]_2$[3] (COD = 1,5-cyclooctadiene) with $i$-$C_3H_7MgBr$ and 1,3-cyclohexadiene proceeding *via* β-elimination of propene from the unstable (1,3-$C_6H_8$)(COD)Ir—$i$-$C_3H_7$ to ($\eta^4$-1,3-cyclohexadiene)($\eta^4$-COD)IrH which has a fluctional structure in solution, can be mentioned[1].

We have now investigated the reaction of $[Ir(COD)Cl]_2$ with $i$-$C_3H_7MgBr$ in ether in the absence of other olefinic ligands: the results indicate that the initial product, the coordinatively unsaturated (COD)Ir—$i$-$C_3H_7$ species is stabilized in an unusual way *via* formation of a polynuclear compound. An orange, diamagnetic complex *(1)*, which is air-stable in the solid state, was isolated; the empirical formula, based on the results of elemental analysis and mass spectroscopy ($M^+$ at $m/e = 1248$, based on $^{193}$Ir), corresponds to $C_{35}H_{56}Ir_4$.

The X-ray diffraction analysis[4] of *(1)* indicated an unexpected structural scheme (cf. Fig. 1). The four iridium atoms are arranged in a "butterfly-shape" and together with the acetylenic C atoms of a propyne unit form a closed six-membered cluster framework of approximate $C_s$-symmetry; compounds $Co_4(CO)_{10}(C_2Et_2)$[5], $Ru_4(CO)_{11}(C_8H_{10})$[6] and $Ir_4(CO)_5(COD)_2(C_8H_{10})$[7] have a similar $M_4C_2$ basic framework. Each Ir atom has an $\eta^4$-bonded COD ligand having the usual boat conformation. If the propyne unit is considered to be a four electron donor, the cluster still needs four electrons to complete the 60 electron configuration required by its structure and diamagnetism. These electrons are contributed by four hydrido ligands whose presence is established spectroscopically.

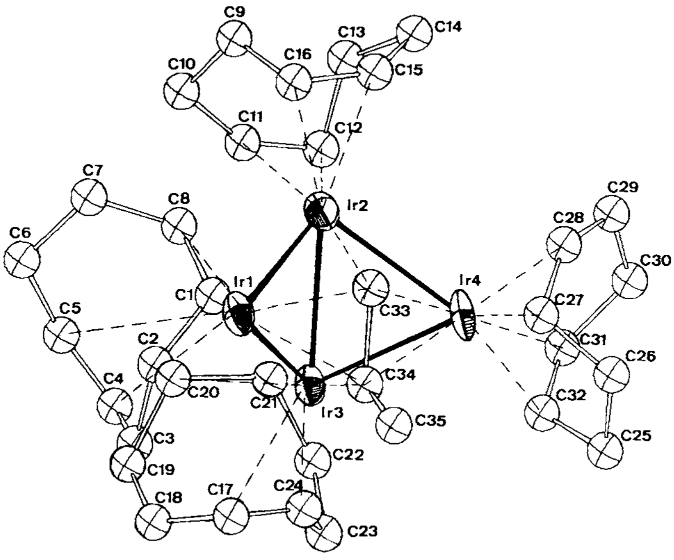


Fig. 1. ORTEP drawing of molecule *(1)*.

| Cluster bond lengths [pm] | | Ir—(COD) bond lengths [pm] | |
|---|---|---|---|
| Ir1—Ir2 | 281.6 | Ir1—C1 | 223.0 |
| Ir1—Ir3 | 281.0 | Ir1—C4 | 231.9 |
| Ir2—Ir3 | 279.8 | Ir1—C5 | 230.7 |
| Ir2—Ir4 | 282.2 | Ir1—C8 | 223.3 |
| Ir3—Ir4 | 278.0 | Ir2—C11 | 238.4 |
| Ir1—C33 | 221 | Ir2—C12 | 227.5 |
| Ir2—C33 | 222 | Ir2—C15 | 231.4 |
| Ir4—C33 | 218 | Ir2—C16 | 211.8 |
| Ir1—C34 | 239 | Ir3—C17 | 224.0 |
| Ir3—C34 | 210 | Ir3—C20 | 241.5 |
| Ir4—C34 | 234 | Ir3—C21 | 230.0 |
| C33—C34 | 156 | Ir3—C24 | 231.0 |
| | | Ir4—C27 | 218.5 |
| | | Ir4—C28 | 228.4 |
| | | Ir4—C31 | 232.8 |
| | | Ir4—C32 | 218.6 |

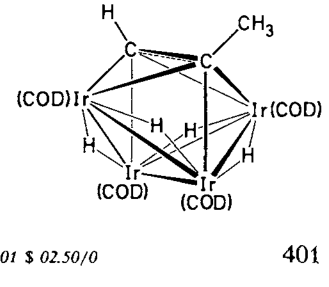


Fig. 2. Structural scheme for *(1)*.

---

[*] Prof. Dr. J. Müller, Dr. H. Menig, Priv.-Doz. Dr. J. Pickardt
Institut für Anorganische und Analytische Chemie
der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] π-Olefin-Iridium Complexes, Part 16. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 5: *J. Müller, W. Hähnlein, H. Menig, J. Pickardt*, J. Organomet. Chem. *197*, 95 (1980).

The IR-spectrum of *(1)* indicates that terminal hydrido hydrogen atoms are absent. In the $^1$H-NMR spectrum (80 MHz, [D$_8$]toluene) two sharp singlets, among other signals, appear at $\delta = -10.36$ and $-13.80$ (2H each), which can be assigned to two groups of $\mu_2$-hydrido bridges, which on the basis of the $C_s$-symmetry of the cluster are chemically non-equivalent. Figure 2 shows the resulting structural scheme of *(1)*. When the temperature is increased, the hydrido signals broaden, collapse together at *ca.* 45 °C and eventually form a sharp signal at $\delta = -12.07$; the other parts of the spectrum are essentially unchanged. At higher temperatures, therefore, a dynamic intramolecular exchange of hydrido hydrogen atoms, involving pairs of non-equivalent H-atoms, occurs.

The protons of the propyne unit in *(1)* can be recognized in the NMR spectrum by two sharp singlets at $\delta = 3.06$ (3H) and 5.72 (1H). These signals are absent in the spectrum of the product of the reaction of $[Ir(COD)Cl]_2$ and $i$-$C_3D_7MgBr$—evidence that the propyne unit originates from the Grignard reagent.

The complex *(1)*, $H_4(COD)_4Ir_4C_3H_4$, is one of the few organometallic clusters which does not contain CO-ligands and to our knowledge is, until now, the only closed hydridometal cluster with exclusively $\pi$-bonded olefinic ligands. In view of this, its thermal stability is surprizingly high; crystals of *(1)* do not decompose under $N_2$-atmosphere at temperatures up to 230 °C and can be vaporized into the mass spectromer at *ca.* 200 °C. It is therefore expected that further complexes of this type are synthesizable.

## *Procedure*

All operations are performed under an inert gas atmosphere. The solution of the Grignard reagent prepared from Mg (65 mg, 2.67 mmol) and $i$-$C_3H_7Br$ (0.3 cm$^3$) in 20 cm$^3$ ether, is dropped over 15 min into a suspension of $[Ir(COD)Cl]_2$ (500 mg, 0.74 mmol) in 20 cm$^3$ ether at $-50$ °C. The mixture is allowed to warm-up to room temperature and the dark brown solution irradiated for 5.5 h with UV light from an Hg high pressure lamp. (Type Q 81, supplied by Heraeus, Hanau.) The solvent is then completely removed, the residue eluted with 100 cm$^3$ hexane and filtered over 3 cm $Al_2O_3$/5% $H_2O$. The solution is concentrated and allowed to stand in the refrigerator, upon which *(1)* precipitates as a dark yellow powder; this is purified by recrystallization from hexane or a little toluene under refrigeration and produces orange red crystals. Yield 55 mg (0.044 mmol; 12%).

Received: October 15, 1980 [Z 742 IE]
German version: Angew. Chem. *93*, 407 (1981)

---

[1] *J. Müller, W. Holzinger, H. Menig,* Angew. Chem. *88*, 768 (1976); Angew. Chem. Int. Ed. Engl. *15*, 702 (1976); *J. Müller, H. Menig, P. V. Rinze,* J. Organomet. Chem. *181*, 387 (1979).

[2] *J. Müller, H. Menig, G. Huttner, A. Frank,* J. Organomet. Chem. *185*, 251 (1980).

[3] *G. Winkhaus, H. Singer,* Chem. Ber. *99*, 3610 (1966).

[4] Triclinic, $P\bar{1}$, $Z=4$; $a=1549.8(4)$, $b=2186.8(7)$, $c=1138.3(3)$ pm, $\alpha=98.82(5)$, $\beta=92.86(5)$, $\gamma=76.40(4)^\circ$. Four-circle diffractometer Syntex $P2_1$, $MoK_\alpha$; of 7164 independent reflections with $2\theta \leq 40^\circ$, 3342 having $I \geq 2\sigma(I)$ were used for the structural determination; $R=0.125$ (Ir anisotropic, C isotropic). The asymmetric unit contains two independent cluster molecules of which only one is described here; the other is, in principle, similarly constructed.

[5] *L. F. Dahl, D. L. Smith,* J. Am. Chem. Soc. *84*, 2450 (1962).

[6] *R. Mason, K. M. Thomas,* J. Organomet. Chem. *43*, C39 (1972).

[7] *G. F. Stuntz, J. R. Shapley, C. G. Pierpont,* Inorg. Chem. *17*, 2596 (1978).

# Chloranil as a Catalyst for the Electrochemical Oxidation of NADH to NAD$^+$[**]

By *Horst Huck* and *Hanns-Ludwig Schmidt*[*]

An "optical test" for the specific determination of substrates by means of NAD$^+$-dependent dehydrogenases is not suitable for the analysis of turbid solutions or for continuous monitoring of concentrations; for these purposes an electrochemical process should be used. A prerequisite for the development of the corresponding "enzyme electrodes" or a preparative method for the specific electrochemical dehydrogenation of substrates is the conception of NADH-oxidizing electrodes. Such electrodes must, in particular, catalyze the dehydrogenation of NADH in an analogous way to the natural process *via* two electron steps, since one electron transitions can lead to decomposition of the coenzymes. Carbon or platinum electrodes are unsuitable because of the correspondingly high overpotentials which could lead to interference from other oxidizable materials present in the sample. A number of investigations to reduce the magnitude of this overpotential have been carried out *e.g.* by oxidative pretreatment of the carbon electrodes (resulting in reduction of the overpotential by *ca.* 200—250 mV)[1], as well as by the use of dissolved or covalently bound *o*-quinones[2]. In both cases the oxidative peak potential could be reduced from 420 to 250 mV relative to an Ag/AgCl-electrode in 0.010 M KCl (from 370 to 200 mV/SCE) in cyclic voltammetry investigations. However, the activity of the bound quinones only remained constant for a few cycles. For our purposes, we considered water-insoluble redox catalysts of sufficiently high activity, more advantageous. Tetrachloro-*p*-benzoquinone (chloranil) seemed to be particularly suitable: it has a standard redox potential of 100 mV/SCE at pH = 7, is stable and spontaneously reacts with dihydro nitrogen heterocycles *via* hydrogen abstraction[3].

Conducting electrodes of this type, consisting of pressed chloranil and graphite powder are already available[4]. However, in our investigations, we treated the basal surfaces of laterally insulated 6 mm diameter graphite electrodes with a solution of chloranil in ether and then removed the solvent by evaporation. The activity of the electrodes was investigated *via* cyclic voltammetric (Fig. 1) and potentiostatic measurements (Fig. 2) of stirred aqueous NADH solutions. The cyclic voltammograms of the NADH oxidation using an unmodified graphite electrode show peak potentials at 320 and 335 mV/SCE for the first (Fig. 1, curve $a_1$) and second (Fig. 1, curve $a_2$) sweeps respectively; the peak height remains constant after the second sweep. Voltammogram b in Figure 1 was obtained in an NADH-free solution using a graphite electrode, which had been treated with 20 µl of a 0.2 mM solution of chloranil (4 nmol): $c_1$ and $c_2$ are the curves obtained from the first and second sweeps, respectively, in the presence of NADH; here again the height of the peak maximum was constant after the second sweep. The peak maximum at 90 mV/SCE in the anodic sweep is more intense in the chloranil catalyzed anodic NADH oxidation; this can be attributed to superposition of the anodic chloranil and anodic NADH peaks. The anodic NADH peaks ob-

---

[*] Prof. Dr. H.-L. Schmidt, Dr. H. Huck
Lehrstuhl für Allgemeine Chemie und Biochemie
der Technischen Universität München
D-8050 Freising-Weihenstephan (Germany)

[**] This work was supported by the Bundesministerium für Forschung und Technologie.

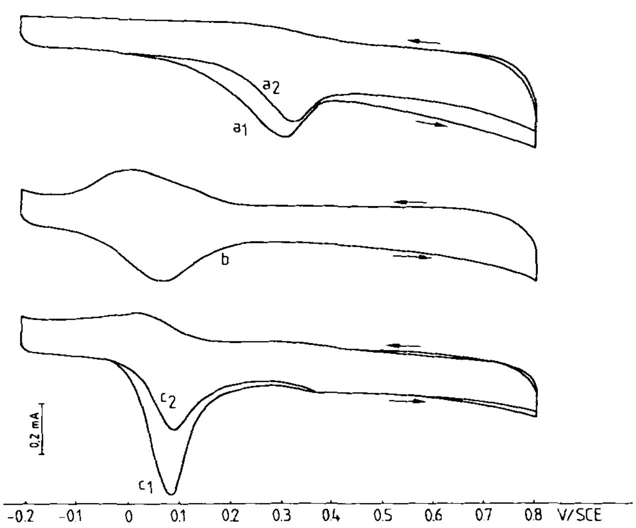


Fig. 1. Cyclic voltammograms for the investigation of the NADH oxidation in a stirred electrolyte. Starting potential −200 mV/SCE, sweep rate 100 mV/s, sensitivity 1 mA/full recorder scale. Electrolyte: 1 mM NADH, 0.1 M phosphate buffer pH 7, 1 M NaCl. $a_1$ unmodified graphite electrode (∅ 6 mm) at the first, $a_2$ at the second sweep. With 4 nmol chloranil modified graphite electrode *in absence of NADH* (b) and in presence of NADH at the first ($c_1$) and the second ($c_2$) sweep under stationary conditions.

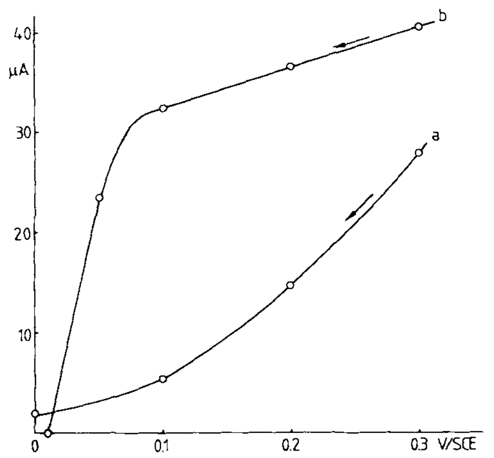


Fig. 2. Stationary current-voltage curves of stirred electrolytes (as in Fig. 1). Curve a, untreated graphite electrode, curve b graphite electrode treated with 120 nmol chloranil.

served at higher potentials are completely absent in the presence of chloranil.

The catalytic effect is particularly conspicuous in the stationary current-voltage curves obtained using controlled electrode potentials (Fig. 2). Here, the electrodes were treated with a large excess of chloranil (20 μl of a 6 mM solution, corresponding to 120 mmol). Measurements of the current were performed 2 min after each adjustment of the potential. The plot of the unmodified electrode (Fig. 2a) corresponds to the exponential course of an irreversible reaction, while that of the modified electrode (Fig. 2b) falls steeply after passing the standard redox potential of chloranil. This characteristic curve-form can be accounted for by the dependence of the potential on the surface concentration of the oxidized form of the redox catalyst, which can be reproduced using the Nernst equation. The limiting current of the plateau is caused by diffusion.

Coulometric data obtained by integrating the area under the potentiostatic current-time curves (5 $cm^3$ 1 mM NADH, 100 mV/SCE, 2 h), in conjunction with the concentration decrease of NADH determined photometrically at 340 nm, show that a two electron transfer occurs with both the modified and unmodified electrodes. No deactivation of the electrodes by fouling was observed in the treated, at 100 mV/SCE, and untreated electrodes, at 300 mV/SCE, after a 2 h investigation. However, fouling occurred with the unmodified electrode at a potential of 100 mV/SCE. Unspecific responses can be eliminated using a differential circuit of an enzyme-chloranil electrode *versus* a chloranil electrode.

The chloranil electrode can also be used with a covering dialysis membrane. However, in order to limit the decrease in sensitivity resulting, the membrane and electrolyte films must be as thin as possible.

The extraordinary activity of chloranil with respect to oxidation of NADH is probably due to formation of a charge-transfer complex. In contrast benzoquinone, whose redox potential is only 30 mV lower, is catalytically inactive. The systematic search for other catalysts for NADH-oxidation, which can be irreversibly adsorbed on carbon electrodes, has led to several heterocyclic compounds[5].

Received: April 28, 1980,
supplemented: December 15, 1980 [Z 746 IE]
German version: Angew. Chem. 93, 421 (1981)

CAS Registry numbers:
NADH, 58-68-4; $NAD^+$, 865-05-4; chloranil, 118-75-2

---

[1] *W. J. Blaedel, R. A. Jenkins*, Anal. Chem. *47*, 1337 (1975).
[2] *D. Chi-Sing, Th. Kuwana*, Anal. Chem. *50*, 1315 (1978).
[3] *E. A. Braude, J. Hannah, R. Linstead*, J. Chem. Soc. *1960*, 3249.
[4] *H. Alt, H. Binder, A. Köhling, G. Sandstede*, Angew. Chem. *83*, 502 (1971); Angew. Chem. Int. Ed. Engl. *10*, 514 (1971).
[5] *H. Huck, H.-L. Schmidt*, unpublished results.

## Axially Unsymmetrical Osmium(II)-Porphyrins with Sulfur and Nitrogen Donors as Models for Cytochrome c[**]

By *Johann Walter Buchler* and *Wolfgang Kokisch*[*]

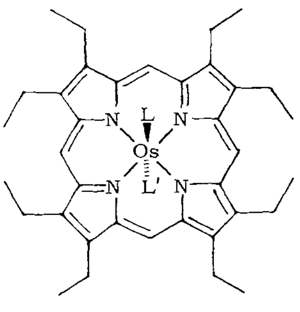
*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

Reduced cytochrome c is an electron transporting heme protein in which the $Fe^{II}$ ion is coordinated axially unsymmetrically by sulfur and nitrogen donors of the protein chain (methionine 80 and histidine 18 respectively)[1]. The central N—Fe—S unit can only be prepared from the protein-free $Fe^{II}$-porphyrin if, as in the "tail-porphyrin" of *Reed et al.*[2], at least one of the donors is covalently fixed to the periphery of the porphyrin by a side chain; otherwise only the axially symmetrical complex with two nitrogen or sulfur donors is isolated because of the kinetic lability of the heme group. In cytochrome c the N—Fe—S unit is stabilized by a double chelate effect. The inherently more stable ligand-osmium bond allowed the synthesis of the axially unsymmetrical bis-ligand-osmium(II) porphyrins *(1)* and *(2)* ("osmochromes"), which are stable without any chelate-effect.

---

[*] Prof. Dr. J. W. Buchler, Dr. W. Kokisch
Fachbereich Anorganische Chemie und Kernchemie der Technischen Hochschule
Hochschulstrasse 4, D-6100 Darmstadt (Germany) (address for correspondence)
and Institut für Anorganische Chemie der Technischen Hochschule
D-5100 Aachen (Germany)

[**] Metal Complexes with tetrapyrrole ligands, Part 25. This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.—Part 24: *J. W. Buchler, K.-L. Lay, H. Stoppa*, Z. Naturforsch. *B 35*, 433 (1980).

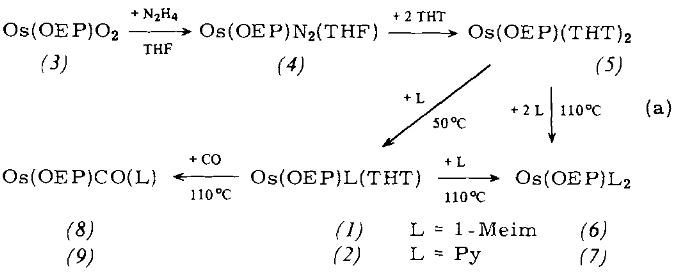


Os(OEP)LL' *(1)-(12)*

| No. | L | L' [a] | No. | L | L' [a] |
|---|---|---|---|---|---|
| *(1)* | 1-Meim | THT | *(7)* | Py | Py |
| *(2)* | Py | THT | *(8)* | 1-Meim | CO |
| *(3)* | O | O | *(9)* | Py | CO |
| *(4)* | $N_2$ | THF | *(10)* | 1-Meim | $P(OMe)_3$ |
| *(5)* | THT | THT | *(11)* | $P(OMe)_3$ | $P(OMe)_3$ |
| *(6)* | 1-Meim | 1-Meim | *(12)* | CO | THT |

[a] Abbreviations: 1-Meim = 1-methylimidazole; Py = pyridine; THF = tetrahydrofuran; THT = tetrahydrothiophene; OEP = octaethylporphyrin.

The dinitrogen complex *(4)*[3] is prepared *in situ* from the dioxoosmium(VI)-porphyrin *(3)* and converted into the bis(tetrahydrothiophene) complex *(5)*, as shown in (a). When *(5)* is warmed to 50 °C in excess 1-methylimidazole or pyridine, only the unsymmetrical osmochromes *(1)* or *(2)*[4], respectively, are formed by displacement of one of the tetrahydrothiophene ligands. In aprotic solvents *(1)* and *(2)* are stable. In methanol, oxygen induced autoxidation to osmium(III) salts ("osmichrome salts") occurs, as recently described for *(6)* and *(7)*[5a].



Above 100 °C, the aforementioned N-donors substitute the second S-donor to give the symmetrical osmochromes *(6)* or *(7)*[5], which can also be obtained directly from *(5)* at this temperature. The reverse reaction, the conversion of *(6)* into *(1)* or *(5)*, does not occur. Apparently, stability increases in the order *(5)* < *(1)* < *(6)*.

Figure 1 shows the electron excitation spectra of *(1)* and *(2)* and Figure 2 the cyclic voltammograms of the 1-methylimidazole complexes *(1)*, *(6)* and *(10)*[6a]. The half-wave potentials of the $Os^{II}/Os^{III}$ transition for systems with $L \neq L'$ lie between those of systems with $L = L'$: *(5)*, −0.26 V; *(1)*, −0.45 V; *(6)*, −0.63 V; *(2)*, −0.30 V; *(7)*, −0.37 V. The voltammograms indicate that the mixed-ligand osmochromes *(1)* and *(2)*, as well as the cytochromes and symmetrical osmochromes[5a], can be considered as reversible one electron redox systems as shown in eq. (b); thus, the osmichrome cations are inert towards substitution as well.

$$Os(OEP)LL' \rightleftarrows [Os(OEP)LL']^{\oplus} + e \qquad (b)$$

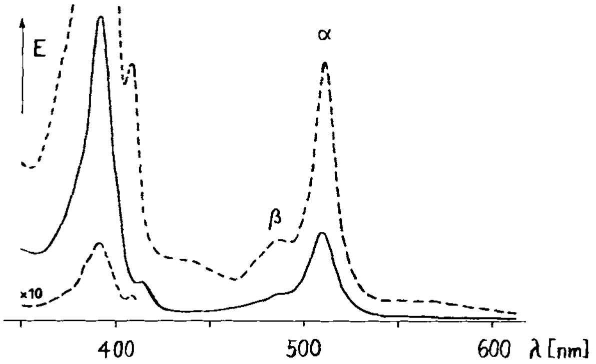


Fig. 1. Electron excitation spectra of the unsymmetrical osmochromes. *(1)* (solid line) and *(2)* (broken line). Values: $\lambda_{max}$ (lg ε): *(1)* 509 (4.37), 486 (3.83), 412 (4.01), 392 (4.90) nm; *(2)* 511 (4.58), 486 (4.08), 408 (4.57), 391 (5.06) nm. Unicam SP 1750, solvent $CH_2Cl_2$.

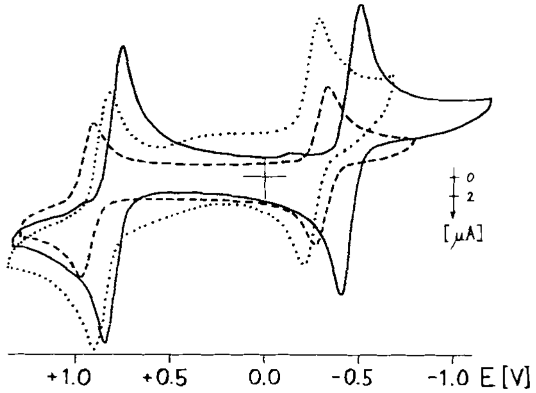


Fig. 2. Cyclic voltammograms of the unsymmetrical osmochromes *(1)* (solid line), *(2)* (broken line) and *(10)* (dotted line). Potentiostat from Princeton Applied Research, scan rate 0.1 $Vs^{-1}$, $NaCl/Hg_2Cl_2$ electrode, $CH_2Cl_2/NBu_4PF_6$. Processes at the right below 0 V are the $Os^{II}/Os^{III}$ steps, those at the left above 0.5 V the $Os^{III}/Os^{IV}$ steps.

Compounds *(1)* and *(2)*, like cytochrome c, are stable towards carbon monoxide at room temperature. As shown in (a), the sulfur donors are partially displaced in *(1)* and completely in *(2)* at 110 °C by CO to form *(8)* and *(9)* respectively[6b]. Compound *(1)* is therefore the more stable system. This is also indicated by the mass spectra. While *(1)* can be vaporized between 165° and 200 °C, without decomposition, to produce the intact molecular ion, the molecular ion from *(2)* is only observed at 170 °C; at 200 °C, apart from ions originating from decomposition of the sulfur donor, only the molecular and fragment ions of *(7)*, formed by transfer of pyrid-

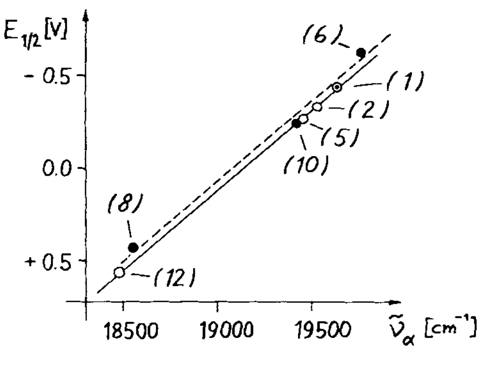


Fig. 3. Correlation between the half-wave potential of the $Os^{II}/Os^{III}$ steps ($E_{1/2}$) and the wave number of the longest wavelength absorption maxima (α-band, $\tilde{\nu}_{max}$) of the osmochromes Os(OEP) (1-Meim)L' [*(1)*, *(6)*, *(8)*, *(10)*: broken line] and Os(OEP)L(THT) [*(1)*, *(2)*, *(5)*, *(12)*; solid line].

ine, are observed. No molecular ion is formed at 180 °C by the relatively labile *(5)*.

The linear relationships between the α-band wave numbers of the absorption spectra, and the $Os^{II}/Os^{III}$-redox potentials shown in Figure 3 ("bathochromic rule"[5b, 6b, 6c]) apply not only to the tetrahydrothiophene derivatives *(1), (2), (5)* and *(12)*[6b] but also to the 1-methylimidazole derivatives *(6), (1), (10)* and *(8)*. A certain π-acceptor capacity can therefore be ascribed to the tetrahydrothiophene ligands. This result, together with the π-donor capacity of the imidazole system[5b] results in a "push-pull" stabilization of *(1)*, and also accounts for the greater chemical stability of *(1)* relative to *(2)*. In view of this inherent stability of the *trans*-arrangement of thioether and imidazole donors, cytochrome c represents a good choice by Nature.

A further detail of the cytochrome model, the difference $\Delta E = E_1 - E_2$ between the metal redox potential $E_1$ of the corresponding symmetrical bis(imidazole) and $E_2$ of the unsymmetrical thioether/imidazole systems, is reproduced by the osmochrome system. For the heme-octapeptide obtained by partial hydrolysis of cytochrome c, $\Delta E = -160$ mV[7], for the "tail-porphyrin", $\Delta E = -167$ mV[2], for the mesoheme with covalently bonded N/N- or S/N-donors, $\Delta E = -147$ mV[8a], and for the osmochromes *(6)* and *(1)*, $\Delta E = -180$ mV[8b]. By comparison of cytochromes $b_5$ and c one finds for the latter $\Delta E = -235$ mV[9]. This larger value may be attributed to a special protein-effect.

### *Procedure*

A solution of *(5)*[10] (64 mg, 7 mmol) in 11 cm³ THF/1-methylimidazole (10:1) is prepared under an argon atmosphere, warmed for 2 h at 50 °C and concentrated in a stream of argon. The residual solution is allowed to stand under argon until crystallization occurs. The black, analytically pure needles of *(1)* which precipitate (51 mg, 65%) are suction filtered, washed with methanol/water (4:1) and dried at 40 °C/$10^{-4}$ torr.

Received: August 27, 1980 [Z 747 IE]
German version: Angew. Chem. *93*, 418 (1981)

Cas registry numbers:
*(1)*, 77450-09-0; *(2)*, 77450-10-3; *(3)*, 51349-77-0; *(4)*, 53352-71-9; *(5)*, 77450-11-4; *(6)*, 74077-51-3; *(7)*, 51286-87-4; *(8)*, 77450-12-5; *(9)*, 51286-85-2; *(10)*, 77450-13-6; *(11)*, 52649-92-0; *(12)*, 77450-14-7

---

[1] *S. Ferguson-Miller, D. L. Brautigan, E. Margoliash* in *D. Dolphin:* The Porphyrins, Vol. 7, Academic Press, New York 1979, p. 149f.; *R. Timkovich, ibid.*, p. 241 f.

[2] *T. Mashiko, J.-C. Marchon, D. T. Musser, C. A. Reed, M. E. Kastner, W. R. Scheidt*, J. Am. Chem. Soc. *101*, 3653 (1979).

[3] *J. W. Buchler, P. D. Smith*, Angew. Chem. *86*, 820 (1974); Angew. Chem. Int. Ed. Engl. *13*, 745 (1974).

[4] All new osmium porphyrins were characterized by elemental analysis, mass-, electron excitation-, ¹H-NMR-, IR-spectroscopy and cyclic voltammetry.

[5] a) *J. Billecke, W. Kokisch, J. W. Buchler*, J. Am. Chem. Soc. *102*, 3622 (1980); b) *J. W. Buchler, W. Kokisch, P. D. Smith*, Struct. Bonding *34*, 79 (1978).

[6] a) The novel Os(OEP)P(OMe)₃(1-Meim) *(10)* can also be prepared by treating Os(OEP)[P(OMe)₃]₂ *(11)* [6b] with excess 1-Meim in boiling $CH_2Cl_2$; however, at 110 °C it does not react to give *(6)*; b) *J. W. Buchler, K. Rohbock*, J. Organomet. Chem. *65*, 223 (1974); c) *J. W. Buchler, W. Kokisch, P. D. Smith, B. Tonn*, Z. Naturforsch. *B 33*, 1371 (1978).

[7] *H. A. Harbury, J. R. Cronin, M. W. Fanger, T. P. Hettinger, A. Murphy, Y. P. Myer, S. N. Vinogradov*, Proc. Natl. Acad. Sci. USA *54*, 1658 (1965).

[8] a) *G. S. Wilson*, Bioelectrochem. Bioenerget. *1*, 172 (1974); b) *Note added in proof:* The osmochromes prepared in the meanwhile and corresponding to *(6)* and *(1)* but having ms-tetra(*p*-tolyl)porphine ligands have $\Delta E = -200$ mV (*J. W. Buchler, K. Oesten*, unpublished).

[9] *G. R. Moore, R. J. P. Williams*, Coord. Chem. Rev. *18*, 125 (1976).

[10] a) Os(OEP)(THT)₂ *(5)* is prepared in a similar manner to Os(OEP)Py₂ *(7)* [10b], by refluxing 50 mg *(3)* in 10 cm³ THF, 0.025 cm³ $N_2H_4 \cdot H_2O$ and 1 cm³ THT and crystallization from the cooled concentrated solution. (yield 82%); b) *A. Antipas, J. W. Buchler, M. Gouterman, P. D. Smith*, J. Am. Chem. Soc. *100*, 3015 (1978).

## Carbonylation of $C_5H_5Fe(CO)(CH_3)L$—a CO-Insertion and No $CH_3$-Migration[**]

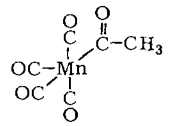
By *Henri Brunner* and *Heinz Vogt*[*]

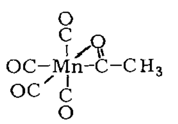
Owing to its industrial importance, CO-insertion in transition metal-alkyl bonds has been the subject of numerous investigations, particularly on the model system

$CH_3Mn(CO)_5 + CO \rightleftarrows (CH_3CO)Mn(CO)_5$[2]

It is assumed that the methyl group migrates from the Mn atom to a *cis*-oriented carbonyl group with formation of the acetyl intermediate *(1)*. The free coordination site becomes occupied by nucleophiles L = CO, PR₃ *etc.* before the square pyramid *(1)* can isomerize. This mode of reaction is supported by calculations[3] and confirmed by labeling experiments, but is not reconcilable with an $\eta^2$-acetyl intermediate *(2)*, formed by insertion of a *cis*-CO ligand in the Mn—CH₃ bond.

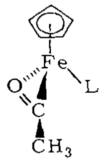
*(1)*

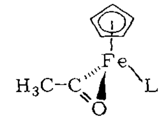




*(2)*

Ligand exchange reactions in optically active Fe-complexes and investigations on ¹³C-labeled and C₅H₅-acyl bridged Fe-complexes showed that the thermal decarbonylation of compounds of the type $C_5H_5Fe(CO)(COCH_3)L$ begins with an intramolecular substitution of the ligand L by the acetyl oxygen with stereospecific formation of the $\eta^2$-acetyl intermediate *(3)*. Ligands L′ = P(CH₃)₃, P(*n*Bu)₃ attack the intermediate *(3)* at the acetyl oxygen and open the $\eta^2$-bond of the acetyl-ligand to give the substitution products $C_5H_5Fe(CO)(COCH_3)L'$ with retention of configuration at the Fe atom. The intermediate *(3)* can rearrange to $C_5H_5Fe(CO)_2CH_3$ and be transformed into its mirror image *(3′)*; the change of configuration is slow compared to the rearrangement[5].





*(3)*, L = CO *(3′)*
*(4)*, L = $P(C_6H_5)_2NCH_3$–(*S*)–$CH(CH_3)(C_6H_5)$ *(4′)*

In the following it is shown that the carbonylation of $(-)_{436}$-*(5)*[1,6] proceeds with stereospecific insertion of the CO group present in the molecule into the Fe—CH₃ bond.

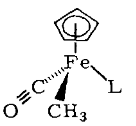
If a solution of optically pure *(5)* in benzene is allowed to stand for 5 d at room temperature under 400 bar CO, *(6)* is formed with a stereoselectivity of over 90%. Comparison of the CD spectra of *(5)* and *(6)* with those of similar complexes of known absolute configuration enables unequivocal assignement of configurations[7]. The reaction *(5)*→*(6)* is not

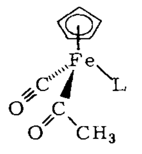
---

[*] Prof. Dr. H. Brunner, Dr. H. Vogt
Institut für Anorganische Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg (Germany)

[**] Optically Active Transition Metal Complexes, Part 75. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, BASF AG, and Dynamit Nobel AG.—Part 74: [1].

compatible with a migration of methyl to give an intermediate analogous to *(1)*, but only with a CO-insertion to give the $\eta^2$-acetyl intermediate *(4)*. The formation of *(4)* from *(5)* can thus be envisioned in terms of the CO ligand being inserted into the Fe—CH$_3$ bond, and the oxygen atom swinging into the position previously occupied by the carbonyl C-atom. In the presence of CO, replacement of the acetyl oxygen in the intermediate *(4)* by the newly entering CO occurs with stereospecific formation of *(6)*. The intermediate *(4)* is formed from *(5)* even at room temperature and is configurationally stable under the conditions of the carbonylation.

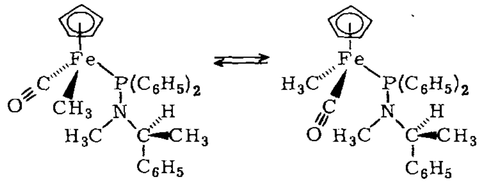




*(5)*, L = P(C$_6$H$_5$)$_2$NCH$_3$–*(S)*–CH(CH$_3$)(C$_6$H$_5$) *(6)*
*(7)*, L = P(C$_6$H$_5$)$_3$ *(8)*

This result is remarkable, because in the photochemical decarbonylation of *(8)* in tetrahydrofuran, the species *(7')* with the opposite configuration to *(7)* at the Fe-atom, is formed, consistent with the concept of a methyl migration into the position vacated by photochemical cleavage of the CO ligand[7b]. It follows, therefore, that the photochemical reaction cannot involve an $\eta^2$-acetyl intermediate, whose carbonylation according to the principle of microscopic reversibility should give the product *(7)*—and not *(7')*, as observed—in view of the stereochemistry of the reaction *(5)*→*(6)*.

*(5)* epimerizes to *(5')* at elevated temperatures. In benzene at 70 °C, approach to the diastereomeric equilibrium *(5)*⇄*(5')* (65:35) is a first order reaction (half-life 81 min) which can be followed NMR spectroscopically[1,6]. Within the limit of error an addition of the aminophosphane contained in *(5)* and *(5')* does not change the rate of the reaction. The epimerization *(5)*⇄*(5')* could be ascribed to a pseudorotation-like rearrangement of the $\eta^2$-acetyl ligand in *(4)* and *(4')*, *e.g.* by rotation about 180°.



*(5)* ⇄ *(5')*

Reaction of *(5)* with the isocyanide CNR* = (−)—CN—*(S)*—CH(CH$_3$)(C$_6$H$_5$) instead of CO in benzene requires about six hours' heating at 70 °C. The product C$_5$H$_5$Fe(COCH$_3$)(CNR*)L has an optical purity of only 50%, since the change of configuration in the intermediate *(4)*⇄*(4')* competes with the trapping reaction *(4)*+CNR*. The carbonylation of *(5)*, on the other hand, leads stereospecifically to *(6)* at room temperature, before the intermediate *(4)* can change its configuration. The variable stereoselectivities observed by *Flood*[8] in the carbonylation of *(7)* to *(8)* might be due to prior change of configuration *(7)*⇄*(7')* at the Fe-atom or, in particular in hexamethylphosphoric triamide, to S$_N$2-inversion at the Fe-atom[5].

Summarizing: Although the fragments (CO)$_3$Mn and C$_5$H$_5$Fe, and thus also the compounds (CO)$_5$MnCH$_3$ and C$_5$H$_5$Fe(CO)$_2$CH$_3$ are isoelectronic, their carbonylation proceeds *via* different routes and *via* different intermediates. This also applies in the case of the photochemical and thermal variants of the carbonylation of C$_5$H$_5$Fe(CO)(CH$_3$)L and of the decarbonylation of C$_5$H$_5$Fe(CO)(COCH$_3$)L.

Received: October 31, 1980 [Z 736 IE]
German version: Angew. Chem. *93*, 409 (1981)

---

[1] *H. Brunner, H. Vogt,* J. Organomet. Chem. *210,* 223 (1981).
[2] a) *A. Wojcicki,* Adv. Organomet. Chem. *11,* 87 (1973); b) *F. Calderazzo,* Angew. Chem. *89,* 305 (1977); Angew. Chem. Int. Ed. Engl. *16,* 299 (1977).
[3] *H. Berke, R. Hoffmann,* J. Am. Chem. Soc. *100,* 7224 (1978).
[4] *T. C. Flood, J. E. Jensen,* Proc. IX. Int. Conf. Organomet. Chem., Sept. 1979, Dijon, D34.
[5] *H. Brunner, H. Vogt,* Chem. Ber., in press.
[6] a) *H. Brunner, G. Wallner,* Chem. Ber. *109,* 1053 (1976); b) *H. Brunner, M. Muschiol, W. Nowak,* Z. Naturforsch. *B 33,* 407 (1978); c) Rate constants and activation enthalpies: *(5)*→*(5')*: $k = 0.54 \times 10^{-4}$ s$^{-1}$, $\Delta G^{\ddagger} = 26.85$ kcal/mol; *(5')*→*(5)*: $k = 0.88 \times 10^{-4}$ s$^{-1}$, $\Delta G^{\ddagger} = 26.52$ kcal/mol.
[7] a) *H. Brunner, E. Schmidt,* J. Organomet. Chem. *36,* C18 (1972); b) *A. Davison, N. Martinez, ibid. 74,* C17 (1974); c) *K. C. Chou, D. L. Miles, R. Bau, T. C. Flood,* J. Am. Chem. Soc. *100,* 7271 (1978).
[8] *T. C. Flood,* private communication.

## *t*Bu$_6$P$_8$ and *t*Bu$_6$As$_8$— Two New Element-Homologous Bicyclic Compounds of Different Structure[**]

By *Marianne Baudler, Jochen Hellmann, Paul Bachmann, Karl-Friedrich Tebbe, Roland Fröhlich* and *Magda Fehér*[*]

*Dedicated to Professor Rolf Appel on the occasion of his 60th birthday*

After successful identification of a large number of polycyclic phosphorus hydrides by mass spectrometric methods[1a] we attempted the synthesis of more stable derivatives[1b,c]. Analogous homonuclear skeletal structures are likely to be found in the corresponding arsanes; this could be confirmed for the pair (Me$_3$Si)$_3$P$_7$[2a] and (Me$_3$Si)$_3$As$_7$[2b]. However, examination of the bicyclic hexa-*tert*-butyloctaphosphane *(1)* and hexa-*tert*-butyloctaarsane *(2)* now gave us the first example showing that homologous phosphanes and arsanes may also display entirely different structures.

The phosphane *(1)* is obtained by cyclocondensation of diphosphorus tetraiodide with 1,2,3-tri-*tert*-butyltriphosphane[3] in the presence of a base.

$$2\ \mathrm{H}(t\mathrm{Bu})\mathrm{P{-}P}(t\mathrm{Bu})\mathrm{{-}P}(t\mathrm{Bu})\mathrm{H} + \mathrm{P_2I_4} \xrightarrow[-4\,\mathrm{Et_3N\cdot HI}]{+4\,\mathrm{Et_3N}} t\mathrm{Bu_6P_8} \qquad (1)$$

As by-products we found the monocyclic phosphanes (*t*BuP)$_3$[4a] and (*t*BuP)$_4$[4b] as well as 1,2-di-*tert*-butyl-1,2-diiododiphosphane[4c] and phosphorus iodides P$_x$I$_y$ with $x > y$. *(1)* is also obtained by dehalogenation of a 3:1 mixture of

---

[*] Prof. Dr. M. Baudler, Dr. J. Hellmann, Dipl.-Chem. P. Bachmann, Prof. Dr. K.-F. Tebbe, Dipl.-Chem. R. Fröhlich, Dr. M. Fehér
Institut für Anorganische Chemie der Universität
Greinstrasse 6, D-5000 Köln 41 (Germany)

[**] Contributions to Phosphorus Chemistry, Part 102, and Contributions to Arsenic Chemistry, Part 4. This work was supported by the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen and the Fonds der Chemischen Industrie. Part 101: *M. Baudler, A. Marx,* Z. Anorg. Allg. Chem., in press; Part 3: *M. Baudler, P. Bachmann,* Angew. Chem. *93,* 112 (1981); Angew. Chem. Int. Ed. Engl. *20,* 123 (1981).

*tert*-butyl(dichloro)phosphane and phosphorus trichloride using magnesium[5].

The octaphosphane *(1)* is a colorless crystalline compound (m.p. 257 °C, dec., closed tube) which remains unaltered on exposure to air, and is only sparingly soluble in the usual solvents. The only fragment in addition to $M^{\oplus}$ ($m/e = 590$, rel. int. 100) found in the mass spectrum (field ionization, 180 °C) is $M^{\oplus}/2$ (295; 17). The $^{31}P\{^1H\}$-NMR spectrum shows two complex multiplets (3 : 1 ratio) at $\delta \approx -45$ for the *tert*-butyl substituted phosphorus nuclei and $-100$ for those bound to phosphorus only. Two singlets at $\delta = 1.27$ and 1.30 (1 : 2) due to the non-equivalent *tert*-butyl groups appear in the $^1H\{^{31}P\}$-NMR spectrum. Lines broaden continuously below $-10$ °C, but coalescence point is not passed down to $-70$ °C[6]. All spectroscopic data are only compatible with the structure of a 2,2′,3,3′,4,4′-hexa-*tert*-butyl-1,1′-bicyclotetraphosphane with the possibility of frozen rotation round the exocyclic P—P bond at low temperature. This structure is also confirmed by X-ray structure analysis (Fig. 1)[7]. All

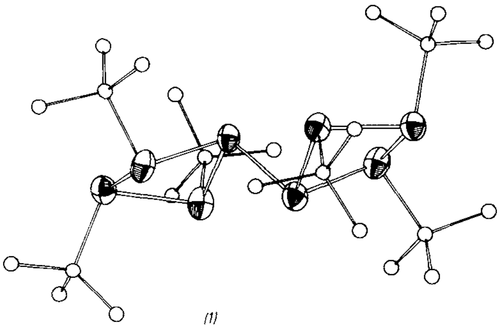

*(1)*

Fig. 1. Crystal structure of *(1)*; parameter ranges and average values of important bond lengths [pm] and angles [°]: $221.4 \leqq d(\text{P—P}) \leqq 223.1$, $\sigma(\text{P—P}) \simeq 0.2$; $\bar{d}(\text{P—P}) = 222.1(6)$; $\bar{d}(\text{P—C}) = 188.7(4)$. $86.8 \leqq \varphi(\text{P—P—P}) \leqq 88.2$, $\sigma(\text{P—P—P}) \simeq 0.6$; $\bar{\varphi}(\text{P—P—P}) = 87.5(6)$ (endocyclic angle); $94.8 \leqq \varphi(\text{P—P—P}) \leqq 98.3$, $\sigma(\text{P—P—P}) = 0.6$; $\bar{\varphi}(\text{P—P—P}) = 96.6(17)$ (angle at the P—P bridge).

P—P distances within the non-planar tetracycles and in the bridge are almost equal. The orientation of the rings as well as the arrangement of the substituents is *all-trans*. Model studies show that strong transannular interactions between the *tert*-butyl groups prevent *(1)* having the 2,3,4,6,7,8-hexa-*tert*-butylbicyclo[3.3.0]octaphosphane structure like $Me_6P_8$, $Et_6P_8$, $iPr_6P_8$[5], and the arsenic compound *(2)*.

The arsane *(2)* was first observed as a by-product of $(t\text{BuAs})_4$, prepared from *tert*-butyl(dichloro)arsane and magnesium, a reaction where, surprisingly, partial cleavage of the As—C bonds takes place; this indicates a remarkable tendency towards the formation of *(2)*. Thus *(2)* is obtained as main product by dehalogenation of a 3 : 1 mixture of *tert*-butyl(dichloro)arsane and arsenic trichloride.

$$6\ t\text{BuAsCl}_2 + 2\ \text{AsCl}_3 + 9\ \text{Mg} \xrightarrow[-9\ \text{MgCl}_2]{} t\text{Bu}_6\text{As}_8 \quad (2)$$

The monocyclic arsanes $(t\text{BuAs})_4$ and $(t\text{BuAs})_5$ are obtained as by-products. The product ratio depends on reactant concentration and time; *(2)* can be isolated pure by means of low temperature crystallization; optimum yield was achieved under $^1H$-NMR-spectroscopic control.

Octaarsane *(2)* forms yellow platelets (m.p. 262–264 °C, closed tube), which are stable in the dark and under inert gas. The crystals are only moderately soluble in tetrahydrofuran (THF) and benzene, less soluble in *n*-pentane or *n*-hexane. Air causes rapid oxidation of *(2)*, particularly in solution. Elemental analysis (As, C, H), cryoscopic determination of the molecular weight (in benzene) and a mass spectrum (field ionization, 140 °C) confirm the composition of *(2)*; other than in *(1)*, only $M^{\oplus}$ ($m/e = 942$) appears, and no $M^{\oplus}/2$ signal. As further confirmed by $^1H$-NMR spectral data (two singlets at $\delta = 1.66$ and 1.58 in a 1 : 2 ratio), this shows that *(2)* is a 2,3,4,6,7,8-hexa-*tert*-butyl-bicyclo[3.3.0]octaarsane. The spectroscopic findings admit two configurations with the *tert*-butyl groups within each five-membered ring in *trans* position and the substituents of different five-membered rings next to the zero bridge in *cis* position. X-ray structure analysis[8] (Fig. 2) shows unambiguously the presence of the sterically preferred isomer with the *tert*-butyl groups in the 3,7 position arranged *trans* with respect to the free electron pairs of the bridgehead arsenic atoms. Both five-membered rings have twisted envelope conformations.

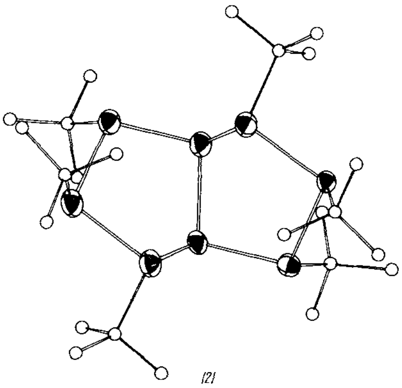

*(2)*

Fig. 2. Crystal structure of *(2)*; parameters, parameter ranges and average values of important bond lengths [pm] and angles [°]: $d(\text{As1—As5}) = 241.4(4)$; $\varphi(\text{As—As(1,5)—As}) = 94.8$, 94.9 (zero bridge); $243.3 \leqq d(\text{As—As}) \leqq 244.4$, $\sigma(\text{As—As}) = 0.4$; $\bar{d}(\text{As—As}) = 243.8(4)$; $\bar{d}(\text{As—C}) = 201(3)$; $97.8 \leqq \varphi(\text{As—As—As}) \leqq 107.3$, $\sigma(\text{As—As—As}) = 0.1$ (arsene pentacycles).

*Procedure*

*(1)*: A solution of 10.0 g (37.6 mmol) 1,2,3-tri-*tert*-butyltriphosphane[3] in 100 cm$^3$ *n*-pentane is vigorously stirred with 10.7 g (18.8 mmol) diphosphorus tetraiodide and 7.7 g (76.1 mmol) triethylamine for 24 h at room temperature. The mixture is then refluxed for 3 h and the solvent is removed, finally in an oil pump vacuum. The residue is dissolved in 150 cm$^3$ THF and is kept at $-78$ °C for 15 h before filtering at the same temperature. After drying, the powdery solid is extracted with 500 cm$^3$ *n*-pentane in a Soxhlet apparatus for 5 h; enriched *(1)* begins to precipitate in the extract after a while. The solution is concentrated to 100 cm$^3$, the crude product is filtered off and is recrystallized from 100 cm$^3$ boiling toluene; yield: 1.5 g (14%) colorless *(1)*.

*(2)*: A solution of 7.0 g (34.5 mmol) *tert*-butyl(dichloro)arsane and 2.1 g (11.6 mmol) arsenic trichloride in 60 cm$^3$ THF is added dropwise within 20 min into 10 cm$^3$ boiling THF containing 3.8 g magnesium. As soon as reaction commences, heating is stopped; the heat of reaction will keep the mixture boiling. While the mixture is still hot, the precipitate is removed by filtration and washed twice with 20 cm$^3$ THF. The combined filtrates are concentrated and the light yellow solid residue treated with 80 cm$^3$ hexane; remaining magnesium chloride is filtered off. The solution contains *ca.* 50 mol% of *(2)*, 30% $(t\text{BuAs})_5$, and 20% $(t\text{BuAs})_4$ (shown by $^1H$-NMR spectrum). Cooling to $-30$ °C for 5 d leads to precipitation of the yellow crude product; excess solution is si-

phoned off in the cold. Renewed dissolution in a minimum quantity of boiling *n*-hexane and crystallization at −30 °C yields 1.9 g of *(2)* with a purity of *ca.* 90% (contaminated with $(t\mathrm{BuAs})_4$); three further recrystallizations yield 1.1 g (20%) of pure *(2)*.

Received: October 2, 1980 [Z 743 IE]
German version: Angew. Chem. *93*, 415 (1981)

CAS Registry numbers:
*(1)*, 77256-90-7; *(2)*, 77256-91-8; $(t\text{-BuAs})_5$, 77256-92-9; $(t\mathrm{BuAs})_4$, 37755-92-3; H(*t*-Bu)P—P(*t*-Bu)—P(*t*-Bu)H, 77256-93-0; $P_2I_4$, 13455-00-0; *t*-$\mathrm{BuAsCl_2}$, 4262-41-3; $\mathrm{AsCl_3}$, 7784-34-1

---

[1] a) *M. Baudler, H. Ständeke, M. Borgardt, H. Strabel, J. Dobbers*, Naturwissenschaften *53*, 106 (1966); also see *M. Baudler*, Pure Appl. Chem. *52*, 755 (1980); b) *M. Baudler, W. Faber, J. Hahn*, Z. Anorg. Allg. Chem., in press; c) *M. Baudler, Y. Aktalay, J. Hahn, E. Därr, ibid.*, in press.

[2] a) *G. Fritz, W. Hölderich*, Naturwissenschaften *62*, 573 (1975); *W. Hönle, H. G. von Schnering*, Z. Anorg. Allg. Chem. *440*, 171 (1978); b) *H. G. von Schnering, D. Fenske, W. Hönle, M. Binnewies, K. Peters*, Angew. Chem. *91*, 755 (1979); Angew. Chem. Int. Ed. Engl. *18*, 679 (1979).

[3] *M. Baudler, J. Hellmann*, Z. Anorg. Allg. Chem., in press.

[4] a) *M. Baudler, J. Hahn, H. Dietsch, G. Fürstenberg*, Z. Naturforsch. *B 31*, 1305 (1976); *M. Baudler, Ch. Gruner, ibid. B 31*, 1311 (1976); b) *K. Issleib, M. Hoffmann*, Chem. Ber. *99*, 1320 (1966); c) *M. Baudler, J. Hellmann*, Z. Anorg. Allg. Chem., in press.

[5] *M. Baudler, Y. Aktalay*, unpublished.

[6] Measurements at lower temperatures were impossible due to the poor solubility of *(1)*.

[7] Space group $P2_1/n$ (No. 14); $a = 1141.6(3)$, $b = 1805.7(2)$, $c = 1764.8(3)$ pm, $\beta = 108.32(2)°$; $V = 3453.6 \cdot 10^6$ pm$^3$, $Z = 4$, $\rho_{\text{rönt.}} = 1.14$ g·cm$^{-3}$. $\mu(\mathrm{Mo_{K\alpha}}) = 3.64$ cm$^{-1}$. Measurement at room temperature, CAD4-Diffractometer (ENRAF-Nonius), $\mathrm{Mo_{K\alpha}}$ radiation, $2\theta \leqq 50°$; 5361 reflections (hkl), 3836 of them with $|Fo| \geqq 4 \cdot \sigma(Fo)$; solution (direct methods) with program SHELX76, refinement (P and C anisotrop, H isotrop), $R = 0.049$, $R_w = 0.051$. *M. Fehér, R. Fröhlich, K.-F. Tebbe*, Z. Kristallogr., in press.

[8] Space group $P2_1/n$ (No. 14); $a = 1836.8(6)$, $b = 1000.8(2)$, $c = 2107.6(7)$ pm, $\beta = 110.20(2)°$; $V = 3636.0 \cdot 10^6$ pm$^3$, $Z = 4$, $\rho_{\text{rönt.}} = 1.72$ g·cm$^{-3}$. $\mu(\mathrm{Mo_{K\alpha}}) = 44.76$ cm$^{-1}$. Conditions see [7], $2\theta \leqq 44°$; 4603 reflections (hkl), 2539 of them with $|Fo| \geqq 4 \cdot \sigma(Fo)$; solution (direct methods) with program system XRAY76, refinement (As and C anisotrop, computed H positions), $R = 0.075$, $R_w = 0.098$. *R. Fröhlich, K.-F. Tebbe*, Z. Kristallogr., in press.

# —P=N— Tetramerization of a Triazaphosphole Induced by Complex Formation[**]

By *Alfred Schmidpeter, Helmut Tautz, Joachim von Seyerl* and *Gottfried Huttner*[*]

*Dedicated to Professor Rolf Appel on the occasion of his 60th birthday*

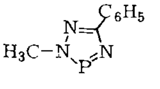
The monophospha analogues of azo compounds occur, in general, not as monomers *(1)* but as the dimers *(2)*, $n = 2$. *P*-amino derivatives with bulky substituents may be stable, at least kinetically, as monomers *(1)*[1]. With substituents having smaller spacial requirements, tri-[2a] and tetrameric[2b] *(2)*, $n = 3$, 4 are found.

*(1)*

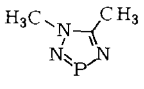
$$n\ {>}P{=}N{<} \rightleftharpoons ({>}P{-}N{<})_n$$

*(2)*

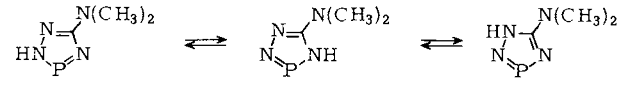
In 1,2,4,3-triazaphospholes[3] such as *(3)*—*(5)*, and other azaphospholes, the with —P=N— unit is incorporated into a 6π-system and does not usually oligomerize.



*(3)*



*(4)*



*(5a)* *(5b)* *(5c)*

In order to investigate the donor properties of the ψ-trigonal nitrogen and phosphorus atoms in these heterocycles, we prepared the $M(CO)_5$-complexes, M = Cr, Mo, W. While *(3)* and *(4)* gave P-coordinated 1:1-complexes[4], *(5)*[5] formed—despite the use of equimolar amounts of educts—complexes in which two molecules of *(5)* are bonded to an $M(CO)_5$ unit, the second apparently indirectly. The $^{31}P\{^1H\}$-NMR spectrum (Fig. 1) shows an $[AB]_2$-system which indicates a dimeric structure. $\delta^{31}P_A$ corresponds to a triply σ-bonded phosphorus and $\delta^{31}P_B$, according to the downfield

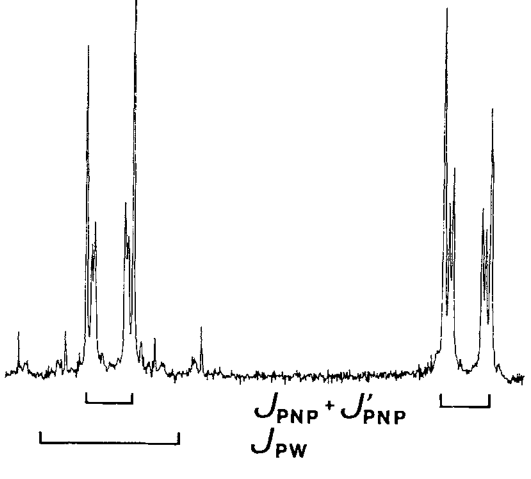


Fig. 1. $^{31}P\{^1H\}$-NMR spectrum of *(6b)* in tetrahydrofuran.

Table 1. Temperature of decomposition and NMR data (in THF) of *(6a)* and *(6b)*.

| Properties | *(6a)* | *(6b)* |
|---|---|---|
| Decomp. [°C] | 195 | 190 |
| $\delta^{31}P$ (A) | 66.4 | 68.9 |
| (B) | 140.5 | 96.8 |
| $J_{PNP} + J'_{PNP}$ [Hz] | 104.0 | 117.4 |
| $J_{PNH}$ (A) [Hz] | 29.9 | 30.2 |
| (B) [Hz] | 22.6 | 22.8 |
| $J_{PW}$ [Hz] | | 340.1 |
| $\delta^1H$, $CH_3$ (A) | 2.72 | 2.72 |
| (B) | 2.81 | 2.80 |

---

[*] Prof. Dr. A. Schmidpeter, Dr. H. Tautz
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)
Prof. Dr. G. Huttner, Dr. J. von Seyerl
Fakultät Chemie der Universität
D-7750 Konstanz (Germany)

[**] Four- and Five-membered Phosphorus Heterocycles, Part 49. This work was supported by the Deutsche Forschungsgemeinschaft and from the Fonds der Chemischen Industrie.—Part 48: *W. S. Sheldrick, D. Schomberg, A. Schmidpeter*, Acta Crystallogr. *B 36*, 2316 (1980); Part 52: *H. Tautz, A. Schmidpeter*, Chem. Ber. *114*, 825 (1981); Part 52: *H. Tautz, A. Schmidpeter*, Chem. Ber. *144*, 825 (1981).

coordination shift[4] (large for M = Cr, small for M = W)[4], to a phosphorus complexed to $M(CO)_5$. The $^{183}W$-satellites of the $P_B$-signal (Fig. 1) confirm this assignment.

An X-ray structure analysis proves the products to be $[M(CO)_5]_2$ complexes *(6)* of a tetramer of *(5)*.

From the solutions of *(6)* colorless crystals of *(6)*·6THF are obtained which lose THF even at 20 °C. The crystal structure was determined on a crystal of *(6a)*·6THF fused into a capillary tube which was partly filled with the mother liquor.

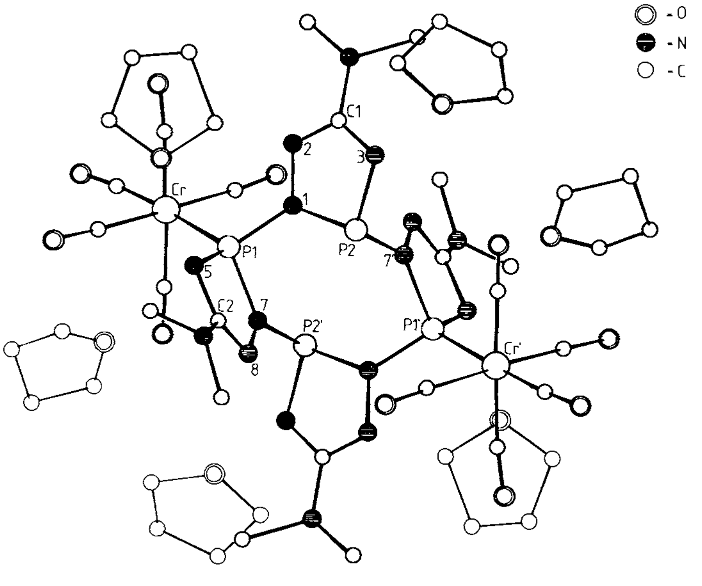
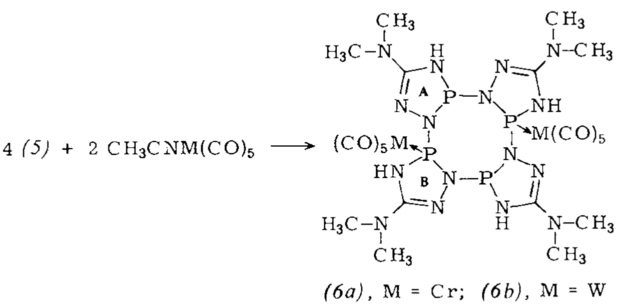


Fig. 2. Structure of the complex *(6a)*·6THF; monoclinic, space group $P2_1/c$, $a = 1987$, $b = 1151$, $c = 2193$ pm, $\beta = 138.88°$, $V = 3300$ Å$^3$, $Z = 2$, $\rho_{calc} = 1.35$ g cm$^{-3}$, $\mu = 5.2$ cm$^{-1}$. 1876 independent reflections (Syntex-P3 diffractometer, $T = -80$ °C, $2.5 \leq 2\theta \leq 40°$, $1.2 \leq \omega \leq 29.3$ s$^{-1}$, ω-scan). Structure solution system Syntex-EXTL, refined with full matrix, partially anisotropic, to $R_1 = 0.114$.

The X-ray structure analysis shows (Fig. 2) the tetramer in complex *(6)* to derive from the 4*H*-tautomer *(5b)*. This suggests that the oligomerization equilibrium *(1)*$\rightleftharpoons$*(2)* lies less to the left side with 4*H*-1,2,3,4-triazaphospholes than with the 2*H*- or 1*H*-isomers: for this reason *(3)* and *(4)*, in which these forms are fixed, behave in a different way to *(5)* when forming complexes.



*(6a)*, M = Cr; *(6b)*, M = W

The chromium complex *(6a)* possesses a crystallographic center of inversion and hence, unlike in octamethylcyclotetra(phosphazane)[2b], the eight-membered ring is not crown shaped. As a consequence of the strain in the five-membered ring, the phosphorus bond angles in the eight-membered ring are smaller (N1—P1—N7 and N1—P2—N7′ 102°) and the nitrogen bond angles larger (P1—N1—P2 126°, P1—N7—P2′ 122°) than in the said cyclotetra(phosphazane) (108 and 112°, respectively). Although two of the four phosphorus atoms are complexed and two are not the bond lengths in the eight-membered ring of *(6a)* are of note since they are almost identical (P1—N1 and P2′—N7 170 pm, P1—N7 and P2—N1 173 pm). The environment around all the nitrogen atoms is almost planar and the $PN_3$-pyramid is only slightly widened out by Cr-coordination. Intramolecular comparison indicates that formation of an $M(CO)_5^-$-complex only exerts a small structural effect on the ligands.

Both PN-bonds in the five-membered ring are lengthened considerably relative to those of a monomeric triazaphosphole[6] (to 173 pm for P1—N5, P1—N7 and P2—N1 and to 170 pm for P2—N3); the internal angles at phosphorus are contracted (to 87° for N5—P1—N7 and 86° for N1—P2—N3). The 4-position of the hydrogen bond manifests itself by the relatively long C2—N5 and C1—N3 bonds (*ca. 139* pm; in comparison C2—N8 and C1—N2 are *ca.* 127 pm). In contrast to cyclodi(phosphazane), the vicinal bonds in cyclotetra(phosphazane) only form a small dihedral angle[2b] and thereby permit the attachment of an almost planar ring (maximum deviation of the ring members from the best plane of the five-membered ring in *(6a):* 8 pm). According to this argument dimerization of an azaphosphole, on the other hand, would seem to be rather impossible.

The tetramer is only stable in the complex. Attempts to displace it using triphenylphosphane resulted in re-formation of the monomer *(5)*. The formation and dissociation of *(6)* suggest for the azaphospholes an equilibrium *(1)*$\rightleftharpoons$*(2)*, as in the analogous acyclic phosphazenes, which mostly lies far on the left-hand side: it may however be displaced to the right by a (soft) acceptor, if the latter prefers the P-atom in *(2)* to the P-atom in *(1)* as the donor[4]. In the opposite sense, with 1,3,2-benzodiazaphospholes[7], the equilibrium is shifted to the left by the *N*-coordinating (hard) acceptor $BF_3$.

## *Procedure*

*(6a, b):* Acetonitrile(pentacarbonyl)chromium or -tungsten (5 mmol) and *(5)* (10 mmol) are refluxed in 50 cm³ $CHCl_3$ for 5 h. After concentration to 10 cm³, *(6)* crystallized out; yield 75—85%.

Received: May 19, 1980
Supplemented: January 29, 1981 [Z 744 IE]
German version: Angew. Chem. *93*, 420 (1981)

CAS Registry numbers:
*(5)*, 76070-34-3; *(6a)*·6THF, 77461-21-3; *(6b)*, 77450-08-9; $CH_3CNCr(CO)_5$, 15228-38-3; $CH_3CNW(CO)_5$, 15096-68-1

---

[1] *E. Niecke, O. J. Scherer,* Nachr. Chem. Tech. *23*, 395 (1975); *O. J. Scherer, W. Glässel,* Chem. Ber. *110*, 3874 (1977).

[2] a) *W. Zeiss, K. Barlos,* Z. Naturforsch. *B 34*, 423 (1979); b) *W. Zeiss, W. Schwarz, H. Hess,* Angew. Chem. *89*, 423 (1977); Angew. Chem. Int. Ed. Engl. *16*, 407 (1977).

[3] *Y. Charbonnel, J. Barrans,* Tetrahedron *32*, 2039 (1976); *A. Schmidpeter, J. Luber, H. Tautz,* Angew. Chem. *89*, 554 (1977); Angew. Chem. Int. Ed. Engl. *16*, 546 (1977).

[4] *J. H. Weinmaier, H. Tautz, A. Schmidpeter, S. Pohl,* J. Organomet. Chem. *185*, 53 (1980).

[5] *A. Schmidpeter, H. Tautz,* Z. Naturforsch. *B 35*, 1222 (1980).

[6] *J.-P. Legros, Y. Charbonnel, J. Barrans, J. Galy,* C. R. Acad. Sci. Ser. *C 286*, 319 (1978); *S. Pohl,* Chem. Ber. *112*, 3159 (1979); both structure determinations relate however to 1*H*-isomers.

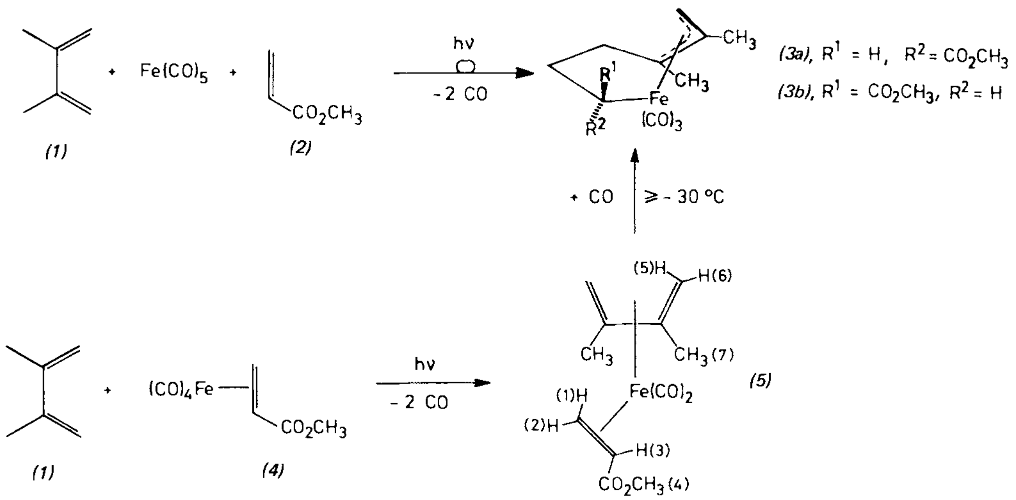
[7] *C. Malavaud, M. T. Boisdon, Y. Charbonnel, J. Barrans,* Tetrahedron Lett. *1979*, 447.

# Photochemical Synthesis of a ($\eta^4$-Diene)($\eta^2$-Olefin)Fe(CO)$_2$ Complex and Subsequent Thermal Coupling of the Ligands

By *Friedrich-Wilhelm Grevels* and *Konrad Schneider*[*]

We previously reported on the coupling of 1,3-dienes and methyl acrylates *(2)* by photochemical reaction with pentacarbonyliron, which leads, both *via* the ($\eta^4$-diene)Fe(CO)$_3$ as well as *via* the ($\eta^2$-olefin)Fe(CO)$_4$ *(4)*, to complexes of the type *(3)*[1a]. We have now succeeded in isolating an intermediate[1], the ($\eta^2$-methyl acrylate)dicarbonyl($\eta^4$-2,3-dimethylbutadiene)iron complex *(5)*.

*(5)* is obtained by irradiation—preferably at low temperature—of *(4)* and *(1)*, if the liberated CO is removed by a stream of argon. *(5)* is stable at 20 °C, but very air-sensitive in solution; in the dark it reacts with CO to give *(3)*.



Thus, it is shown that CO in Fe(CO)$_5$ is first replaced photochemically by the unsaturated ligands *(1)* and *(2)*—a process which without irradiation requires rather drastic conditions and is frequently accompanied by decomposition—and this is followed by thermal C—C coupling of the ligands with re-uptake of one CO. This reaction starts at *ca.* −30 °C and affords the isomers *(3a)* and *(3b)* in a ratio which is temperature-dependent (Fig. 1). $^{13}$C-labeled CO is distributed equally among the three CO positions of *(3a)* and *(3b)* ($^{13}$C-NMR, MS).

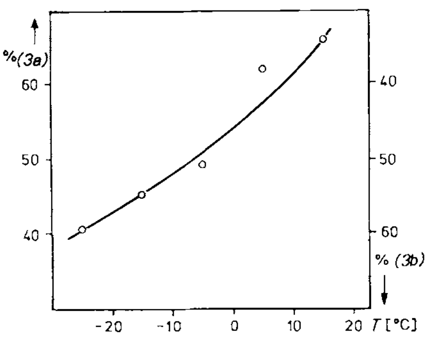
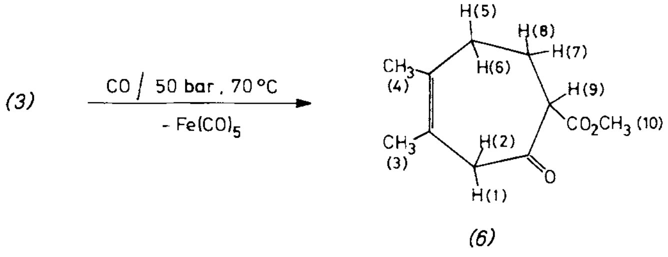


Fig. 1. Product ratio *(3a)/(3b)* in the reaction of *(5)* with CO as a function of temperature.

Although ($\eta^4$-diene)Fe(CO)$_3$ loses CO in good quantum yields[2], and coordinatively unsaturated $\eta^4$-(diene)Fe(CO)$_2$ has also been detected spectroscopically in low-temperature matrices[3], attempts to obtain *(5)* also from ($\eta^4$-diene)Fe(CO)$_3$ and *(2)* have so far failed.

The IR spectrum shows that *(5)* is present as a mixture, presumably of three or four species. In the metal-carbonyl region, instead of the expected two bands a total of five bands (some slightly broadened) are observed (*n*-hexane; 2023, 2018, 1981, 1977.5, 1968 cm$^{-1}$), while two bands appear in the ester-carbonyl region (1724, 1711 cm$^{-1}$). The position of the CO-stretching vibration bands—taking into account substituent-determined shifts—resembles those of known dicarbonyl($\eta^4$-cyclobutadiene)($\eta^2$-olefin)iron complexes[4a]. The $^1$H-NMR spectrum ([D$_8$]toluene) of *(5)* at 20 °C shows only one set of signals each for the olefin [$\delta = 2.20$ (1-H), 3.12 (2-H), 2.60 (3-H), 3.50 (4-H); $J_{1,2} \lesssim 3$, $J_{1,3} \approx 7$, $J_{2,3} \approx 11$ Hz] and the diene [$\delta = -0.21$, $-0.40$ (5-H, 5′-H), 1.09, 0.63 (6-H, 6′-H), 1.98, 1.83 (7-H, 7′-H)], which, however, are partly split at lower temperatures. Accordingly, the system is fluxional, with rapid exchange—presumably through rotation of the olefin[4] and of the diene[4b]—at room temperature. The changes in the spectrum on cooling are not complete until −80 °C. The relative concentrations of the precursors of *(3a)* and *(3b)*, however, do not appear to be temperature-dependent, since the intensity ratios of the carbonyliron bands in the IR spectrum of *(5)* do not change between +20 and −50 °C. It can therefore be concluded that the temperature-dependence of the product ratio *(3a)/(3b)* is kinetically determined.

As with CO, *(5)* also reacts with phosphanes, isocyanides *etc.* with coupling of the diene and the olefin to give Fe(CO)$_2$L complexes analogous to *(3)*[5].



*(6)*

Detachment of the C$_6$-chain from the metal in *(3)* is accomplished, *inter alia*, with CO. Insertion of CO takes place

---

[*] Dr. F.-W. Grevels, K. Schneider
Institut für Strahlenchemie
im Max-Planck-Institut für Kohlenforschung
Stiftstrasse 34—36, D-4330 Mülheim a. d. Ruhr (Germany)

0570-0833/81/0404-0410 $ 02.50/0

with formation of the cycloheptenone derivative *(6)*[6] along with other products. The $Fe(CO)_5$ that is formed could be used again for the synthesis of *(3)*; so ultimately *(6)* is synthesized from *(1)*, *(2)*, and CO. This reaction sequence be possibly can used preparatively for the synthesis of substituted cycloheptenones[7].

*Procedure*

A solution of *(4)*[8] (2.54 g, 0.01 mol) and *(1)* (4.10 g, 0.05 mol) in diethyl ether (130 $cm^3$) is irradiated for 2.5 h at −40 °C (immersion-lamp apparatus of Solidex glass, Philips HPK 125 W Hg-lamp), with concomitant passage of Ar. The solution is evaporated down *in vacuo* and the residue chromatographed on silica gel at −40 °C. Diene-$Fe(CO)_3$ and *(4)* are eluted with pentane, and then *(5)* is eluted with pentane/diethyl ether (4+1). The oily crude product is dissolved in 5 $cm^3$ hexane; on cooling to −78 °C yellow crystals of *(5)* are formed (0.75 g, 27%), m.p. 24—25 °C.

Received: May 13, 1980 [Z 745 IE]
German version: Angew. Chem. *93*, 417 (1981)

CAS Registry numbers:
*(1)*, 513-81-5; *(2)*, 96-33-3; *(3a)*, 61867-50-3; *(3b)*, 61950-05-8; *(4)*, 12287-67-1; *(5)*, 77257-30-8; *(6)*, 77256-94-1; $Fe(CO)_5$, 13463-40-6

---

[1] a) *F.-W. Grevels, U. Feldhoff, J. Leitich, C. Krüger*, J. Organomet. Chem. *118*, 79 (1976); b) *M. Bottrill, R. Davies, R. Goddard, M. Green, R. P. Hughes, B. Lewis, P. Woodward*, J. Chem. Soc. Dalton Trans. *1977*, 1252.

[2] *O. Jaenicke, R. C. Kerber, P. Kirsch, E. A. Koerner von Gustorf, R. Rumin*, J. Organomet. Chem. *187*, 361 (1980).

[3] *G. Ellerhorst, W. Gerhartz, F.-W. Grevels*, Inorg. Chem. *19*, 67 (1980).

[4] a) *P. Reeves, J. Henery, R. Pettit*, J. Am. Chem. Soc. *91*, 5888 (1969); b) *J. W. Faller*, Adv. Organomet. Chem. *16*, 211 (1977).

[5] *F.-W. Grevels*, unpublished results.

[6] *(6)*, m.p. 50 °C; $^1$H-NMR ($C_6D_6$, 20 °C): $\delta = 2.96$, 2.82 (1-H, 2-H, $J_{1,2} = 15.5$ Hz), 1.37, 1.39 (3-H, 4-H), 1.82, 1.80 (5-H, 6-H, m), 1.64, 2.20 (7-H, 8-H, m), 3.30 (9-H, $J_{7,9} \approx J_{8,9} \approx 7$ Hz), 3.32 (10-H); IR (*n*-hexane): $\tilde{\nu}(CO) = 1753$, 1717.5 $cm^{-1}$; MS: $m/e = 196$ ($M^+$), 165, 164, 149, 136, 122, 109, 93, 82, 67 (100%), 55, 41 *etc.*

[7] See *e.g.* *R. Noyori*, Acc. Chem. Res. *12*, 61 (1979) (synthesis of seven-membered rings from $\alpha,\alpha'$-dibromoketones and 1,3-dienes with $Fe_2(CO)_9$).

[8] *E. Weiss, K. Stark, J. E. Lancaster, H. D. Murdoch*, Helv. Chim. Acta *46*, 288 (1963).

## BOOK REVIEWS

*H. Staudinger, H. Mark* and *K. H. Meyer*—**Thesen zur Grösse und Struktur der Makromoleküle** (*H. Staudinger, H. Mark* and *K. H. Meyer*—Theses on the Size and Structure of Macromolecules). By *C. Priesner*. Verlag Chemie, Weinheim 1980. x, 389 pages, cloth, DM 98.00.

This is a "contribution to the history of macromolecular chemistry" in which the author limited himself intentionally to "a comprehensive and comparatively detailed presentation of one very important aspect", as stated in the title of the book. The main intention was to demonstrate that also during this phase of scientific evolution "the major lines of development..." emerged "from the work and ideas of many people", even though "Hermann Staudinger was one of the best known pioneers of modern high polymer chemistry".

The book is arranged in such a way that the author's presentation is supported mainly by abstracts of publications or communications. The evidence is often impressive and speaks for itself, so that only a few commentative sentences are necessary to make correlations. The first nonsystematic and systematic experiments on polymers are described in Part 1, beginning with the establishment of *Berzelius'* concept of "Polymerism" in 1833. This part ends with a detailed discussion of the work reported at the 89th Meeting of the Society of German Scientists and Physicians at Düsseldorf in 1926.

Part 2 occupies a central place and covers the subsequent period up to 1937. The feuds between *Staudinger* and *K. H. Meyer/H. Mark* as well as others, documented by substantial original material, fall into this period and are interpreted mainly as differences about priority rather than conflicts of views.

A concluding evaluation is attempted in the last part, entitled "Commentary". In all, it must be said that *Priesner* has succeeded in producing an exceptionally exciting work, even though the modern expert reader will not easily follow all reasoning, arguments, and counterarguments contained in the original texts. The many-sided views expressed with definite terminology by organic chemists, colloid chemists, physicists, and physical chemists required a veritable polymath to interpret, weigh up, and sometimes criticize, and the author rose fully to the occasion. In his rather more reserved over-all judgment of *Staudinger*, especially concerning the priority argument, the younger specialists are more likely to follow him than the older ones, or even former students of *Staudinger*.

Naturally, not everything is well done. The merits of *Pickles* are quite rightly pointed out. But *Staudinger* already mentions *Pickles* and his suggested structure of rubber in the first work "Concerning Polymerization", and not only in the fifth, which appears twice in the index (references 39 and 79). *Paul J. Flory*, who commences his well-known standard work of 1953 with an excellent historical introduction, also rightly emphasizes *Pickles'* importance, so the impression can hardly arise that his work has not been sufficiently observed (p. 22).

The "modern interpretation" on p. 120, second paragraph, is not clear. The reviewer prefers the preceding original text from *Staudinger*, which sounds remarkably up-to-date if the term "association" is replaced by "entanglement".

Did *Staudinger* win the Nobel prize in 1953 for the "viscosity formula", as claimed at the top of p. 121?

Here and there one has the impression that the author should have consulted other recognized books on polymer chemistry and polymer physics in addition to the Römpp and the Ullmann.

Full marks to Verlag Chemie for the book's layout. Pity about some printing errors.

*Heinz-Hermann Meyer* [NB 535 IE]

## Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Spectral and Chemical Characterization of Organic Compounds.** By *W. J. Criddle* and *G. P. Ellis.* John Wiley & Sons. New York 1980. xi, 115 pp., carton, £ 4.50.—ISBN 471-27812-2

**An Introduction to Synthesis Using Organocopper Reagents.** By *G. H. Posner.* John Wiley & Sons, New York 1980. xvii, 140 pp., bound, £ 12.50.—ISBN 0-471-69538-6

**Quantum Dynamics of Molecules.** Edited by *R. G. Woolley.* Plenum Press, New York 1980, xiv, 557 pp., bound, $ 59.50.—ISBN 0-306-40462-1

**Perspectives in Peptide Chemistry.** Edited by *A. Eberle, R. Geiger,* and *T. Wieland.* S. Karger, Basel 1981. xi, 443 pp., bound, DM 174.00.—ISBN 3-8055-1297-X

**The Infrared Spectra of Complex Molecules.** Vol. 2. 2nd Edit. By *L. J. Bellamy.* Chapman and Hall, New York 1980. xi, 299 pp., bound, £ 15.00.—ISBN 0-412-22350-3

**Coordination Chemistry.** Edited by *D. Banerjea.* Pergamon Press, Oxford 1980. xi, 275 pp., bound, £ 34.00.—ISBN 0-08-023942-0

**International Thermodynamic Tables of the Fluid State—7 Propylene (Propene).** Edited by *S. Angus, B. Armstrong,* and *K. M. de Reuck.* Pergamon Press, Oxford 1980. xxiii, 273 pp., bound, $ 100.00.—ISBN 0-08-022373-7

**The Analysis and Control of Less Desirable Flavours in Foods and Beverages.** Edited by *G. Charalambous.* Academic Press, New York 1980. ix, 358 pp., bound, $ 24.50.—ISBN 0-12-169065

**Medizinische Psychologie, Medizinische Soziologie.** Examensfragen Medizin. Edited by *W. Rathgeber.* edition medizin im Verlag Chemie, Weinheim 1980. xi, 187 pp., bound, DM 32.00.—ISBN 3-527-15031-5

**Molecular Shapes.** By *J. K. Burdett.* John Wiley & Sons, New York 1980. x, 287 pp., bound, £ 15.75.—ISBN 0-471-07860-3

**Qualitative Analysis of Flavor and Fragrance Volatiles by Glass Capillary Gas Chromatography.** By *W. Jennings* and *T. Shibamoto.* Academic Press, New York 1980. vi, 472 pp., bound, $ 39.00.—ISBN 0-12-384250-6

**Physical Methods in Modern Chemical Analysis.** Edited by *Th. Kuwana.* Academic Press, New York 1980. xi, 411 pp., bound, $ 45.00.—ISBN 0-12-430802-3

**Medizinisch-Psychologische Anthropologie.** Edited by *W. Bräutigam.* Wissenschaftliche Buchgesellschaft, Darmstadt 1980. 439 pp., bound, DM 94.00 (for members DM 58.00).—ISBN 3-534-07973-6

**Pflanzen der Götter.** By *R. E. Schultes* and *A. Hofmann.* Hallwag Verlag, Bern 1980. 191 pp., bound, DM 48.00.—ISBN 3-444-10282-8

**Liquid Crystals of One- and Two-Dimensional Order.** Edited by *W. Helfrich* and *G. Heppke.* Springer Verlag, Berlin 1980. xii, 416 pp., bound, DM 69.00.—ISBN 3-540-10399-6

**Anorganische Chemie.** By *K. Westermann, K.-H. Näser,* and *G. Brandes.* VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1980. 11th Edit. 670 pp., bound, *ca.* DM 40.00.

**Tabellenbuch Chemie.** Numerous Authors. VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1980. 8th Edit. 312 pp., bound, *ca.* DM 23.00

**Chemische Reaktionsdetektoren für die schnelle Flüssigkeits-Chromatographie.** By *G. Schwendt.* Hüthig-Verlag, Heidelberg 1980. 213 pp., bound, DM 28.00.—ISBN 3-7785-0687-0

## Corrigendum

The following corrections should be made to the short communication entitled "Polymethinic Ring Compounds and the Polymethinic Carbonyl Group" by *Siegfried Kulpe,* Angew. Chem. Int. Ed. Engl. *20,* 271 (1981):

On p. 271, second paragraph, second line, "di- and triaminobenzoquinones" should read "di- and tetraaminobenzoquinones".

On p. 272, first paragraph, left-hand column, delete the words "tetra- and".

On p. 272, the first sentence, right-hand column, should read "The heteropolarity of this bond does *not* lead to stretching as would have to exist according to *(2b)* and *(2c)*".

---

**Editorial office:** Boschstrasse 12, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

**Editor:** *O. Smrekar.* **Translation Editors:** *I. G. Neil* and *A. Stimson.*

**Publishers:** Verlag Chemie GmbH. (Managing Directors *Dr. Helmut Grünewald* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany, Telephone Weinheim (06201) 14031 <602-1>. Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English

Volume 20 · Number 5
May 1981
Pages 413–486

# The Transition Metal-Nitrogen Multiple Bond

**By Kurt Dehnicke and Joachim Strähle**[*]

*Dedicated to Professor Josef Goubeau on the occasion of his 80th birthday*

Numerous nitrido complexes of transition metals show very short metal-nitrogen bond lengths, suggesting M≡N-triple bonds. At present, compounds of this type are being intensively investigated. In particular the molybdenum complexes are considered as model substances for the study of at least an intermediate step of $N_2$-assimilation. This article contains a review of the structure and bonding, as well as syntheses and reactions of these complexes.

## 1. Introduction

Apart from the carbyne ligand, the nitrido ligand is the strongest known π-electron donor. As a terminal ligand M≡N: its formal bond order corresponds to a triple bond. Here, the three bond lines represent one σ and two π bonds, the latter resulting from overlap of occupied π orbitals of the nitrogen with two unoccupied, symmetry allowed d-orbitals of the metal. An important reason for the high bond order is the relatively low electronegativity of the nitrogen, which qualifies it for optimal overlap in the series

$$\mathrm{M{\equiv}N{:}} \qquad \mathrm{M{=}\ddot{O}{:}} \qquad \mathrm{M{-}\ddot{F}{:}}$$

Although higher bond orders are possible in transition metal-oxygen and transition metal-fluorine bonds, the facts are on the whole expressed by the above formulation. The second condition for the occurrence of a high bond order is a sufficient supply of unoccupied d-orbitals in the transition metal, which, as a result, exists in general in a high oxidation state. Hitherto, MN multiple bonds have been found with following elements:

| | | | | | |
|---|---|---|---|---|---|
| Ti | V | Cr | Mn | Fe | |
| | Nb | Mo | (Tc) | Ru | |
| | Ta | W | Re | Os | Ir |

The most favorable conditions are provided by the elements Mo, W, Re, Ru and Os.

## 2. Bonding

### 2.1. Terminal Ligand M≡N:

The terminal nitrido ligand occurs, for example, in the tetragonal pyramidal complex anions $[MNCl_4]^-$ (M = Mo, W, Re, Ru, Os)[1-4] (see Fig. 1). The M≡N bond is ex-

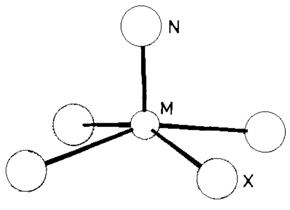


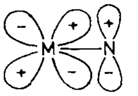
Fig. 1. Structure of anions $[MNX_4]^-$ (M = Mo, Re, Ru, Os; X = F, Cl, Br, I) with terminal nitrido ligands.

---

[*] Prof. Dr. J. Strähle [+]
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)
Prof. Dr. K. Dehnicke
Fachbereich Chemie der Universität
Lahnberge, D-3550 Marburg/Lahn (Germany)
[+] Author to whom correspondence should be addressed.

tremely short; values range between 157 pm (Ru) and 166 pm (Mo). The triple bond can be understood as a superposition of one σ bond *(1)* and two (degenerate) π bonds *(2)*.

*(1)*



*(2)*

The lone pair of electrons only bestows weak basic properties to the nitrido ligand.

## 2.2. Asymmetrical $\overset{\ominus}{M}\equiv\overset{\oplus}{N}$—M Bridges

Under certain conditions, the free electron pair at the nitrido ligand is able to form a second, significantly weaker bond to the adjacent transition metal center. The continuance of the bond axis, according to M≡N—M≡N—, leads to columnar structures, as in $ReNCl_4$[5] (Fig. 2) and $K_2ReN(CN)_4 \cdot H_2O$[6]. The ReN bond lengths differ greatly: 158 and 248 pm, 153 and 244 pm respectively. Whereas the short bond can be interpreted in the same way as the terminal one, the long bond is a σ-type, in which the occupied sp-hybrid orbital of the nitrogen overlaps with an unoccupied $d^2sp^3$-hybrid orbital of the metal, as indicated in *(3)*.

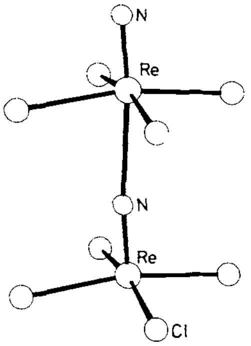
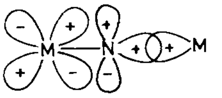


Fig. 2. Structure of $ReNCl_4$ with asymmetric nitrido bridges.

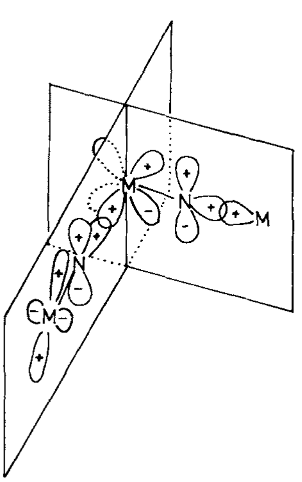


*(3)*

In this arrangement, the $d_{z^2}$- and $p_z$-orbitals involved in the hybridization of the metal are strongly and unequally involved in the σ-part of the M≡N triple bond, and hence the σ-interaction in the position *trans* to the π bond is only very weak.

A much more favorable arrangement is that shown in *(4)*, in which the second σ bond is achieved *via* an orbital perpendicular to the z-axis.

Consequently, a rectangular bonding system is formed, giving tetrameric units of type *(5)* (see Fig. 3). A zig-zag chain, which is equally possible, has not yet been observed.



*(4)*

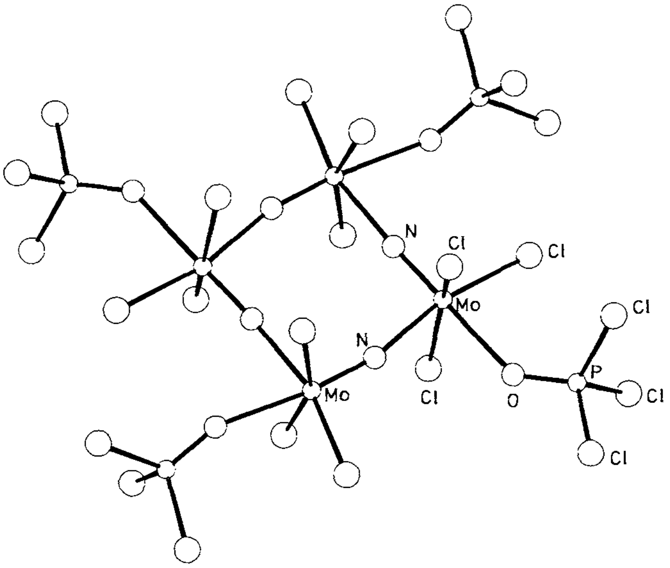
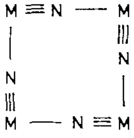
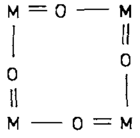


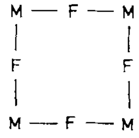
Fig. 3. Structure of the tetramer $[MoNCl_3 \cdot OPCl_3]_4$ with asymmetric nitrido bridges.



*(5)*



*(6)*



*(7)*

In fact, such tetramers occur far more frequently than polymers of the type $ReNCl_4$, as illustrated by the examples $[MoNCl_3]_4$[7] and $[MNCl_3 \cdot POCl_3]_4$ (see Fig. 3) (M = Mo, W, Re[8-10]). The long Re—N bond in the tetrameric rhenium complex is even reduced to 217 pm. It is interesting to compare these nitrido complexes with the tetrameric oxo *(6)* and fluoro complexes *(7)*, in which the differences between the alternating bond lengths decrease in the succession $[MoNCl_3 \cdot POCl_3]_4$[8], $[NbOCl_3 \cdot POCl_3]_4$[11] and $[NbF_5]_4$[12]:

| Mo≡N—Mo | Nb≡N—Nb | Nb—F—Nb | |
|---|---|---|---|
| 166 216 | 174 209 | 207 207 | [pm] |

The solvating $POCl_3$ molecules are always arranged *trans* to the π bonded ligand and are coordinated to the metal center *via* the oxygen atom (see Fig. 3). Accordingly, the bonding in the trinuclear nitridomolybdenum complex $[\{(Et_2NCS_2)_3Mo{\equiv}N\}_2Mo(S_2CNEt_2)_3]^{3+}$, which contains the Mo≡N—Mo—N≡Mo group as a structural element can be understood[13]. The structures of these types of compounds are discussed in Section 6.3.

### 2.3. Symmetrical $\overset{\frac{1}{2}\ominus}{M}=\overset{\oplus}{N}=\overset{\frac{1}{2}\ominus}{M}$ Bridges

Symmetrical nitrido bridges are observed in some binuclear complexes, *e.g.* in the recently prepared ion $[Ta_2NBr_{10}]^{3-}$[14] (see Fig. 4). The TaN bonds (185 pm) can be interpreted as double bonds. In this case, apart from two $\sigma$ bonds, the nitrido ligand forms, using the two perpendicular occupied $\pi$ orbitals, two degenerate $d\pi$-$p\pi$-$d\pi$ three centered $\pi$ molecular orbitals, each being occupied by one electron pair (see Fig. 8)[15].

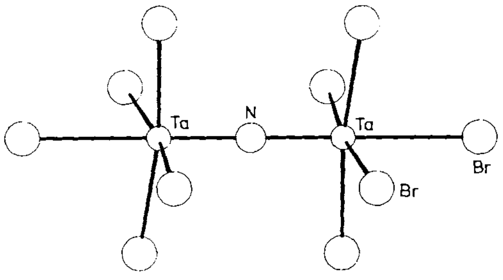
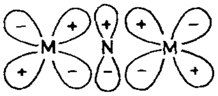


Fig. 4. Structure of the anion $[Ta_2NBr_{10}]^{3-}$ with symmetric nitrido bridges.



(8)

The factors responsible for the formation of symmetrical or asymmetrical bridges have not yet been completely clarified (Section 6.4). An intermediate situation is found with the nitrido bridge in the complex ion $[W_2NCl_{10}]^{2-}$[16], which contains a long (207 pm) and a short WN bond (166 pm), but where the long WN bond shows an even more distinct share of multiple bonding. This could be a consequence of one of the tungsten atoms being pentavalent and the other hexavalent, which would explain the asymmetry of the bridge. A symmetrical bridge also occurs in μ-nitrido-bis(porphyrinato)iron. To date, it is the only known nitridoiron complex[17] (see Section 6.4 for structures of these complexes).

### 2.4. N-Bridges ("Nitrido Bridges") of the Type $\overset{\ominus}{M}=\overset{\oplus}{N}=X$ (X = O, S, $PR_3$)

N-bridges of this type with X = O or S, occur in nitrosyl or thionitrosyl complexes. Nitrosyl complexes have been adequately reviewed[18] so there is no need to discuss them here further. Formally, the nitrosyl ligand is considered to be $NO^+$, which explains its extremely strong back-bonding behavior. In principle, it is suitably described by the linear arrangement M=N=O. Similar considerations seem to apply to the thionitrosyl ligand. In the complex $\pi$-$C_5H_5Cr(CO)_2NS$ it is also linear, the bond lengths CrN (169 pm) as well as NS (155 pm) suggesting $\pi$ bonding[19]. In both cases the formal oxidation number of the N atom is +3, so that these compounds are actually not real nitrido complexes.

On the other hand, this does not apply to phosphaneiminato complexes of transition metals with a linear arrangement $M=N=PPh_3$, of which three examples have already been examined by crystallographic methods[20-22]. In these complexes, real nitrido bridges are found. In the compounds $[Cl_4M=N=PPh_3]_2$ (M = Nb, Ta) (see Fig. 5) the MN- (178 pm and 180 pm respectively) and PN-bonds (164 and 159 pm respectively) can be understood as double bonds on account of their lengths; the bond angle of the bridge (171 and 177° respectively) practically corresponds to an sp-hybridization of the N atom, so that the phosphaneiminato complexes are closely related to the type discussed in Section 2.3, and should be formulated as follows:

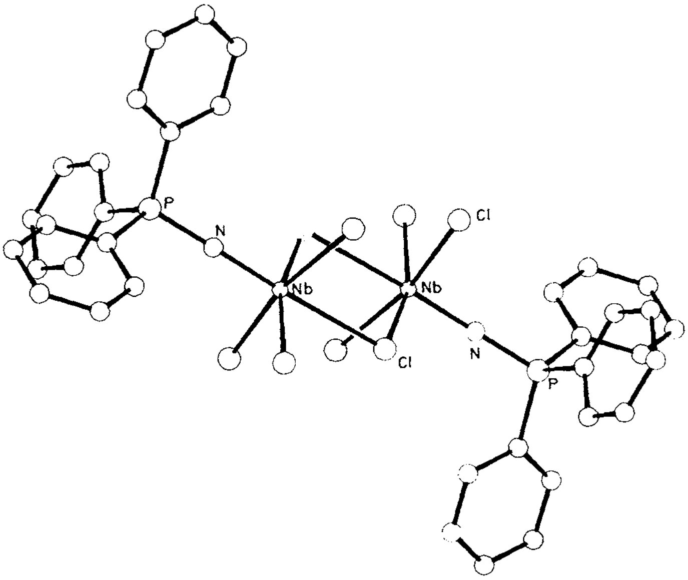


Fig. 5. Structure of the phosphaneiminato complex $[Cl_4NbNPPh_3]_2$.

$$\overset{\ominus}{M}=\overset{\oplus}{N}=PPh_3 \leftrightarrow \overset{2\ominus}{M}\equiv\overset{\oplus}{N}-\overset{\oplus}{P}Ph_3$$

### 2.5. N-Bridges ("Nitridobridges") of the Type $\overset{\ominus}{M}\equiv\overset{\oplus}{N}-X$, $M=\ddot{N}\diagdown X$ and $\overset{\ominus}{M}=\overset{\oplus}{N}R_2$

Compounds with these types of bridges have recently been reviewed[23], so they need not be discussed here in detail (for structures see Section 6.5). The ligands X, among others, are hydrogen, halogens (see Fig. 6), alkyl, aryl, silyl, $NR_2$ groups; $M\ddot{N}X$, X = $NR_2$ is a hydrazido(2−) complex.

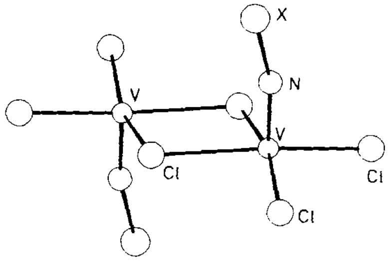
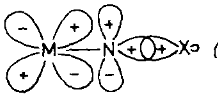


Fig. 6. Structure of the complexes $Cl_3VNX$ (X = Cl or I).

With the exception of NR and $NR_2$ respectively, all these ligands, X, in complexes of the type

$$\overset{\ominus}{M}=\overset{\oplus}{N}=\ddot{N}R \text{ or } \overset{2\ominus}{M}=\overset{\oplus}{N}=\overset{\oplus}{N}R_2$$

the ligands X show no tendency to π-bond with the central nitrogen atom, so that the N—X group has σ-character. The bonds can be interpreted in a similar way as those of M≡N—M (Section 2.2); *(9)* shows only one of the doubly degenerate π bonds of the M≡N bond.



*(9)*

The N—X σ bond thus arises *via* overlap of an sp-hybrid orbital of nitrogen with a hybrid orbital of the X-group. The bond is, contrary to the easily cleaved long bonds in the M≡N—M bridges, very stable. It should be noted that the M≡N bond of nitrene complexes (Section 6.5) should only be regarded as a triple bond when the MNX-axis is linear. This claim is supported by numerous nitrene complexes, although smaller bond angles (up to 139°) are known.

In some diazenido-complexes, which contain the $\overset{\ominus}{M}\equiv\overset{\oplus}{N}-NR_2$ group, the NN bond is shorter than a N—N single bond, so that the form $\overset{2\ominus}{M}=\overset{\oplus}{N}=\overset{\oplus}{N}R_2$ is justified.

A selection of the numerous recent examples of these types of bonds has been compiled in Table 1 (for further examples see [23]).

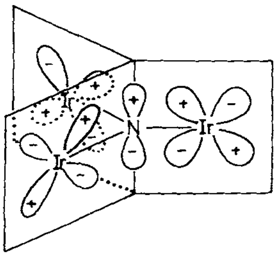
Table 1. Examples of structures with the characteristic groups $\overset{\ominus}{M}\equiv\overset{\oplus}{N}-X$, $\overset{\ominus}{M}=\overset{\oplus}{N}=\bar{N}R$, $\overset{\ominus}{M}\equiv\overset{\oplus}{N}-\bar{N}R_2$ and $\overset{\ominus}{M}=\overset{\oplus}{N}R_2$.

| Complex | Group | M—N [pm] | M—N—X [°] | Ref. |
|---|---|---|---|---|
| $Cl_3VNI$ | $\overset{\ominus}{V}-\overset{\oplus}{N}-I$ | 165 | 163 | [24] |
| $[(\eta^5\text{-}C_5H_5)_2VN(SiMe_3)]$ | $\overset{\ominus}{V}-\overset{\oplus}{N}-Si$ | 167 | 178 | [25] |
| $[MoCl_4(POCl_3)(NC_2Cl_5)]$ | $\overset{\ominus}{Mo}-\overset{\oplus}{N}-C$ | 169 | 172 | [26] |
| $[Mo(NC_6H_4Me\text{-}p)Cl_2(p\text{-}MeC_6H_4N_2COPh)(PMe_2Ph)]$ | $\overset{\ominus}{Mo}-\overset{\oplus}{N}-C$ | 173 | 177 | [27] |
| $[MoCl_2(NH)O(EtPh_2PO)_2]$ | $\overset{\ominus}{Mo}-\overset{\oplus}{N}-H$ | 170 | 157 | [28] |
| $[MoCl(N_2COPh)(NHNCOPh)(PMe_2Ph)]$ | $\overset{\ominus}{Mo}-\overset{\oplus}{N}-N$ | 178 | 174 | [29] |
| $[Mo(N_2Ph)_2(S_2CNMe_2)_2]$ | $\overset{\ominus}{Mo}-\overset{\oplus}{N}-N$ | 174 | 170 | [30] |
| $[MoI(N_2C_6H_{11})(diphos)_2]$ [a] | $\overset{\ominus}{Mo}-\overset{\oplus}{N}-N$ | 183 | 177 | [31] |
| $[Mo(NMe_2)_4]$ | $\overset{\ominus}{Mo}=\overset{\oplus}{N}R_2$ | 193 | 123 | [32] |
| $AsPh_4^+[Cl_5W(NC_2Cl_5)]^-$ | $\overset{\ominus}{W}-\overset{\oplus}{N}-C$ | 168 | 168 | [33] |
| $[WBr(diphos)_2(N_2CCl_2)]^+PF_6^-$ [a] | $\overset{\ominus}{W}-\overset{\oplus}{N}-N$ | 175 | 169 | [34] |
| $[(\eta^5\text{-}C_5H_5)W(CO)_2(N_2CH_3)]$ | $\overset{\ominus}{W}-\overset{\oplus}{N}-N$ | 186 | 173 | [35] |
| $[ReCl_4(POCl_3)(NC_2Cl_5)]$ | $\overset{\ominus}{Re}-\overset{\oplus}{N}-C$ | 169 | 169 | [36] |
| $[IrCl(N_2C_5Cl_4)(PPh_3)_2(C_7H_8)]$ | $\overset{\ominus}{Ir}-\overset{\oplus}{N}-N$ | 182 | 173 | [37] |

[a] diphos = ethylenebis(diphenylphosphane).

### 2.6. Nitride Bridges of the Type $M_3N$

This type of bridge has hitherto only been described in the iridium complex $(NH_4)_4[Ir_3N(SO_4)_6(H_2O)_3]$. The group $Ir_3N$ is trigonal planar; the Ir—N bond length (192 pm) indicates appreciable π bonding[38]. As shown in *(10)* the bond system can be described by three IrN σ bonds and ($p_\pi$-$d_\pi$) overlap of the occupied N($p_z$) orbital with each Ir($d_{xz}$) orbital.



*(10)*

## 3. Syntheses

The following contains a review of the most important reactions for the syntheses of nitrido compounds of transition metals. A comprehensive review, up to 1971, has been put forward by *W. P. Griffith*[39]. As far as the organoimido complexes (Section 6.5) are concerned we shall only deal with those syntheses not covered in [23].

### 3.1. Decomposition of Azides

The most effective preparative method is the reaction of azides, mostly with transition metal halides. The halogen azides, chlorine azide and because of the higher polarity of the I—N bond iodine azide, have proved to be of special utility. Thus, for example, tungsten hexachloride[40] or the pentachlorides of niobium, tantalum[41], molybdenum[40] and rhenium[42] react with chlorine azide, to form metal chloride azides:

$$WCl_6 + ClN_3 \xrightarrow[CCl_4]{} WCl_5N_3 + Cl_2 \tag{1}$$

$$MoCl_5 + ClN_3 \rightarrow MoCl_5N_3 + 1/2\,Cl_2 \tag{2}$$

The explosive metal chloride azides of molybdenum, tungsten and rhenium can be thermally decomposed in solution without any risk:

$$MCl_5N_3 \rightarrow MNCl_3 + N_2 + Cl_2 \tag{3}$$

M = Mo, W, Re

This reaction is completed within a few hours, even at room temperature[40,42]. On the other hand, the azides of niobium and tantalum are more stable and have not yet been thermally converted into nitrido complexes.

The tantalum azide $[TaCl_4N_3]_2$ has been characterized by single crystal structure analysis[41]. However, decomposition of the azides $[MN_3Cl_4]_2$ (M = Nb, Ta), occurs at room temperature upon addition of a Lewis base such as triphenylphosphane. In an analogous Staudinger reaction[43], the phosphaneiminato complexes $[Cl_4M{=}N{=}PPh_3]_2$ are obtained[21,22].

The azides $ClN_3$[44], $IN_3$[45] and $PhN_3$[46] undergo a remarkable reaction with vanadium tetrachloride; here, the NX bond of the $XN_3$ molecules is preserved and the nitrene complexes $Cl_3V{\equiv}N{-}X$ are formed (see Section 6.5). The mechanism of this reaction has not yet been clarified. In the reaction with $IN_3$, the formation of ICl and the consumption of two mol $IN_3$ per mol $VCl_4$ suggest the following reaction equation:

$$VCl_4 + 2\,IN_3 \rightarrow Cl_3V{\equiv}N{-}I + 2\,1/2\,N_2 + ICl \tag{4}$$

In the case of $ClN_3$, the intermediate azide $VCl_4N_3$ can be isolated. It presumably decomposes [eq. (6)] in a manner analogous to the Curtius reaction[47] [eq. (5)], in which an isocyanate is formed by anionotropic migration of the group R:

$$R{-}CO{-}N_3 \rightarrow R{-}N{=}C{=}O + N_2 \tag{5}$$

$$Cl_4VN_3 \rightarrow Cl_3V{\equiv}N{-}Cl + N_2 \tag{6}$$

It has been known for some time, that the reaction of organoazides with metal compounds yields nitrene complexes[23]. $MoNCl_3$ can also be prepared from $MoCl_5$ and $IN_3$; under mild conditions it is even possible to isolate an intermediate compound with an N—N bond[48]:

$$2\,MoCl_5 + 2\,IN_3 \rightarrow Cl_4Mo{=}N{-}N{=}MoCl_4 + 2\,ICl + 2\,N_2 \tag{7}$$

which can be converted into $MoNCl_3$ by thermal dissociation of $Cl_2$.

Reactions with iodine azide are transferable to metal bromides, as demonstrated by the examples for the preparation of $MoNBr_3$[49] and $WNBr_3$[72]:

$$MoBr_4 + IN_3 \xrightarrow[-IBr]{} MoBr_3N_3 \xrightarrow[-N_2]{} MoNBr_3 \tag{8}$$

$$WBr_6 + IN_3 \rightarrow WNBr_3 + IBr + Br_2 + N_2 \tag{9}$$

According to *Chatt et al.*[50], complex chloro(nitrido) compounds can be obtained by reaction of trimethylsilyl azide with molybdenum tetrachloride dissolved in acetonitrile, in the presence of complex donor molecules[50]:

$$\begin{aligned} MoCl_4(MeCN)_2 + Me_3SiN_3 + bpy \rightarrow MoNCl_3(bpy) +& \\ N_2 + 2\,MeCN + Me_3SiCl& \end{aligned} \tag{10}$$

In a similar way, the azidonitrido complexes $MoN(N_3)_3(bpy)$[51] (see Fig. 7) or $MoN(N_3)_3(py)$[52] (see Fig. 8) respectively result from the reaction of excess trimethylsilyl azide with the molybdenum(IV) complexes $MoCl_4(bpy)$ and $MoCl_4(py)_2$.

Equally, the only presently known nitrido iron complex was prepared by thermal decomposition of an azide. Azido-(α,β,γ,δ tetraphenylporphyrinato)iron(III) $(FeTPP)N_3$ reacts to form $(FeTPP)_2N$[53] with a symmetrical $Fe{=}N{=}Fe$ bridge[17]:

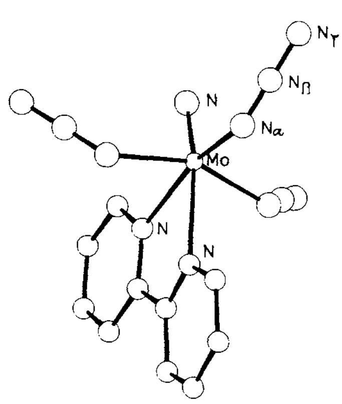


Fig. 7. Structure of the triazido(nitrido) complex $MoN(N_3)_3(bpy)$.

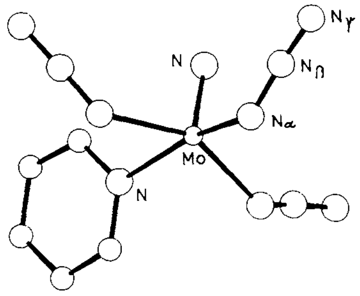


Fig. 8. Structure of the triazido(nitrido) complex $MoN(N_3)_3(py)$.

$$2\,(FeTPP)N_3 \rightarrow (FeTPP)_2N + 2\,1/2\,N_2 \tag{11}$$

Here, the nitrido ligand is able to stabilize iron in the formal oxidation state +3.5.

Even dinitrogen complexes can occasionally be converted into nitrido complexes[54]:

$$Mo(N_2)_2(diphos)_2 \xrightarrow{Me_3SiN_3} MoN(N_3)(diphos)_2 \tag{12}$$

Lastly, tetrachloronitridomolybdate is obtained from a straight-forward reaction of azide ions with molybdenum pentachloride[55]:

$$MoCl_5 + N_3^- \rightarrow [MoNCl_4]^- + N_2 + 1/2\,Cl_2 \tag{13}$$

### 3.2. Ammonolysis Reactions

The preparation of the nitridoosmate $[OsO_3N]^-$ from osmium tetraoxide and aqueous ammonia[56] has been known for some considerable time.

$$OsO_4 + NH_3 + KOH \rightarrow K[OsO_3N] + 2\,H_2O \tag{14}$$

The same holds for nitridorhenates prepared from rhenium heptaoxide[57]:

$$Re_2O_7 + 3\,KNH_2 \rightarrow K_2[ReO_3N] + K[ReO_4] + 2\,NH_3 \tag{15}$$

Recently, nitrido complexes were also prepared by thermolysis of ammonium salts[14]:

$$2\,NH_4Br + 2\,NH_4TaBr_6 \rightarrow (NH_4)_3[Ta_2NBr_{10}] + 4\,HBr \tag{16}$$

### 3.3. Reactions with Nitrogen Trichloride

Nitrogen trichloride dissolved in carbon tetrachloride reacts with $ReCl_5$ at slightly elevated temperatures[58]:

$$ReCl_5 + NCl_3 \rightarrow ReNCl_3 + 2.5\,Cl_2 \qquad (17)$$

The corresponding reaction, carried out at 0 °C, leads to the thermally sensitive nitridochloride of the heptavalent rhenium[5]:

$$ReCl_5 + NCl_3 \rightarrow ReNCl_4 + 2\,Cl_2 \qquad (18)$$

A very effective way is the synthesis of $MoNCl_3$ and $WNCl_3$ from the corresponding hexacarbonyl compounds[59]:

$$W(CO)_6 + NCl_3 \rightarrow WNCl_3 + 6\,CO \qquad (19)$$

As it is possible to obtain $NCl_3$ and $NBr_3$ from ammonium salts and halogens, the syntheses of halogeno(nitrido) complexes from ammonium halometalates and chlorine at 400—500 °C[60,61] are included in this section:

$$(NH_4)_2OsCl_6 + Cl_2 \rightarrow Os_2NCl_5 + \cdots \qquad (20)$$

Simultaneous use of ammonia and sodium hypochlorite recently led to the first nitrido[tetra(*p*-tolyl)porphyrinato]manganese(v) complex[62]:

$$Mn(TPP)OMe + NH_3 + NaOCl \rightarrow MnN(TPP) + NaCl + H_2O + MeOH \qquad (21)$$

### 3.4. Reactions with Hydrazine

Complexes of the type $ReNCl_2(PR_3)_3$ and $ReNCl_2(PR_3)_2$ can be obtained from the oxo complexes $ReOCl_3(PR_3)_2$ with hydrazine in the presence of ethanol[63–65].

### 3.5. Reaction of Vanadium Nitride with Chlorine

A method for the synthesis of halonitrene complexes, which up till now has only been verified in one case, is the reaction of vanadium nitride with gaseous chlorine; this proceeds even at 120 °C yielding $Cl_3VNCl$, as well as a small amount of $VCl_4$[66]:

$$VN + 2\,Cl_2 \rightarrow Cl_3VNCl \qquad (22)$$

Under analogous conditions, all other metal nitrides investigated yielded only pure metal halides[67].

## 4. Chemical Properties

### 4.1. Addition Reactions

Many of the reactions dealt with in this section result in formation of novel complexes with metal-nitrogen multiple bonds and are therefore useful synthetic routes to these complexes. Thus, the ternary nitridohalides $MNCl_3$ (M = Mo, W, Re, Os) and the nitridobromide $MoNBr_3$, which are associated in the crystal lattice, can be transformed into the tetrahalogeno(nitrido) complexes by treatment with the corresponding tetraphenylarsonium halides[68–71]:

$$MNCl_3 + AsPh_4Cl \xrightarrow[CH_2Cl_2]{} AsPh_4[MNCl_4] \qquad (23)$$

$$MoNBr_3 + AsPh_4Br \xrightarrow[CH_2Br_2]{} AsPh_4[MoNBr_4] \qquad (24)$$

The complex anions form tetragonal pyramids having $C_{4v}$ symmetry with the terminal nitrido ligand in an axial position.

The use of the smaller tetraethylammonium ion allowed the preparation of the six-coordinated molybdenum complex $(NEt_4)_2[MoNCl_5]$[73].

The nitrene complexes $Cl_3V{\equiv}N{-}Cl$ and $Cl_3PO(Cl_4)M{\equiv}N{-}R$ (M = Mo, W, Re; R = $CCl_3$, $C_2Cl_5$) are also capable of forming chloro complexes[33,74–76]:

$$Cl_3V{\equiv}N{-}Cl + Cl^- \rightarrow [Cl_4V{\equiv}N{-}Cl]^- \qquad (25)$$

$$Cl_3PO(Cl_4)M{\equiv}N{-}R + Cl^- \rightarrow [Cl_5M{\equiv}N{-}R]^- + POCl_3 \qquad (26)$$

In both cases, the linear group $M{\equiv}N{-}R$ is preserved. $ReNCl_4$, which is sensitive to redox reactions, is smoothly reduced to the rhenium(vi) complex by chloride or azide ions[69]:

$$ReNCl_4 + Cl^- \rightarrow [ReNCl_4]^- + 1/2\,Cl_2 \qquad (27)$$

$$ReNCl_4 + N_3^- \rightarrow [ReNCl_4]^- + 1\,1/2\,N_2 \qquad (28)$$

Phosphoryl chloride solvates the nitridohalides, forming tetrameric units having alternating long and short MN bonds. The O atom of the $POCl_3$ molecule is always arranged *trans* to the N atom at the end of the short MN bond[8–10] (see Fig. 3):

$$4\,MNCl_3 + 4\,POCl_3 \rightarrow [MNCl_3 \cdot POCl_3]_4 \qquad (29)$$

M = Mo, W, Re

In addition, the lattice of the complexes with M = W and Re contains two $POCl_3$ molecules per tetrameric unit[9,10]. With chelate ligands, such as α,α′-bipyridyl, monomeric six-coordinated complexes can be prepared[77]:

$$MoNCl_3 + bpy \rightarrow MoNCl_3(bpy) \qquad (30)$$

Relative to the strongly electrophilic character of the metal atoms, as expressed in reactions (23)—(30), the nucleophilic character of the nitrido ligand is, in general, not very distinct. Thus, neither $MoNCl_3$ nor the ion $[MoNCl_4]^-$ coordinate *via* the N atom with the strong Lewis acid $SbCl_5$. Only when the order of the MoN bond is reduced to $Mo{=}\ddot{N}$ by competitive π-interaction of fluorine ligands, is adduct formation at the nitrido ligand possible[78]:

$$[MoNF_4]^- + BF_3 \rightarrow [F_4MoN{-}BF_3]^- \qquad (31)$$

Furthermore, the oxidation state of the metal center seems to influence the donor properties of the nitrido ligand, since the rhenium(v) complexes $ReNX_2(PEt_2Ph)_3$ (X = Cl, Br) form complexes of the type $(PEt_2Ph)_3X_2Re{\equiv}N{-}BX_3$ with boron trihalides[78].

The reactions of $Cl_3V{\equiv}N{-}Cl$ with Lewis acids and Lewis bases[79] have been thoroughly investigated. Lewis bases such as phosphane or nitrogen bases always attack at the metal center. As illustrated by a crystal structure analysis of $Cl_3(bpy)VNCl$, the $V{\equiv}N{-}Cl$ group remains in linear array. $Cl_3VNCl$ does not react with Lewis acids as a base. $SbCl_5$ was used to prepare the thermally unstable trinuclear complex $Cl_3VNCl(SbCl_5)_2$, in which $Cl_3VNCl$ is linked to two molecules of $SbCl_5$ *via* Cl-bridges[79].

Sufficient nucleophilic character of the nitrido ligand is presumably a prerequisite for the formation of thionitrosyl complexes from nitrido complexes and elemental sulfur or disulfur dichloride[80]:

$$[MoN(S_2CNR_2)_3] + S \xrightarrow[CH_3CN]{} [Mo(NS)(S_2CNR_2)_3] \tag{32}$$

$R_2 = Me_2, Et_2, (CH_2)_5$

$$[ReCl_2N(PR_3)_3] + 1/2\,S_2Cl_2 \rightarrow [ReCl_2(NS)(PR_3)_3] + 1/2\,Cl_2 \tag{33}$$

$$[OsCl_3(N)L_2] + 1/2\,S_2Cl_2 \rightarrow [OsCl_3(NS)L_2] + 1/2\,Cl_2 \tag{34}$$

$L = AsPh_3, PMe_2Ph, 1/2\,bpy$

The nitrido complexes are recovered from the thionitrosyl compounds by means of tertiary phosphanes[80].

Only in the cases of ruthenium, osmium and rhenium has it been possible to obtain phosphaneiminato complexes of transition metals, containing the characteristic group $M{=}N{=}P$, using nitrido complexes and triphenylphosphane as starting materials[81,82,77]:

$$ReNCl_4 + 2\,PPh_3 \rightarrow [(Ph_3P)Cl_4Re{=}N{=}PPh_3] \tag{35}$$

More convenient for this purpose is the Staudinger reaction[21]:

$$[NbCl_4N_3]_2 + 2\,PPh_3 \rightarrow [Cl_4Nb{=}N{=}PPh_3]_2 + 2\,N_2 \tag{36}$$

The type of reaction (36) also applies to ionic azido complexes[83,84]:

$$[Cl_5MN_3]^- + PPh_3 \rightarrow [Cl_5M{=}N{=}PPh_3]^- + N_2 \tag{37}$$

$$[Br_5MN_3]^- + PPh_3 \rightarrow [Br_5M{=}N{=}PPh_3]^- + N_2 \tag{38}$$

$M = Nb, Ta$

UV-irradiation of $[Cl_5NbN_3]^-$ yielded the arsaneiminato complex $[Cl_5Nb{=}N{=}AsPh_3]^-$[84]. Several phosphaneiminato complexes of titanium and vanadium have recently been prepared by ligand exchange reactions[85]:

$$TiCl_2(S_2CNEt_2)_2 + Me_3SiNPPh_3 \rightarrow [TiCl(NPPh_3)(S_2CNEt_2)_2] + Me_3SiCl \tag{39}$$

$$VOCl_3 + 2\,Me_3SiNPPh_3 \rightarrow [VOCl(NPPh_3)_2] + 2\,Me_3SiCl \tag{40}$$

### 4.2. Substitution Reactions

Reactions of this type occur at the $M{\equiv}N$ bond as well as at the other metal-ligand bonds, resulting in the latter case, in new nitrido compounds. In general, the $M{\equiv}N$ bond is sensitive to hydrolysis, yet nitrido complexes are known which are resistant to moisture. Thus, the red $AsPh_4[MoNCl_4]$ reacts in moiste air to form the green oxo complex $AsPh_4[MoOCl_4]$[1]. The two compounds are isostructural, and the reaction could also be carried out in a single crystal. In boiling dichloromethane, the convertion of the nitrido complex into the oxo complex can even be achieved using dry oxygen[70]:

$$2[MoNCl_4]^- + O_2 \rightarrow 2[MoOCl_4]^- + N_2 \tag{41}$$

Reaction (41) is remarkable inasmuch as molybdenum(VI) is reduced to molybdenum(V) by $O_2$; however, the process cannot be reversed. The $Os{\equiv}N$ bond of the $[OsO_3N]^-$ ion is surprisingly inert towards water; the ion is transformed into the chloro(nitrido) complex by hydrochloric acid in the presence of potassium chloride[86]:

$$K[OsO_3N] + 6\,HCl + KCl \rightarrow K_2[OsNCl_5] + 3\,H_2O + Cl_2 \tag{42}$$

Recrystallization of this complex from water causes the chlorine ligand *trans* to the nitrido ligand to exchange as follows[87]:

$$K_2[OsNCl_5] + H_2O \rightarrow K[OsNCl_4(H_2O)] + KCl \tag{43}$$

Analogous reactions of the bromonitrido complexes of osmium are known[88].

Treatment of tetraphenylarsonium tetrachloro(nitrido)rhenate(VI) with thiocyanate ions in boiling methanol gives the corresponding pentakis(isothiocyanato)nitridorhenate(VI)[89]:

$$AsPh_4[ReNCl_4] + 4\,SCN^- + AsPh_4SCN \xrightarrow[CH_3OH]{} (AsPh_4)_2[ReN(NCS)_5] + 4\,Cl^- \tag{44}$$

In this complex the coordinatively unfavored position *trans* to the nitrido ligand is also occupied by an NCS group; however, the Re—N bond length is 231 pm, in contrast to a mean length of 202 pm for the four *cis*-NCS groups. The position *trans* to the nitrido ligand remains uncoordinated in exchange reactions of the $[MoNCl_4]^-$ ion[90,91]:

$$AsPh_4[MoNCl_4] + 4\,AgF \xrightarrow[CH_3CN]{} AsPh_4[MoNF_4] + 4\,AgCl \tag{45}$$

$$AsPh_4[MoNCl_4] + 4\,AgN_3 \xrightarrow[CH_2Cl_2]{} AsPh_4[MoN(N_3)_4] + 4\,AgCl \tag{46}$$

Chelate ligands such as α,α′-bipyridyl, slowly displace one chloro ligand, resulting in nitrido complexes with six-coordinated metal centers[77]:

$$[MNCl_4]^- + bpy \rightarrow [MNCl_3(bpy)] + Cl^- \tag{47}$$

$M = Mo, W, Re$

Of note is the fact that tribromonitridomolybdenum undergoes a substitution reaction with tetraphenylporphyrin[77]:

$$MoNBr_3 + H_2TPP \rightarrow [MoN(TPP)]^+Br_3^- + H_2 \tag{48}$$

The reaction of the *N*-iodine compound, $Cl_3VNI$, with bromine or chlorine produces the corresponding *N*-halogen derivatives by halogen exchange[45]:

$$Cl_3V{\equiv}N{-}I + Br_2 \rightarrow Cl_3V{\equiv}N{-}Br + IBr \tag{49}$$

$$Cl_3V{\equiv}N{-}I + Cl_2 \rightarrow Cl_3V{\equiv}N{-}Cl + ICl \tag{50}$$

Furthermore, with iodine azide, exclusively the N—I ligand reacts, to form the highly explosive *N*-azide[70]:

$$Cl_3V{\equiv}N{-}I + IN_3 \rightarrow Cl_3V{\equiv}N{-}N_3 + I_2 \qquad (51)$$

which is also obtained from the reaction of $Cl_3VNCl$ with $ClN_3$[92].

$Cl_3VNCl$ can transfer the nitrogen to 4d and 5d elements[58,70]:

$$Cl_3V{\equiv}N{-}Cl + MCl_5 \rightarrow MNCl_3 + VCl_4 + Cl_2 \qquad (52)$$
$$M = Mo,\ Re$$

The primary product is presumably $Cl_4M{-}N{\equiv}VCl_3$, in which two different metals compete for π-interaction with the nitrogen. As the d-orbitals of the 4d and 5d metals are more extensive than those of vanadium, the M≡N bond (M = Mo, Re) is favored over the VN bond, and hence the latter is cleaved.

## 5. Vibrational Spectra

In general, it is possible to determine nitrido groups or nitrene groups quickly and reliably by infrared spectroscopy, since the stretching vibrations of MN multiple bonds give rise to very strong absorptions at characteristic frequencies (for examples see Table 2). Because of the intense color of most of the substances, the vibrational data are, on the whole, confined to IR spectra; Raman spectra have only been recorded in a very few cases.

Compounds with terminal bonds of the type M≡N: normally exhibit a very intense MN stretching vibration in the region 1000—1100 cm$^{-1}$, when the metals have the oxidation number (+VI). The MN-vibration thus occurs at least 100 cm$^{-1}$ higher than the corresponding MO stretching modes, so that they can generally be easily distinguished. An exception is ν(MoN) in $[MoNF_4]^-$ at 969 cm$^{-1}$; this is, however, a result of the competitive π bonding of the fluorine ligands. When the metal is reduced to the oxidation state (+V) or (+IV), the wave number of the MN vibration is lowered to about 950 cm$^{-1}$. In structurally comparable species, depending on the position of the metal within the periodic table, the wave numbers increase from left to right along a period and generally down a group, as shown by the following examples:

$[WNCl_4]^-$ 1036 cm$^{-1}$ [68], $[ReNCl_4]^-$ 1085 cm$^{-1}$ [69],
$[OsNCl_4]^-$ 1123 cm$^{-1}$ [100],
$[RuNCl_3(AsPh_3)_2]$ 1023 cm$^{-1}$ [82], $[OsNCl_3(PEt_3)_2]$ 1070 cm$^{-1}$ [82]

The reason for this appears to be the increased ability of transition metals to effect π-overlap, which proceeds in the same direction.

Table 2. Selected frequencies of MN stretching vibrations in complexes with MN multiple bonds. 0 = P or As.

| Terminal Type M≡N: | ν(M≡N:) [cm$^{-1}$] | Ref. | Bridge Type $\overset{\ominus}{M}{\equiv}\overset{\oplus}{N}{-}M$ | ν(M≡N) [cm$^{-1}$] | Ref. |
|---|---|---|---|---|---|
| $AsPh_4[MoNF_4]$ | 969 | [90] | $[MoNCl_3]_4$ | 1045 | [40] |
| $AsPh_4[MoNCl_4]$ | 1054 | [68] | $[MoNBr_2]_\infty$ | 951 | [101] |
| $AsPh_4[MoNBr_4]$ | 1060 | [71] | $[WNCl_3]_\infty$ | 1068, 1084 | [40] |
| $[MoN(S_2CNMe_2)_3]$ | 1019 | [50] | $(AsPh_4)_2[W_2NCl_{10}]$ | 944, 1015 | [16] |
| $[MoNCl_2(bpy)]$ | 948 | [50] | $[ReNCl_3]_\infty$ | 1080 | [58] |
| $AsPh_4[WNCl_4]$ | 1036 | [68] | $[ReNCl_4]_\infty$ | 944, 995, 1011 | [5] |
| $AsPh_4[ReNCl_4]$ | 1085 | [69] | | | |
| $K_2[ReO_3N]$ | 1022 | [98, 99] | | | |
| $[RuNCl_3(AsPh_3)_2]$ | 1023 | [82] | | | |
| $AsPh_4[OsNCl_4]$ | 1123 | [100] | | | |
| $K_2[OsNCl_5]$ | 1073<br>($^{15}N$: 1041) | [97] | | | |
| $[OsNCl_3(PEt_3)_2]$ | 1070 | [82] | | | |

| Type $\overset{\ominus}{M}{\equiv}\overset{\oplus}{N}{-}X$ | ν(M≡N) [cm$^{-1}$] | ν(NX) [cm$^{-1}$] | Ref. | Type $\overset{\ominus}{M}{=}\overset{\oplus}{N}{=}Q$ | $\nu_{as}$(MNQ) [cm$^{-1}$] | $\nu_s$(MNQ) [cm$^{-1}$] | Ref. |
|---|---|---|---|---|---|---|---|
| $Cl_3VNCl$ | 1107 | 510 | [44] | | | | |
| $Cl_3VNBr$ | 1032 | 435 | [45] | $[TiCl_2(NPPh_3)_2]$ | 1090,<br>1110 | | [85] |
| $Cl_3VNI$ | 963 | 390 | [45] | | | | |
| $AsPh_4[Cl_5MoNCCl_3]$ | 1200 | 928 | [75] | $PPh_4[Cl_5Nb(NPPh_3)]$ | 1138 | 580 | [83] |
| $[WF_5(NR)]^-$ | 1286-1332 | | [102] | $PPh_4[Br_5Nb(NPPh_3)]$ | 1131 | 575 | [84] |
| $AsPh_4[WCl_5(NCCl_3)]$ | 1265 | | [33] | $AsPh_4[Cl_5Nb(NAsPh_3)]$ | 1155 | 525 | [83] |
| $AsPh_4[Cl_5ReNCCl_3]$ | 1240 | 851 | [76] | $[RuCl_3(NPEt_3)(PEt_3)_2]$ | 1099 | | [82] |
| $[ReCl_3(NMe)(QR_3)_2]$ | 1190-1196 | | [65, 103] | $[OsCl_3(NPEt_3)(PEt_3)_2]$ | 1125 | | [82] |
| $[OsO_3(NR)]$ | 1184-1215 | | [86, 104] | | | | |

A similar spectroscopic situation is found in compounds with M≡N—M bridges. A strong absorption in the region of 1000—1100 cm$^{-1}$, which is occasionally split, corresponds to the stretching vibration of the short MN bond. No data is available on the vibrational frequency of the long MN bond, however this is expected to occur at very low wave numbers (<200 cm$^{-1}$). This is also the reason for the absence of significant coupling: ν(M≡N) for this type of bridge occurs in the same region as ν(M≡N) for the terminal type. The few spectra of complexes with symmetrical M=N=M bridges hitherto reliably studied, form a similar picture. Here, the two stretching vibrations should be regarded as $\nu_s$(M=N=M) and $\nu_{as}$(M=N=M); the latter appear again between 1000 and 1100 cm$^{-1}$. Since the symmetrical vibration leaves the N atom unmoved, it has a very low wave number.

An interesting aspect of the vibrational spectra of anions of the type $[X_5M{=}N{=}MX_5]^{n-}$ and of the corresponding μ-oxo complexes is a strong, sharp band which occurs at

520—540 cm$^{-1}$ in the μ-nitrido compounds and at 400—470 cm$^{-1}$ in the μ-oxo compounds, first mentioned by *Mattes et al.*[93].

Its assignment is problematic, since except for the asymmetric vibration of the bridge $\nu_{as}(M_2N)$, no absorption is expected above 500 cm$^{-1}$, this being the upper limit of the characteristic region for metal-halogen stretching vibrations. *Mattes et al.* assigned this vibration to a $\rho$(XMO) or $\rho$(XMN) mode of the species $E_u$. The IR spectrum of the anion $[Ta_2NBr_{10}]^{3-}$, apart from $\nu_{as}(Ta_2N)$ at 985 cm$^{-1}$, also shows a band of medium intensity at 735 cm$^{-1}$. This has been tentatively assigned to the bridge deformation vibration $\delta(M_2N)$[14], which due to the high mass of the $TaBr_5$ groups lies at a higher wave number than the symmetrical vibration of the bridge $\nu_s(M_2N)$.

Apparently, the situation in the anion $[W_2NCl_{10}]^{2-}$ cannot be compared herewith; this ion contains an asymmetric nitrido bridge. Here, two absorptions occur at 1015 cm$^{-1}$ and 944 cm$^{-1}$, which are assigned to WN stretching modes[16].

The vibrations of bridges of the types $M{=}N{=}X$ and $M{\equiv}N{-}X$ have to be regarded in a somewhat different way. Depending on the frequency of the NX stretching vibration, strong couplings are observed in some cases, which permit the MN stretching mode to be considered as a characteristic vibration, to a limited extent. In the phosphaneiminato complexes, significant π bonding of the $M{=}N{=}P$ type can be attributed to the PN bond on account of its short length. Here, a strong band, generally above 1100 cm$^{-1}$ is usually found (occasionally split into a doublet as a consequence of Fermi resonance), and a second band appears between 500 cm$^{-1}$ and 600 cm$^{-1}$. The former is normally described as $\nu$(PN), the latter as $\nu$(MN); more correctly these should be $\nu_{as}$(MNP) and $\nu_s$(MNP). Undoubtedly the frequencies of both vibrations are influenced by strong coupling, which accounts for the low wave number of the MN stretching vibration. Similar conditions are encountered in nitrosyl metal complexes where the MNO group is linear:

$$\overset{\ominus}{M}{=}\overset{\oplus}{N}{=}\ddot{\underset{\cdot\cdot}{O}} \quad \text{or} \quad \overset{2\ominus}{M}{-}\overset{\oplus}{N}{\equiv}\overset{\oplus}{O}{:}$$

In these cases $\nu$(NO) is assigned to frequencies between 1600 and 1700 cm$^{-1}$, and $\nu$(MN) to that at *ca.* 500 cm$^{-1}$.

On the other hand, in compounds with $M{\equiv}N{-}X$ bridges in which the ligand X does not display π bonding to the N atom, $\nu$(MN), by analogy with nitrosyl complexes, appears shifted to shorter and $\nu$(NX) to longer wave lengths as a result of vibrational coupling. The decreasing influence of coupling is especially evident in the series of compounds $Cl_3V{\equiv}N{-}X$, in which the linear arrangement of the VNX group has been confirmed by crystal structure analyses ($X = Cl$[94]; $X = I$[95]):

| | $Cl_3V{\equiv}N{-}Cl$ [44] | $Cl_3V{\equiv}N{-}Br$ [45] | $Cl_3V{\equiv}N{-}I$ [45] |
|---|---|---|---|
| $\nu$(VN) | 1107 | 1032 | 963 |
| $\nu$(NX) | 510 | 435 | 390 |

When X is an organic group, $\nu$(MN) appears at even shorter wavelengths, generally between 1200 cm$^{-1}$ and 1300 cm$^{-1}$; in this case $\nu$(NC) is shifted to longer wavelengths by more than 100 cm$^{-1}$ relative to uncoupled $\nu$(NC) stretching vibrations. Similar behavior is found in the carbyne complexes $M{\equiv}C{-}R$[96], which are related to the bridges of the type $M{\equiv}N{-}X$.

## 6. Crystal Structures

A remarkable feature of all crystal structures of nitrido and nitrene complexes (Section 6.5) is the extremely short metal-nitrogen bond length and the distinct *trans*-effect of the π bonded nitrogen ligand.

After a brief consideration of the *trans*-effect, the compounds will be discussed in detail. Characteristic data of selected compounds are compiled in Tables 3 to 7 (for the problem bond length/bond order in MoN bonds see [105]).

### 6.1. The *trans*-Effect

The *trans*-effect is the weakening of the bond to a ligand, coordinated in a position *trans* to a ligand which is particularly strongly bonded, so that substitution reactions preferentially take place at this site (see Section 4.2). Not only is the weakening evident in reactions but it is also expressed by the differences observed in the bond lengths between the central atom and *cis* or *trans*-positioned ligands: this difference can amount to 30 pm in mononuclear complexes. In the previously mentioned complex, $[ReN(NCS)_5]^{2-}$[89], the Re(NCS) bond length is 202 pm for the *cis*-ligand (relative to the nitrido nitrogen) and 231 pm for the *trans*-ligand. A similar situation is found in $[OsNCl_5]^{2-}$ (236 pm and 261 pm respectively)[106] (Fig. 9).

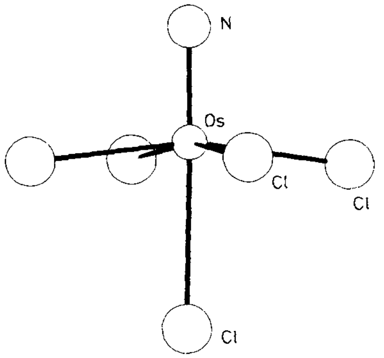


Fig. 9. Structure of the anion $[OsNCl_5]^{2-}$ with a terminal nitrido ligand.

Frequently, the *trans*-effect is so strong, that the *trans*-position is not occupied at all. As a result, in a solution of pentachloro(nitrido)molybdate in $CH_2Cl_2$, an equilibrium is observed:

$$[MoNCl_5]^{2-} \rightleftharpoons [MoNCl_4]^- + Cl^-$$

In the azido(nitrido) complex $MoN(N_3)_3(bpy)$[51] (Fig. 7) the bipyridyl ligand is bonded asymmetrically, since the nitrogen atom in the *trans*-position to the nitrido ligand can only bond very weakly to the molybdenum atom. In attempts to prepare the analogous pyridine complex, the *trans*-position remains unoccupied and the resulting compound, $MoN(N_3)_3(py)$[52] with coordination number five is formed (Fig. 8).

In general, the *trans*-effect has been attributed to electronic influences. According to *Grinberg*[107], an easily polarizable ligand causes polarization at the central atom, giving rise to an accumulation of negative charge at the *trans*-position, and, in consequence, to repulsion of the *trans*-ligand's electron sphere.

*Chatt et al.*[108] and *Orgel*[109] have interpreted the *trans*-effect as deriving from a strong $\pi$ bond. As two ligands located in *trans*-position to each other compete for the same atom orbitals, increased overlap on one side of the central atom results in a decrease of electron density and thus a weakening of the bond on the other side. This interpretation explains the distinct *trans*-effect of the nitrido ligand, which is exceedingly strongly bonded by two $\pi$ bonds in planes perpendicular to one another. It is however possible to account for the *trans*-effect with purely steric arguments. This opinion was first expressed by *Bright* and *Ibers*[106] and later by the authors[5,8]. Accordingly, the *trans*-effect is a consequence of the mutual repulsion of the ligands. The nitrido atom, which is extremely close to the central atom, displaces the *cis*-positioned ligands to the other side of the central atom. The latter atom is therefore situated above the plane of the four *cis*-positioned ligands in an octahedral coordination. Thus, the sixth coordination site can be occupied only by a weakly bonded ligand at a greater distance.

In this model it is assumed that the six ligands bonded to the same central atom already have the minimum distance to each other. If the central atom bonds especially strongly to one ligand, it is displaced from the center of the octahedron towards this ligand, thus weakening the bond to the *trans*-position.

This concept is supported by the fact that the *trans*-effect occurs particularly frequently in the sterically unfavorable square planar coordination.

Both $ReNCl_2(PPh_3)_2$[110], coordinated in the form of a tetragonal pyramid, and the octahedral $ReNCl_2(PEt_2Ph)_3$[111], have been investigated crystallographically by *Ibers et al.*, and clearly show the steric influence. In the latter six-coordinate complex the inter-ligand repulsion is so strong, that even the nitrido ligand is forced away to a bond length of 179 pm. In the five-coordinate complex only two bulky phosphane ligands are bonded to rhenium. The ReN bond length is 160 pm, which is the value expected for a triple bond. It is interesting to note, that the analogous tris(triphenylphosphane) complex $ReNCl_2(PPh_3)_3$ does not exist, presumably for similar steric reasons.

## 6.2. Structures of Mononuclear Nitrido Complexes with Square Pyramidal and Octahedral Coordination

Nitrido complexes having the stoichiometry $[MNX_4]^-$ (M = Mo, Re, Ru, Os; X = F, Cl, Br, I, $N_3$) form tetragonal pyramids with the nitrido ligand at the apex (Fig. 1). In all cases the metal atom M is situated about 55 pm above the pyramid's base. All complexes $[MNX_4]^-$, which were investigated crystallographically, have tetraphenylarsonium ions as cations since this combination was found to produce readily crystallizable products. An interesting crystallographic publication concerning AB types with $EPh_4^+$ ions (E = P, As, Sb) should be mentioned here[112]. The most important geometrical details of the complex ions are specified in Table 3, including the compounds $MoN(N_3)_3(py)$[52], $ReN(S_2CNEt_2)_2$[113] and $ReNCl_2(PPh_3)_2$, in which the coordination of the central atom is also approximately tetragonal pyramidal.

Table 3. Characteristic bond lengths and angles in selected mononuclear nitrido complexes with tetragonal pyramidal coordination.

| Compound | Bond length [pm] $M{\equiv}N$ | $M{-}X$ | Angle [°] NMX | Ref. |
|---|---|---|---|---|
| $AsPh[MoNF_4]$ | 183 | 173 | 99 | [90] |
| $AsPh_4[MoNCl_4]$ | 166 | 234.5 | 101.5 | [1] |
| $AsPh_4[MoNBr_4]$ | 163 | 248.8 | 103 | [71] |
| $AsPh_4[MoN(N_3)_4]$ | 163.0 | 206.8 | 99.5 | [91] |
| $MoN(N_3)_3(py)$ | 163.5 | 204.3 | 102.2 | [52] |
| $AsPh_4[ReNCl_4]$ | 162 | 232.2 | 103.5 | [69] |
| $ReN(S_2CNEt_2)_2$ | 165.6 | 239.1 | 107.7 | [113] |
| $ReNCl_2(PPh_3)_2$ | 160.3 | 237.7 [a] | 109.7 [a] | [110] |
| | | 244.8 [b] | 98.4 [b] | |
| $AsPh_4[RuNCl_4]$ | 157.0 | 231.0 | 104.6 | [3] |
| $AsPh_4[OsNCl_4]$ | 160 | 231.0 | 104.6 | [4] |
| $AsPh_4[OsNI_4]$ | 163 | 266.2 | 103.7 | [114] |

[a] X = Cl. [b] X = P.

It is interesting to compare the structures of $MoN(N_3)_3(py)$[52] and $[MoN(N_3)_4]^-$[91]. In the complex $MoN(N_3)_3(py)$ (Fig. 8), steric effects cause the azide groups to arrange so that the free electron pair of the $sp^2$-hybridized $N_\alpha$ atom points radially away from the nitrido ligand. The same configuration exists in three of the four azide groups of $[MoN(N_3)_4]^-$. The fourth group, which occupies the site of the pyridine ligand, is oriented in the op-

Table 4. Characteristic bond lengths and angles in selected mononuclear nitrido complexes with octahedral coordination.

| Compound | Bond length [pm] $M{\equiv}N$ | $M{-}X_{cis}$ | $M{-}X_{trans}$ | Average Angle [°] NMX | Ref. |
|---|---|---|---|---|---|
| $K_2[OsNCl_5]$ | 161 | 236.2 | 260.5 | 96.2 | [106] |
| $AsPh_4[ReN(NCS)_5]$ | 166 | 202.1 | 230.1 | 96.0 | [89] |
| $ReNCl_2(PEt_2Ph)_3$ | 179 | 245.4 [a] | 256.3 | 99.2 [a] | [111] |
| | | | | 92.2 [b] | |
| $MoN(N_3)_3(bpy)$ | 164.2 | 224.0 [c] | 241.9 | 92.0 [c] | [51] |
| | | | | 100.6 [d] | |

[a] X = Cl. [b] X = P. [c] X = bpy. [d] X = $N_3$.

posite direction, so that its free electron pair is located in the vicinity of the nitrido ligand.

Complexes with the coordination number five generally have the sterically favorable trigonal pyramidal geometry. In the nitrido complexes, however, the *trans*-effect of the nitrido ligand forces the formation of a tetragonal pyramid. In some cases the tetragonal pyramid can be replenished to form an octahedron by an additional, less tightly bonded ligand (Fig. 9). Some selected complexes of this kind are given in Table 4. Even in the octahedral complexes, the central atom is situated above the plane of the *cis*-positioned ligands. Yet the distance here (about 20 pm) is smaller than in the tetragonal pyramids.

Except for two examples, the M≡N bond lengths range from 157 to 166 pm. A comparison of the values in Tables 3 and 4 shows that oxidation state and coordination number have practically no effect on the bond lengths, which correspond to M≡N triple bonds. In $[MoNF_4]^-$[90] the $\pi$-donor ability of the fluorine ligands accounts for the very long MoN bond length which is equivalent to a low bond order, as determined from the low frequency of the MoN stretching vibration (Section 5).

Steric reasons account for the great length of the ReN bond in $ReNCl_2(PEt_2Ph)_3$[111] (Section 6.1).

### 6.3 Structures of Polynuclear Complexes with Asymmetrical Nitrido Bridges $\overset{\ominus}{M}\equiv\overset{\oplus}{N}-M$

As mentioned in Section 2.1, the free electron pair of the nitrido ligand renders it weakly basic and it can form a weak dative bond with another metal atom, resulting in a linear, highly asymmetrical nitrido bridge. This type of bridge gives rise to binuclear, trinuclear and tetranuclear complexes, as well as polymeric structures. The anion $[W_2NCl_{10}]^{2-}$[16] has hitherto been the only example of the species $[M_2YX_{10}]^{n-}$ with M = transition metal, Y = O or N and X = Cl or Br, in which an asymmetric bridge is observed. Here, it is assumed that the different oxidation states of the tungsten atoms are the decisive factor. Participation of the $d^1$ system of the tungsten(v) atom, leading to Jahn-Teller stabilization, in the $[W_2NCl_{10}]^{2-}$ ion also seems to be evident from the W...W distance (373 pm). This is significantly shorter than the W...W distance in $[WNCl_3\cdot POCl_3]_4\cdot 2\,POCl_3$ (386 pm)[9], but exactly the same as in $(HNMe_3)_2[W_4O_8Cl_4(OH_2)_4]\cdot 2\,H_2O$, which contains linear WOW bridges with alternating $W^V$ and $W^{VI}$ atoms[115].

Table 5. Characteristic bond lengths and angles in selected polynuclear complexes with asymmetric nitrido bridges $\overset{\ominus}{M}\equiv\overset{\oplus}{N}-M$.

| Compound | Bond length [pm] | | | | Angle [°] | | Ref. |
|---|---|---|---|---|---|---|---|
| | M≡N | M—N | M—$X_{cis}$ | M—$X_{trans}$ | M≡N—M | N≡M—$X_{cis}$ | |
| *mononuclear* | | | | | | | |
| $(AsPh_4)_2[W_2NCl_{10}]$ | 166 | 207 | 231.1 | 242.6 | 177 | 92 | [16] |
| *dinuclear* | | | | | | | |
| $[Et_2NCS_2)_3Mo{\equiv}N]_2$<br>$[Mo(S_2CNEt_2)_3](PF_6)_3$ | 166 | 213 | — | — | 180 | — | [13] |
| *tetrameric* | | | | | | | |
| $[MoNCl_3]_4$ | 166 | 217 | 227 [a] | 288 [a] | 173 | 99 | [7] |
| $[MoNCl_3\cdot OPCl_3]_4$ | 166 | 216 | 229 [a] | 237 [b] | 172 | 98 | [8] |
| $[WNCl_3\cdot OPCl_3]_4\cdot 2\,POCl_3$ | 167 | 215 | 232 [a] | 231 [b] | 171 | 99 | [9] |
| *polymeric* | | | | | | | |
| $[ReNCl_4]_\infty$ | 158 | 248 | 227 | — | 174 | 97 | [5] |
| $\{K_2[ReN(NC)_4]\cdot H_2O\}_\infty$ | 153 | 244 | 213 [c] | — | 180 | 100 | [6] |

[a] X = Cl. [b] X = O. [c] X = N.

Further evidence should be provided by the planned structural analyses of complexes of the type $(PMe_2Ph)_3$-$Cl_2ReNMoCl_4(NCEt)$[116], which exhibit a nitrido bridge between different metal atoms.

In the trinuclear complex $[(Et_2NCS_2)_3Mo{\equiv}N]_2$-$Mo(S_2CNEt_2)_3(PF_6)_3$[13], the central Mo atom accepts the free electron pairs of two neighboring Mo≡N: groups forming a slightly bent chain Mo≡N—Mo—N≡Mo. The bond lengths in the Mo≡N—Mo bridges are, within the limits of error, the same as in $[MoNCl_3]_4$[7].

The numerous tetrameric cyclic structures are completely planar and approximately square, the edges being formed by the M≡N—M bridges (Fig. 3). The small deviation of the nitrido bridge from linearity is caused by steric effects. The van der Waals distances of neighboring N atoms within the MN eight-membered ring are comparatively short; hence, these atoms are pushed outwards slightly. Again, the strong *trans*-effect (see Section 6.1.) directs the most weakly bonded ligand to occupy a position *trans* to the nitrido ligand. In $[MoNCl_3]_4$, a Cl atom of a neighboring tetramer occupies this position and forms a very weak Cl bridge. In the $POCl_3$ adducts, $[MNCl_3\cdot OPCl_3]_4$ (Fig. 3), the *trans*-position is occupied by the oxygen atom of the Lewis base $POCl_3$. The Mo—N eight-membered ring has the same geometry in the adduct as in pure $[MoNCl_3]_4$.

$ReNCl_4$[5] and $K_2[ReN(CN)_4]\cdot H_2O$[6] form polymeric linear chains. Here, the ReN single bonds are very long (248 and 244 pm) in contrast to the other complexes with asymmetrical bridges, since they are located in *trans*-positions and are sterically influenced by the ligands in the *cis*-positions.

It is interesting to note that the MN bond length is evidently not significantly affected by the donating function of the free electron pair. The M≡N bond lengths of the tetrameric complexes in Table 5 are therefore, within the limits of error, the same as in the compounds with terminal nitrido ligands (Tables 3 and 4). Extremely short ReN bond lengths are observed in the polymers $[ReNCl_4]_\infty$[15]

and $\{K_2[ReN(CN)_4]\cdot H_2O\}_\infty$[6], however, these values have relatively high standard deviations.

## 6.4. Structures of Binuclear Complexes with Symmetrical Nitrido Bridges $\overset{\frac{1}{2}\ominus}{M}=\overset{\oplus}{N}=\overset{\frac{1}{2}\ominus}{M}$

Symmetrical nitrido bridges, $M=N=M$, are exclusively observed in binuclear complexes. When the bridges are linearly continued to form oligomeric and polymeric chains, *e.g.* in $[(Et_2NCS_2)_3Mo\equiv N]_2Mo(S_2CNEt_2)_3(PF_6)_3$[13] and in $[ReNCl_4]_\infty$[5], the *trans*-effect prevents formation of symmetrical nitrido bridges. It is however surprising, that asymmetrical bridges also occur in the tetrameric ring structures of the type $[MoNCl_3]_4$[7], since the *trans*-effect has no direct influence there. It might be possible—as in the *trans*-effect—to invoke steric effects to account for the formation of an asymmetrical bridge. The MN eight-membered ring is strained, because neighboring N atoms in the ring are situated very close to each other. Consequently, the ring is extended slightly and the nitrido bridge bonds consequently lengthened. In a symmetrical bridge this lengthening would unfavorably affect π overlap, whereas in an asymmetrical arrangement it would only influence the σ bond which is known to tolerate longer bond lengths.

In accord with this supposition, an increase in the metal-metal bond lengths of the nitrido bridges from dimeric (332—370 pm) to tetrameric (381—384 pm) and polymeric (397—406 pm) complexes is observed.

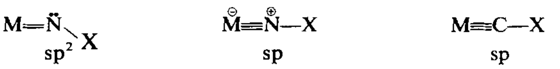
Metal-metal distances as short as 332 pm (in the iron complex $[Fe(TPP)]_2N$[17]) are possible in the symmetrical nitrido bridges of binuclear complexes, since the *cis*-positioned ligands can move away from both sides of the nitrido ligands. Thus, the metal atoms are located about 20—30 pm above the plane of the *cis*-ligands. The *trans*-position either remains unoccupied, as in the porphyrinatoiron complex, or is coordinated by a relatively weakly bonded ligand. In the ruthenium complex $[Ru_2NCl_8(H_2O)_2]^{3-}$[117] (Table 6), this ligand is a water molecule, and in $[Ta_2NBr_{10}]^{3-}$[14] a bromine atom, with a TaBr bond 23 pm longer than the bonds of the *cis*-ligands.

The metal-nitrogen bond lengths (Table 6) in the symmetrical nitrido bridges are, in view of their double bond character, longer than those in terminal nitrido ligands (Table 3). They correspond well to the values[118] expected for double bonds. In agreement with the conception of the $(d_\pi\text{-}p_\pi\text{-}d_\pi)\text{-}\pi$ overlap (Section 2.3.) in the nitrido bridge, the *cis*-ligands of the two metal atoms are arranged in eclipsed positions to each other. The complexes $[Ru_2NCl_8(H_2O)_2]^{3-}$, $[Os_2NCl_{10}]^{4-}$ and $[Ta_2NBr_{10}]^{3-}$ have $D_{4h}$ symmetry. However, it is surprising to find a staggered configuration in the iron complex $[Fe(TPP)]_2N$ with the porphyrinato ligands twisted at a torsion angle of 58°.

## 6.5. Structures of Complexes with N-Bridges ("Nitrido Bridges") $\overset{\ominus}{M}\equiv\overset{\oplus}{N}-X$ and $M=\ddot{N}\diagdown_{X}$

Complexes with the groups $M\equiv N-X$ or $M=\ddot{N}-X$ are formally derived from amines $H_2N-X$, by substitution of the two hydrogen atoms by a metal atom. In the case of transition metals in high oxidation states, the free electron pair of the nitrogen atom participates in the MN bond, resulting in a linear MNX-arrangement with a $M\equiv N$ triple bond. A bent MNX structure with an $sp^2$-hybridized nitrogen atom is only observed when the metal atom attains an inert gas configuration without the free electron pair of the nitrogen. In contrast to this, corresponding compounds of the main group elements always show a bent arrangement[79].

In order to distinguish both types, we have proposed the terms "imido" and "nitrene" complexes[79]:



$$M=\ddot{N}\diagdown_{X} \qquad \overset{\ominus}{M}\equiv\overset{\oplus}{N}-X \qquad M\equiv C-X$$

$sp^2$ | sp | sp

imido complex | nitrene complex | carbyne complex

In the electrophilic nitrene complexes a nitrene $\underset{\cdot\cdot}{\ddot{N}}-X$ is formally stabilized by bonding to the transition element. This makes them formally similar to the carbyne complexes. The nucleophilic imido complexes, on the other hand, are characterized by a free electron pair at the nitrogen atom.

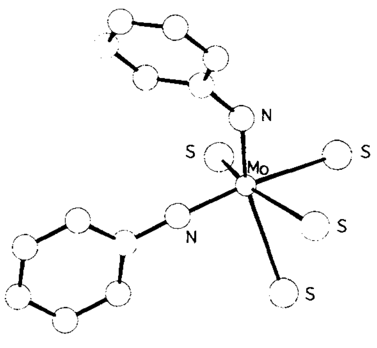


Fig. 10. Detail from the structure of the *cis*-bis(diethyldithiocarbamato)bis(phenylimido)molybdenum complex $Mo(NPh)_2(S_2CNEt_2)_2$ with bent imido and linear nitrene geometry. For the sake of clarity, only the S atoms of the diethyldithiocarbamato ligands are shown.

Table 6. Characteristic bond lengths and angles in binuclear complexes with symmetrical nitrido bridges $\overset{\frac{1}{2}\ominus}{M}=\overset{\oplus}{N}=\overset{\frac{1}{2}\ominus}{M}$.

| Compound | Bond length [pm] | | | Angle [°] | | Ref. |
|---|---|---|---|---|---|---|
| | $M=N$ | $M-X_{cis}$ | $M-X_{trans}$ | $M=N=M$ | $N=M-X_{cis}$ | |
| $K_3Ru_2NCl_8(OH_2)_2$ | 172.0 | 236 [a] | 218 [b] | 180 | 94.7 | [117] |
| $(NH_4)_3Ru_2NCl_8(OH_2)_2$ | 172.5 | 238 [a] | 220 [b] | 180 | 95 | [119] |
| $Cs_4Os_2NCl_{10}$ | 177.8 | 237.1 | 243.4 | 180 | 93.7 | [123] |
| $(NH_4)_3Ta_2NBr_{10}$ | 184.9 | 251.4 | 273.8 | 180 | 94.1 | [14] |
| $Os_2N(S_2CNMe_2)_5$ | 166.1 | 240 | 242 | 165 | 98 | [120] |
| $[(TPP)Fe]_2N$ | 176 | 199.1 [c] | — | 180 | 99.2 | [17] |

[a] X = Cl. [b] X = O. [c] X = N.

Complexes with a bent "imido" geometry have hitherto been rarely observed; in addition, the expected bond angle of 120° for $sp^2$-hybridization is significantly exceeded, whereas in compounds of main group elements, the corresponding angle is 120° or usually even smaller.

An example of an imido transition metal complex is the molybdenum compound $MoOCl_2(NH)(OPEtPh_2)_2$[28] in which the angle is 157°. The complexes *cis*-$Mo(NPh)_2(S_2CNEt_2)_2$[30] (Figure 10) and $OsO_2[NC(CH_3)_3]_2$[121] each contain a bent and a linear MNR group (see Table 7).

Table 7. Characteristic bond lengths and angles of selected imido and nitrene complexes M—N—X.

| Compounds | Bond length [pm] MN | N—X | Angle [°] MNX | Ref. |
|---|---|---|---|---|
| $Cl_3VNCl$ (solid) | 164.2 | 158.8 | 175.2 | [94] |
| $Cl_3VNCl$ (gas) | 165.1 | 159.7 | 170 | [122] |
| $Cl_3VNCl(SbCl_5)_2$ | 165.5 | 160.3 | 179.5 | [79] |
| $Cl_3(bpy)VNCl$ | 168.8 | 158.5 | 175.0 | [79] |
| $Cl_3VNI$ | 165 | 193 | 163 | [95] |
| $Cl_3PO(Cl_4)MoNC_2Cl_5$ | 169.2 | 145 | 171.8 | [26] |
| $AsPh_4[Cl_5WNC_2Cl_5]$ | 168.4 | 147 | 163 | [33] |
| *cis*-$Mo(NPh)_2(S_2CNEt_2)_2$ | 175.4<br>178.9 | 138.6<br>139.2 | 169.4<br>139.4 | [30] |
| $MoOCl_2(NH)(OPEtPh_2)_2$ | 170 | 92 | 157 | [28] |
| $OsO_3$(N-Adamantyl) | 169.7 | 144.8 | 171.4 | [121] |
| $OsO_2[NC(CH_3)_3]_2$ | 171.0<br>171.9 | 143<br>145 | 178.9<br>155.1 | [121] |
| $RuCl_3(NPEt_2Ph)(PEt_2Ph)_2$ | 184.1 | 158.6 | 174.9 | [20] |
| $[NbCl_4(NPPh_3)]_2$ | 177.6 | 163.7 | 171.1 | [21] |
| $[TaCl_4(NPPh_3)]_2$ | 180.1 | 159.3 | 176.8 | [22] |

The metal-nitrogen distance in nitrene complexes is consistent with the value expected for a triple bond. A lengthening of the MN bond in the linear form $M{\equiv}N{-}X$ is only observed in the latter cases, in which there is a large supply of electrons and one of the two MNX groups is bent.

It is interesting to consider the NX bond lengths in the nitrene complexes more closely. On account of sp-hybridization of the nitrogen atom, the bonds are always significantly shorter than in $sp^3$-hybridization. In $Cl_3V{\equiv}N{-}Cl$[94] and $Cl_3V{\equiv}N{-}I$[95] (Fig. 6), for example, the shortest hitherto measured N—Cl and N—I bond lengths have been observed (Table 7): the values being respectively *ca.* 17 and 22 pm smaller than in halogen amines. Approximately the same difference is found in C—Cl bonds in halogen alkanes and alkynes.

Apart from halogens, organic groups and amino groups, the substituent, X, in nitrene complexes can also be an organophosphorus group. The resulting phosphaneiminato complexes also exhibit an almost linear configuration of the $M{=}N{=}PR_3$ group (see Fig. 5), in which the following mesomeric structures can be assumed on account of the observed bond lengths:

$$\overset{2\ominus}{M}{\equiv}\overset{\oplus}{N}{-}\overset{\oplus}{P}R_3 \leftrightarrow \overset{\ominus}{M}{=}\overset{\oplus}{N}{=}PR_3$$

In all cases the MNP unit is slightly bent, the bond angle being about 174°. This can be explained by $p_\pi$-$d_\pi$ overlap in the NP bond, since in the tetrahedral coordination of the phosphorus only the less favorable orbitals $d_{z^2}$ or $d_{x^2-y^2}$ can be utilized for the π bond[20].

## 7. Future Prospects

Since the fundamental investigations of *Goubeau*[124], who suggested that multiple bonds between two elements outside the first row of eight elements can occur under certain conditions, many examples have been found experimentally. Transition metals can form multiple bonds with each other, as well as with carbon, nitrogen and oxygen. The still new field of metal-nitrogen multiple bonds is rapidly expanding. Apart from the attractive structural chemistry and the remarkable bonding of these compounds, considerable stimulus has arisen from attempts to develop models of $N_2$-assimilation. Starting with the fixation of a $N_2$ molecule at a molybdenum center, the formation of the nitridomolybdenum group is an important step towards the production of ammonia in which the nitrogen is transformed into a form utilizable by plants. However, much still has to be done to clarify the complex paths of such sequences of reactions and to simulate them in the laboratory.

*We thank the Verband der Chemischen Industrie and the Deutsche Forschungsgemeinschaft for their generous financial support of our investigations. We also wish to extend our thanks to the many co-workers who have contributed significantly to this field.*

Received: December 1, 1980 [A 365 IE]
German version: Angew. Chem. *93*, 451 (1981)

---

[1] *B. Knopp, K.-P. Lörcher, J. Strähle*, Z. Naturforsch. *B 32*, 1361 (1977).
[2] *W. Liese, K. Dehnicke, R. D. Rogers, R. Shakir, J. L. Atwood*, J. Chem. Soc. Dalton Trans. *1981*, 1061.
[3] *F. L. Phillips, A. C. Skapski*, Acta Crystallogr. *B 31*, 2667 (1975).
[4] *S. R. Fletcher, W. P. Griffith, D. Pawson, F. L. Phillips, A. C. Skapski*, Inorg. Nucl. Chem. Lett. *9*, 1117 (1973).
[5] *W. Liese, K. Dehnicke, I. Walker, J. Strähle*, Z. Naturforsch. *B 34*, 693 (1979).
[6] *W. O. Davies, N. P. Johnson, P. Johnson, A. J. Graham*, Chem. Commun. *1969*, 36.
[7] *J. Strähle*, Z. Anorg. Allg. Chem. *375*, 238 (1970); *380*, 96 (1971).
[8] *J. Strähle, U. Weiher, K. Dehnicke*, Z. Naturforsch. *B 33*, 1347 (1978).
[9] *W. Musterle, J. Strähle, W. Liebelt, K. Dehnicke*, Z. Naturforsch. *B 34*, 942 (1979).
[10] *W. Liese, K. Dehnicke, I. Walker, J. Strähle*, Z. Naturforsch. *B 35*, 776 (1980).
[11] *G. Münninghoff, E. Hellner, M. El Essawi, K. Dehnicke*, Z. Kristallogr. *147*, 231 (1978).
[12] *A. J. Edwards*, J. Chem. Soc. *1964*, 3714.
[13] *M. W. Bishop, J. Chatt, J. R. Dilworth, M. B. Hursthouse, M. Motevalli*, J. Chem. Soc. Chem. Commun. *1976*, 780.
[14] *K.-P. Frank, J. Strähle, J. Weidlein*, Z. Naturforsch. *B 35*, 300 (1980).
[15] *J. Dunitz, L. E. Orgel*, J. Chem. Soc. *1953*, 2594.
[16] *F. Weller, W. Liebelt, K. Dehnicke*, Angew. Chem. *92*, 211 (1980); Angew. Chem. Int. Ed. Engl. *19*, 220 (1980).
[17] *W. R. Scheidt, D. A. Summerville, I. A. Cohen*, J. Am. Chem. Soc. *98*, 6623 (1976).
[18] *B. F. G. Johnson, J. A. McCleverty*, Prog. Inorg. Chem. *7*, 277 (1966); *N. G. Conally*, Inorg. Chim. Acta, Rev. *6*, 48 (1972); *J. A. Enemark, R. D. Feltham*, Coord. Chem. Rev. *13*, 339 (1974); *J. Eisenberg, C. D. Meyer*, Acc. Chem. Res. *8*, 26 (1975); *K. G. Coulton*, Coord. Chem. Rev. *14*, 317 (1975); *E. I. Stiefel*, Prog. Inorg. Chem. *22*, 1 (1977).
[19] *T. J. Greenhough, B. W. S. Kolthammer, P. Legzdins, J. Trotter*, J. Chem. Soc. Chem. Commun. *1978*, 1036.
[20] *F. L. Phillips, A. C. Skapski*, J. Chem. Soc. Dalton Trans. *1976*, 1448.
[21] *H. Bezler, J. Strähle*, Z. Naturforsch. *B 34*, 1199 (1979).
[22] *H. Bezler*, Dissertation, Universität Tübingen 1980.
[23] *W. A. Nugent, B. L. Haymore*, Coord. Chem. Rev. *31*, 123 (1980).
[24] *G. Beindorf, J. Strähle, W. Liebelt, F. Weller*, Z. Naturforsch. *B 35*, 153 (1980).
[25] *N. Wiberg, H.-W. Häring, U. Schubert*, Z. Naturforsch. *B 35*, 599 (1980).

[26] *K. Dehnicke, U. Weiher, D. Fenske,* Z. Anorg. Allg. Chem. *456,* 71 (1979).

[27] *M. W. Bishop, J. Chatt, J. R. Dilworth, M. B. Hursthouse, S. A. Jayaweera, A. Quick,* J. Chem. Soc. Dalton Trans. *1979,* 914.

[28] *J. Chatt, R. Choukroun, J. R. Dilworth, J. Hyde, P. Vella, J. Zubieta,* Transition Met. Chem. *4,* 59 (1979).

[29] *A. V. Butcher, J. Chatt, J. R. Dilworth, G. J. Leigh, M. B. Hursthouse, S. A. A. Jayaweera, A. Quick,* J. Chem. Soc. Dalton Trans. *1979,* 1979.

[30] *J. Chatt, B. A. L. Crichton, J. R. Dilworth, P. Dahlstrom, G. Gutkeska, J. A. Zubieta,* Transition Met. Chem. *4,* 271 (1979).

[31] *C. S. Day, V. W. Day, T. A. George, I. Tavanaiepour,* Inorg. Chim. Acta *45,* L54 (1980).

[32] *M. H. Chisholm, F. A. Cotton, M. W. Extine,* Inorg. Chem. *17,* 1329 (1978).

[33] *U. Weiher, K. Dehnicke, D. Fenske,* Z. Anorg. Allg. Chem. *457,* 105 (1979).

[34] *H. M. Colquhoun, T. J. King,* J. Chem. Soc. Chem. Commun. *1980,* 879.

[35] *G. L. Hillhouse, B. L. Haymore, W. A. Herrmann,* Inorg. Chem. *18,* 2423 (1979).

[36] *U. Weiher, K. Dehnicke, D. Fenske,* Z. Anorg. Allg. Chem. *457,* 115 (1979).

[37] *K. D. Schramm, J. A. Ibers,* Inorg. Chem. *19,* 1231 (1980).

[38] *M. Ciechanowicz, W. P. Griffith, D. Pawson, A. C. Skapski,* Chem. Commun. *1971,* 876.

[39] *W. P. Griffith,* Coord. Chem. Rev. *8,* 369 (1972).

[40] *K. Dehnicke, J. Strähle,* Z. Anorg. Allg. Chem. *339,* 171 (1965).

[41] *J. Strähle,* Z. Anorg. Allg. Chem. *405,* 139 (1974).

[42] *K. Dehnicke, W. Liese, P. Köhler,* Z. Naturforsch. *B 32,* 1487 (1977).

[43] *H. Staudinger, J. Mayer,* Helv. Chim. Acta *2,* 635 (1919).

[44] *J. Strähle, K. Dehnicke,* Z. Anorg. Allg. Chem. *338,* 287 (1965).

[45] *K. Dehnicke, W. Liebelt,* Z. Anorg. Allg. Chem. *453,* 9 (1979).

[46] *U. Künzel,* Dissertation, Universität Tübingen 1980.

[47] *T. Curtius,* Ber. Dtsch. Chem. Ges. *27,* 778 (1894).

[48] *W. Liebelt, K. Dehnicke,* Z. Naturforsch. *B 34,* 7 (1979).

[49] *K. Dehnicke, N. Krüger,* Z. Naturforsch. *B 33,* 1242 (1978).

[50] *J. Chatt, J. R. Dilworth,* J. Chem. Soc. Chem. Commun. *1974,* 517.

[51] *E. Schweda, J. Strähle,* Z. Naturforsch. *B 35,* 1146 (1980).

[52] *E. Schweda,* Dissertation, Universität Tübingen 1980.

[53] *D. A. Summerville, I. A. Cohen,* J. Am. Chem. Soc. *98,* 1747 (1976).

[54] *J. Chatt, J. R. Dilworth,* J. Chem. Soc. Chem. Commun. *1975,* 983.

[55] *R. D. Bereman,* Inorg. Chem. *11,* 1149 (1972).

[56] *J. Fritsche, H. Struve,* J. Prakt. Chem. *41,* 97 (1847).

[57] *A. F. Clifford, R. R. Oesen,* Inorg. Synth. *6,* 167 (1960).

[58] *W. Liese, K. Dehnicke,* Z. Naturforsch. *B 33,* 1061 (1978).

[59] *K. Dehnicke, U. Weiher, J. Strähle,* Z. Naturforsch. *B 32,* 1484 (1977).

[60] *N. I. Kolbin, I. N. Semenov, Y. M. Shutov,* Russ. J. Inorg. Chem. *8,* 1270 (1963).

[61] *M. J. Cleare, W. P. Griffith,* J. Chem. Soc. *A 1970,* 1117.

[62] *J. W. Buchler, K. L. Lay,* Chemiedozententagung, Erlangen 1980.

[63] *J. Chatt, G. A. Rowe,* J. Chem. Soc. *1962,* 4019.

[64] *J. Chatt, J. D. Garforth, N. P. Johnson, G. A. Rowe,* J. Chem. Soc. *1964,* 1012.

[65] *J. Chatt, C. D. Falk, G. J. Leigh, R. J. Poske,* J. Chem. Soc. *A 1969,* 2288.

[66] *J. Strähle, H. Bärnighausen,* Angew. Chem. *78,* 450 (1966); Angew. Chem. Int. Ed. Engl. *5,* 417 (1966).

[67] *N. P. Johnson, M. E. L. Pickford,* Inorg. Nucl. Chem. Lett. *39,* 819 (1977).

[68] *K. Dehnicke, W. Kolitsch,* Z. Naturforsch. *B 32,* 1485 (1977).

[69] *W. Liese, K. Dehnicke, R. D. Rogers, R. Shakir, J. L. Atwood,* J. Chem. Soc. Dalton Trans. *1981,* 1061.

[70] *K. Dehnicke,* unpublished results.

[71] *K. Dehnicke, N. Krüger, R. Kujanek, F. Weller,* Z. Kristallogr. *153,* 181 (1980).

[72] *P. Ruschke, K. Dehnicke,* Z. Naturforsch. *B 35,* 1589 (1980).

[73] *W. Kolitsch, K. Dehnicke,* Z. Naturforsch. *B 25,* 1080 (1970).

[74] *G. Beindorf, J. Strähle, W. Liebelt, K. Dehnicke,* Z. Naturforsch. *B 35,* 522 (1980).

[75] *F. Weller, U. Müller, U. Weiher, K. Dehnicke,* Z. Anorg. Allg. Chem. *460,* 191 (1980).

[76] *K. Dehnicke, U. Weiher,* Z. Anorg. Allg. Chem. *469,* 45 (1980).

[77] *K. Dehnicke, H. Prinz, W. Kafitz, R. Kujanek,* Liebigs Ann. Chem. *1981,* 20.

[78] *J. Chatt, B. J. Heaton,* J. Chem. Soc. *A 1971,* 705.

[79] *K. P. Lörcher, J. Strähle, I. Walker,* Z. Anorg. Allg. Chem. *452,* 123 (1979).

[80] *M. W. Bishop, J. Chatt, J. R. Dilworth,* J. Chem. Soc. Dalton Trans. *1979,* 1.

[81] *W. P. Griffith, D. Pawson,* J. Chem. Soc. Chem. Commun. *1973,* 418.

[82] *D. Pawson, W. P. Griffith,* Inorg. Nucl. Chem. Lett. *10,* 253 (1974).

[83] *R. Dübgen, U. Müller, F. Weller, K. Dehnicke,* Z. Anorg. Allg. Chem. *471,* 89 (1980).

[84] *U. Müller, R. Dübgen, K. Dehnicke,* Z. Anorg. Allg. Chem. *473,* 115 (1981).

[85] *R. Choukroun, D. Gervais, J. R. Dilworth,* Transition Met. Chem. *4,* 249 (1979).

[86] *A. F. Clifford, C. S. Kobayashi,* Inorg. Synth. *6,* 204 (1960).

[87] *A. Werner, K. Dinklage,* Ber. Dtsch. Chem. Ges. *34,* 2698 (1901).

[88] *A. Werner, K. Dinklage,* Ber. Dtsch. Chem. Ges. *39,* 499 (1906).

[89] *M. A. A. F. de C. T. Carrondo, R. Shakir, A. C. Skapski,* J. Chem. Soc. Dalton Trans. *1978,* 844.

[90] *D. Fenske, W. Liebelt, K. Dehnicke,* Z. Anorg. Allg. Chem. *467,* 83 (1980).

[91] *K. Dehnicke, J. Schmitte, D. Fenske,* Z. Naturforsch. *B 35,* 1070 (1980).

[92] *J. Strähle,* Dissertation, Universität Stuttgart 1965.

[93] *R. Mattes, M. Moumen, I. Pernoll,* Z. Naturforsch. *B 30,* 210 (1975).

[94] *J. Strähle, H. Bärnighausen,* Z. Anorg. Allg. Chem. *357,* 325 (1968).

[95] *G. Beindorf, J. Strähle, W. Liebelt, F. Weller,* Z. Naturforsch. *B 35,* 153 (1980).

[96] *E. O. Fischer, N. Q. Dao, W. R. Wagner,* Angew. Chem. *90,* 51 (1978); Angew. Chem. Int. Ed. Engl. *17,* 50 (1978).

[97] *W. P. Griffith,* J. Chem. Soc. *1965,* 3694.

[98] *B. Krebs, A. Müller,* J. Inorg. Nucl. Chem. *30,* 463 (1968).

[99] *A. Müller, B. Krebs, W. Höltje,* Spectrochim. Acta *A 23,* 2753 (1967).

[100] *W. P. Griffith, D. Pawson,* J. Chem. Soc. Dalton Trans. *1973,* 1315.

[101] *N. Krüger, K. Dehnicke,* Z. Naturforsch. *B 34,* 1343 (1979).

[102] *O. R. Chambers, M. E. Harman, D. S. Rycroft, D. W. A. Sharp, J. M. Winfield,* J. Chem. Res. (M) *1977,* 1846.

[103] *L. F. Dahl, P. D. Frisch, G. R. Guest,* J. Less-Common Met. *36,* 255 (1974).

[104] *A. O. Chong, K. Oshima, K. B. Sharpless,* J. Am. Chem. Soc. *99,* 3420 (1977).

[105] *J. C. J. Bart, V. Ragaini,* Acta Crystallogr. *B 36,* 1351 (1980).

[106] *D. Bright, J. A. Ibers,* Inorg. Chem. *8,* 709 (1969).

[107] *A. A. Grinberg,* Acta Physicochim. URSS *3,* 573 (1935).

[108] *J. Chatt, L. A. Düncouson, L. M. Venanzi,* J. Chem. Soc. *1955,* 4456.

[109] *L. F. Orgel,* J. Inorg. Nucl. Chem. *2,* 137 (1956).

[110] *R. J. Doedens, J. A. Ibers,* Inorg. Chem. *6,* 204 (1967).

[111] *P. W. R. Corfield, R. J. Doedens, J. A. Ibers,* Inorg. Chem. *6,* 197 (1967).

[112] *U. Müller,* Acta Crystallogr. *B 36,* 1075 (1980).

[113] *S. R. Fletcher, A. C. Skapski,* J. Chem. Soc. Dalton Trans. *1972,* 1079.

[114] *F. L. Phillips, A. C. Skapski, M. J. Withers,* Transition Met. Chem. *1,* 28 (1975/1976).

[115] *Y. Yeannin, J.-P. Launnay, J. Livage, A. Nel,* Inorg. Chem. *17,* 377 (1978).

[116] *J. R. Dilworth,* personal communication.

[117] *M. Ciechanowicz, A. C. Skapski,* J. Chem. Soc. *A 1971,* 1972.

[118] *L. Pauling:* The Nature of the Chemical Bond, 3rd edition, Cornell University Press, New York, 1960.

[119] *R. J. Gee, H. M. Powell,* J. Chem. Soc. *A 1971,* 1795.

[120] *K. W. Given, L. H. Pignolet,* Inorg. Chem. *16,* 2982 (1977).

[121] *W. A. Nugent, R. L. Harlow, R. J. McKinney,* J. Am. Chem. Soc. *101,* 7265 (1979).

[122] *H. Oberhammer, J. Strähle,* Z. Naturforsch. *A 30,* 296 (1975).

[123] *H. G. von Schnering,* personal communication.

[124] *J. Goubeau,* Angew. Chem. *69,* 77 (1957); *78,* 565 (1966); Angew. Chem. Int. Ed. Engl. *5,* 567 (1966).

# Photoelectron Spectra and Molecular Properties: Real-Time Gas Analysis in Flow Systems[**]

**New analytical methods (20)**

By Hans Bock and Bahman Solouki[*]

*Dedicated to Professor Heilbronner on the occasion of his 60th birthday*

For the analysis and optimization of numerous gas phase reactions in flow-systems, photoelectron spectroscopy has proven most valuable. This real-time measuring probe allows one to determine—with millimol quantities and within a few hours—the temperatures for different decomposition channels. Simultaneously, main products are characterized and, if need be, their yield can be improved. By careful performance of the experiment, short-lived and/or reactive molecules such as $P_2$, thioformaldehyde or silabenzene can be detected. PE-spectroscopic gas analysis is of particular advantage in the search for heterogeneous catalysts; they can be tested within a day using gas mixtures of varying composition over the temperature range from 300 K to 1300 K. In addition, PE-spectrometers are well-suited for on-line connection to computers; portable instruments for laboratory use are under development.

> *"Besser ist's doch wie gar nichts"*
> (Karl Valentin[1])

## 1. Introduction

The diversity and extent of instrumental analysis in the chemist's everyday routine foster scepticism towards any further method of measurement. Nonetheless, it will be attempted in this publication to present the scope of an analytical procedure for flowing gases and at the same time to focus one's attention more strongly on preparative gas phase reactions.

The topic in question is photoelectron spectroscopy, on whose "inner annular rings"—development of the method[2-5], commercial availability of high-resolution spectrometers, and the measurement of the ionization energies of thousands of molecules[2-9]—is now growing throughout the world, a more applications-related "bark". PE-spectroscopic band patterns can serve as "molecular fingerprints" for visually monitoring the course of gas phase reactions. Those of the parent molecules vanish, whereas those of the products emerge. In the following, we will report on how to "read" these band patterns[11-12], on some technical aspects of the apparatus, and on examples for gas phase reactions that can be PE-spectroscopically optimized[3,10]. This last topic ranges from temperature-dependent equilibria *via* pyrolyses, partly with detection of short-lived intermediates, to syntheses, especially with regard to heterogeneous catalysis. In the closing sections, an up-to-date summary will attempt to point out strengths and weaknesses of PE-spectroscopic gas analysis, especially in comparison to other well-established analytical methods such as gas chromatography, mass or vibrational spectroscopy.

## 2. Ionization Patterns as "Molecular Fingerprints"

Figure 1 shows a dozen PE-spectra which have been chosen as close to reality as possible in such a way that the molecules presented could occur as components of a synthesis gas mixture, an alkane bromination, or a cracking product fraction. Here, they serve as an introduction to "reading" ionization band patterns—divided according to number, shapes and regions of characteristic ionization bands. In conclusion we shall deal with how to make a qualitative estimation of expected values for ionization energies[3-7,12,13], or how to calculate them using different approximation methods and outline which criteria the ionization pattern must fulfill in order to enable a PE spectroscopic gas analysis.

### 2.1. Number of Bands

In general, PE-spectra in the range between 9 and 18 eV suffice for gas analyses (Fig. 1). The usual complete helium(I) measuring range of an instrument extends from 6 eV to 21 eV and encompasses, *e.g.*, the first ionization energy, amounting to $IE_1 = 6.01$ eV, of the phosphorus ylide

---

[*] Prof. Dr. H. Bock, Dr. B. Solouki
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

[**] Photoelectron Spectra and Molecular Properties, Part 100.—Part 99: *H. Bock, G. Brähler, D. Dauplaise, J. Meinwald,* Chem. Ber. *114* (1981), in press. Also 8th essay on molecular properties and models.—7th essay: *H. Bock, G. Brähler, W. Kaim, M. Kira, B. Roth, A. Semkow, U. Stein, A. Tabatabai,* "Novel Radical Ions: Generation and Properties—An Interim Report on PES and ESR Investigations by the Frankfurt Photoelectron Group" *in J. Bargon:* Computational Methods in Chemistry, Plenum Press, New York 1980, p. 103f.—Based on lectures at the 26th IUPAC Congress in Tokyo (1977), at the ACHEMA Frankfurt (1979), at the European Conference on Molecular Spectroscopy in Frankfurt (1979), at the Mass Spectroscopy Congress in Darmstadt (1979), at the Bayer AG Leverkusen (1978), at the Dow Chemical Corporation Midland/Michigan (1980), at the Dow Corning Midland (1978), at the Fritz-Haber-Institute of the Max Planck Society Berlin (1978), at the IBM Research Center San José (1980), at the ICI Central Research Department Runcorn (1977), at the Catalysis Institute Cracow (1978), at the Max-Planck-Institute for Coal Research Mülheim (1976), at the Monsanto Central Research Department St. Louis (1977), at the Polish Academy of Sciences Warsaw (1978), at the SOHIO Research Center Cleveland (1977) as well as at numerous universities.

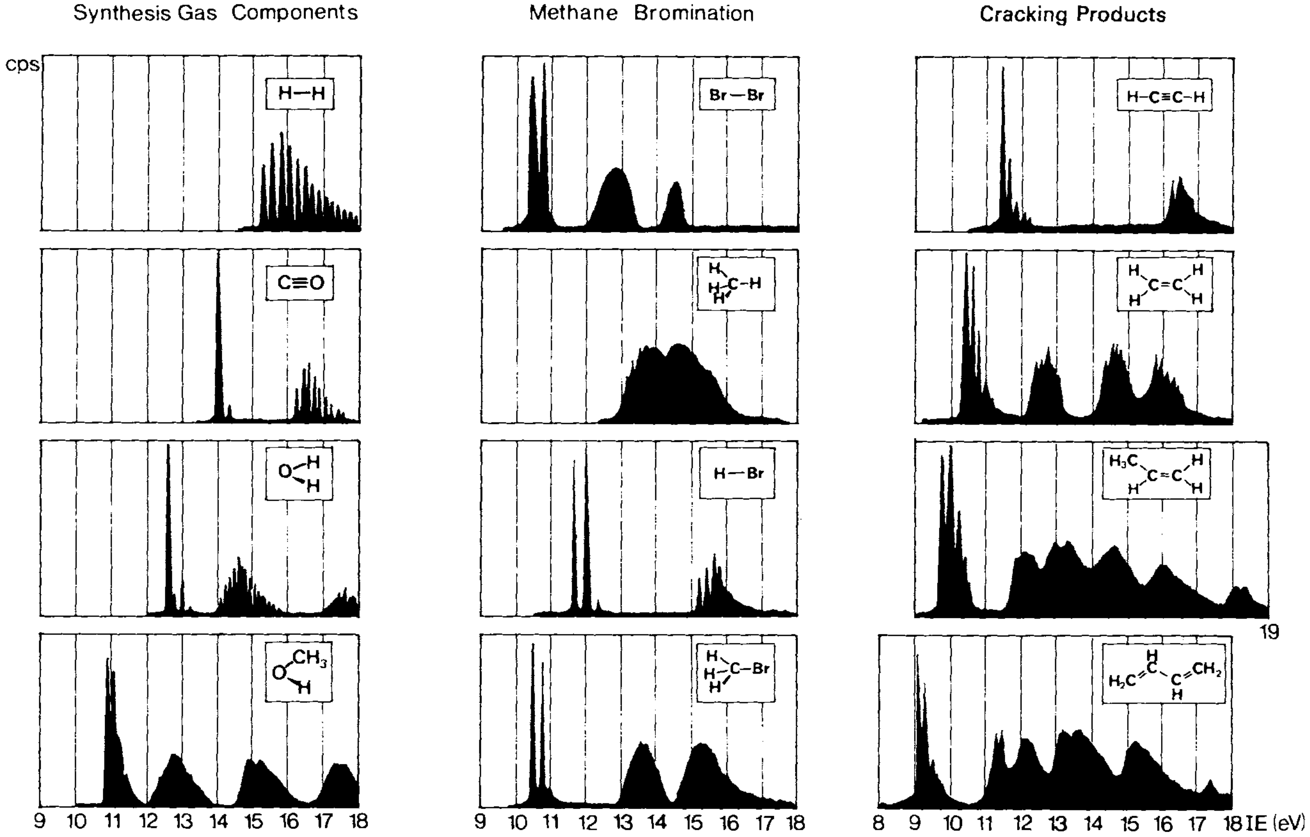


Fig. 1. Diagram containing a dozen helium(I)-photoelectron spectra of molecules as they could occur in a synthesis gas mixture, in an alkane bromination, or in a cracking products fraction. One recognizes the different band types—from sharp needles to broad hills of partially overlapping ionizations, with or without vibrational fine structure, as well as the double peaks of bromine derivatives with their distance determined by spin/orbit-coupling. The characteristic ionization patterns of the different molecules are discussed in the text arranged according to number, form, and energy range of the bands (see also Table 1).

Table 1. Additional data from the photoelectron spectra in Figure 1: number of valence electrons ($np_X + 1s_H$), from half the sum of which the number of bands in the HeI-range usually follows; recognizable radical cation vibrational fine structure $\nu_m^{\oplus}$ [cm$^{-1}$] ± 100 cm$^{-1}$ in relation to the corresponding vibrational frequency $\nu_m$ [cm$^{-1}$] of the neutral molecule; and qualitative partial assignment of the radical cation states generated by the three lowest ionizations ($IE_1$ to $IE_3$).

| | H—H | C≡O | HOH | $H_3COH$ | Br—Br | $CH_4$ | H—Br | $H_3C$—Br | HC≡CH | $H_2C$=$CH_2$ | $C_3H_6$ | $C_4H_6$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $np_X$ | | 2+4 | 4 | 2+4 | 2·5 | 2 | 5 | 2+5 | 2·2 | 2·2 | 3·2 | 4·2 |
| $1s_H$ | 2 | | 2 | 4 | | 4 | 1 | 3 | 2 | 4 | 6 | 6 |
| bands | 1 | 3 [a] | 3 | 5 [b] | 5 [c] | 3 [b] | 3 | 5 [b] | 3 [d] | 4 | 6 | 7 |
| $\nu_m^{\oplus}$ [cm$^{-1}$] [e] | 2260 [2] | 2160 [4] | 3200 [2] | 700 [9] | 300 [4] | 1700 [4] | 2420 [2] | 1300 [17] | 1830 [2] | 1230 [2] | 1340 [4] | 1520 [2] |
| $\nu_m$ [cm$^{-1}$] | 4280 | 2170 | 3652 | (1034) [f] | 320 | (2900) [g] | 2560 | 1400 | 1983 | 1623 | 1652 | 1643 |
| $IE_1$ | $\sigma_{HH}$ | $n_C + n_O$ | $n_O^{\pi}$ | $n_O^{\pi}$ | $n_{Br}$ | $\sigma_{CH}$ | $n_{Br}$ | $n_{Br}$ | $\pi$ | $\pi$ | $\pi$ | $\pi_1$ |
| $IE_2$ | | $\pi_{CO}$ [a] | $n_O^{\sigma}$ | $n_O^{\sigma}$ | $n_{Or}$ [h] | $\sigma_{CH}$ [b] | $n_{Br}$ [h] | $n_{Br}$ [h] | $\pi$ [d] | $\sigma_{CH}$ | $\sigma$ | $\pi_2$ |
| $IE_3$ | | $\pi_{pCO}$ | $\sigma$ | $\sigma$ | $\sigma$ | $\sigma_{CH}$ | $\sigma$ [i] | $\sigma_{CBr}$ | $\sigma$ | $\sigma_{CC}$ | $\sigma$ | $\sigma$ |

[a] $\pi$-double band at 16.5 eV. [b] $\sigma_{CH}$-multiple band between 14–16 eV. [c] $n_{Br}$-double band at 13 eV. [d] $\pi$-double band at 11.5 eV. [e] Only highest observed frequency given; for detailed discussion cf. [3, 4]. [f] Assignment not certain. [g] Spin/Orbit coupling $\Delta IE_{1,2} = 0.35$, 0.33 and 0.32 eV [17]. [h] Strong Jahn/Teller-distortion [3, 4]. [i] In the 3rd band $\nu_m^{\oplus} = 1290$ cm$^{-1}$ drops to nearly half that value.

$(H_5C_6)_3P{=}CH(C_6H_5)$[14] as well as the sixth of ethane, $IE_6 = 20.4$ eV[2,4,9,15]. The ionization of *a single electron at a time* occurs *via* transfer of the energy of photons generated in a helium gas discharge (see Section 3). In this way, the molecule *M* is transferred into its radical cation $M^{\ddagger}$ as well as the excited states of the latter[7]. In contrast to the electronic excitations in the visible and ultraviolet spectral regions with their selection rules, *all* single ionizations are usually allowed and therefore observable. A simplifying rule-of-thumb[6] states that in the so-called "helium(I)"-range 6 eV—21 eV *the number of observable ionizations should be equal to half the number of all element p- and hydrogen 1s-electrons formally present in the molecule*[16].

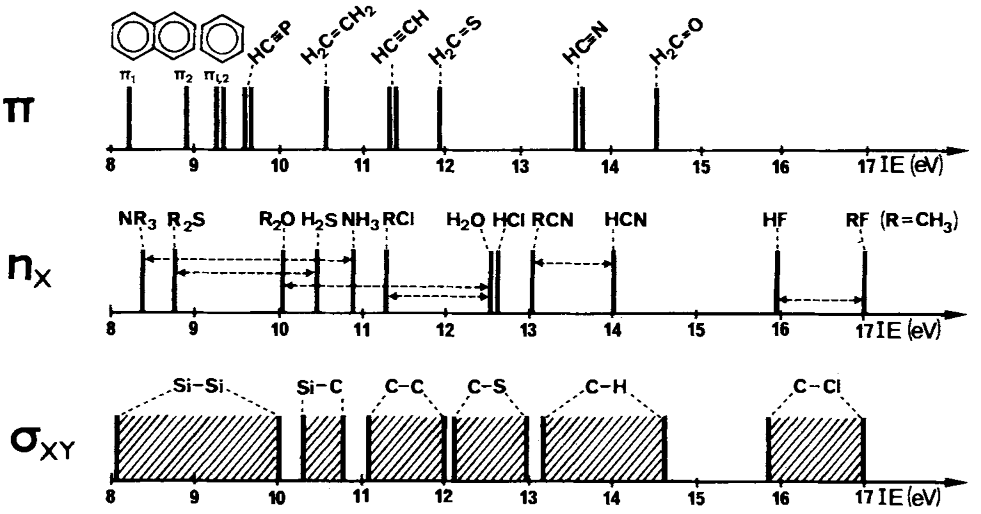
In this respect, the PE-spectra shown in Figure 1 can be viewed as follows: for the molecule H—H one expects and finds one band (with extensive vibrational fine structure); carbon monoxide formally has $2(2p_C)$- and $4(2p_O)$-valence electrons and therefore exhibits one single and one double band in the region up to 18 eV (cf. also [2-4]), water as expected shows $[2(1s_H) + 4(2p_O)] \times 1/2 = 3$ ionization bands in the He(I)-range. Methanol formally possesses $4(1s_H) + 2(2p_C) + 4(2p_O) = 10$ valence electrons and the PE spectrum up to 21 eV consequently shows five ionization bands including the double band at 15–16 eV while butadiene $C_4H_6$ shows $14/2 = 7$ He(I)-bands, two of which overlap at 13—14 eV. This counting of bands in the PE-spectra of molecules has been compiled in Table 1 together with the PE-spectroscopic information obtained from band shapes with or without vibrational fine structure, which is subsequently discussed, as well as the qualitative assignment of the radical cation states $M^{+\cdot}$ generated by the three lowest ionization energies.

## 2.2. Band Shape

The photoionization process $M + h\nu \rightarrow M^{+\cdot} + e$ occurs unimaginably fast within about $10^{-16}$ seconds. The radical cation $M^{+\cdot}$ produced by this "vertical" electron ejection therefore cannot "relax" into an equilibrium structure with a more favorable charge distribution[7], not even through molecular vibrations, which, with a period of about $10^{-14}$ seconds, take considerably more time. On the other hand, the ionizations of the neutral molecule do not only lead to electronically excited states of the radical cation $M^{+\cdot}$—as discussed previously for the example of the number of bands—but also to vibrationally excited ones[2-4]. Depending on the number of possible $M^{+\cdot}$-vibrations and the difference in their frequencies, there result in the photoelectron band patterns either needles separated from one another, or, in the case of their overlapping, broad ionization hills. Thus by inspection of the PE-spectra (Fig. 1) the following simplified band shapes can be distinguished:

- ⇒ single needles (CO, $OH_2$, $Br_2$, HBr, $H_3CBr$), which in general are assigned to the ionizations of "lone" electron pairs (Table 1). Here the constant distance of the double bands of halogen derivatives R—X (Fig. 1 and Table 1: $n_{Br}$) is due to spin/orbit-coupling which increases with ascending atomic numbers ($n_{Cl} < 0.1$, $n_{Br} \approx 0.3$, $n_I \approx 0.6$ eV[17,18]).
- ⇒ peak sequences with a width of up to about 1 eV (for example $HC{\equiv}CH$, $H_2C{=}CH_2$, $H_3C{-}CH{=}CH_2$, $H_2C{=}CH{-}HC{=}CH_2$) in most cases belong to $\pi$-ionizations, as a rule the first ionization is the most intense[3,4].
- ⇒ unstructured broad bands ($CH_4$ or derivatives $H_3C{-}X$ at $IE > 14.5$ eV) in general arise from ionizations of the $\sigma$ molecular frame, in which case numerous $M^{+\cdot}$-bands overlap.
- ⇒ peak sequences with a width of more than 1 eV ($H_2$, higher $IE_n$ of $OH_2$ or HBr): in the case of smaller molecules with only few vibrations, often at high frequencies, $\sigma$-ionizations can also exhibit vibrational fine structure.

A comparison of the vibrational frequencies before ($\nu_m$) and after ($\nu_m^{\oplus}$) ionization can be interpreted according to the size of the difference $\nu_m - \nu_m^{\oplus}$ as though "bonding" (Table 1: $H_2$ or $H_2C{=}CH_2$) or "nonbonding" (Table 1: CO, $Br_2$, HBr or $H_3CBr$) valence electrons have been ionized and therefore provides arguments for the assignment of the PE-spectra (Fig. 1 and Table 1). Own experience gathered over the years shows that gases with needle-like ionization bands can be readily analyzed PE-spectroscopically even in mixtures (cf. *e.g.* [10, 19-27]).



(1)

## 2.3. Band Ranges

From the PE-spectra (Fig. 1), chosen for their proximity to practical experience, characteristic ionization regions can be extracted according to the previously discussed partial assignment (Table 1: $IE_1$ to $IE_3$): thus $\pi_{CC}$-ionizations can be found between 9 eV—11.5 eV, the bands assigned to "lone" electron pairs $n_X$ lie for $n_O$ between 11 eV—14 eV or for $n_{Br}$ between 10.5 eV—12 eV, and $\sigma_{CH}$-ionizations in most cases occur between 13 eV—16 eV. A scale of typical $\pi_{XY}$, $n_X$ or $\sigma_{XY}$ ionization regions [see (1)], expanded for other heteroatoms, reflects the influence of the effective nuclear charge acting on the valence electrons, as already discussed for "s" and "p" electrons during the estimation of the number of PES bands[16]: fluorine derivatives are difficult and Si-compounds easy to ionize[6,7]. The upper and lower boundaries of the particular regions are also easy to comprehend and/or predict on the basis of substituent effects with which all chemists are familiar: thus methylation lowers the respective ionization energy by up to 2 eV (Fig. 1: cf. also $\Delta n_O(H{-}OH \rightarrow H_3C{-}OH)$, $\Delta n_{Br}(H{-}Br \rightarrow H_3C{-}Br)$, and, as a further example, $\Delta\pi_{CC}(H{-}HC{=}CH_2 \rightarrow H_3C{-}HC{=}CH_2$[29]). Enlarging the $\pi$ system *e.g.* by a vinyl group leads to $\pi$-splitting[5,6] (Fig. 1: ethene with $IE^{\pi} = 10.51$ eV → butadiene with $IE_1^{\pi} = 9.03$ eV and $IE_2^{\pi} = 11.46$ eV).

Beyond such considerations of plausibility, substituent effects can, in a simple way, be parametrized PE-spectroscopically and the expected values for similar compounds be estimated from them: in this way it is possible to determine, *e.g.* from the PE-spectra of the 1,1- and 1,2-dichloroethenes, the (coulomb) parameters $\alpha_\pi$ and $\alpha_{Cl}$ of the partial systems as well as the parameter $\beta_{\pi Cl}$ for the π interaction between them[30]:

$$\left.\begin{aligned}\alpha_\pi &= -10.85\ \text{eV}\\ \alpha_{Cl} &= -12.64\ \text{eV}\\ \beta_{\pi Cl} &= -\ 1.80\ \text{eV}\end{aligned}\right\}\Rightarrow\left\{\begin{array}{lll} & \text{Calc.} & \text{Obs.}\\ IE_1(H_2C{=}CH{-}Cl) & 10.09\ \text{eV} & 10.15\ \text{eV}\\ IE_2(H_2C{=}CH{-}Cl) & 13.28\ \text{eV} & 13.07\ \text{eV}\\ IE_1(Cl_2C{=}CCl_2) & 9.39\ \text{eV} & 9.35\ \text{eV}\end{array}\right. \quad (2)$$

Substituting the parameters into interaction determinants, or respectively into the equations derived from them—in the simplest case (2) into the relation

$$\begin{aligned}IE_{1,3} &= (\alpha_\pi+\alpha_{Cl})/2 \pm \sqrt{(\alpha_\pi-\alpha_{Cl})^2/4-\beta_{\pi Cl}^2}\\ &= 23.49/2\\ &\qquad \pm\sqrt{1.79^2/4-1.8^2}\\ &= 11.75 \pm 1.56\ \text{eV}\end{aligned}$$

which can be solved using any pocket calculator—in most cases yields reliable expectation values (cf. *e.g.* [4-7,28-31]). Excellent correlations between calculated and PE-spectroscopic ionization energies such as in (2) demonstrate once again the *usefulness of comparisons of equivalent states of chemically related compounds*[7], a method well suited to the chemical point of view, and which consequently makes reading PE-spectroscopic band patterns easier.

### 2.4. Calculation of Ionization Patterns

An additional advantage of PE spectroscopy consists in the possibility to calculate vertical ionization energies on different levels of approximation with the available quantum mechanical computational methods[32], *e.g.* for thioformaldehyde[13] (Fig. 2).

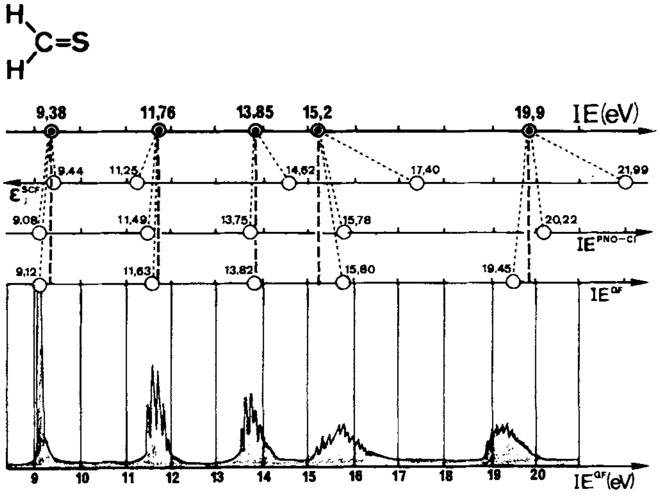
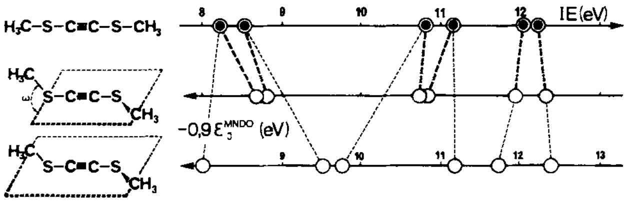


Fig. 2. Vertical PE-spectroscopic ionization energies *IE*[eV] of thioformaldehyde (⊙) and their correlation with *ab initio* SCF eigenvalues $-\varepsilon_J^{SCF}$, with energy state differences $IE^{PNO-CI}$ obtained by means of "*P*seudo *N*atural *O*rbital-*C*onfiguration *I*nteraction", and with ionization energies from *G*reen-*F*unction calculations $IE^{GF}$ (see text). The ionization pattern shown is a computer simulation based on many-body Green-function calculations [33]; it differs only slightly [7] from the authentic PE spectrum of thioformaldehyde [13].

It is quite obvious that the experimental ionization energies of $H_2C{=}S$ are only unsatisfactorily approximated by *ab initio* SCF eigenvalues $-\varepsilon_J^{SCF}$[13]; Koopman's defects, that is deviations from Koopmans' theorem $IE_n^v = -\varepsilon_J^{SCF}$[3,4,16,32], of over 2 eV occur. However, calculations of molecular states which, to a large extent, include correlation effects, such as the *p*seudo *n*atural *o*rbital-*c*onfiguration *i*nteraction method, can reproduce ionization energies to within about ±0.3 eV[13]. The ionization pattern shown was calculated using many-body Green-function techniques[33] and was drawn by a mechanical plotter (!) with the additional use of some experimental results; it differs only in insignificant details[7] from the PE spectrum of thioformaldehyde.

For molecules which are either larger than, for example, benzene or have lower symmetry, exact computation takes too long. Here, the faster semi-empirical "four-letter"-methods such as the well-proven MNDO method[32] become advantageous. Although their exactness especially for radical cation state energy differences of less than 1 eV is often overestimated, they nonetheless reproduce ionization patterns in a satisfactory way, *e.g.* for bis(methylthio)acetylene[27] which can be generated by gas phase thermal decomposition of 3,4-bis(methylthio)-1,2-cyclobutenedione [see (3)].



(3)

According to electron diffraction measurements bis(methylthio)acetylene does indeed display a dihedral angle of $\omega = 86°$[34], and therefore possesses two partial π systems of the same kind, S—C═C(—S) and (S—)C═C—S[27]. As the example given here shows, the calculation of ionization patterns frequently yields further useful information beyond expectation values important for gas analysis, *e.g.* on the feasibility of oxidation to the radical cation in solution[35].

### 2.5. Ionization Patterns of Gaseous Mixtures

The PE spectra (Fig. 1) previously discussed one by one, have been placed together in the three columns "synthesis components", "methane bromination", or "cracking products". Arranging the spectra in applications-related groups was undertaken for the didactic reason of illustrating certain criteria of the PE spectroscopic analysis of gaseous mixtures:

⇒ $H_2$, CO, $H_2O$ and $H_3COH$: here the last three compounds can be recognized visually without much trouble by their separated single needles at 10.94 eV[9], 12.61 eV[2] and 14.01 eV[2] even in concentrations of only about 5 to 10%. The gaseous mixtures may additionally contain other molecules of the same composition as synthesis gas $\{n\cdot CO + m\cdot H_2\}$ with characteristic single peaks such as $H_2C{=}O$ ($IE_1 = 10.88$ eV)[9],

$HCOOCH_3$ ($IE_1 = 11.00$ eV[36]), or O=CH—HC=O ($IE_2 = 12.20$ eV[9])[36]. The only difficulties arise from the analysis of $H_2$ in mixtures of all components, since then the "observation windows" between 15—16 eV (next to CO) and 16—17 eV (next to $H_2O$ and $H_3COH$) do not lie in the same region. Our own experience[36] shows nonetheless that the distinctive vibrational fine structure (Fig. 1 and Table 1) which extends over a range of 3 eV frequently allows at least a qualitative detection.

⇒ $Br_2 + CH_4 \rightarrow HBr + H_3C—Br$: this example of a gas phase reaction shows the limits of PE-spectroscopic real time analysis, since the overlapping double bands of the educt $Br_2$ ($IE_1 = 10.53$ eV, $IE_2 = 10.85$ eV[41]), and of the product $H_3C—Br$ ($IE_1 = 10.53$ eV, $IE_2 = 10.85$ eV[17]) cannot be resolved anymore. The temperature dependence of the methane bromination, as a function of a heterogenous catalyst which is to be optimized, would have to be monitored only by means of the HBr being formed. Moreover, $CH_4$ cannot be visually detected in mixtures with $Br_2$ and $H_3C—Br$ (Fig. 1). It must, however, be pointed out that the overlap of $Br_2$ and RBr-bands, so unfortunate in this case, does not occur with other gas phase brominations[24] (cf. Fig. 10: $F_3CH + Br_2 \rightarrow F_3CBr + HBr$).

⇒ Acetylene, ethene, propene and butadiene: in each case the first bands and those assigned to π ionizations (Fig. 1 and Table 1) between 9 and 11.5 eV allow a simultaneous analysis of all components down to concentrations of about 10%. This accuracy, which is obtained by visually comparing band intensities, can be considerably increased by computerized evaluation of the spectra.

The question whether a given gas reaction in a flow system can be monitored with PE-spectroscopy, is—if the PE-spectra of all components are known—most favorably answered by means of a computer: the basis for this is the linear relationship, verified experimentally many times, between the concentrations of molecules in the gaseous mixture and their (relative) band intensities (cf. *e.g.* [37-42]). For example, mixtures with known ratios of hydrogen cyanide : cyanogen were analyzed PE-spectroscopically and the band areas planimetrically determined: this verification gave satisfactory agreement[23]. In the meantime, *e.g.* a simple program PESIMU[43] allows one to store PE spectra in 0.05 eV steps in a computer and, within minutes, to print out the expected PE spectra for gaseous mixtures composed from the constituents in any way[10,23]. This is based on the assumption of comparable photoionization cross sections, usually valid for chemically related compounds. It is on purpose that the little structured PE-spectra of the chlorosilanes $H_2SiCl_2$ and $HSiCl_3$[44], the ratio of which is important in the manufacture of pure silicon, have been chosen here as example of an application (Fig. 3).

PE-spectroscopic analysis is more complicated for $H_2SiCl_2/HSiCl_3$ mixtures than for the examples discussed up to now (Fig. 1), because the spectra are of the same type, and contain only three prominent bands: for $H_2SiCl_2$ $IE_1 = 12.53$ eV and for $HSiCl_3$ $IE_3 = 13.07$ eV and $IE_7 = 18.14$ eV[44]. It is nonetheless evident that it would be possible to carry out an optimization of reaction conditions with the aim of a maximum $H_2SiCl_2$ yield, relying on the relative intensities of the bands marked by arrows. It would of course be more favorable if the gas analysis could be performed using a small molecule such as HCl, the PE spectrum of which contains characteristic needle-like peaks (cf. Fig. 1: HBr).

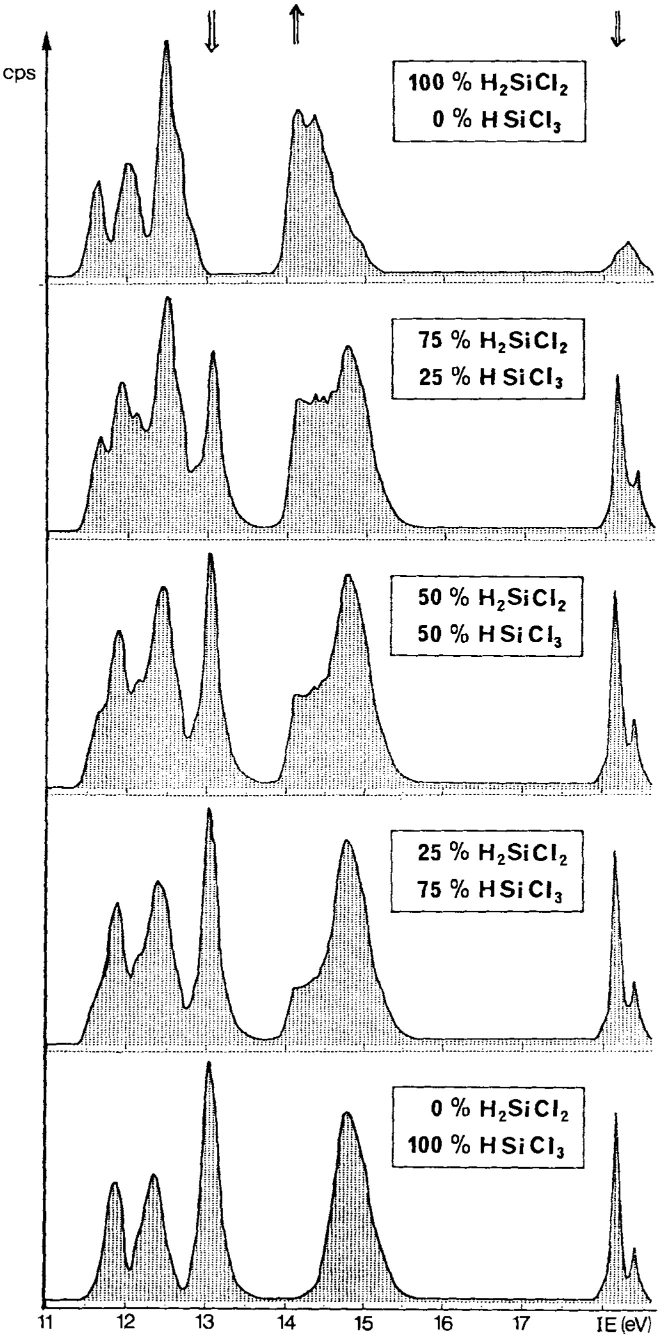


Fig. 3. Computerized PE spectra of the chlorosilanes $H_2SiCl_2$ and $HSiCl_3$ [43, 44], and computer simulation of the PE spectra of their mixtures in the ratios 75:25, 50:50, and 25:75.

### 2.6. Gas Analysis by Means of Ionization Patterns

The preceeding introduction into band number, band shape and band energy ranges of helium(I) photoelectron spectra is intended to let an observer less proficient in their interpretation recognize that their daily use does not raise any particular difficulties, just as with IR vibrational frequencies, mass spectroscopic fragments or NMR couplings. In order to identify molecules by means of their ionization patterns, it is advisable to record spectra of probable reaction products in advance. Starting from the discussed rules, a specific search among the thousands of known PE spectra is often successful, starting with looking them up in the available PE spectra collections[2-4,6,8,9], or in the original literature *via* the entries "photoelectron spectrum" in the Chemical Abstracts Chemical Compounds Register. A library of PE spectra on recall from a graphic display is currently being established at the University of Frankfurt (DEC 10 *via* PDP 11/40 terminal)[45]. For hitherto unknown PE spectra, especially for molecules produced for the first time in the gas phase, the assignment *via* a comparison of states with chemically related compounds or the quantum mechanical calculation of vertical ionization energies remain as additional possibilities, besides questioning knowledgeable colleagues. As an expansion of the above discussion, the feasibility of PE spectroscopic analyses in gaseous mixtures can be judged by comparison, projection of the spectra upon one another, or computer mixing of the PE spectra of the main components. Here needle-like PE bands as they occur on ionization of "electron pairs" or of "π systems" of smaller molecules are favorable. The scope as well as the advantages and disadvantages of PE spectroscopic gas analysis will be discussed in a final comparison (Section 5) with "competing" methods of gas analysis such as gas chromatography, mass spectroscopy or infrared spectroscopy.

## 3. Gas Analysis with Photoelectron Spectrometers

The working principle of a photoelectron spectrometer is well documented[2-6] and so lucid that it is excellently suited for the treatment of the experimental determination of ionization energies in introductory chemistry lectures[11] (cf. Fig. 4B): helium atoms are excited in a gas discharge and give off photons of energy $h\nu = 21.21$ eV. In the ionization chamber, these impact on molecules drawn into the chamber by the PE spectrometer's high vacuum system. By photoionization $h\nu + M \rightarrow M^{+\cdot} + e$, *i.e.* by supplying the respective ionization energies $IE_n$, electrons with well defined kinetic energies $E_{kin} = 21.21\ \text{eV} - IE_n$ are generated, then sorted according to energy in an electrostatic analyzer, and finally counted (cf. Fig. 1: ordinate in "counts per second", abscissa from left to right $IE_n$ and from right to left $E_{kin}$). Starting from this common working principle, useful details on the instruments and apparatus for gas analysis in flow systems have been compiled and are presented in the following sections.

### 3.1. Comments on the Instrumentation: PE Spectrometers

Of the numerous kinds of PE spectrometers two extremes will be presented here: on the one hand, a high performance instrument for research purposes (Fig. 4A), remaining at the same location in an instrument room, and to which the apparatus for the preparation of the species under investigation is connected, and, on the other, a prototype of a simple portable instrument (Fig. 4C), which is connected to a fixed apparatus for measurements.

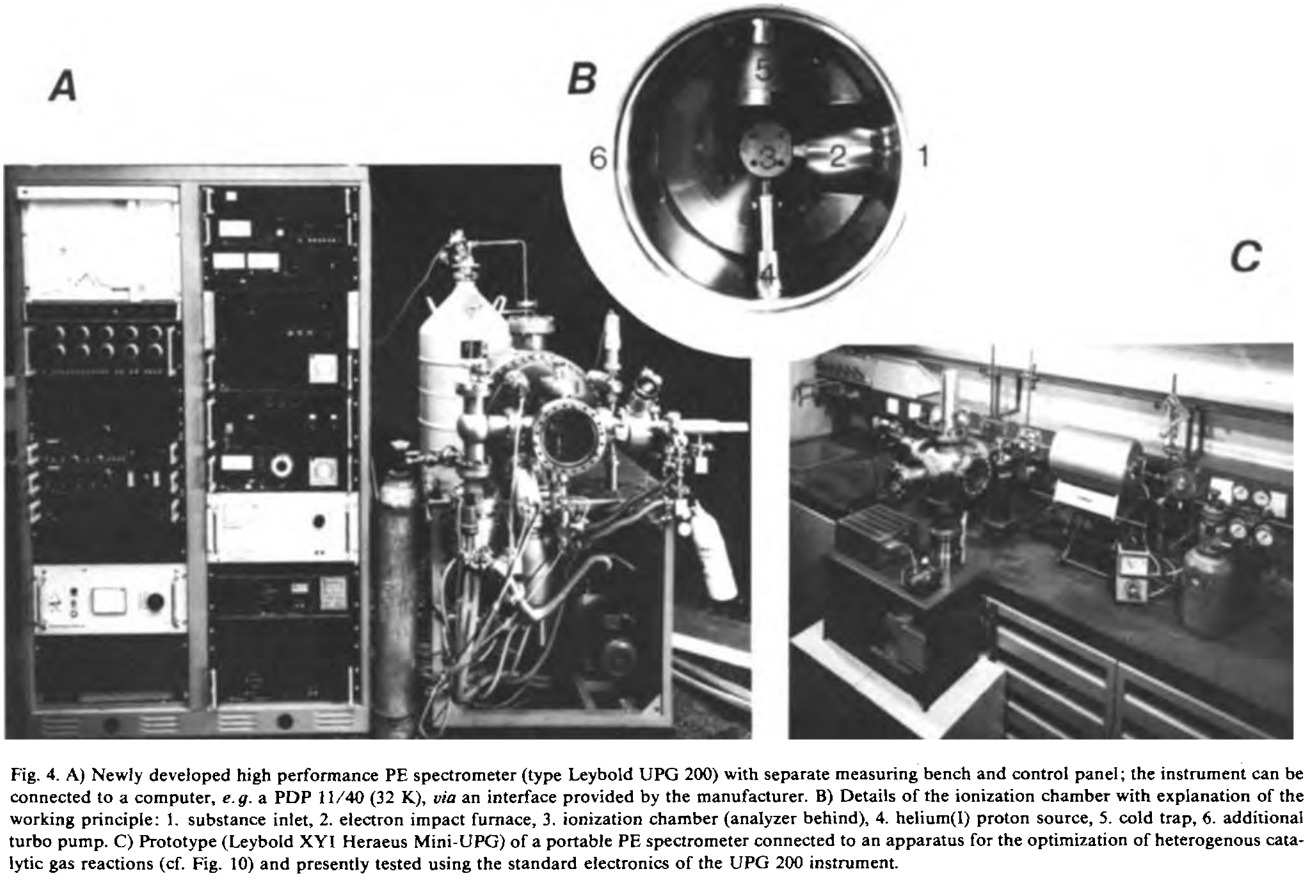


Fig. 4. A) Newly developed high performance PE spectrometer (type Leybold UPG 200) with separate measuring bench and control panel; the instrument can be connected to a computer, *e.g.* a PDP 11/40 (32 K), *via* an interface provided by the manufacturer. B) Details of the ionization chamber with explanation of the working principle: 1. substance inlet, 2. electron impact furnace, 3. ionization chamber (analyzer behind), 4. helium(I) proton source, 5. cold trap, 6. additional turbo pump. C) Prototype (Leybold XYI Heraeus Mini-UPG) of a portable PE spectrometer connected to an apparatus for the optimization of heterogenous catalytic gas reactions (cf. Fig. 10) and presently tested using the standard electronics of the UPG 200 instrument.

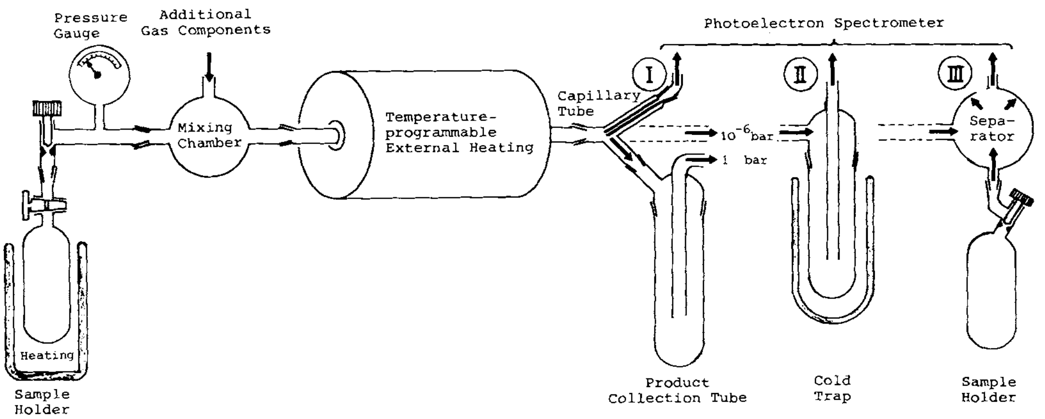


Fig. 5. Assembly kit for the apparatus needed for PE spectroscopic gas phase reactions, comprising (from left to right): substance inlet, pressure gauge for stoichiometric mixing of gases with given partial pressures, heated reaction tube (optionally empty, or filled with quartz wool or a catalyst) and some means for trapping reaction products [10]: I) For pressures of about 1 bar, reduction to the PE spectrometer's working pressure of $10^{-5}$ to $10^{-7}$ bar can be effected using a capillary tube, depending on its length and diameter. Products can be collected in a conventional way, and can be subjected to a further preparative or analytical workup, if so wished. This "capillary bleeding" is advantageous especially with hot gases [46]. II) For gas phase reactions at PES working pressures, identification of certain components in product mixtures with strongly overlapping PE-spectra is often possible by freezing out in a cold trap followed by fractional evaporation. III) Some components can be eliminated from product mixtures by an additional gas phase reaction in a separator bulb, such as *e.g.* $HCl + NH_3 \rightarrow NH_4Cl$ [13].

Both types of instruments are constructed according to the working principle described above and are comparable concerning most of the measuring conditions specified below. The following differences catch the eye: the electrostatic analyzer is built into the horizontal vacuum chamber, separate from the ionization chamber (Fig. 4A) or connected to it in the cross flange (Fig. 4C). In A, an additional turbomolecular pump makes it possible to guide the beam of molecules in a largely separate way. Resolution (A 15 meV, C < 100 meV) and maximum possible intensity (A > 100000 cps, C 30000 cps) as well as operating options and gauges for helium lamp, vacuum system or electronics are in keeping with their respective operating purposes and the very different cost of the instruments. The following comments on the instruments are subdivided according to the operating conditions, the "real time" measuring process, and the extension of the range of application:

- ⇒ operating conditions: in both types of PE spectrometers (Fig. 4A and C) the beam of molecules is pumped from a storage vessel to a cold trap in a flow system at a pressure of about $10^{-5}$ to $10^{-8}$ bar. As a rule-of-thumb, only about 1 millimol of a compound is needed for a series of measurements lasting from 6 to 10 h. Since the He(I) photons are generated in an open gas discharge, the PE spectrometer is filled with a partial pressure of helium; for calibration of the spectra one adds argon ($^2P_{3/2} = 15.76$ eV) and/or xenon ($^2P_{3/2} = 12.13$ eV)[2].
- ⇒ "real time" measurement: as already mentioned, the ionization process occurs within $10^{-16}$ s; the time needed for the measurement is, however, considerably longer: this is mainly due to the gas flow in both types of spectrometer (Fig. 4A and 4C) having to be pumped from the (usually heated) reaction zone to the ionization chamber. "Real time" measurement is therefore understood as continuous measuring without an additional delay caused by the instrument, as *e.g.* in gas chromatography. According to the rate of feed chosen, registration of a complete spectrum from 6 to 21 eV takes between 3 and 20 min with a recorder, and about $10^{-2}$ s per measured point electronically.
- ⇒ extension of the range of applications: of the innumerable possibilities, reactions at higher pressure and shorter contact time should be emphasized. The reduction of pressure between reaction tube and PE spectrometer can be effected by means of various "bleeding"-valves or, most simply—especially in the case of hot gases—by means of a reducing capillary (Fig. 5)[46]. For flow velocities which can be varied only within a limited range[3] the contact time is preferentially shortened by reducing the distance between the reaction zone and the ionization chamber—down to about 1 cm[3,47-49], depending on the type of spectrometer used (cf. Fig. 8A). The spectrometer shown (Fig. 4B: 2) is fitted with an electron impact heating system which allows one to reach temperatures of above 1500 K with a minimum distance of 2 cm between the end of the reaction zone and the ionization chamber.

Short-lived species produced thermally, by microwave discharge or by chemical reactions, and detected PE-spectroscopically (cf. *e.g.* [3,10,47]) will be reported upon in Section 4.3.

### 3.2. Comments on the Apparatus for Reactions

How to carry out gas phase reactions at various pressures and temperatures has already been discussed on a number of occasions[3,10,47,50-52]. Here a few additional useful tips concerning apparatus and reaction conditions for PE spectrometers will be given, based on experience gathered by the Frankfurt PES group[53] since 1973[10,13,21,46,49,53]. The starting point is the standard assembly (Fig. 4C or 10)[46], which can be modified in nu-

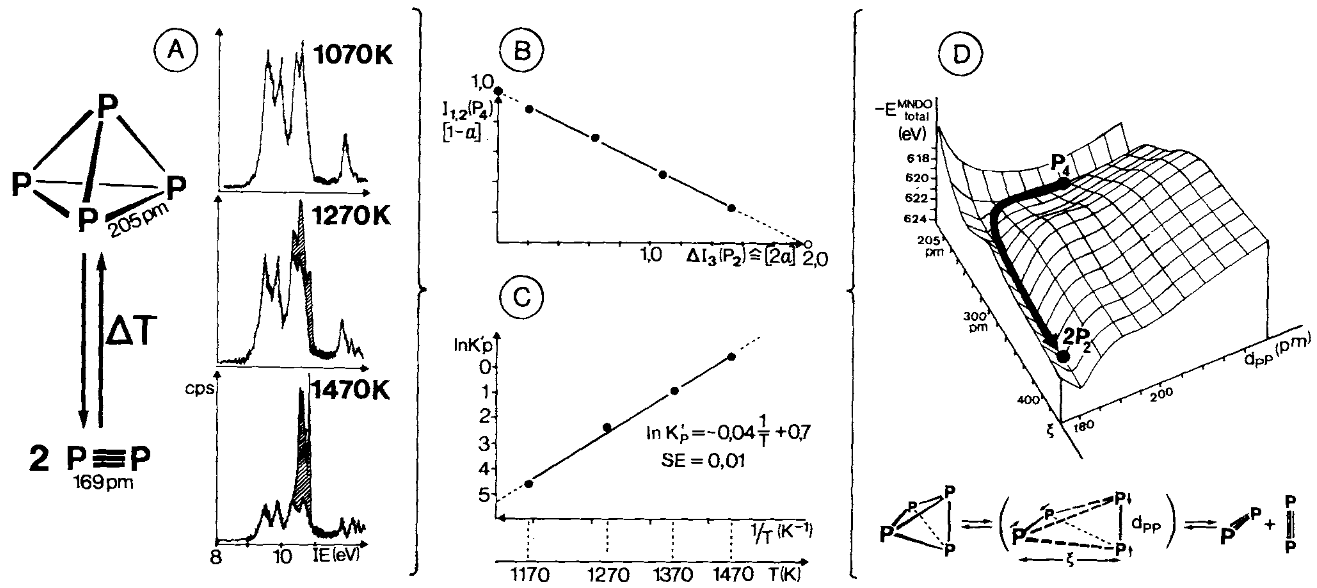


Fig. 6. The thermal equilibrium $P_4 \rightleftarrows 2P_2$. A) White phosphorus, pre-dried with acetone and distilled in a brown glass apparatus over $CaH_2$ [56], is vaporized in a PES pyrolysis assembly (Fig. 5: substance inlet without mixing bulb, oven, direct connection to the PE spectrometer). The PE spectra of the gas flow change between the temperatures of the oven given above: the intensity of the $P_4$ ionization pattern at 9—11 eV decreases, that of the $P_2$ ionization pattern at 10.5—11 eV (shaded area) increases. If the band area corresponding to the $P_4$ intensity ratio $IE_{1,2}:IE_3$ is subtracted from this band, the band intensities $IE_{1,2}(P_4) \triangleq [1-\alpha]$ and $\Delta I_3(P_2) \triangleq [2\alpha]$, proportional to the partial pressures $p$, can be plotted against one another assuming temperature independent and comparable ionization cross sections. B) The points of the resulting straight line can be converted according to $\ln K_p' = 4\alpha^2 P/(1-\alpha^2)$ and afford C) the temperature dependence of the equilibrium constant $K_p'$. The experimental values agree satisfactorily with those found in the literature (*e.g.* for 1370 *K*: at $p = 0.04$ mbar $\ln K_p' = -0.89$; literature [56], at 0.19 mbar $\ln K_p' = -0.81$) as well as with the difference in the calculated MNDO enthalpies of formation $\Delta H_{total}^{MNDO} = 180$ kJ/mol (dissociation energy [56] $E_D = 217$ kJ/mol). D) The MNDO hypersurface was calculated using the simplifying assumption that dissociation proceeded along the coordinate $\xi$ with reduction of the bond length $d_{PP}$ from 205 pm ($P_4$) to 169 pm ($P_2$), in spite of the symmetry forbidden process $T_d \rightarrow D_{2d} \rightarrow D_{\infty h}$. The PE spectroscopic measurements were carried out with 100 mg of white phosphorus during one day.

merous ways very much as with an assembly kit[10] (Fig. 5). Depending on the choice of parts for substance inlet, reaction zone and product isolation, different types of gas phase reactions, from the thermal decomposition of a compound to the heterogeneously catalyzed reaction of several components, can be analyzed PE spectroscopically and their reaction conditions optimized.

⇒ substance inlet: the vaporizing of molecules that can be brought into the gas phase without decomposition offers no difficulties, especially under vacuum conditions, and can be effected in a separate preheated oven around the extended reaction tube *e.g.* for pyrolyses of high-boiling solids. Mixing several gases is best accomplished by passing them at right angles to each other and to the reaction tube into a mixing bulb, preferentially filled with Raschig rings and heated if necessary (Fig. 5). The possibility of carrying out reactions in flow systems, *e.g.* sulfur chloride and methylamine[54] [cf. (18)] with a Daniell type burner extending into the reaction zone should also be mentioned here.

⇒ Reaction zone: generally quartz or steel tubes of 10 to 30 mm in diameter and about 400 mm long are used; lengths of the reaction zone of up to 2 m can be obtained by using spiral tubes in ovens with openings of large diameter[21]. Heterogeneous catalysts can be packed in between quartz wool wads; if necessary, the reaction tube can be positioned vertically. Ovens that can be swung open allow a faster change of tubes. The heating tube of a "flash vacuum pyrolysis" apparatus[50,51] can be installed instead of the oven and the temperature for the preparative isolation of the compound formed can be optimized. A thermocouple on the outside of the reaction vessel is sufficient for determining *relative decomposition temperatures*; in order to minimize temperature dependent equilibrium shifts after leaving the reaction zone, one has to pay attention to maintaining as short as possible a distance to the ionization chamber of the PE spectrometer. Finally, mention must be made of the protecting helium atmosphere in the PE spectrometer, which is advantageous for measurements of oxygen-sensitive compounds such as silanes $Si_nH_{2n+2}$[55], phosphorus ylides[14], or of the $P_4/P_2$ equilibrium[56] (Fig. 6).

⇒ Isolation of products: the numerous possible variations include condensation at atmospheric pressure (Fig. 5 I), freezing out with subsequent fractional evaporation of the product mixture (Fig. 5 II) or separating certain compounds as solids (Fig. 5: III). Poisonous reaction components such as cyanogen and hydrocyanic acid[46] can be rendered inoffensive by, *e.g.*, freezing them out on the surface of the cold trap of the PE spectrometer, and allowing them to thaw in a suitable decontaminating solution after removal from the spectrometer.

All in all, carrying out reactions in PE spectrometers is very versatile as far as the apparatus is concerned; the thermal energy supply in use for most preparative aims can be replaced by microwave generators or by electric discharges (Section 4.3[3,47]). When operating in a vacuum, the reaction conditions are often similar to those of the well-established "flash vacuum pyrolysis"[50,51]. Beyond this, the scope of PE spectroscopic gas analysis, discussed in the following sections with selected examples, also encompasses reactions at normal pressure, gas phase syntheses and heterogenously catalyzed reactions.

## 4. Examples of PE Spectroscopically Optimized Gas Phase Reactions

The scope and possibilities of PES gas phase analysis, both from the spectroscopic point of view and as regards the apparatus, will now be demonstrated in closer detail by means of the following selected examples:

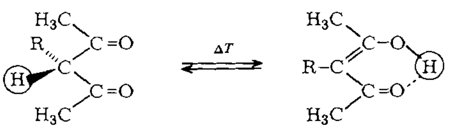
- ⇒ the measurement of the temperature dependence of equilibrium constants by means of the dissociation $P_4 \rightleftarrows 2P_2$[56],
- ⇒ the investigation of thermal reaction channels by means of the pyrolysis of vinyl azide[26,57],
- ⇒ the detection of short-lived intermediates using as example the formation of silabenzene[49,58],
- ⇒ gas phase syntheses by the reaction of thionyl chloride with ammonia to form sulfinyl imide[59],
- ⇒ the optimization of gas phase reactions with heterogeneous catalysis, using as example the bromination of trifluoromethane[24].

For each example, further literature on other reactions of that type will be cited.

### 4.1. Measurement of the Temperature Dependence of Equilibria

So far, gas phase equilibria have been investigated PE spectroscopically only in isolated instances (Table 2). Nevertheless, this type of reaction takes the lead in the examples of applications, as it can be used to demonstrate that the comparison of PE band intensities makes possible quantitative statements under certain conditions and within certain limits of error.

Already in 1974 the temperature dependence of keto/enol-tautomeric equilibria was determined from PE spectroscopic band intensities[37]; in agreement with IR or mass spectroscopic results, *e.g.*, 76% acetylacetone is found to be present in the keto form at room temperature [see eq. (4), R = H][37].



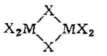
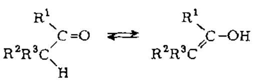
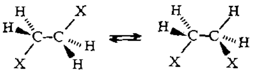
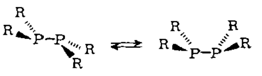
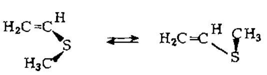
(4)

R = H, CH$_3$

The basic assumptions—*temperature independent* PE band intensities for keto- and enol-tautomers in a ratio of 1 : 1, ionization cross sections and asymmetry parameters[37]—have proven their value also in measurements on other *temperature dependent* gas phase equilibria[38–41,56,60–64] (Table 2).

The PE spectroscopic measurements of temperature dependent equilibria (Table 2) encompass reactions such as dissociations or rearrangements and phenomena of molecular dynamics such as the barriers of rotamers or vibrational excitations. Mention must be made of many other gas phase reactions (Section 4.2—4.5), for which temperature dependent yields have been optimized without, however, evaluating band intensity ratios. The survey (Table 2) shows molecular sizes between 2 atoms ($O_2$, $Cl_2$) and 16 atoms ($H_5C_6$—$SCH_3$); the range of temperatures extends from 210 K with cooling of the flow system ($N_2O_4$) to light red heat ($P_4 \rightleftarrows 2P_2$). The experimental results enable one to estimate equilibrium constants[37–39,56] or energy barriers[38,39,41,63,64] in usually satisfactory agreement with thermodynamic data from the literature, and moreover to characterize the respective partners of the equilibrium.

Table 2. Types of gas phase equilibria investigated by means of PE spectroscopy.

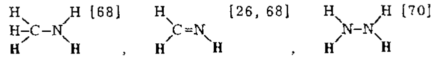
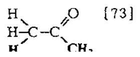
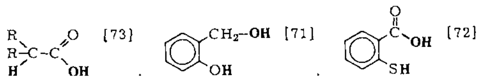
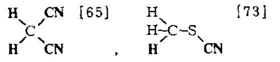
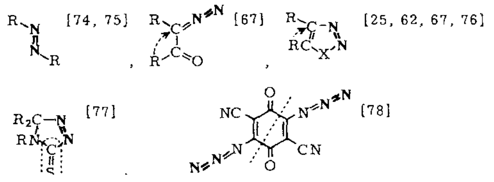
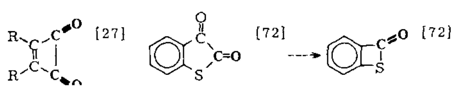
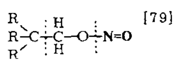
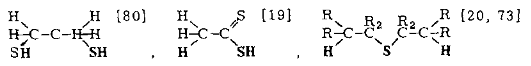
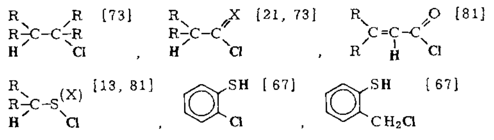
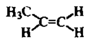
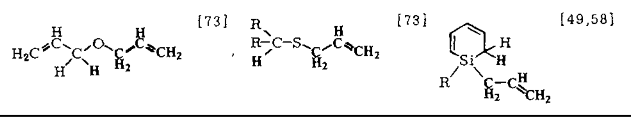
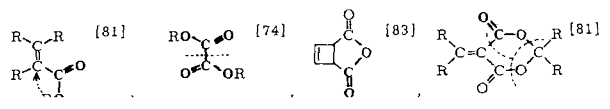
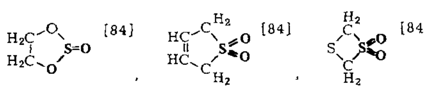
| Gasphase equilibrium | Ref. | *T*-range | Remarks |
|---|---|---|---|
| *Dissociation* | | | |
|  ⇄ 2 MX$_3$ | [60] | 340– 500 | 440 K: 50% MX$_3$ |
| $O_2N{-}NO_2 \rightleftarrows 2\ NO_2$ | [61] | 290– 210 | 210 K: 20% N$_2$O$_4$ |
| $P_4 \rightleftarrows 2\ P_2$ | [56] | 1000–1500 | 1270 K: 50% P$_2$ |
| *Rearrangement* | | | R$^1$ = CH$_3$, R$^2$ = H,<br>R$^3$ = CH$_3$CO, |
|  | [37] | 295– 520 | 295 K: 76% keto form |
|  | [62] | 295– 500 | 313 K: 80% oxadiazole |
| *Rotation* | | | |
|  | [63] | 300– 570 | 293 K: 76% trans |
|  | [41] | 300– 530 | 295 K: 60% trans |
|  | [38] | | |
|  | | 340– 860 | cis: 10 kJ/mol more stable |
| R = H | [64] | 300– 800 | high *T*: – H$_2$S |
| R = CH$_3$ | [39] | 295– 770 | barrier: 3 kJ/mol |
| *Vibrational excitation* | | | |
| $O_2 \rightleftarrows O_2^*$ | [40] | 295– 685 | $\nu_{OO} = 1460 \pm 260\ cm^{-1}$ |
| $Cl_2 \rightleftarrows Cl_2^*$ | [40] | – 390 | $\nu_{ClCl} = 1048 \pm 240\ cm^{-1}$ |

The equilibrium of dissociation $P_4 \rightleftarrows 2P_2$[56] has been chosen as an example that should be discussed in detail (Fig. 6) for it requires comparatively high temperatures (Table 2), illustrates the advantages of the protecting helium atmosphere in the PE spectrometer (cf. Section 3.1) and at the same time is a prerequisite for further attempts at reactions such as (5). The experimental expenditure is comparatively small (Fig. 5 and 6): 100 mg of the phosphorus vapor, which is dangerous at high temperatures, is sufficient for the one day neccessary to carry out the experiment. As can be seen from the illustration (Fig. 6A), the PES band intensities change markedly upon heating; the planimetric evaluation of the band areas yields the equilibrium constitution of P$_4$ and P$_2$ (Fig. 6B) and, after conversion, the temperature dependence of the equilibrium constant $K_p'$ (Fig. 6C). The PE spectroscopic results can be compared with thermodynamic data from the literature[56] as well as with the MNDO energy hypersurface calculated along the coordinate $\xi$ using highly simplifying assumptions (Fig. 6D). According to the latter, P$_4$ and P$_2$ lie in comparatively deep "potential energy troughs"; the difference in their MNDO total energies is very near to the considerable experimental dissociation energy of 217 kJ/mol[56]. These findings are consistent with the observed low reactivity of $P_4$ and $P_2$; thus according to further PE spectroscopic investigations[65] the equilibrium mixture does not react with cyanogen even at 1250 K:

$$\{P_4 \rightleftarrows 2\,P_2\} + NCCN \overset{\text{to 1250 K}}{\nrightarrow} P(CN)_3,\ (NC)_2PP(CN)_2\ldots \quad (5)$$

Using the assembly kit for the apparatus (Section 3.2), reactions such as (5) can also be tested PE spectroscopically on a millimole scale within one day, and—if necessary—their reaction conditions optimized.

Table 3. A selection of PE spectroscopically analyzed thermal decompositions arranged according to increasing molecular weight of the "leaving" molecule (set off in the formulas); further decomposition products are indicated by broken lines.

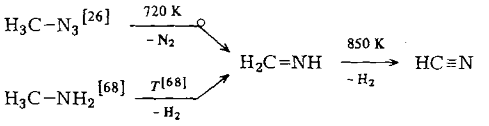
| Leaving molecule | Examples |
|---|---|
| HH |  [68], [26, 68], [70] |
| $CH_4$ |  [73] |
| HOH |  [73], [71], [72] |
| HCN |  [65], [73] |
| NN |  [74, 75], [67], [25, 62, 67, 76], [77], [78] |
| CO |  [27], [72], [72] |
| NO |  [79] |
| HSH |  [80], [19], [20, 73] |
| HCl |  [73], [21, 73], [81], [13, 81], [67], [67] |
|  |  [73], [73], [49,58] |
| OCO |  [81], [74], [83], [81] |
| OSO |  [84], [84], [84] |

### 4.2. Investigation of Thermal Reaction Channels

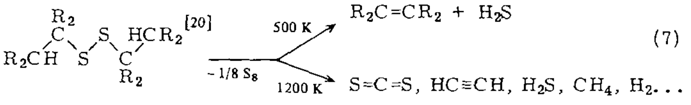
Pyrolyses in flow systems can be excellently monitored using PES gas phase analysis: the bands present vanish, new ones appear, and the temperature dependent changes allow one to optimize the conditions of decomposition, and to identify decomposition products by means of their ionization patterns. As an admittedly extreme example the pyrolysis of vinyl azide, which explodes at 70 °C[66], yielding 2*H*-azirine[66] and/or acetonitrile[57] (Fig. 7C and D) will be presented here and discussed using a section of an energy hypersurface (Fig. 7A and 7B) which has been calculated in advance.

The temperature dependent rearrangements of vinyl azide expected from the partial $C_2H_3N$-hypersurface (Fig. 7B) can be detected PE spectroscopically (Fig. 7D) if the experiments are carried out in a suitable way (Fig. 7C): the pyrolysis of vinyl azide leads, with $N_2$ elimination, mainly to 2*H*-azirine at temperatures below 650 K and to increasing amounts of acetonitrile above 650 K. Whether these two pyrolyses occur simultaneously or *via* 2*H*-azirine as an intermediate product cannot be established by the decomposition of 1,2,3-triazole, either: the $N_2$-elimination from the five-membered ring requires a higher decomposition temperature of 820 K, at which acetonitrile is observed exclusively[67].

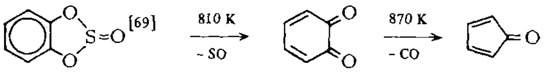
Other PE spectroscopically optimized gas phase pyrolyses (cf. Table 3) also shown several thermal decomposition channels. Examples are reactions (6)—(8).



(6)



(7)



(8)

Evidently reactions of different starting materials such as $H_3C—N_3$[26] and $H_3C—NH_2$[68] can proceed *via* the same decomposition channel (6), or one precursor such as R—SS—R[20] or $H_4C_6O_2SO$[69] can exhibit different decomposition channels as a function of temperature [(7) and (8)]. These can be independent of one another as in (7) or presumably follow each other as in (6), (8) and the reaction in Figure 7. The molecular skeleton remains unchanged at low decomposition temperatures; at higher temperatures rearrangements occur more frequently, finally leading to formation of the thermodynamically most stable products. The formation of $CS_2$ from a dialkyl disulfide, which lacks a C-atom with two CS-bonds, as observed in (7), ought to warn against hasty formulations of thermal decomposition mechanisms.

Published decomposition temperatures often differ considerably [cf. *e.g.* for (6)[26,28] or for (8)[69]], since they depend on the working pressure or on the kind of apparatus

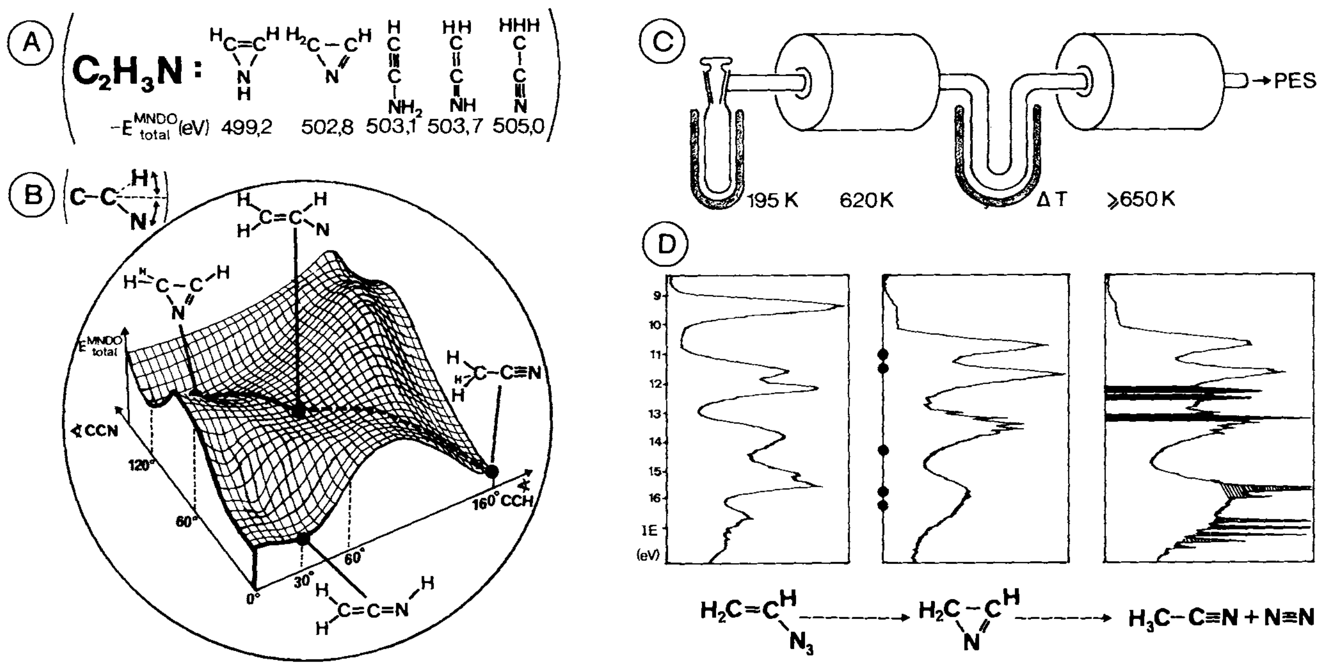
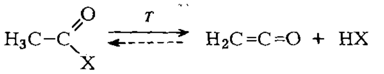


Fig. 7. A) Among its topologically possible constitutional isomers the ensemble $C_2H_3N$ comprises five molecules of "normal valence" as shown above; according to their MNDO total energies, their stability increases from 1*H*-azirine to acetonitrile. For $n=6$ atoms, a twelve-dimensional hyperspace is formed according to the $3n-6$-rule: using the angle changes Δ∢ CCN and Δ∢ CCH as coordinates, and subsequently performing a force field geometry optimization for each structure, the section B) can be calculated as an MNDO-total-energy (partial) hypersurface [57]: passing over the lowest barrier, vinyl nitrene $H_2C{=}CH\ddot{N}$, which also belongs to the $C_2H_3N$ ensemble, ought to close the ring to form 2*H*-azirine as shown in the illustration (unbroken line), and at still higher temperatures, the latter should open the ring again to form acetonitrile (broken line). In order to test this prediction, small amounts of vinyl azide (which detonates at 70 °C) were synthesized following a known procedure [66] by first reacting Cl—$H_2C$—$CH_2$—OTos with $NaN_3$ and treating the resulting Cl—$H_2C$—$CH_2$—$N_3$ with KOH. C) Vinyl azide can be vaporized without decomposition from a cooling trap at 195 K and its PE spectrum (D) can be registered [57]. By heating the quartz reaction tube filled with quartz wool to 620 K in the first oven, freezing out all condensable pyrolysis products in a U-tube cooled to 77 K and subsequent fractionated vaporization it is possible to measure the PE spectrum of 2*H*-azirine [57] (D) assigned according to $IE_n = -\varepsilon_J^{MNDO}$ (●). If the cooling bath is removed from the U-tube, and the second oven in C) is heated to temperatures above 650 K, the continuously registered PE spectra increasingly show the characteristic bands of acetonitrile (black) besides those of 2*H*-azirine (white) and $N_2$ (shaded bands) [57].

used, especially as regards diameter, length, and filling of the pyrolysis tube. In contrast to this, relative temperatures can often be given to within ±10° for comparable conditions of thermolysis using the same apparatus and internal calibration, *i.e.* reading off the temperature always at the same PES peak heights of educt and product. It is remarkable that the lowest thermal decomposition channel such as (7) at 500 °C often yields uniform products such as the alkenes. This finding is surprising in view of the usually obscure energy transmission *via* wall contacts and/or molecular collisions, and the generally unknown partition function for the vibrational and rotational degrees of freedom. The preparative possibilities to be found here are increasingly made use of, *e.g.*, in the "flash vacuum pyrolysis" technique[50-52]. A selection of the many PE spectroscopically analyzed gas phase thermolyses (Table 3) is most suitably arranged according to the smaller "leaving" molecules eliminated in each case.

The "leaving molecules" found in the Table range from molecular weight 2 (HH) to 64 (OSO); the examples chosen (cf. reviews such as [3,4,47,50,51]) together with the thermolyses (6) to (9), are only intended to illustrate the possible scope of application: Thus, cyclic sulfites, apart from $SO_2$[84] (see Table 3), can eliminate SO[69] [see (8)]. Unsaturated hydrocarbons are represented here by propene alone (Table 3), since experience has proven its value as an excellent leaving group in the gas phase generation of unstable species such as thioacrolein $H_2C{=}CH{-}HC{=}S$[73] or silabenzene $C_5SiH_6$[49,58] (Section 4.3), and since the allylic function is easily introduced into compounds, *e.g.*, *via* Grignard reactions. Special mention must be made, *e.g.*, of acetylene, which occurs as a thermodynamically favored pyrolysis product at higher temperatures[20,73]. The likewise favorable elimination of HCN has been little investigated so far; furthermore, there is a lack of PE spectroscopically determined elimination temperatures for common "leaving" molecules (Table 3) for a comparable type of reaction, such as the formation of ketene from carboxylic acid derivatives[73] [Reaction (9)].

 (9)

$$H_3C{-}C(=O)X \underset{}{\overset{T}{\rightleftarrows}} H_2C{=}C{=}O + HX \qquad (9)$$

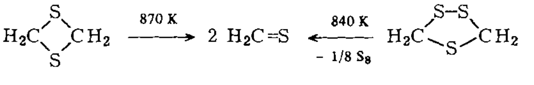
| HX | $HOCOCH_3$ | HCl | HBr | HOH | $HOC_2H_5$ | $HCH_3$ ... |
|---|---|---|---|---|---|---|
| *T* [K] | 570 | 580 | 650 | 720 | 740 | 1130 |

In this context the empirical inquiry into favorable *"thermal leaving molecules"* for specific thermolyses is of special interest. However, a numerical comparison is difficult (the heats of formation of the elements are zero by definition). As one of the "rules-of-thumb" in circulation the classification of di- and tri-atomic species *M* according to the sum of their bond dissociation energies $\sum D(XY)$ might be mentioned, which *e.g.* for HCN consists of

$HCN \rightarrow H^{\odot} + CN^{\odot} \rightarrow C + N^{\odot}\ (+H^{\odot})$[85]:

| *M* | HCN | CO | $SO_2$ | $N_2$ | $H_2O$ | $H_2S$ | HCl | HBr... | |
|---|---|---|---|---|---|---|---|---|---|
| $\sum D(XY)$ [kJ/mol] | 1270 | 1075 | 1070 | 949 | 920 | 720 | 431 | 364 | (10) |

For larger molecules, better quantitative criteria are the sums of the energies of all bonds formally involved in the decomposition, supplemented by contributions *e.g.* from reduced steric hindrance or $\pi$ systems formed[85]. The simplicity of PE spectroscopic analysis must be stressed here, which with only 1 mmol, and using an apparatus (Fig. 5) readily constructed from an assembly kit usually yields the *experimental result* in a single day!

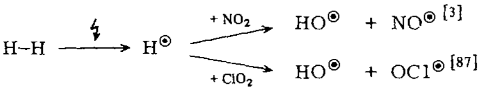


(11)

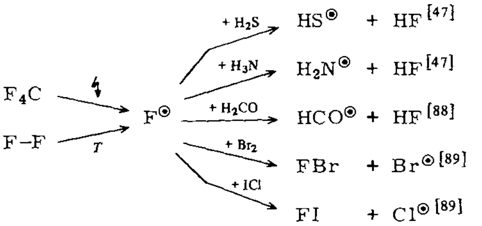
Thermal decompositions which give rise to only one volatile product, such as *e.g.* in (11)[22,71], are especially advantageous in generating short-lived molecules (Section 4.3) such as thioformaldehyde[13], first detected in interstellar space.

### 4.3. Detection of Reactive Intermediates

The detection method discussed previously—one registers changes in the PE spectroscopic band patterns (Fig. 1) of a flowing gas (Fig. 4 or 5) while varying the reaction conditions (Fig. 6 or 7) — is well suited for the detection of numerous atoms and molecules which cannot be "put into bottles" at room temperature (Table 4). Both the given conditions of the apparatus (vacuum, comparatively small amounts of the compounds, species being usually formed in their neutral ground state) and the possibility of identifying the reactive intermediates by Koopmans correlations[16] with their calculated ionization patterns $-\varepsilon_J^{SCF} = IE_n^V$ [cf. (3) or Fig. 2] are particularly advantageous.



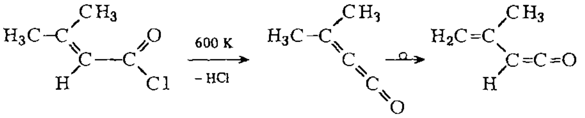
(12)



(13)

Usually the particles formed have a rather high energy, with only a few exceptions such as $O_2N{-}NO_2$[61] which is produced by cooling; they are predominantly generated using three methods: external heating of the gaseous flow, if necessary up to 2900 K[47], electrodeless microwave discharge[3,47] (Table 4: ↯), or reaction (Table 4: R) with atoms such as $H^{\odot}$[3,47,86,87] or $F^{\odot}$[3,47,88,89] formed thermally or in discharges.

A disadvantage of the microwave method is the high electron and energy density in the discharge zone, which is about 5 cm long[3,47]. Often the desired product is formed unspecifically in admixture with others, so that special methods of evaluation[3,47], such as "spectra stripping"[68], must be used in order to separate the overlapping PES bands. In comparison, reactions of atoms from microwave discharges such as $H^{\odot}$ and $F^{\odot}$ [reactions (12) and (13)] show a more homogeneous behavior[3,47]. The detection of short-lived species requires as short as possible a distance between reaction zone and ionization chamber: at a minimum distance of 1 cm particles with half-lives of about $10^{-3}$ s ought to be observable according to an estimation of the gas flow rate[26]. Thus during the thermal elimination of HCl from 3-methylcrotonic chloride the PE spectrum of the more stable tautomeric vinyl ketene is observed instead of that of the first formed isopropylidene ketene, if the distance from the pyrolysis tube to the place of measurement exceeds approximately 20 cm [reaction (14)][81].



(14)

Many transients, however, possess longer lifetimes, ranging from the order of minutes, such as HN=NH, to several hours, such as S=S=O (cf. *e.g.* the literature cited in [3]).

Since 1970, many types of "reactive intermediates" have been identified and characterized PE spectroscopically: atoms, radicals, radical anions such as $H_2C^{\cdot -}$[90], valence unsaturated molecules (Table 4), up to molecules such as $O_3$[91] or $O_2N{-}NO_2$[61], which under standard conditions quickly react to form thermodynamically more favorable products. A representative selection is presented in Table 4 (cf. [3,10,47] as well as Section 4.2).

The lifetimes of the compounds listed in Table 4 range from short-lived $^{\odot}NF_2$ or also the vibrationally excited nitrogen molecule[3,128] to those that can be isolated in pure form for short times or at low temperatures such as OOO or HCP. Many of them are not generated by thermal decomposition (Section 4.2) or in a microwave discharge [reactions (12) and (13)], but *via* the reaction of gases with solids, thus:

Table 4. "Reactive intermediates" of molecular size $M$ (x = number of atoms) which have been identified and characterized PE spectroscopically, listed according to increasing group and periodic numbers of the elements. Radicals are characterized by $M^{\odot}$, special, *i.e.* non-thermal, ways for their generation by (⊙) for (microwave) discharge and (R) for chemical reaction.

| x | *M* | Examples |
|---|---|---|
| 1 | A | H (↯) [86], N (↯) [86], O (↯) [86, 92], F [89] (↯) [3, 47, 88], Cl (↯) [3], Br (↯) [3], Ba [3, 93], Zn [3, 4, 93] |
| 2 | AB$^{\odot}$ | HO$^{\odot}$ (R) [3, 47], HS$^{\odot}$ (R) [47], OCl$^{\odot}$ (R) [87], OBr$^{\odot}$ (R) [47] |
|  | AA | OO (↯→singlet $^1\Delta_g$) [3, 94], PP [3, 47, 56], SS [3, 95], SeSe [95], TeTe [95], ArAr [96], KrKr [96], XeXe [96] |
|  | AB | CS (↯) [97], SiO [3, 47], GeO [98], GeS [99], SnS [99], PbTe [99], NP [100], NS [101] (↯, R) [101], OS (↯, R) [102], FBr [89], FI [89] |
| 3 | AB$_2^{\odot}$ | NF$_2^{\odot}$ [103], O$_2$Cl$^{\odot}$ [103] |
|  | ABC$^{\odot}$ | HCO$^{\odot}$ [88] |
|  | AAA | OOO [91] |
|  | AB$_2$ | H$_2$C$^{\cdot -}$ [90], CF$_2$ [91], SiF$_2$ (R) [104], OCl$_2$ [105], OS$_2$ (R) [53, 106], F$_2$S (R) [107] |
|  | ABC | HBS (R) [108], BSCl (R) [109], HCP (↯) [110], CFP [111] |
| 4 | *M*$^{\odot}$ | H$_3$C$^{\odot}$ (R) [74, 79, 112] |
|  | *M* | H$_2$CS [13, 73, 113], HNNH (↯) [70], HNSO (R) [59], NSSN [114] |
| 5 | *M*$^{\odot}$ | O$_3$FS$^{\odot}$ [103] |
|  | *M* | H$_2$CNH [26, 68], H$_2$CCS [19], H$_2$CCSe [25, 72, 76, 115], H$_2$CSO [73, 82] |
| ≥6 | *M*$^{\odot}$ | H$_5$C$_2^{\odot}$ [79], H$_5$C$_3^{\odot}$ [116], H$_9$C$_4^{\odot}$ [74, 117], H$_7$C$_7^{\odot}$ [118], H$_5$C$_6$O$^{\odot}$ [119], (F$_3$C)$_2$NO$^{\odot}$ [103] |
|  | *M* | (cf. Table 3), quinodimethane [120], cyclobutabenzene [121], 1-substituted silabenzene [49, 58], R$_2$CNR [122], 6-methylene-2,4-cyclohexan-1-one [124], (RCOOH)$_2$ [123], R$_2$CCCO [81], R$_2$CS [125], R$_2$CCS [126], R$_2$CCSe [73, 127], N$_2$O$_4$ [61] |

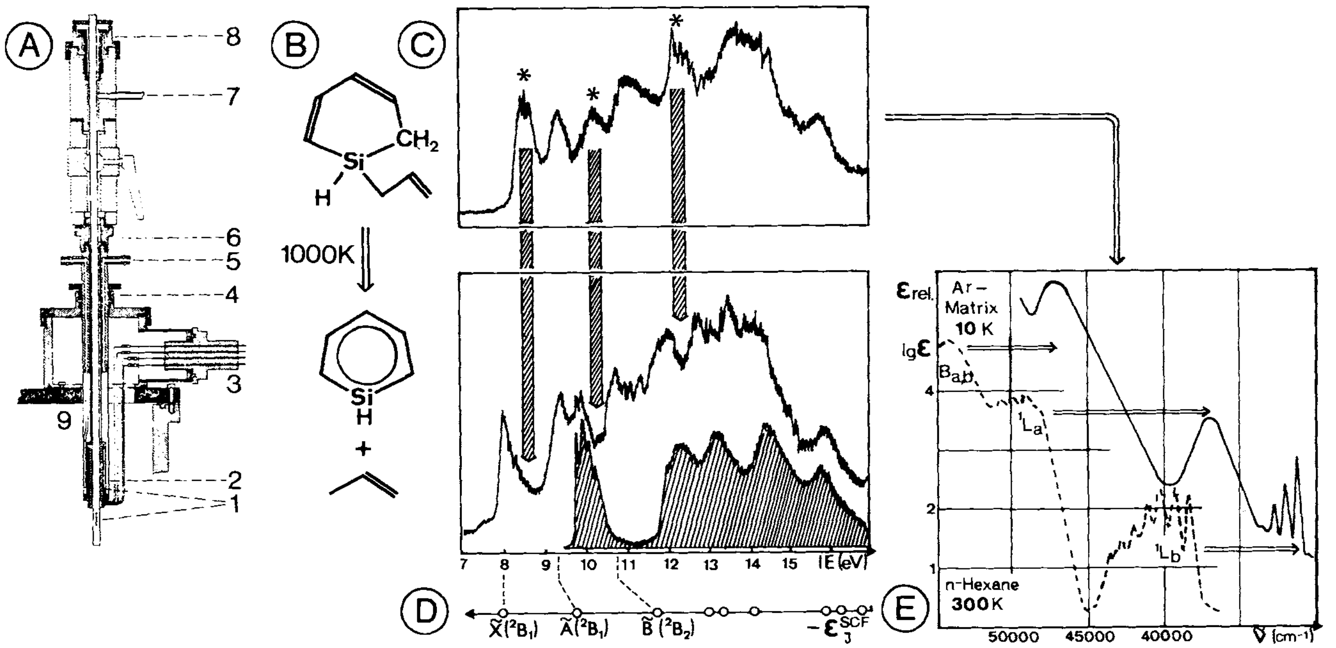


Fig. 8. PE spectroscopic detection of silabenzene [49] and its matrix isolation [131]: A) short path pyrolysis apparatus (1. Furnace over electron exit slit, 2. water cooling mantle, 3. current feed, 4. locking nut, 5. water cooling, 6. centering device, 7. backing pump connection, 8. adjusting device for internal tube, 9. PE spectrometer cavity); B), the precursor 1-allyl-1-sila-2,4-cyclohexadiene, which splits off propene quantitatively at an oven temperature of 1000 K; C) PE spectra (*: vanishing bands, shaded area: PE spectrum of propene, to be substracted); D) assignment of the three lowest radical cation states by means of an SCF calculation with a 2s(H), 7s/3p(C) and 9s/5p(Si) basis set; E) UV-spectrum of silabenzene in an Ar matrix at 10 K with band displacements of 8100, 12200 and 7000 cm⁻¹ relative to UV spectrum of benzene (broken lines).

$$\begin{array}{llll} H_2S & + (B)_\infty & \rightarrow HBS + H_2 & [108] \\ SiF_4 & + (Si)_\infty & \rightarrow SiF_2 & [104] \\ OSCl_2 & + (Ag_2S)_\infty & \rightarrow OSS + (AgCl)_\infty & [53, 106] \\ F_3CPH_2 & + (KOH)_\infty & \rightarrow FCP + (KF+H_2O)_\infty & [111] \end{array} \qquad (15)$$

In conclusion, the usefulness of PE spectroscopic investigations for the preparative isolation of a reactive intermediate will be discussed using silabenzene as an example (Table 3 and Fig. 8).

As a 6π-electron system of $C_{2v}$ symmetry, silabenzene has been the aim of numerous theoretical and experimental efforts[129]: SCF calculations have suggested its viability[49]; π ionization energies of 8.2, 9.2 and 11.5 eV were predicted from perturbation treatments[7]. However, attempts to thermolize derivatives of 1-sila-2,4-cyclohexadiene $H_7C_5SiX$ for a long time met without success because of unfavorable choice of leaving groups such as HCl [see (10)]. It was only the elimination of propene that made it possible to trap adducts[129]. The detection of silabenzene[49,58] was accomplished in the short path pyrolysis apparatus shown (Fig. 8 A). The assignment of the PE spectrum relies on an SCF calculation with a large basis set[130] (Fig. 8 C and 8 D). Using PE spectroscopically optimized conditions for the pyrolysis, the mass spektrum could be subsequently measured[130], and the preparative isolation accomplished[131]. The comparison of the UV spectrum recorded in an Ar matrix at 10 K with that of benzene (Fig. 8 E) leads us full circle: as can be calculated, the perturbations[130] show that silabenzene has a similar π electron system as benzene.

### 4.4. Testing Gas Phase Syntheses

Stoichiometric reactions of gases can often be adjusted and examinated advantageously by means of PE spectroscopy: thus one succeeds in obtaining a pure gaseous flow of the reactive intermediate sulfinylimide O=S=NH[59] (Fig. 9 and Table 4).

The gas + gas synthesis of OSNH (Fig. 9) complements the already discussed types of reactions of gases such as pyrolyses (Figs. 6—8 and Tables 2—4), discharges [Table 4 and (12), (13)] or reactions with solids [Table 4 and (15)]. Thus PE spectrometers are in general well suited for monitoring gaseous streams of pure compounds, for example to simplify the determination of structures by microwave and especially electron diffraction methods.

Gas + gas reactions can formally be subdivided into acid/base and redox reactions. Of the numerous possible applications the following should be emphasized:

⇒ detection and characterization of donor/acceptor complexes (Lewis base/Lewis acid adducts) in the gas phase, *e.g.*

$$\begin{array}{l} R_3N + Br_2 \rightarrow R_3N\cdot Br_2 \; [132] \\ R_2O + HCl \rightarrow R_2O\cdot HCl \; [133] \end{array} \qquad (16)$$

⇒ separation of gases *via* the formation of salts, *e.g.* according to

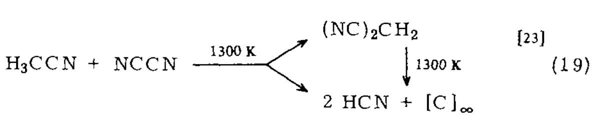
$$H{-}M{-}Cl \xrightarrow{\Delta T} \{M + HCl\} \xrightarrow{NH_3} [NH_4^{\oplus}\, Cl^{\ominus}]_\infty + M \qquad (17)$$

In this way it is possible to register the PE spectra of pure compounds such as $M = H_2C{=}S$[13], $H_2C{=}S{=}O$[73,82] or $R_2C{=}C{=}O$[73,81].

⇒ syntheses of new compounds (cf. Fig. 9), *e.g.*:

$$H_3C{-}NH_2 + SCl_2 \xrightarrow{NH_3} H_3C{-}NS + 2\,[H_3C{-}NH_3^{\oplus}\,Cl^{\ominus}]_\infty \;[54]$$
$$P_4 + 8\,NO + [C]_\infty \xrightarrow{1800\,K} 4\,PN + 2\,N_2 + 8\,CO \;[100] \qquad (18)$$

⇒ fast elucidation of gas phase reactions, *e.g.*:



$$H_3CCN + NCCN \xrightarrow{1300\,K} (NC)_2CH_2 \;[23] \xrightarrow{1300\,K} 2\,HCN + [C]_\infty \qquad (19)$$

Evidently a thermal synthesis of malononitrile from acetonitrile and cyanogen is thwarted by the fact that at the temperature necessary for the reaction the desired product already decomposes to hydrocyanic acid and graphite [cf. (10)].

The last mentioned possible application of PES analysis—elucidation of gas phase reactions including their temperature dependence within a few hours—will probably become more important with the availability of portable PE spectrometers (Fig. 4C), especially for the testing of solid state contacts for heterogeneously catalyzed gas phase reactions (Section 4.5).

### 4.5. Testing Solid State Catalysts for Gas Phase Reactions

This last section dealing with "examples of PE spectroscopically optimized gas phase reactions" should be regarded as an outlook on future developments of preparative syntheses, since according to the literature only the following three heterogenous catalyses have so far been worked out using PE spectroscopic analysis:

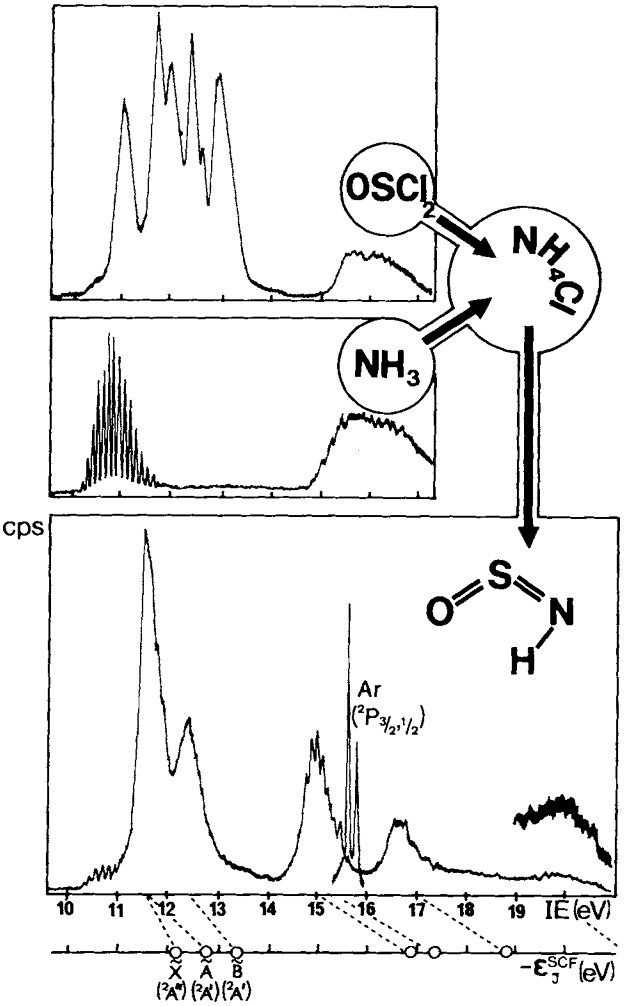
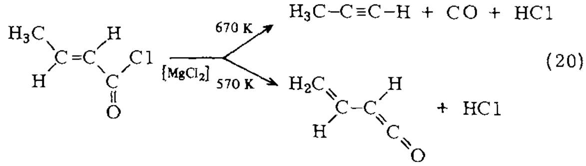
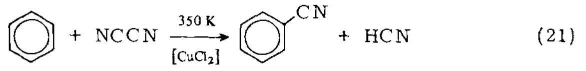


Fig. 9. The PE spectroscopically controlled gas phase synthesis of sulfinylimide: ammonolysis of sulfinyl chloride occurs both spontaneously and quantitatively upon mixing the gaseous reactants in a reaction flask. The PE spectra of the precursors and the product which do not overlap in essential regions allow one to quickly adjust the 3 : 1 stoichiometry, and to monitor it continuously. In the OSNH spectrum chosen here one recognizes a small excess of $NH_3$ by the band with its vibrational fine structure at 10.5 to 11 eV. The PE spectrum, calibrated with the Ar double peak (15.76/15.94 eV) has been assigned using an SCF calculation [59]; according to it one expects still within the He(I) range a seventh radical cation state of OSNH which can be recognized at 20.15 eV with a higher count rate.

⇒ reduction of the pyrolysis temperature of crotonic acid chloride; the catalyst is $MgCl_2$ or "didymium chloride" on γ-aluminum oxide[10,73]:



⇒ cyanylation of benzene; catalyst $CuCl_2$ (partially reduced) on γ-aluminum oxide[46]:



⇒ bromination of trifluoromethane (Fig. 10); catalyst $CuF_2$ (from $CuCl_2$ by heating in an $F_3CH$ stream, 800 K, 5h) on charcoal[24]:

$$F_3CH + Br_2 \xrightarrow[\text{[CuF}_2\text{]}]{400\,K} F_3CBr + HBr \qquad (22)$$

The gas phase bromination of trifluoromethane is of technical interest, since the bromotrifluoromethane formed is used as an effective fire extinguishing agent for the protection of valuable goods. The search for suitable catalysts is worthwhile because of the corrosion problems at higher reaction temperatures. Their effectiveness is judged from the temperatures at which the PE bands of $Br_2$ and HBr are at the same height (Fig. 10). An additional advantage of PES analysis is the possibility of recognizing the initial fluorination, at high temperatures, of oxidic carriers by $F_3CH$ *via* the appearance of bands of $H_2O$, CO or $CO_2$. The exactness which can be obtained with PE spectroscopy does not exceed ±2% even in favorable cases[23] so that subsequently a refining optimization on a preparative scale had to be carried out using conventional recycling apparatus[24]. Nevertheless, there results a considerable saving of time when searching for catalysts: two tests per day and per PE spectrometer can be carried out over the temperature range of interest. Furthermore, "real time" gas analysis with a PE spectrometer set up near the catalyst zone responds without delay to the ratio of reactants, which can be adjusted smoothly at the valves.

## 5. Outlook: PE Spectroscopic Gas Analysis as a Complementary Method and as a Measuring Procedure Capable of Development

Many different methods of measurement are available for the analysis of gases in flow systems, among which gas chromatography (GC)[134,135], mass spectrometery (MS)[136-138] and vibrational spectroscopy[139-140] are well established and have been abundantly applied. With reference to PE spectroscopic gas analysis, as presented above, one must therefore inquire which advantages and disadvantages these methods possess, broadly speaking, and to what extent they complement each other.

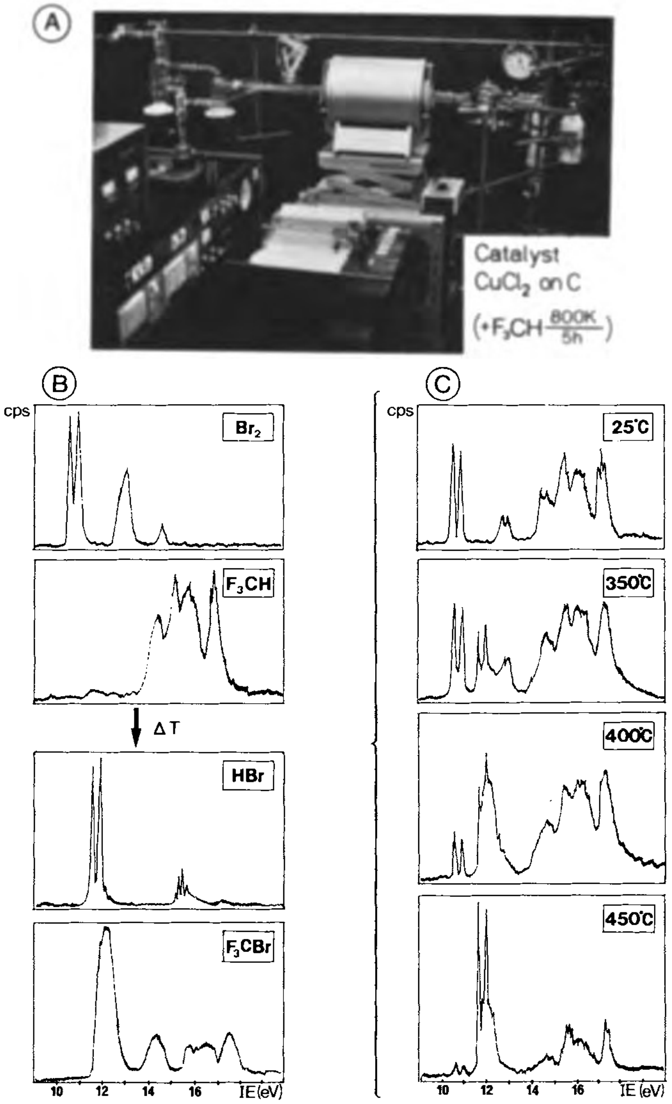


Fig. 10. The PE spectroscopic optimization of the heterogeneously catalyzed thermal bromination of trifluoromethane. A) Apparatus (from right to left): steel bottles with $F_3CH$ and $Br_2$, mixing bulb filled with Raschig rings, adjustable oven, capillary tube outlet into the PE spectrometer (cf. Fig. 5), cold traps and (not visible) oil pump. B) PE spectra of the components of the reaction, the band patterns of which obviously do not overlap completely. Particularly advantageous for gas analysis are the double peaks of HBr and $Br_2$ (cf. Fig. 1). C) Temperature dependence of the course of the Cu-catalyzed gas phase bromination: Increase and decrease of all components of the reaction can be monitored by comparison with the spectra of the pure compounds in B.

*Gas chromatography:*

advantages: well suited for mixtures and their simultaneous separation, simple as far as the instrument is concerned[134, 135]

disadvantages: no real-time measurement, unknown compounds and especially reactive intermediates can be identified only with difficulty or not at all, no information on structures or states.

*Mass spectrometry:*

advantages: even big molecules can be identified by their isotopic patterns, high sensitivity[137], elaborate measuring techniques with many extensions such as chemical ionization[138], large data bank[136].

disadvantages: fragmentation patterns of unknown products only predictable under certain conditions, digitalization[136] required for quantitative analysis, no immediate structural information, instrumentation sometimes expensive.

*Vibrational spectroscopy:*

advantages: (to be differentiated for FIR, IR and Raman, with or without Fourier transform technique) "molecular fingerprint" method with information on structure and state, sensitive, suited for kinetic investigations.

disadvantages: selection rules require many small molecules to be IR inactive, interpretation of spectra *via* normal coordinate analysis difficult, especially FIR not well suited for hot gases (emissions!), instrumental expense sometimes high.

*Photoelectron spectroscopy:*

advantages: molecular "fingerprints" with information on structure and state, favorable interpretation of spectra with MO methods, instrumentally simple, well suited for temperature dependent investigations.

disadvantages: not well suited for multicomponent mixtures and large molecules.

As can be seen from this greatly simplified comparison, none of these methods for gas analysis is perfect in every respect. In practical applications combinations such as GC/MS or PES+MS have therefore proven valuable; in many cases GC/PES would also complement each other[142].

For photoelectron spectroscopy numerous extensions of the range of applications are either now available, under development, or conceivable. Thus negative ions in the gaseous phase[3,90] or molecules adsorbed on a surface[141] can be investigated with PE spectroscopy. Portable instruments for laboratory use (Fig. 4C) and extensive computer programs[45] (multiple scan, reduction and simulation of spectra, spectral data bank for comparison) are available or presently being developed. One would also appreciate the availability of multichannel analyzers for fast registration as well as simultaneous registration of many components. As a wild speculation, one might dream of miniaturized PES probes in the flow tube and especially in the reaction zone itself.

By means of photoelectron spectroscopy, our knowledge of radical cation states has been greatly extended over the past few years, quantum mechanical calculation techniques have been tested using ionization patterns, many reactive intermediates could be characterized for the first time, and, finally, heterogeneously catalyzed gas phase reactions are being optimized. Starting from this successful balance, one may expect for the future—together with systematic investigations *e.g.* of the margins of error—a further development of photoelectron spectroscopic gas phase analysis in flow systems.

*The Frankfurt photoelectron spectroscopy group thanks Professor Edgar Heilbronner "in cumulo" for much good advice, his interest and his advancement of our research. The investigations in PE spectroscopic gas analysis were carried out together with S. Aygen, G. Bert, R. Dammel, T. Hirabayashi, S. Mohmand, H. Müller, M. Pohlenz, U. Stein, and J. Wittmann, whose impetus and dedication should be emphasized. Here as well P. Rosmus and A. Semkov have contributed to the successful outcome with their quantum mechanical calculations, H. J. Arpe (Hoechst AG) and J. Mintzer with their advice for the development of catalysts. Joint ventures were carried out together with R. Appel (Bonn), T. J. Barton (Ames, Iowa), G. Becker (Marburg), E. Block (St. Louis, Missouri), L. Horner (Mainz), G. Maier (Giessen), W. Ried (Frankfurt), H. W.Roesky (Göttingen), J. Russow (Hoechst AG), and R. Steudel (Berlin). The University of Frankfurt and the State of Hesse provided the PE spectrometers and supported the investigations; we gratefully acknowledge the additional support of the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the Hoechst AG, the Max-Buchner- and Hermann-Schlosser-Foundations.*

Received: March 6, 1981 [A 363 IE]
German version: Angew. Chem. *93*, 425 (1981)
Translated by *R. Dammel*, Universität Frankfurt, Germany.

---

[1] *Karl Valentin* in "Tingeltangel", (transl. "Its still better than nothing at all"), cf. Gesammelte Werke, R. Piper & Co., München 1961, p. 147, or in *E. Heilbronner, H. Bock:* The HMO Model and its Application, Vol. 1, Verlag Chemie, Weinheim 1968, p. 386.

[2] *D. W. Turner, C. Baker, A. D. Baker, C. R. Brundle:* Molecular Photoelectron Spectroscopy, Wiley-Interscience, London 1970, give a first summary, together with hundreds of illustrated. He(I)-photoelectron spectra.

[3] *A. D. Baker, C. R. Brundle:* Electron Spectroscopy: Theory, Techniques and Applications. Vol. 1-3, Academic Press, London 1977 to 1979, gives a comprehensive survery of the topic, including X-ray photoelectron spectroscopy, in individual contributions written by experts. Special attention is drawn to the contribution by *J. M. Dyke, N. Jonathan, A. Morris:* Ultravoilet Photoelectron Spectroscopy of Transient Species, Vol. 3, p. 189f., and references cited therein.

[4] *J. W. Rabalais:* Principles of Ultraviolet Photoelectron Spectroscopy, Wiley & Sons, New York 1977, claims special mention among the numerous available monographs because of its comprehensive review of the literature, the interesting arrangement, and the lucid presentation.

[5] *E. Heilbronner*, laid the ground work for the photoelectron spectroscopy of organic compounds in fundamental publications. Of his more than 100 publications on "Applications of Photoelectron Spectroscopy" especially noteworthy are the summaries in Pure Appl. Chem. *7*, 9 (1971); in Isr. J. Chem. *10*, 143 (1972); in *R. Daudel, B. Pullman:* The World of Quantum Chemistry, D. Reidel, Dordrecht 1974, p. 211f., in [3] (together with *J. P. Maier*), in: Reports of the 6th Conference of Molecular Spectroscopy, Durham 1976; in Helv. Chim. Acta *60*, 2248 (1977) and references cited therein; in Phys. Scr. *16*, 202 (1977) (together with *T. B. Jones, E. Kloster-Jensen, J. P. Maier*).

[6] *H. Bock, B. G. Ramsey*, Angew. Chem. *85*, 773 (1973); Angew. Chem. Int. Ed. Engl. *12*, 734 (1973), report on the interpretation of the PE-Spectra of organic and non metallic-organic compounds by means of comparisons of equivalent states of chemically related compounds, based on simple MO-methods.

[7] *H. Bock*, Angew. Chem. *89*, 631 (1977); Angew. Chem. Int. Ed. Engl. *16*, 613 (1977) discusses, among other things, the interpretation of radical cation states by means of PE-spectra with use of molecular orbitals.

[8] In the Specialist Periodical Reports of the Chemical Society on Electronic Structure and Magnetism of Inorganic Compounds, Vol. 1 (1970) through Vol. 3 (1972), *A. F. Orchard, S. Evans,* and *A. Hamnett* give a comprehensive literature review on technical details of the apparatus as well as on the PE-spectra of small molecules.

[9] *K. Kimura, S. Katsumata*, Monograph 25, Res. Inst. Appl. Electricity, Hokkaido Univ., Sapporo, Japan 1978 give a useful compilation of PE-spectra of common organic molecules.

[10] On future trends see *e.g, H. Bock, B. Solouki, S. Aygen, G. Bert, T. Hirabayashi, S. Mohmand, P. Rosmus, J. Wittmann*, Nachr. Chem. Tech. Lab. *26*, 634 (1978); cf. also Chimia *32*, 434 (1978); J. Mol. Struct. *60*, 31 (1980).

[11] Cf. *H. Bock, P. D. Mollère*, J. Chem. Educ. *51*, 506 (1974).

[12] Cf. *E. Heilbronner, H. Bock:* Das HMO-Modell und seine Anwendung, Vol. 1, 2nd edit. Verlag Chemie, Weinheim 1978.

[13] Cf. *e.g. B. Solouki, P. Rosmus, H. Bock*, J. Am. Chem. Soc. *98*, 6054 (1976).

[14] *K. A. Ostoja-Starzewski, H. Bock*, J. Am. Chem. Soc. *98*, 8486 (1976).

[15] *G. Bieri, F. Burger, E. Heilbronner, J. P. Maier*, Helv. Chim. Acta *60*, 2213 (1977).

[16] According to *Koopmans'* theorem [2-12], $IE_n = -\varepsilon_j^{SCF}$, J = n ionizations correspond to the J doubly occupid molecular orbitals. The different effective nuclear charges for p- and s-electrons enter the SCF-calculations as parameters; cf. *e.g. J. A. Pople, D. L. Beveridge:* Approximate Molecular Orbital Theory, McGraw-Hill, New York 1970, p. 71: C(2p) 10.7 eV compared to C(2s): 19.4 eV or O(2p): 15.9 eV compared to O(2s): 32.4 eV. This is why SCF molecular orbitals used for the assignment of PE-spectra possess high p-atomic orbital contributions for low ionization energies and high s-atomic orbital contributions for high ionization energies. A pefect PE-spectroscopic example for s-type ionizations are the helium(II)spectra of organic molecules studied by *E. Heilbronner* et al. [5, 15].

[17] Cf. *e.g. F. Brogli, E. Heilbronner*, Helv. Chim. Acta *54*, 1423 (1971), and references cited therein.

[18] Cf. *e.g. K. Wittel, H. Bock, R. Manne*, Tetrahedron *30*, 651 (1974).

[19] *H. Bock, B. Solouki, G. Bert, P. Rosmus*, J. Am. Chem. Soc. *99*, 1663 (1977).

[20] *H. Bock, S. Mohmand*, Angew. Chem. *89*, 105 (1977); Angew. Chem. Int. Ed. Engl. *16*, 104 (1977).

[21] *H. Bock, T. Hirabayashi, S. Mohmand, B. Solouki*, Angew. Chem. *89*, 106 (1977); Angew. Chem. Int. Ed. Engl. *16*, 105 (1977).

[22] *H. Bock, B. Solouki, S. Mohmand, E. Block, L. K. Revelle*, J. Chem. Soc. Chem. Commun. *1977*, 287.

[23] *H. Bock, B. Solouki, J. Wittmann*, Angew. Chem. *90*, 985 (1978); Angew. Chem. Int. Ed. Engl. *17*, 932 (1978).

[24] *H. Bock, J. Mintzer, J. Wittmann, J. Russow*, Angew. Chem. *92*, 136 (1980); Angew. Chem. Int. Ed. Engl. *19*, 147 (1980).

[25] *H. Bock, S. Aygen, P. Rosmus, B. Solouki*, Chem. Ber. *113*, 3187 (1980).

[26] *H. Bock, R. Dammel, L. Horner*, Chem. Ber. *114*, 220 (1981); cf. *R. Dammel*, Diplomarbeit, Universität Mainz 1980.

[27] *H. Bock, U. Stein, W. Ried*, Chem. Ber. *114*, 673 (1981).

[28] Cf. *e.g. W. Ensslin, H. Bock, G. Becker*, J. Am. Chem. Soc. *96*, 2757 (1974).

[29] *M. Beez, G. Bieri, H. Bock, E. Heilbronner*, Helv. Chim. Acta *56*, 1028 (1973).

[30] *K. Wittel, H. Bock*, Chem. Ber. *107*, 317 (1974).

[31] *H. Bock, G. Wagner, K. Wittel, J. Sauer, D. Seebach*, Chem. Ber. *107*, 1869 (1974).

[32] Cf. here the reviews by *R. Janoschek and also R. Janoschek, H. Stoll:* Theorien auf dem Prüfstand, Nachr. Chem. Tech. Lab. *26*, 653 and 720 (1978), and references cited therein. For MNDO cf. *M. J. S. Dewar, W. Thiel*, J. Am. Chem. Soc. *99*, 4899 (1977) and *100*, 3607 (1978).

[33] *W. van Niessen, L. S. Cederbaum, W. Domcke, H. Diercksen*, J. Chem. Phys. *66*, 4893 (1977).

[34] *B. Beagley, V. Ulbrecht, S. Katsumata, D. R. Lloyd, J. A. Connor, G. A. Hudson*, J. Chem. Soc. Faraday Trans. II, *73*, 1278 (1977).

[35] Cf. *e.g. H. Bock, W. Kaim, A. Semkow, H. Nöth*, J. Am. Chem. Soc. *102*, 4421 (1980); *H. Bock, W. Kaim, ibid. 102*, 4429 (1980), and references cited therein.

[36] *H. Bock, J. Dörr, M. Haun, J. Mintzer*, unpublished; cf. Diplomarbeiten by *J. Dörr* and *M. Haun*, Universität Frankfurt 1981.

[37] *A. Schweig, H. Vermeer, U. Weidner*, Chem. Phys. Lett. *26*, 229 (1974), and references cited therein.

[38] *C. Müller, W. Schäfer, A. Schweig, N. Thon, H. Vermeer*, J. Am. Chem. Soc. *98*, 5440 (1976).

[39] *A. Schweig, N. Thon*, Chem. Phys. Lett. *38*, 482 (1976).

[40] *P. Dechant, A. Schweig, N. Thon*, J. Electron Spectrosc. Relat. Phenom. *12*, 443 (1977).

[41] *A. Schweig, N. Thon, H. Vermeer*, J. Am. Chem. Soc. *101*, 80 (1979); J. Electron Spectrosc. Relat. Phenom. *15*, 65 (1979), and references cited therein.

[42] *H. Bock, H. Müller*, unpublished; cf. *H. Müller*, Dissertation, Universität Frankfurt 1980.

[43] *B. Solouki, H. Bock*, unpublished. The program PESIMU is adapted for a PDP 11/40 and will be sent on request. Examples of applications can be found in the literature [10, 23].

[44] *D. C. Frost, F. G. Herring, A. Katrib, R. A. N. McLean, J. E. Drake, N. P. C. Westwood*, Can. J. Chem. *49*, 4037 (1971).

[45] *P. Rosmus, M. Grimm, R. Klein, B. Solouki, H. Bock*, unpublished.

[46] *H. Bock, B. Solouki, J. Wittmann, H.-J. Arpe*, Angew. Chem. *90*, 986 (1978); Angew. Chem. Int. Ed. Engl. *17*, 933 (1978).

[47] In addition to the review in [3] with 173 literature citations (!) see also *J. Dyke, N. Jonathan, A. Morris,* J. Electron Spectrosc. Relat. Phenom. *15,* 45 (1979), and references cited therein.

[48] Cf. also *A. Houle, J. L. Beauchamp,* J. Am. Chem. Soc. *100,* 3290 (1978), and references cited therein.

[49] *B. Solouki, P. Rosmus, H. Bock, G. Maier,* Angew. Chem. *92,* 56 (1980); Angew. Chem. Int. Ed. Engl. *19,* 51 (1980).

[50] For a recent review see especially: *R. F. C. Brown:* Pyrolytic Methods in Organic Chemistry, Academic Press, New York 1980. Details of the apparatus are summarized in Chapter 2, p. 21–43; cf. [51].

[51] Flash vacuum pyrolysis methods are summarized in *G. Seybold,* Angew. Chem. *89,* 377 (1977); Angew. Chem. Int. Ed. Engl. *16,* 365 (1977).

[52] Cf. also the detailed instructions for gas phase reactions in books on laboratory practice such as *G. Brauer:* Präparative anorganische Chemie, Vol. 1–3. 3rd Edit. Thieme, Stuttgart 1979–1981; *L. Kolditz:* Anorganikum. 8th Edit. VEB Deutscher Verlag der Wissenschaften, Berlin 1978.

[53] *H. Bock, B. Solouki, P. Rosmus, R. Steudel,* Angew. Chem. *85,* 987 (1973); Angew. Chem. Int. Ed. Engl. *12,* 933 (1973).

[54] *B. Solouki, P. Rosmus, H. Bock, H.-W. Roesky,* unpublished results. Generation of $(H_3C)_2N{-}N{=}S$ see *K. Emmert,* Diplomarbeit, Universität Frankfurt 1980.

[55] *H. Bock, W. Ensslin, F. Fehér, R. Freund,* J. Am. Chem. Soc. *98,* 668 (1976).

[56] *H. Bock, H. Müller,* unpublished; *H. Müller,* Dissertation, Universität Frankfurt 1980. The PE spectrum of $P_2$ has been observed by *D. K. Bulgin, J. M. Dyke, A. Morris,* J. Chem. Soc. Faraday Trans. II, *72,* 2225 (1976); cf. *A. W. Potts, K. G. Glenn, W. C. Price,* Faraday Discuss. Chem. Soc. *54,* 65 (1972). Thermodynamic data: Gmelins Handbuch der Anorganischen Chemie. 8th Edit. Phosphor, Part B, Verlag Chemie, Weinheim 1964.

[57] *H. Bock, S. Aygen, R. Dammel,* unpublished.

[58] *H. Bock, R. A. Bowling, B. Solouki, T. J. Barton, G. T. Burns,* J. Am. Chem. Soc. *102,* 429 (1980).

[59] *B. Solouki, P. Rosmus, H. Bock,* Angew. Chem. *88,* 381 (1976); Angew. Chem. Int. Ed. Engl. *15,* 384 (1976).

[60] *M. F. Lappert, J. B. Pedley, G. J. Sharp, N. P. C. Westwood,* J. Electr. Spectrosc. Relat. Phenom. *3,* 237 (1974); an excellent example for a dissociation equilibrium is the cyclopentadiene polymerization, cf. *A. Schweig, N. Thorn,* J. Electr. Spectrosc. Relat. Phenom. *16,* 1991 (1980).

[61] *T. Yamakazi, K. Kimura,* Chem. Phys. Lett. *43,* 502 (1976); cf. *T. H. Gan, J. P. Peel, G. D. Willett,* J. Chem. Soc. Faraday Trans. II *73,* 1459 (1977); *D. L. Ames, D. W. Turner,* Proc. R. Soc. London *A 348,* 175 (1976).

[62] *R. Schulz, A. Schweig,* Angew. Chem. *91,* 737 (1979); Angew. Chem. Int. Ed. Engl. *18,* 692 (1977) cf. also Tetrahedron Lett. *1979,* 59 and *1980,* 343.

[63] *T. H. Gan, J. B. Peel, G. D. Willett,* J. Chem. Soc. Faraday Trans. II, *73,* 965 (1977).

[64] *H. Bock, A. Tabatabai,* unpublished results; *A. Tabatabai,* Diplomarbeit, Universität Frankfurt 1976.

[65] *H. Bock, J. Wittmann,* unpublished results; *J. Wittmann,* Diplomarbeit, Universität Frankfurt 1977.

[66] Vinyl azide was synthesized according to the procedure of *R. H. Wiley, J. Moffat,* J. Org. Chem. *22,* 995 (1957); cf. the review by *G. L'abbé,* Angew. Chem. *87,* 831 (1975); Angew. Chem. Int. Ed. Engl. *14,* 775 (1975), and references cited therein, as well as the microwave structure by *R. Ford,* J. Am. Chem. Soc. *99,* 2389 (1977).

[67] *H. Bock, S. Aygen,* unpublished; cf. *S. Aygen,* Dissertation, Universität Frankfurt 1981.

[68] *J. B. Peel, G. D. Willett,* J. Chem. Soc. Faraday Trans. II, *71,* 1799 (1975). The observed higher decomposition temperatures of 1230 K and 1540 K are in part due to higher pressure and different oven arrangement (cf. [26]).

[69] *T. König, M. Smith, W. Snell,* J. Am. Chem. Soc. *99,* 6663 (1977); *V. Eck, G. Lauer, A. Schweig, H. Vermeer,* Z. Naturforsch. *A 33,* 383 (1978).

[70] *D. C. Frost, S. T. Lee, C. A. McDowell, N. P. C. Westwood,* Chem. Phys. Lett. *30,* 26 (1975); J. Chem. Phys. *64,* 4719 (1976).

[71] *V. Eck, A. Schweig, H. Vermeer,* Tetrahedron Lett. *1978,* 2433.

[72] *R. Schulz, A. Schweig,* Tetrahedron Lett. *1979,* 59.

[73] *H. Bock, T. Hirabayashi, S. Mohmand,* unpublished; cf. *S. Mohmand,* Dissertation, Universität Frankfurt 1981.

[74] *T. König, T. Balle, W. Snell,* J. Am. Chem. Soc. *97,* 662 (1975); *T. König, W. Snell, J. C. Chang,* Tetrahedron Lett. *1976,* 4569.

[75] *J. Dyke, N. Jonathan, E. Lee, A. Morris, M. Winter,* Phys. Scr. *16,* 197 (1977).

[76] *R. Schulz, A. Schweig,* Angew. Chem. *92,* 52 (1980); Angew. Chem. Int. Ed. Engl. *19,* 69 (1980); cf. also [72].

[77] *D. C. Frost, W. P. C. Westwood, N. H. Werstink, L. Cabelkova-Taguchi, J. Warkenkin,* Can. J. Chem. *55,* 3677 (1977).

[78] *A. Hotzel, R. Neidlein, R. Schulz, A. Schweig,* Angew. Chem. *92,* 751 (1980); Angew. Chem. Int. Ed. Engl. *19,* 739 (1980).

[79] *F. A. Houle, J. L. Beauchamp,* J. Am. Chem. Soc. *101,* 4067 (1979); cf. also Chem. Phys. Lett. *48,* 457 (1977).

[80] *W. Schäfer, A. Schweig,* Z. Naturforsch. *A 30,* 1785 (1975).

[81] *S. Mohmand, T. Hirabayashi, H. Bock,* Chem. Ber. *114,* (1981), in press.

[82] *E. Block, H. Bock, S. Mohmand, P. Rosmus, B. Solouki,* Angew. Chem. *88,* 380 (1976); Angew. Chem. Int. Ed. Engl. *15,* 383 (1976).

[83] *V. Eck, G. Lauer, A. Schweig, W. Thiel, H. Vermeer,* Z. Naturforsch. *A 33,* 383 (1978).

[84] *E. Block, E. R. Corey, R. E. Penn, T. L. Renken, L. K. Revelle, P. F. Sherdin, H. Bock, T. Hirabayashi, S. Mohmand, B. Solouki,* J. Am. Chem. Soc., in press; see also *H. Zacharias,* Diplomarbeit, Universität Frankfurt 1976.

[85] Cf. *e.g.* the tables of thermodynamic properties in the "Handbook of Chemistry and Physics", CRS Press, Cleveland/Ohio, which usually suffice for these estimations.

[86] *N. Jonathan, A. Morris, D. J. Smith, K. J. Ross,* Chem. Phys. Lett. *7,* 497 (1970); J. Chem. Phys. *53,* 3758 (1970); *54,* 4954 (1971).

[87] *D. K. Bulgin, J. M. Dyke, N. K. Fayad, A. Morris,* J. Chem. Soc. Faraday Trans. II, *75,* 456 (1979).

[88] *J. M. Dyke, N. Jonathan, A. Morris, M. J. Winter,* Mol. Phys. *39,* 629 (1980).

[89] *E. A. Colbourn, J. M. Dyke, N. K. Fayad, A. Morris,* J. Electron Spectrosc. Relat. Phenom. *14,* 443 (1978).

[90] *P. F. Zittel, G. B. Ellison, S. V. O'Neil, E. Herbst, W. C. Lineberger, W. P. Reinhardt,* J. Am. Chem. Soc. *98,* 3731 (1976).

[91] *J. M. Dyke, L. Golob, N. Jonathan, A. Morris, M. Okuda,* J. Chem. Soc. Faraday II, *70,* 1828 (1974). The PE spectrum of $O_3$ was published independently by *D. C. Frost, S. T. Lee, C. A. McDowell,* Chem. Phys. Lett. *24,* 149 (1973).

[92] Cf. also *J. A. R. Samson, V. E. Petrosky,* J. Electron Spectrosc. Relat. Phenom. *3,* 461 (1974); Phys. Rev. *A 9,* 2449 (1974); *P. M. Dehmer, J. Berkowitz, W. A. Chupka,* J. Chem. Phys. *59,* 5777 (1973).

[93] For the PE spectra of metal atoms cf. *e.g.* for Ba: *B. Brehm, K. Höfer,* Int. J. Mass Spectrom. Ion Phys. *17,* 371 (1975); for Zn/Cd: *T. E. H. Walker, J. Berkowitz, J. L. Dehmer, J. T. Waber,* Phys. Rev. Lett. *11,* 678 (1973).

[94] *N. Jonathan, A. Morris, M. Okuda, K. J. Ross, D. J. Smith,* J. Chem. Soc. Faraday Trans. II, *70,* 1810 (1974).

[95] *J. Berkowitz,* J. Chem. Phys. *62,* 4674 (1975); *J. M. Dyke, L. Golob, N. Jonathan, A. Morris,* J. Chem. Soc. Faraday Trans. II, *71,* 1026 (1975); for $Se_2$ and $Te_2$ cf. especially *D. G. Streets, J. Berkowitz,* J. Electron Spectrosc. Relat. Phenom. *9,* 269 (1976).

[96] *P. M. Dehmer, J. L. Dehmer,* J. Chem. Phys. *67,* 1774 (1977); *69,* 125 (1978)..

[97] Cf. *N. Jonathan, A. Morris, M. Okuda, K. J. Ross, D. J. Smith,* Faraday Discuss. Chem. Soc. *54,* 48 (1972); *G. H. King, H. W. Kroto, R. J. Suffolk,* Chem. Phys. Lett. *13,* 457 (1972); *D. C. Frost, S. T. Lee, C. A. McDowell, N. P. C. Westwood, ibid. 17,* 153 (1972).

[98] *E. A. Colbourn, J. M. Dyke, A. Fackerell, A. Morris, I. R. Trickle,* J. Chem. Soc. Faraday Trans. II, *74,* 2278 (1978).

[99] *M. Wu, T. P. Fehlner,* J. Am. Chem. Soc. *98,* 7578 (1976).

[100] *M. Wu, T. P. Fehlner,* Chem. Phys. Lett. *36,* 114 (1975); *D. K. Bulgin, J. M. Dyke, A. Morris,* J. Chem. Soc. Faraday Trans. II, *72,* 983 (1976).

[101] *J. M. Dyke, A. Morris, I. R. Trickle,* J. Chem. Soc. Faraday Trans. II, *72,* 147 (1976).

[102] *J. M. Dyke, L. Golob, N. Jonathan, A. Morris, M. Okuda, D. J. Smith,* J. Chem. Soc. Faraday Trans. II, *70,* 1818 (1974), and references cited therein.

[103] *A. B. Cornford, D. C. Frost, F. G. Herring, C. A. McDowell,* Faraday Discuss. Chem. Soc. *54,* 56 (1972); for $NF_2$ also J. Chem. Phys. *54,* 1872 (1971).

[104] *T. P. Fehlner, D. W. Turner,* Inorg. Chem. *13,* 754 (1974); *N. P. C. Westwood,* Chem. Phys. Lett. *25,* 558 (1974).

[105] *A. B. Cornford, D. C. Frost, F. G. Herring, C. A. McDowell,* J. Chem. Phys. *55,* 2820 (1971).

[106] *D. C. Frost, S. T. Lee, C. A. McDowell,* Chem. Phys. Lett. *22,* 243 (1973).

[107] *D. M. DeLeeuw, R. Mooyman, C. A. de Lange,* Chem. Phys. *34,* 287 (1978).

[108] *H. W. Kroto, R. J. Suffolk, N. P. C. Westwood,* Chem. Phys. Lett. *22,* 495 (1973); *T. P. Fehlner, D. W. Turner,* J. Am. Chem. Soc. *95,* 7175 (1973).

[109] *C. Kirby, H. W. Kroto, N. P. C. Westwood,* J. Am. Chem. Soc. *100,* 3760 (1978).

[110] *D. C. Frost, S. T. Lee, C. A. McDowell,* Chem. Phys. Lett. *23,* 472 (1973).

[111] *H. W. Kroto, J. F. Nixon, N. P. C. Simmons, N. P. C. Westwood,* J. Am. Chem. Soc. *100,* 446 (1978).

[112] *J. Dyke, N. Jonathan, E. Lee, A. Morris,* J. Chem. Soc. Faraday Trans. II, *72,* 1385 (1976), and references cited therein.

[113] *H. W. Kroto, R. J. Suffolk,* Chem. Phys. Lett. *15,* 545 (1972); *H. W. Kroto, B. M. Landsberg, R. J. Suffolk, A. Vodden, ibid. 29,* 265 (1974).
[114] *D. C. Frost, M. R. LeGeyt, N. L. Paddock, N. P. C. Westwood,* J. Chem. Soc. Chem. Commun. *1977,* 217.
[115] Selenoketene has already been prepared and its structure been determined: *A. Holm, C. Berg, C. Bjerre, B. Bak, H. Svanholt,* J. Chem. Soc. Chem. Commun. *1979,* 99, and references cited therein.
[116] *F. A. Houle, J. L. Beauchamp,* J. Am. Chem. Soc. *100,* 3290 (1978).
[117] *J. Dyke, N. Jonathan, E. Lee, A. Morris, M. Winter,* Phys. Scr. *16,* 197 (1977).
[118] *T. Koenig, J. C. Chong,* J. Am. Chem. Soc. *100,* 2240 (1978).
[119] *M. J. S. Dewar, D. E. David,* J. Am. Chem. Soc. *102,* 7389 (1980).
[120] *T. Koenig, R. Wielesek, W. Snell, T. Balk,* J. Am. Chem. Soc. *97,* 3225 (1975).
[121] *T. Koenig, D. Imre, J. A. Hoobler,* J. Am. Chem. Soc. *101,* 6447 (1979).
[122] *D. C. Frost, B. McDonald, C. A. McDowell, N. P. C. Westwood,* J. Electron Spectrosc. Relat. Phenom. *14,* 379 (1978).
[123] *R. K. Thomas,* Proc. R. Soc. London *A 331,* 249 (1972).
[124] *V. Eck, A. Schweig, H. Vermeer,* Tetrahedron Lett. *1978,* 2433.
[125] *H. W. Kroto, B. M. Landsberg, R. J. Suffolk, A. Vodden,* Chem. Phys. Lett. *29,* 265 (1974).
[126] Cf. *e.g. R. Schulz, A. Schweig,* Angew. Chem. *92,* 751, 752 (1980); Angew. Chem. Int. Ed. Engl. *19,* 739, 740 (1980).
[127] Cf. *e.g. R. Schulz, A. Schweig,* Angew. Chem. *92,* 52 (1980); Angew. Chem. Int. Ed. Engl. *19,* 69 (1980).
[128] *J. M. Dyke, N. Jonathan, A. Morris, T. J. Sears,* J. Chem. Soc. Faraday Trans. II, *72,* 597 (1976).
[129] *T. J. Barton, G. T. Burns,* J. Am. Chem. Soc. *100,* 5246 (1978).
[130] *H. Bock, G. Maier, P. Rosmus, B. Roth, B. Solouki,* unpublished.
[131] *G. Maier, G. Mihm, H. P. Reissenauer,* Angew. Chem. *92,* 58 (1980); Angew. Chem. Int. Ed. Engl. *19,* 52 (1980).
[132] *C. Utsunomiya, T. Kobayashi, S. Nagakura,* Chem. Phys. Lett. *39,* 245 (1976).
[133] *F. Carnovale, M. K. Livett, J. B. Peel,* J. Am. Chem. Soc. *102,* 569 (1980).
[134] Cf. *e.g. R. L. Grob:* Modern Practice of Gas Chromatography. Wiley, New York 1977.
[135] Cf. *e.g. G. Schomburg, F. Weeke, B. Weimann, E. Ziegler,* Angew. Chem. *84,* 390 (1972); Angew. Chem. Int. Ed. Engl. *11,* 366 (1972), and references cited therein.
[136] Cf. *e.g. D. Henneberg, K. Casper, E. Ziegler, B. Weimann,* Angew. Chem. *84,* 381 (1972); Angew. Chem. Int. Ed. Engl. *11,* 357 (1972), and references cited therein.
[137] Cf. *e.g. W. D. Lehmann, H. R. Schulten,* Angew. Chem. *90,* 233 (1978); Angew. Chem. Int. Ed. Engl. *17,* 221 (1978), and references cited therein.
[138] Cf. e.g. *W. J. Richter, H. Schwarz,* Angew. Chem. *90,* 449 (1978); Angew. Chem. Int. Ed. Engl. *17,* 424 (1978), and references cited therein.
[139] Cf. *e.g. S. D. Ross:* Inorganic Infrared and Raman Spectra, McGraw-Hill, London 1972.
[140] Cf. *e.g. A. E. Martin:* Infrared Interferometric Spectrometers, Elsevier, New York 1980.
[141] Cf. *e.g. A. M. Bradshaw, L. S. Cederbaum, W. Domcke,* Struct. Bonding *24,* 133 (1975).
[142] *D. Betteridge, A. D. Baker, P. Bye, S. K. Hassannudin, N. R. Kemp, M. Thompson,* J. Electron Spectrosc. Relat. Phenom. *4,* 163 (1974).

# Structure and Bonding in Cyclic Sulfur-Nitrogen Compounds—Molecular Orbital Considerations

**By Rolf Gleiter**[*]

*Dedicated to Professor Edgar Heilbronner on the occasion of his 60th birthday*

The molecular structures of monocyclic sulfur-nitrogen ring systems, such as $S_2N_2$, $S_3N_3^{\ominus}$, $S_4N_3^{\oplus}$ and $S_5N_5^{\oplus}$, can be considered as examples of electron rich $(4n+2)\pi$ systems. The structures of $S_4N_4$, $S_4N_4^{2\oplus}$, $P_4S_4$, $As_4S_4$ and the bicyclic structures $S_4N_5^{\ominus}$, $S_4N_5^{\oplus}$ as well as $S_5N_6$ can be rationalized on the basis of a planar tetrasulfur tetranitride with $12\pi$ electrons.

## 1. Introduction

Since the fifties, when *Becke-Goehring et al.*[1] started a revival of sulfur-nitrogen chemistry, the syntheses and structures of a large number of cyclic and bicyclic ring systems containing sulfur and nitrogen only have been reported[2]. The recent discovery of the solid state properties of $(SN)_x$ and the observation that electron rich sulfur-nitrogen compounds can serve as donors in charge-transfer complexes has spurred interest in this class of compounds. From the viewpoint of an organic chemist, accustomed to relatively straightforward synthesis, the reported procedures of preparation very often seem strange and accidental. This can be seen from Figure 1, which shows schematically the most important paths from $S_4N_4$ to various cyclic sulfur-nitrogen compounds. The structural variety is also puzzling, at least at first glance. An attempt is made in the following to rationalize the structures of most mono- and bicyclic SN compounds based on a molecular orbital (MO) model, using arguments from perturbation theory[3]. The explanations put forward rest on molecular orbital calculations using semiempirical procedures or *ab initio* methods. Both types of calculation have been proven to be reliable, at least to rationalize the gross structural features. The compounds which will be discussed in detail are shown in Figures 2 and 3, together with their most relevant structural details.

## 2. Planar Rings and the Hückel Rule

If we divide the six valence electrons of sulfur and the five valence electrons of nitrogen in a planar ring system,

---

[*] Prof. Dr. R. Gleiter
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

0570-0833/81/0606-0444 $ 02.50/0

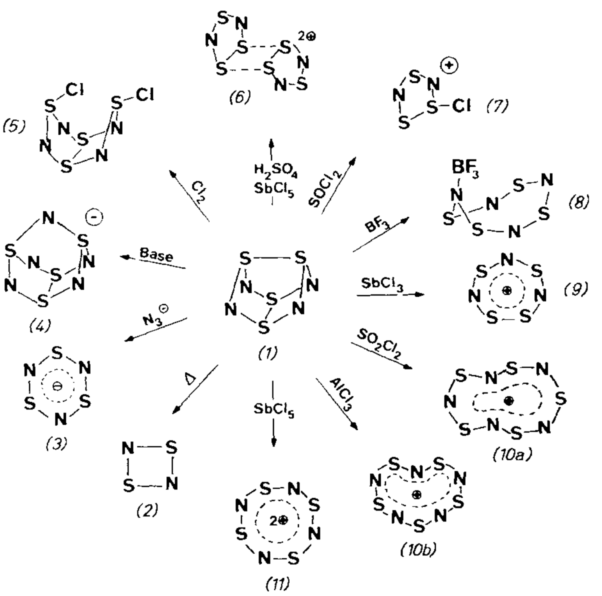


Fig. 1. Formation of various cyclic SN-compounds from $S_4N_4$.

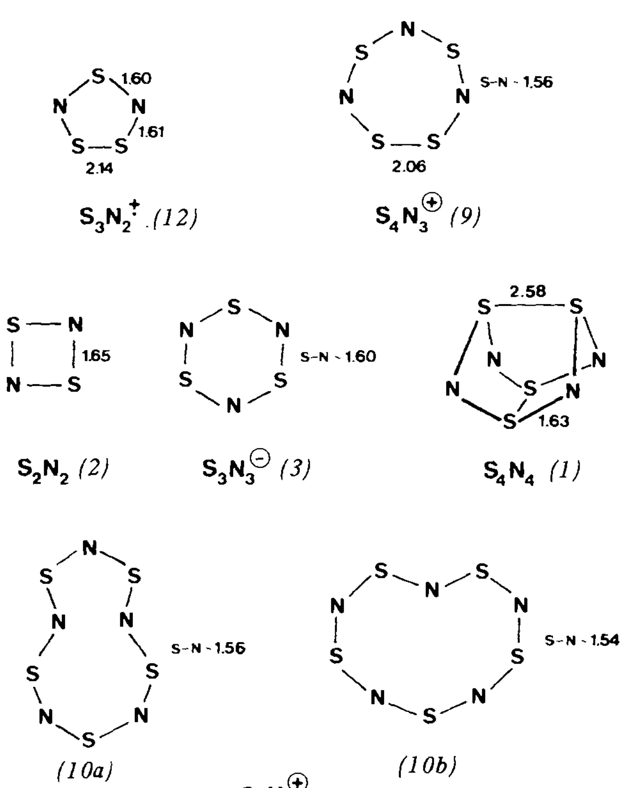
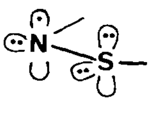


Fig. 2. Most prominent structural features of monocyclic SN-compounds of general formulae $(SN)_x$ and $S_2N(SN)_y$.

in such a way that each atom contributes one electron to a σ bond and two electrons to a lone pair, then two π-electrons are left on sulfur and one on nitrogen.



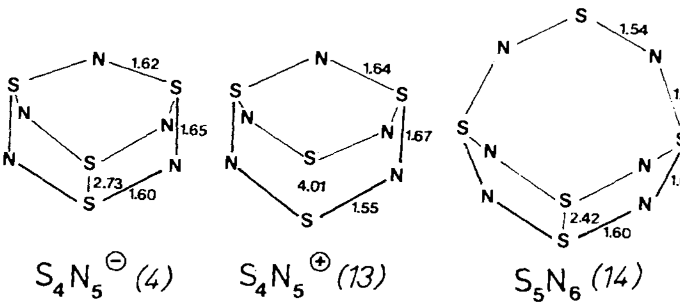


Fig. 3. Most prominent structural features of the bicyclic SN-compounds $S_4N_5^{\ominus}$, $S_4N_5^{\oplus}$ and $S_5N_6$.

Bearing this division scheme in mind, the following numbers of π-electrons for the simple monocyclic systems listed in Figure 2 can be counted:

| No. of π-electrons | Ring system | |
|---|---|---|
| 6π | $S_2N_2$ | *(2)* |
| 10π | $S_3N_3^{\ominus}$ | *(3)* |
| 10π | $S_4N_3^{\oplus}$ | *(9)* |
| 14π | $S_5N_5^{\oplus}$ | *(10)* |

In fact, planar structures have been reported[5-9] for all four systems possessing $(4n+2)\pi$-electrons[4]. This suggests that Hückel's rule[4] works well for these systems. In contrast to the case of stable organic π-systems, antibonding π* levels are also occupied in the SN rings (electron rich $(4n+2)\pi$-systems[10]). The relative stability of these systems might be due to two factors:

1) The higher electronegativity of nitrogen compared to carbon or sulfur[11], lowers the antibonding π* levels towards the bonding region.
2) The larger SN bond length in these rings reduces the mutual repulsion of any pairs of electrons relative to the corresponding hydrocarbon π-system. Thus, the total energy of the π-system is lowered[3b].

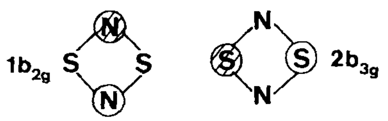
## 3. Monocyclic SN-Rings of the Type $(SN)_x$

### 3.1. Disulfur Dinitride $S_2N_2$

X-ray diffraction measurements on $S_2N_2$ *(2)* in the solid state at −130°C indicate a cyclic square planar molecule ($D_{2h}$) with a common SN bond length of 1.65 Å[5].

A detailed investigation of the electronic structure of *(2)* using *ab initio* techniques[12] and semiempirical methods[13] confirms the simple picture presented in Section 2. Using the Edmiston-Ruedenberg localization procedure[14], the set of eight canonical σ-type MO's of *(2)* can be transformed to a set of four SN σ bonds and one lone pair at each center[13a]. The remaining three occupied π-MO's from *(2)* are just the ones anticipated for a cyclobutadiene dianion. The two highest occupied MO's of *(2)* are, on theoretical grounds, predicted to be nearly degenerate and to belong to the irreducible representations $B_{3g}$ and $B_{2g}$.

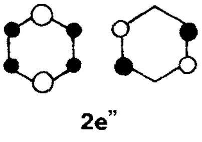
The orbital sequence predicted by several methods of calculation has been confirmed by X-ray[15] and UV-photoelectron spectroscopy[16]. It is found that inclusion of sul-



fur 3d-functions improves the numerical results, but does not change the overall picture; 3d-functions act as polarization functions. All calculations predict a surplus of negative charge at the nitrogen centers (*ca.* 0.4 e).

### 3.2. The Trisulfur Trinitride Anion $S_3N_3^\ominus$

The crystal and molecular structure of $[n\mathrm{Bu}_4\mathrm{N}^\oplus][\mathrm{S}_3\mathrm{N}_3^\ominus]$ has been determined by X-ray analysis. For the anion *(3)* a six-membered, essentially planar ring with SN bond lengths in the range 1.58 to 1.63 Å is found[6]. *Ab initio* calculations (Hartree-Fock approximation)[6] confirm the picture derived from a simple HMO treatment: the highest occupied π-MO's (2e'', see below) are π* in character and thus essentially reduce the π bond order to the contribution from the lowest lying π-orbital.



The UV spectrum (broad band at 360 nm) has been assigned to a $2a_2(\pi^*) \leftarrow 2e''(\pi^*)$ transition[6].

### 3.3. Tetrasulfur Tetranitride ($S_4N_4$)

$S_4N_4$ *(1)* is formed by reaction of $NH_3$ with sulfur chlorides having the composition, "$SCl_3$". The orange crystalline compound has been known since 1835[17]. The speculation over the structure of *(1)* has been brought to an end by an X-ray structure analysis which indicates that $S_4N_4$ has a cradle shaped structure belonging to point group $D_{2d}$[18,19]. In order to use our simple rules to deduce and understand the structure of $S_4N_4$ it has been assumed to be planar with $D_{4h}$ symmetry. The resultant π-orbital scheme is shown in Figure 4[20]. Because nitrogen has a higher electronegativity than sulfur[11] the $b_{2u}$-orbital lies below the $b_{1u}$-orbital in the MO scheme (Fig. 4).

Using Hund's rule, the twelve π electrons doubly occupy the orbitals $a_{2u}$, $e_g$, $b_{2u}$ and $b_{1u}$, while each of the components of the higher $e_g$ orbital accommodates a single electron. Thus, the $D_{4h}$ model predicts a triplet ground state and leads one to expect a Jahn-Teller effect. There are two possible ways to obtain a stable singlet ground state of $S_4N_4$: either the degeneracy of the half occupied $e_g$ level is effectively split or $e_g$ is destabilized and $a_{2u}$ stabilized. Both possibilities are shown in Figure 5.

As with other eight-membered ring systems such as cyclooctatetraene or sulfur ($S_8$), bond alternation or ring puckering might be envisaged. Examination of six possible slight deformations of $S_4N_4$ shows no or no significant splitting or switching of the orbitals and thus, no change in the multiplicity is expected[20].

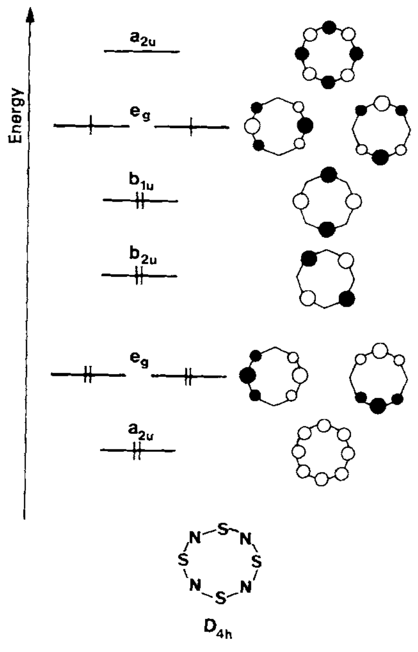


Fig. 4. π-MO scheme of the hypothetical planar $S_4N_4$.

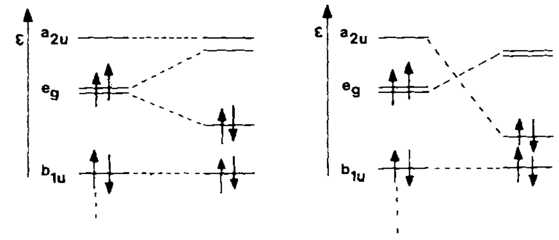


Fig. 5. Possible ways for stabilization of the singlet ground state of $S_4N_4$.

Larger effects are expected from transannular interactions: between pairs of bonds which face each other, as in the tub-form, and between opposite pairs of atoms, as in the crown or cradle conformation. The transannular interaction between opposite bonds does not lead to splitting of $e_g$ or to lowering of $a_{2u}$. The second type of transannular interaction is shown in the correlation diagram in Figure 6[20]. In the crown conformation the $a_{2u}$ level is stabilized but the $b_{1u}$ is destabilized; Formation of two transannular bonds gives a singlet ground state (Fig. 6, right)[20].

Consideration of symmetry arguments alone indicates that coupling of *two* transannular bonds leads to stabilization of the ground state. Molecular orbital calculations indicate that bond formation between the sulfur atoms in $S_4N_4$ is more efficient than between the nitrogen atoms[20,21].

A decisive factor in the stabilization of the singlet ground state is the strong interaction of the 3p orbitals of sulfur over a distance of 2.58 Å; for bond lengths between 2.8 and 2.0 Å the $3p_\sigma$-$3p_\sigma$ overlap of the two sulfur atoms is much larger than the $2p_\sigma$-$2p_\sigma$ overlap of the two nitrogen centers (Fig. 7)[20].

Using CNDO type wave functions, localized molecular orbitals for $S_4N_4$ have been derived[21a]: it is found that both the SS and the SN bonds are slightly bent single bonds with pure p-character. Electron delocalization occurs by transfer of electron density from the lone pairs on

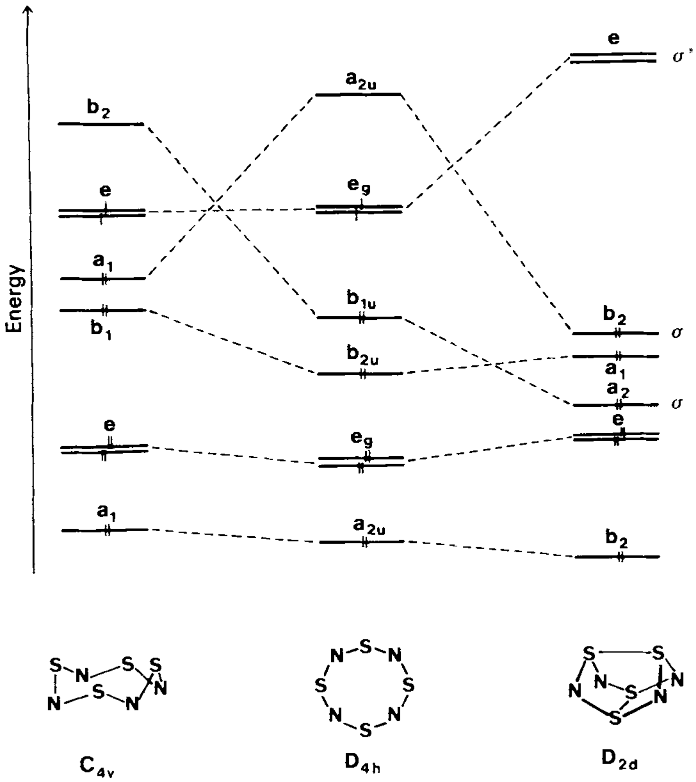


Fig. 6. Correlation between the π-MO's of a planar $S_4N_4$ with the valence MO's of $S_4N_4$ in the crown and cradle conformations.

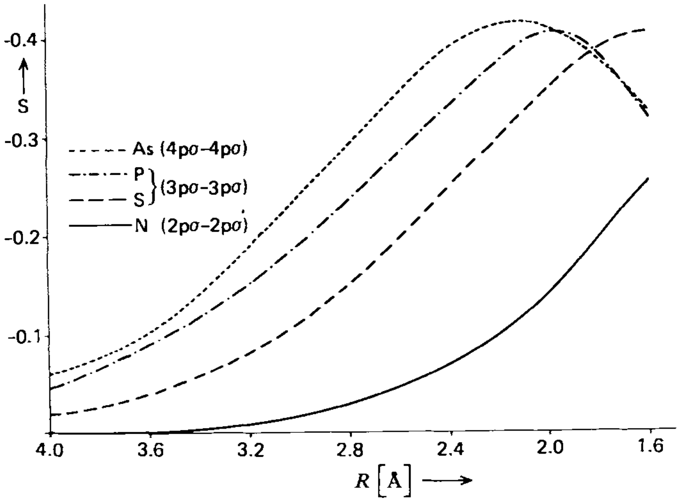
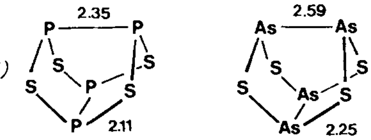


Fig. 7. $p_\sigma$-$p_\sigma$ overlap integrals S as a function of distance $R$ for N ($2p_\sigma$-$2p_\sigma$), S, P ($3p_\sigma$-$3p_\sigma$) and As ($4p_\sigma$-$4p_\sigma$).

nitrogen to the neighboring sulfur atoms[13c,21]. The results obtained by semiempirical calculations have been confirmed by *ab initio* methods[16b] and X-ray and UV-photoelectron spectroscopy[16b,22] on $S_4N_4$.

### 3.4. Structures Related to $S_4N_4$

From Figure 7 it can be seen that the $p_\sigma$-$p_\sigma$ overlap integrals for P($3p_\sigma$-$3p_\sigma$) and As($4p_\sigma$-$4p_\sigma$) are larger than those for S($3p_\sigma$-$3p_\sigma$) and N($2p_\sigma$-$2p_\sigma$). From the arguments in the previous section it is understandable that in realgar, $As_4S_4$ *(16)*[23], and α-$P_4S_4$ *(15)*[24], the sulfur atoms occupy the positions "in the plane", while the transannular bonds are formed between As and P atoms respectively (Fig. 8).



*(15)* *(16)*

Fig. 8. Structures of realgar ($As_4S_4$) and α-$P_4S_4$.

$S_4N_4$ forms adducts with Lewis acids for which two types of structures result: If only one Lewis acid is bound, the $S_4N_4$ structure is changed completely and the eight-membered ring adopts a saddle-type structure (Fig. 9). Examples are the adducts with $BF_3$[25] (Fig. 9), $SbCl_5$[26], $SO_3$[27] and $FeCl_3$[28]. If $S_4N_4$ behaves as a bidentate ligand *e.g.* with CuCl, CuBr, and $CuCl_2$, the cage-like structure is retained[29]. The complexes with $BF_3$, $SbCl_5$ and $FeCl_3$ are reminiscent of the structure of $S_4N_4O_2$[30] (Fig. 9).

In the saddle-like structures, seven centers are arranged in an almost planar fashion. The resulting system is similar to a heptatrienyl fragment with ten π-electrons. In the case of adducts with Lewis acids, homoconjugation between the sulfur centers is suggested by MO calculations[31].

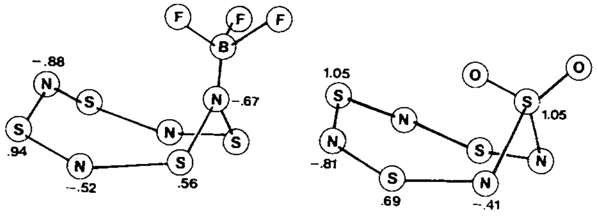


Fig. 9. Structure of $S_4N_4 \cdot BF_3$ and $S_4N_4O_2$ together with MNDO calculated net charges.

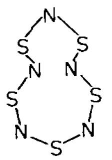
From the MO model discussed for a planar $S_4N_4$ (Section 3.3), it follows that the dianion and dication of $S_4N_4$ should have a "closed-shell" structure. Both systems, if planar, satisfy Hückel's rule[4] for aromatic 10 π- and 14 π-systems. For the dication *(11)*, three different planar structures have recently been reported[33], one with equal bond lengths and two with alternating bonds. This result can be interpreted as meaning that the energy difference between a totally delocalized species and a system with alternating bonds is small.

The structure of $S_4N_4$ can also be varied by replacement of two opposite sulfur centers by centers or fragments which provide less π-electrons, such as B—R or C—R. In the case of two boron atoms in the ring an 8 π-, and with two carbon atoms a 10 π-system, is expected. The results of preliminary calculations[31] and recent experiments[34] support this view, although things are not so simple as they appear at first sight. This is best seen from the structures which result by formally replacing two sulfur centers by an $AsR$[35,36] fragment. In the case of R = phenyl, X-ray investigations[36] clearly point out that two NSN units and two $AsC_6H_5$ units are present in the almost planar molecule, *i.e.* a delocalization of electrons by an intramolecular redox reaction has not occured.

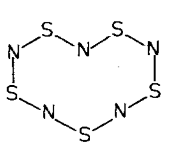
### 3.5. The Pentasulfur Pentanitrogen Cation $S_5N_5^{\oplus}$

The results on the structure of $S_5N_5^{\oplus}$ *(10)* are puzzling. To date, two different structures are known: a heart shaped *(10b)* and an azulene-like structure *(10a)* (Fig. 2). The heart shaped structure occurs with $AlCl_4^{\ominus}$[8a] or $FeCl_4^{\ominus}$[8b], while the azulene-like structure has been found with $S_3N_3O_2^{\ominus}$ or $[SnCl_5(OPCl_3)]^{\ominus}$ as anions [9]. Both ring structures are almost planar and both have a 14π-system. Somewhat unusually, the SNS bond angles in *(10b)* are close to 180° at the N1 and N2 centers and relatively large temperature factors for N1, S2 and N2 around the tip of the heart occur (cf. Fig. 10b).

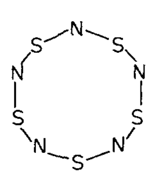
A theoretical investigation of the six possible conformers *(10a)*—*(10f)* of an $(SN)_5$ ring using the Extended Hückel (EH) method shows the problems encountered in $S_5N_5^{\oplus}$[37] are similar to those in [10]annulene[38]: the lone pairs at the sulfur and nitrogen centers restrict the number of favorable conformers to two, the heart shaped and azulene-like structures *(10b)* and *(10a)* respectively. The qualitative result of the Extended Hückel calculations can be summarized as follows: In the case of the regular 10-membered ring *(10c)* ($D_{5h}$), the angle strain reaches its maximum. In the azulene-like structure with a relatively short transannular SS separation *(10e)*, the lone pair-lone pair interaction is at a maximum. A minimum in angle strain and lone pair-lone pair interaction occurs in *(10a)*. The predicted energy difference of 2 eV between *(10a)* and *(10b)* is unusually large for two stable isomers and hence correctness of the structural data reported for *(10b)* seems doubtful. Together with the already mentioned large temperature factors for *(10b)* it seems reasonable to suggest[39] that the apparently heart shaped structure may be caused by superposition of two azulene-like structures (see Fig. 10).



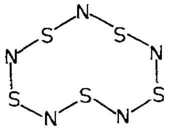
*(10a)*



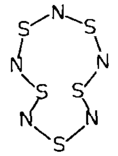
*(10b)*



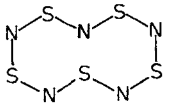
*(10c)*



*(10d)*



*(10e)*



*(10f)*

The explanation summarized in Fig. 10, however, is questionable if the results of recent MNDO calculations are considered[31]. The minimization of the total energy as a function of the geometrical parameters of *(10b)* and *(10a)* leads to almost identical energies with bond lengths and bond angles close to the experimental ones.

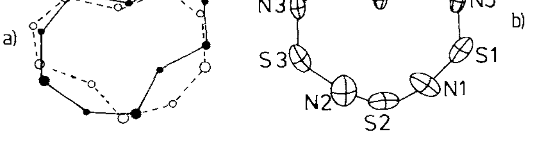


Fig. 10. a) Superposition of two azulene-like structures *(10a)* of $S_5N_5^{\oplus}$. b) Thermal ellipsoids of $S_5N_5^{\oplus}$ as reported for the heart shaped structure [8].

To clarify whether *(10b)* exists in Nature or arises from the superposition of two azulene-like structures *(10a)* (disorder or dynamic processes), a careful re-examination of the structural data is necessary. Diffraction experiments are probably the only method of reaching a decision; other methods, *e.g.* electron spectroscopy are of little help, since the electronic absorption spectra of *(10a)* and *(10b)* [40] in the visible or near UV region are predicted to be very similar, due to the similar energy of the π-levels[37].

## 4. Ring Systems of the Type $S_2N(SN)_x$

### 4.1. The Radical Cation $S_3N_2^{\oplus}$ *(12)* and its Dimer $S_6N_4^{2\oplus}$

The simplest ring system in this category is $S_3N_2$. Counting the electrons as in Section 2, leaves eight electrons for the π-system. According to the π-MO diagram (which is based on an MNDO calculation on $S_3N_2^{\oplus}$[41]) a triplet ground state seems likely, since the separation between $2a_2$ and $3b_1$ is predicted to be small (Fig. 11). One way of achieving a closed shell system is to remove or fill-in two electrons. In the case of the doubly charged cation, a stable system seems likely. For the dianion, however, two antibonding π* levels have to be occupied and thus the molecule might avoid this by fragmentation. While the dianion and dication of $S_3N_2$ are unknown, the radical cation *(12)* has been generated and investigated in solution by ESR spectroscopy and in the solid state by X-ray structure, analysis. By treating $S_4N_4$ with strong Lewis acids and sulfuric acid, $S_3N_2^{\oplus}$ *(12)* is generated[42,43], but its nature was not recognized until recently[44a]. Comparing the observed $^{33}S$ coupling constants and the results of MNDO calculations it was concluded that $S_3N_2^{\oplus}$ has a $^2A_2$ ground state[41]. Its structure in the solid state has recently been determined[45]: bond lengths and bond angles are shown in Figure 2.

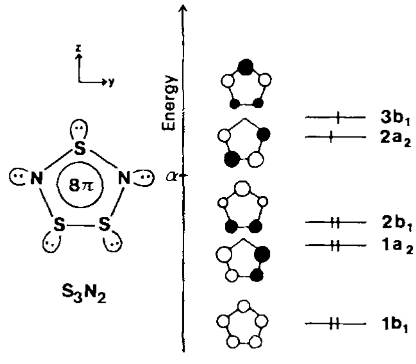


Fig. 11. Qualitative MO scheme of $S_3N_2$. For the numbering of the levels only the valence orbitals were considered.

$S_3N_2Cl^{\oplus}$ *(7)*[46] and $S_3N_2NP_3N_3F_5$ *(17)*[2] are related to $S_3N_2^{\oplus}$ *(12)* (Fig. 12). The 6π-electrons in *(7)* and *(17)* occupy the three lowest π-orbitals ($\psi_1$ to $\psi_3$) derived from a linear combination of the $p_\pi$ orbitals from the four remaining centers (Fig. 13). The resulting molecular orbitals are closely related to those of the corresponding π-system of butadiene, the main difference being that in butadiene *two,*

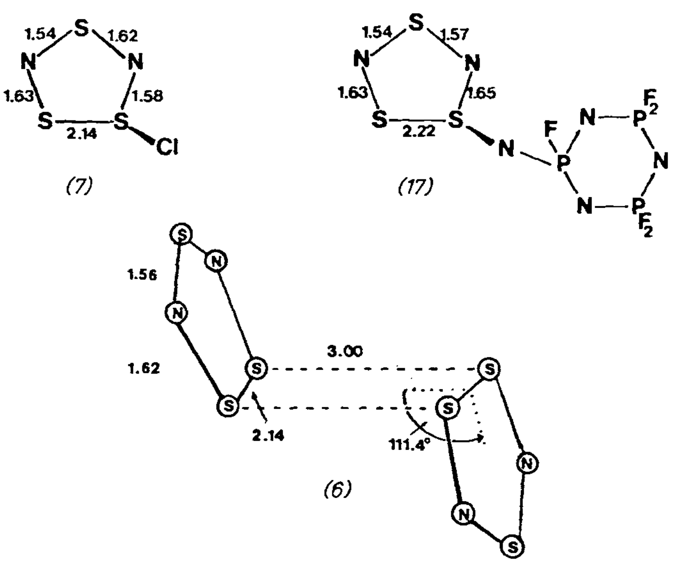


Fig. 12. Bond lengths of $S_3N_2Cl^{\oplus}$, $S_3N_2NP_3N_3F_5$ and $[S_6N_4]^{2\oplus}$.

and in $S_3N_2Cl^{\oplus}$ *three* π-levels are occupied. As a consequence of this difference, bond alternance should be less pronounced in $S_3N_2Cl^{\oplus}$. A similar conclusion is reached by considering the most likely valence structures of *(7)*[44a] and by semiempirical calculations involving all the valence electrons[44b]. These qualitative arguments agree with the experimental bond lengths (Fig. 12) found for *(7)* and *(17)* as well as for related species[2]. The MO picture of *(12)* and its congeners also allows an explanation of why other tautomers of *(7), e.g. (7a)* or *(7b)* are not found[41].

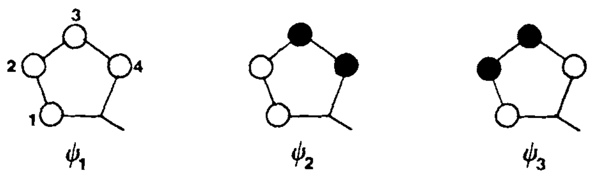
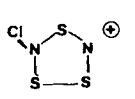
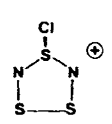


Fig. 13. Schematic representation of the occupied π-MO's of *(7)* or *(17)*.

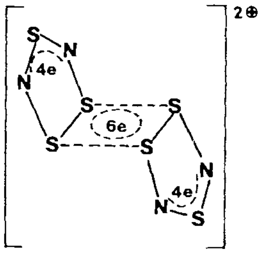
*(7a)*



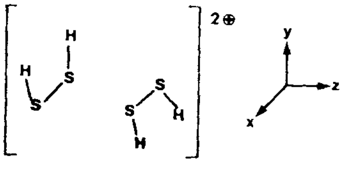


*(7b)*

If the radical cation *(12)* finds no substrate to react with, stabilization *via* dimerization is possible. The structure of the dimer $S_6N_4^{2\oplus}$ *(6)* has been determined using X-ray techniques[47]. The most interesting feature is the long SS bond (Fig. 12) between the two $S_3N_2^{\oplus}$ moieties. Considering the values of overlap integrals shown in Figure 7 and using arguments from perturbation theory, it can be shown[41] that other possible structures for a dimer are not likely. Model calculations carried out on $[H_2S_2]_2^{2\oplus}$ reveal[41] that the bonding between the two $S_3N_2^{\oplus}$ moieties can best be described as an electron-rich four-center bond. The orbital energies of the four molecular orbitals, which arise from the four $3p_z$-atomic orbitals on the sulfur centers of $[H_2S_2]_2^{2\oplus}$ *(18)*, are shown in Figure 14. The resulting linear combinations (Fig. 14) transform according to the irreducible representations $A_g$, $B_u$, $A_u$ and $B_g$ in point group $C_{2h}$. In our model dication *(18)* three MO's ($a_g$, $b_u$, $a_u$) are occupied and one MO ($b_g$) unoccupied. At large values of $R$ (>4 Å) the resulting MO's are similar to those of two isolated $H_2S_2^{\oplus}$ units. The two orbitals of π-type ($a_g$, $b_u$) and those of π*-type ($a_u$, $b_g$) are close in energy. Reduction of the distance R between the two moieties leads to stabilization of both the $a_g$ and $a_u$ levels, while the $b_u$ and $b_g$ orbitals are strongly destabilized. It is interesting to note, that



*(6)*



*(18)*

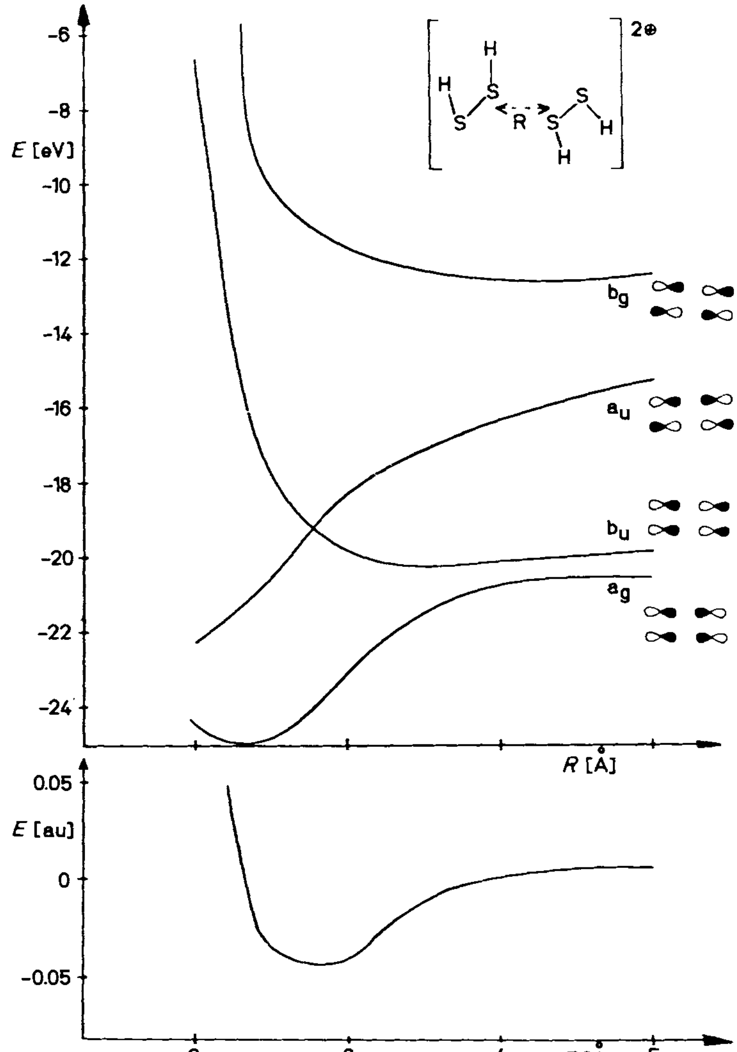


Fig. 14. Energy of the highest occupied MO's and lowest unoccupied MO's of $[H_2S_2]_2^{2\oplus}$ as a function of the distance $R$ (above), and total energy of $[H_2S_2]_2^{2\oplus}$ as a function of R (below) according to an *ab initio* calculation.

down to 3 Å the positive slope of $a_g$ and $a_u$ is larger than the negative slope of the antibonding combinations. Thus the total energy is lowered, since nuclear-nuclear repulsion is still small at these distances and reaches a minimum at around 3 Å.

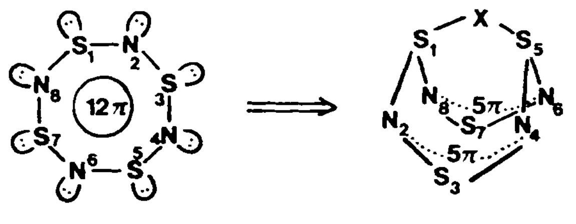
### 4.2. The Tetrasulfur Trinitrogen Cation $S_4N_3^{\oplus}$

X-ray investigations on salts containing $S_4N_3^{\oplus}$ *(9)* units[7,48] indicate planar seven-membered rings with one S—S bridge (Fig. 2). The electronic structure of *(9)* can be satisfactorily described by assuming a 10π-system. Consideration of the p-orbitals only, leads to excellent reproduction of the absorption spectrum. The first two bands in the electronic spectrum of $S_4N_3^{\oplus}$ can be assigned to $\pi^* \leftarrow \pi$ transitions[49]. The π bond-orders obtained, approximately parallel the reported bond lengths and the calculated π-electron densities are in qualitative agreement with the result of an $^{15}$N-NMR study[50].

## 5. Bicyclic Structures $S_4N_5^{\ominus}$, $S_4N_5^{\oplus}$, $S_5N_6$

Recently, bicyclic structures have also been reported in SN-chemistry: $S_4N_5^{\ominus}$ *(4)*[51], $S_4N_5^{\oplus}$ *(13)*[52] and $S_5N_6$ *(14)*[53]. Structural details are collected in Figure 3. Formally, all three can be derived from $S_4N_4$ by replacing one transannular SS bond by a nitrogen atom or an NSN-fragment. The most striking structural difference between *(4)* and *(13)* is the S3—S7 distance [cf. Fig. 3 and *(19)*], which is found to be 2.73 Å and 4.01 Å respectively. In *(14)*, as in *(4)*, a relatively short S3—S7 distance is again reported (2.92 Å)[53]. The structural differences have been rationalized using arguments from MO theory[54].

The starting point is the hypothetical planar $S_4N_4$ discussed in Section 3.3. From the twelve π-electrons in this species two π-electrons are taken from two opposite sulfur centers, *e.g.* S1 and S5, to form σ-bonds with a bridging atom X. This leaves ten π-electrons for the centers N2—S3—N4 and N6—S7—N8 in *(19)*.



*(19)*

The π MO's of these two allylic moieties are shown in Figure 15 for large (right) and small (left) S3—S7 distances, derived from an extended Hückel calculation[54]. For large distances the energy levels anticipated are those of two separate allylic π-levels, for small distances, however, considerable interaction between those MO's belonging to the irreducible representations $A_1$ and $B_2$ is predicted. The bonding combinations, with respect to a transannular interaction ($1a_1$ and $2a_1$), will be lowered in energy by reduction of the S3—S7 distance, while the antibonding combinations ($1b_2$, $2b_2$) will be raised in energy. In Figure 15 the $2p_\pi$-orbital of a bridging atom (*e.g.* N) has been added (irreducible representation $B_2$). Because of small overlap and large energy difference of the basis orbitals, their interaction with other orbitals of the same symmetry can be neglected. The corresponding energy level is indicated in Figure 15 by a broken line. Having constructed the π-MO scheme for *(19)*, it must be filled with π-electrons: in *(4)* the nitrogen bridge formally contributes two electrons, in *(13)* formally zero. Thus, in our π-molecular orbital scheme (Fig. 15), six MO's in *(4)* and five MO's in *(13)* are occupied. The occupation of six MO's results in no splitting between $2a_1$ and $2b_2$ at large S3—S7 distances. This indicates a triplet ground state and thus an unstable structure. A slight distortion towards a shorter S3—S7 distance. enlarges the HOMO-LUMO gap[55] and leads to a net stabilization. This explains the short distance in *(4)*. Occupation of five MO's (cation) leads, at short S3—S7 distances, to a small but for large S3—S7 distances to a large HOMO-LUMO gap. In addition to this electronic effect a smaller nuclear-nuclear repulsion term at large S3—S7 distances arises. Both effects shift the energy minimum for the cation to a structure with large S3—S7 distances. The π MO-schemes just discussed for *(4)* and *(13)* can be generalized: stable cage structures with short S3—S7 distances can exist if the bridge X in *(19)* provides high lying filled orbitals (*e.g.* $N^{\ominus}$, O, S, $CR_2$, $C_2H_2$, NSN, $C_3H_3^{\ominus}$...). Structures with long S3—S7 bonds are predicted if the bridging atom or group provides low lying empty orbitals (e.g. $N^{\oplus}$, $CR^{\oplus}$, BR, $C_3H_3^{\oplus}$, $NSN^{2\oplus}$...). Examples which fit into this scheme are *(14)*[53], β-$P_4S_5$ *(20a)*[56], $As_4S_5$ *(20b)*[57], $S_4N_5O^{\ominus}$ *(21)*[58], $P_4S_7$ *(22)*[59], $P_9(CH_3)_5$ *(23)*[60], as well as structures with two electron-rich substituents on S1 and S5, *e.g.* the compounds *(24)*—*(26)*[61-63]. By replacing the bridgehead sulfur atoms of *(19)* with tetravalent atoms of the fourth group, *e.g.* C or Si, the two π-fragments N2—S3—N4 and N6—S7—N8 only contain a total of eight π-electrons, since the bridgehead atoms formally contribute no π-electrons, *e.g.* in *(28)*.

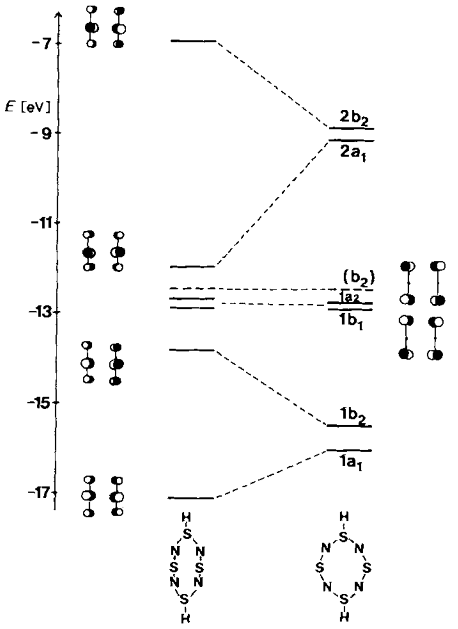
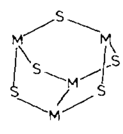
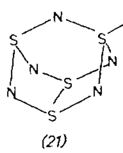


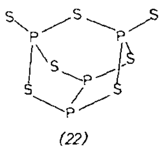
Fig. 15. Energies of the π-MO's of model compound *(19)* according to an EH-calculation of S3—S7 = 2.7 Å (left) and S3—S7 = 4.0 Å (right).



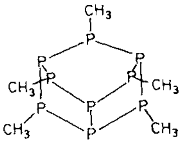
*(20a)*, M = P
*(20b)*, M = As



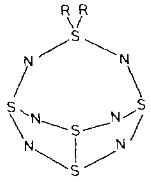
*(21)*



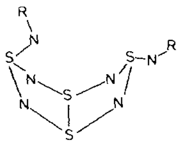
*(22)*



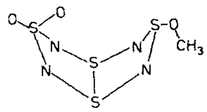
*(23)*



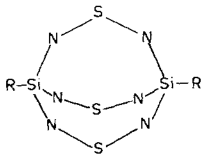
*(24)*, R = Alkyl



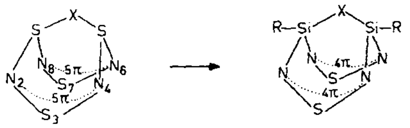
*(25)*, R = P(Ph)$_3$



*(26)*



*(27)*



*(19)* *(28)*

Accordingly, the π-system in *(27)* should contain two electrons less than that of *(14)* and a "long" S3—S7 bond relative to that of *(14)* is therefore expected for *(27)*: this is corroborated by experiment[63].

## 6. Outlook

Our knowledge of reactions of SN compounds rests mainly on isolated crystalline products which can be studied by X-ray investigation. This limitation often only allows a minor insight into what really happens during a reaction and thus, necessarily, many reactions seem very strange. So far, most of the known cyclic SN compounds have been prepared from $S_4N_4$ (Fig. 1). The products obtained under various reaction conditions indicate smaller fragment intermediates in these reactions. A promising step forward has been the isolation and characterization of a key intermediate, $S_4N^{\ominus}$ by *Chivers et al.* [64].

An alternative approach for the synthesis of novel SN-cycles by building larger systems from small fragments with proper leaving groups has been recently advocated by different groups[2a,9a,35,51,66].

The advent of $^{15}$N-NMR spectroscopy (FT-technique) has enabled reactions to be followed spectroscopically, kinetic studies to be carried out and hence the characterization of most important reaction products [67]. MO calculations of potential surfaces of cyclic and open chain SN compounds, in close connection with experimental studies, are necessary to elucidate reaction paths and the structure of key intermediates. The results show that recent MO methods are able to treat these systems properly and initial calculations of potential energy surfaces of small SN molecules[64,65] confirm this optimism.

A further problem awaiting solution is the rationalization of correlations between bond lengths and coordination number or bond lengths and bond angles, discovered recently in several laboratories[2a,39], on an MO basis. Furthermore the electron spectra of most SN compounds must be investigated in more detail: this provides an excellent test of the efficiency of theoretical models.

The role of 3d-orbitals in the bonding of the cyclic SN compounds has not been considered in this review for two reasons: 1) The qualitative explanations given for the structures are not improved by inclusion of 3d-orbitals on sulfur and 2) accurate calculations on small sulfur-nitrogen systems indicate that the 3d-orbital participation is small.

*My own work started in Basel, generously supported and stimulated by Professor E. Heilbronner. I am very grateful to R. Bartetzko who carried out most of the calculations cited. Financial assistance from the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and BASF AG. is acknowledged.*

Received: June 30, 1980 [A 366 IE]
Revised: March 17, 1981
German version: Angew. Chem. *93*, 442 (1981)

---

[1] *M. Goehring:* Ergebnisse und Probleme der Chemie der Schwefelstickstoffverbindungen. Akademie-Verlag, Berlin 1957; *M. Becke-Goehring,* Prog. Inorg. Chem. *1*, 207 (1959).

[2] a) Reviews: *H. W. Roesky,* Angew. Chem. *91*, 112 (1979); Angew. Chem. Int. Ed. Engl. *18*, 91 (1979); b) *A. J. Banister,* MTP Int. Rev. Sci. Ser. 2, Inorg. Chem. *3*, 41 (1975).

[3] a) *E. Heilbronner, H. Bock:* Das HMO-Modell und seine Anwendung. Verlag Chemie, Weinheim 1968; b) *M. J. S. Dewar:* The Molecular Orbital Theory of Organic Chemistry. McGraw-Hill, New York 1969.

[4] *E. Hückel,* Z. Phys. *70*, 204 (1931).

[5] *C. M. Mikulski, P. J. Russo, M. S. Saran, A. G. MacDiarmid, A. F. Garito, A. J. Heeger,* J. Am. Chem. Soc. *97*, 6358 (1975).

[6] *J. Bojes, T. Chivers, W. G. Laidlaw, M. Trsic,* J. Am. Chem. Soc. *101*, 4517 (1979).

[7] *J. Weiss,* Z. Anorg. Allg. Chem. *333*, 314 (1964).

[8] a) *A. J. Banister, P. J. Dainty, A. C. Hazell, R. G. Hazell, J. G. Lomberg,* Chem. Commun. *1969*, 1187; *A. C. Hazell, R. G. Hazell,* Acta Chem. Scand. *26*, 1987 (1972); *A. J. Banister, H. G. Clarke,* J. Chem. Soc. Dalton Trans. *1972*, 2661; b) *U. Thewalt,* Anorg. Allg. Chem., in press.

[9] a) *H. W. Roesky,* Z. Naturforsch. *B 31*, 680 (1976); b) *A. J. Banister, J. A. Durant, I. Rayment, H. M. M. Shearer,* J. Chem. Soc. Dalton Trans. *1976*, 928.

[10] *A. J. Banister,* Nature, London, Phys. Sci. *237*, 92 (1972); *B. M. Gimaric, N. Trinajstić,* Pure Appl. Chem. *52*, 1443 (1980).

[11] *L. Pauling:* The Nature of the Chemical Bond. Cornell University Press, Ithaca 1960.

[12] *M. Kertész, S. Suhai, A. Ažman, D. Kocjan, A. I. Kiss,* Chem. Phys. Lett. *44*, 53 (1976); *D. R. Salahub, R. P. Messmer,* J. Chem. Phys. *64*, 2039 (1976); *M. P. S. Collins, B. J. Duke,* J. Chem. Soc. Chem. Commun. *1976*, 707; *J. A. Jafri, M. D. Newton, T. A. Pakkanen, J. L. Whitten,* J. Chem. Phys. *66*, 5167 (1977); *P. W. Deutsch, L. A. Curtiss,* Chem. Phys. Lett. *51*, 125 (1977); *A. Karpfen, P. Schuster, J. Petkov, H. Lischka,* J. Chem. Phys. *68*, 3884 (1978).

[13] a) *R. R. Adkins, A. G. Turner,* J. Am. Chem. Soc. *100*, 1383 (1978); b) *T. Yamabe, K. Tanaka, K. Fukui, H. Kato,* J. Phys. Chem. *81*, 727 (1977); c) *R. D. Harcourt,* Inorg. Nucl. Chem. *39*, 237 (1977).

[14] *C. Edmiston, K. Ruedenberg,* Rev. Mod. Phys. *35*, 457 (1963).

[15] *J. Sharma, D. S. Downs, Z. Iqbal, F. J. Owens,* J. Chem. Phys. *67*, 3045 (1977).

[16] a) *D. C. Frost, M. R. LeGeyt, N. L. Paddock, N. P. C. Westwood,* J. Chem. Soc. Chem. Commun. *1977*, 217; b) *R. H. Findlay, M. H. Palmer, A. J. Downs, R. G. Egdell, R. Evans,* Inorg. Chem. *19*, 1307 (1980).

[17] *M. Gregory,* J. Pharm. *21*, 315 (1835).

[18] *G. S. Lu, J. Donohue,* J. Am. Chem. Soc. *66*, 818 (1944).

[19] *D. Clark,* J. Chem. Soc. *1952*, 1615; *B. D. Sharma, J. Donohue,* Acta Crystallogr. *16*, 891 (1963).

[20] *R. Gleiter,* J. Chem. Soc. *A 1970*, 3174.

[21] a) *M. S. Gopinathan, M. A. Whitehead,* Can. J. Chem. *53*, 1343 (1975); b) *A. G. Turner, F. S. Mortimer,* Inorg. Chem. *5*, 906 (1966); *P. Cassoux, J.-F. Labarre,* J. Mol. Struct. *13*, 405 (1972).

[22] *W. R. Salanek, J. W. Lin, A. Paton, C. B. Duke, G. P. Ceasar,* Phys. Rev. *B 13*, 4517 (1976).

[23] *T. Ito, N. Morimoto, R. Sadanaga,* Acta Crystallogr. *5*, 775 (1952).

[24] *P. C. Minshall, G. M. Sheldrick,* Acta Crystallogr. *B 34*, 1326 (1978).

[25] *M. G. B. Drew, D. H. Templeton, A. Zalkin*, Inorg. Chem. *6*, 1906 (1967).
[26] *D. Neubauer, J. Weiss*, Z. Anorg. Chem. *303*, 28 (1960).
[27] *A. Gieren, B. Dederer*, Z. Anorg. Allg. Chem. *440*, 119 (1978).
[28] *U. Thewalt*, Z. Naturforsch. *835*, 855 (1980).
[29] *U. Thewalt*, Angew. Chem. *88*, 807 (1976); Angew. Chem. Int. Ed. Engl. *15*, 765 (1976); Z. Anorg. Allg. Chem. *462*, 221 (1980).
[30] *H. W. Roesky, W. Grosse-Böwing, I. Rayment, H. M. M. Shearer*, J. Chem. Soc. Chem. Commun. *1975*, 735.
[31] *R. Gleiter, R. Bartetzko*, unpublished results using the MNDO method [32] and Z. Naturforsch. *B*, in press.
[32] *M. J. S. Dewar, W. Thiel, J. Am. Chem. Soc. 99*, 4899 (1977); *M. J. S. Dewar, M. L. McKee, H. Rzepa, ibid. 100*, 3607 (1978).
[33] *R. J. Gillespie, D. R. Slim, J. D. Tyrer*, J. Chem. Soc. Chem. Commun. *1977*, 253.
[34] *D. Wenkert*, Ph. D. thesis, Harvard 1979.
[35] *O. J. Scherer, R. Wies*, Angew. Chem. *83*, 882 (1971); *84*, 585 (1972); Angew. Chem. Int. Ed. Engl. *10*, 812 (1971); *11*, 529 (1972).
[36] *N. W. Alcock, E. M. Holt, J. Kuyper, J. J. Mayerle, G. B. Street*, Inorg. Chem. *18*, 2235 (1979).
[37] *R. Bartetzko, R. Gleiter*, Inorg. Chem. *17*, 995 (1978).
[38] *S. Masamune, N. Darby*, Acc. Chem. Res. *5*, 272 (1972) and references therein.
[39] *A. J. Banister, J. A. Durrant*, J. Chem. Res. *1978*, 1910.
[40] *R. Zahradnik, A. J. Banister, H. G. Clarke*, Collect. Czech. Chem. Commun. *38*, 998 (1973).
[41] *R. Gleiter, R. Bartetzko, P. Hofmann*, Z. Naturforsch. *B 35*, 1166 (1980).
[42] *D. Chapman, A. G. Massey*, Trans. Faraday Soc. *58*, 1291 (1962); *D. A. C. McNeil, M. Murray, M. C. R. Symmons*, J. Chem. Soc. *A 1967*, 1019; *J. R. W. Warn, D. Chapman*, Spectrochim. Acta *22*, 1371 (1966).
[43] *S. A. Lipp, J. J. Chang, W. L. Jolly*, Inorg. Chem. *9*, 1970 (1970).
[44] a) *R. J. Gillespie, P. R. Ireland, J. E. Vekris*, Can. J. Chem. *53*, 3147 (1975); b) *D. B. Adams, A. J. Banister, D. T. Clark, D. Kilcast*, Int. J. Sulfur Chem. *A 1*, 143 (1971).
[45] *R. J. Gillespie, J. P. Kent, J. F. Sawyer*, J. Am. Chem. Soc., in press.
[46] *A. Zalkin, T. E. Hopkins, D. H. Templeton*, Inorg. Chem. *5*, 1767 (1966).
[47] *A. J. Banister, H. G. Clarke, I. Rayment, H. M. M. Shearer*, Inorg. Nucl. Chem. Lett. *10*, 647 (1976); *B. Krebs, G. Henkel, S. Pohl, H. W. Roesky*, Chem. Ber. *113*, 226 (1980); *U. Thewalt, M. Burger*, Z. Naturforsch. *B 36*, 293 (1981).
[48] *A. W. Cordes, R. F. Kruh, E. K. Gordon*, Inorg. Chem. *4*, 681 (1965); *B. Kruss, M. L. Ziegler*, Z. Anorg. Chem. *388*, 158 (1972); *T. N. Guru-Row, P. Coppens*, Inorg. Chem. *17*, 1670 (1978).
[49] *D. A. Johnson, G. D. Blyholder, A. W. Cordes*, Inorg. Chem. *4*, 1790 (1965); *P. Friedman*, ibid. *8*, 6921 (1969).
[50] *N. Logan, W. L. Jolly*, Inorg. Chem. *4*, 1508 (1965).
[51] *W. Flues, O. J. Scherer, J. Weiss, G. Wolmershäuser*, Angew. Chem. *88*, 411 (1976); Angew. Chem. Int. Ed. Engl. *15*, 379 (1976).
[52] *T. Chivers, L. Fielding, W. G. Laidlaw, M. Trsic*, Inorg. Chem. *18*, 3379 (1980).
[53] *T. Chivers, J. Proctor*, J. Chem. Soc. Chem. Commun. *1978*, 642; *H. W. Roesky, M. N. Sudheendra Rao, T. Nakajima, W. S. Sheldrick*, Chem. Ber. *112*, 3531 (1979).
[54] *R. Bartetzko, R. Gleiter*, Chem. Ber. *113*, 1138 (1980).
[55] *R. G. Pearson:* Symmetry Rules for Chemical Reactions. Wiley, New York 1976.
[56] *A. M. Griffin, G. M. Sheldrick*, Acta Crystallogr. *B 31*, 2738 (1975).
[57] *H. J. Whitefield*, J. Chem. Soc. Dalton Trans. *1973*, 1740.
[58] *P. Luger, H. Bradaczek, R. Steudel*, Chem. Ber. *109*, 3441 (1976).
[59] *A. Vos, H. Wiebenga*, Acta Crystallogr. *8*, 217 (1955); *9*, 92 (1956).
[60] *M. Baudler, Y. Aktaly, J. Hahn, E. Därr*, Z. Anorg. Allg. Chem. *473*, 20 (1981).
[61] *W. S. Sheldrick, M. N. Sudheendra Rao, H. W. Roesky*, Inorg. Chem. *19*, 538 (1980). *H. W. Roesky, C. Graf, M. N. Sudheendra Rao, B. Krebs, G. Henkel*, Angew. Chem. *91*, 846 (1979); Angew. Chem. Int. Ed. Engl. *18*, 780 (1979).
[62] *J. Bojes, T. Chivers, A. W. Cordes, G. Maclean, R. T. Oakley*, Inorg. Chem. *20*, 16 (1981).
[63] *H. W. Roesky, M. Witt, B. Krebs, G. Henkel, H. J. Korte*, Chem. Ber. *114*, 201 (1981).
[64] *T. Chivers, W. G. Laidlaw, R. T. Oakley, M. Trsic*, J. Am. Chem. Soc. *102*, 5773 (1980).
[65] *R. Gleiter, R. Bartetzko*, Z. Naturforsch., *B 36*, 492 (1981).
[66] *W. Lidy, W. Sundermeyer, W. Verbeck*, Z. Anorg. Allg. Chem. *406*, 228 (1974).
[67] *T. Chivers, R. T. Dakley, O. J. Scherer, G. Wolmershäuser*, Inorg. Chem. *20*, 914 (1981).

# COMMUNICATIONS

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

## Photochemical Synthesis of Bis($\eta^2$-methyl acrylate)tricarbonylruthenium[**]

By *Friedrich-Wilhelm Grevels, Johannes G. A. Reuvers*, and *Josef Takats*[*]

The photochemical reaction of pentacarbonyliron with suitable olefins leads, *via* ($\eta^2$-olefin)Fe(CO)$_4$, to ($\eta^2$-olefin)$_2$Fe(CO)$_3$[1a] and, finally, with linkage of the olefinic ligands, to carbonylferracyclopentane derivatives[1]. As we

---

[*] Dr. F.-W. Grevels, Dr. J. G. A. Reuvers, Prof. Dr. J. Takats [***]
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
Stiftstrasse 34—36, D-4330 Mülheim a. d. Ruhr (Germany)

[**] This work was supported by the Alexander von Humboldt Foundation through a stipend (to J. T.). We thank Herr *K. Schneider* for technical assistance.

[***] Permanent address: Department of Chemistry, University of Alberta, Edmonton, Alberta T6G 2G2 (Canada)

have already described the photochemical preparation of ($\eta^2$-olefin)Ru(CO)$_4$ complexes[2a], we report here on the conversion of these compounds into the novel ($\eta^2$-olefin)$_2$Ru(CO)$_3$ complexes.

($\eta^2$-Olefin)tetracarbonylruthenium is obtained by irradiation of dodecacarbonyltriruthenium *(2)* with visible light in the presence of excess olefin[2]. By means of an appropriate filter ($\lambda \gtrsim 370$ nm)[2a], the reaction with olefins yields ($\eta^2$-olefin)Ru(CO)$_4$ exclusively, whereas the analogous reaction with phosphorus ligands results in formation of both LRu(CO)$_4$ and L$_2$Ru(CO)$_3$ as primary products[3]. It has been postulated that the isomerization and hydrosilylation of alkenes, which is photocatalyzed by *(2)*, involves the "Ru(CO)$_3$" moiety[3a]; as yet no bis($\eta^2$-olefin) complexes containing this unit have, however, been isolated or detected.

We have now found that UV-irradiation of the colorless ($\eta^2$-olefin)Ru(CO)$_4$ complexes leads to substitution of one carbon monoxide ligand by an olefin. It is not necessary to isolate the complexes. For example, continued irradiation (through Solidex glass, $\lambda \gtrsim 280$ nm; preferably at a somewhat lower temperature) of *(2)* in the presence of excess methyl acrylate produces, *via* intermediate *(1)*, bis($\eta^2$-methyl acrylate)tricarbonylruthenium *(3)* in good yield. *(3)* can be isolated as white crystals.

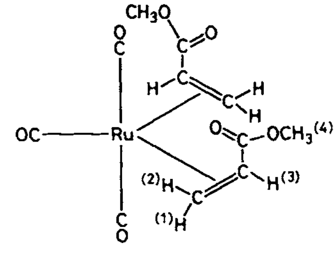
$$\underset{(2)}{\tfrac{1}{3}\,Ru_3(CO)_{12}} + CH_2{=}CH{-}CO_2CH_3 \xrightarrow{h\nu} \underset{(1)}{(CH_2{=}CH{-}CO_2CH_3)Ru(CO)_4}$$

$$\xrightarrow[+\,CH_2{=}CH{-}CO_2CH_3]{h\nu,\ -CO} \underset{(3)}{(CH_2{=}CH{-}CO_2CH_3)_2Ru(CO)_3}$$

Complex *(3)* is more stable than the analogous iron compound, which in solution loses one of the two olefinic ligands reversibly[1a]. A corresponding equilibrium involving a ($\eta^4$-methyl acrylate)Ru(CO)$_3$ species is not observed in the case of *(3)*. However, one methyl acrylate ligand can be substituted by other ligands, as described below. Pure *(3)* is stable at ambient temperature in the solid state. In solution it has limited stability, decomposition being however substantially slower than for the tetracarbonyl complex *(1)*.

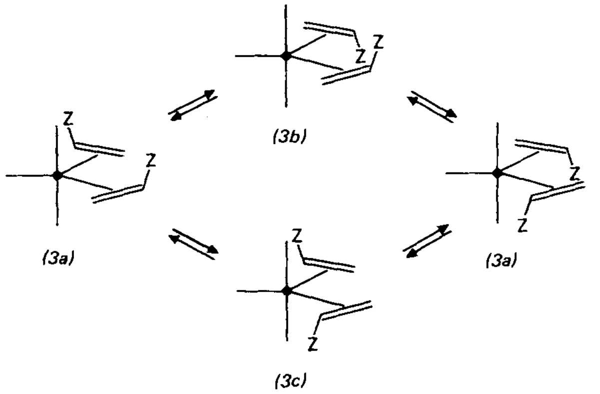
The molecular ion is not observed in the mass spectrum of *(3)*; it does, however, show the successive loss of CO ($m/e$ = 330, 302, 274; $^{102}$Ru) and/or the elimination of the olefinic ligand ($m/e$ = 272, 244, 216, 188, 186, 158, 130, and 102) as well as the formation of fragments at $m/e$ = 85, 55 (base peak), 42, 28, and 27.

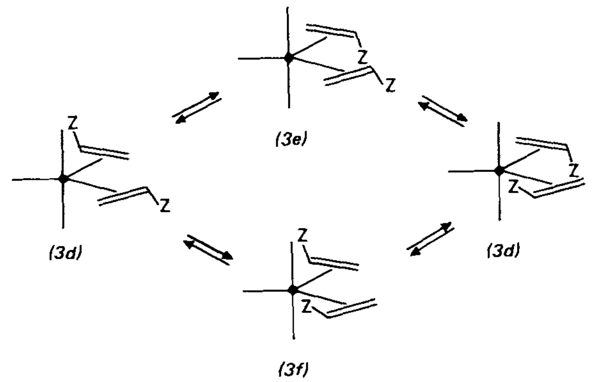
The metal carbonyl stretching bands in the infrared spectrum of *(3)* appear at 2109 (w, $A_1^{(1)}$), 2036 (st, $B_1$), and 2026/2019 (m, $A_1^{(2)}$) cm$^{-1}$. The splitting of the last band into two components, as well as the appearance of two bands at 1723/1716 cm$^{-1}$ in the ester carbonyl region, point to the presence of more than one species in solution—as will be discussed below. The intensity ratio of the metal carbonyl bands indicates local $C_{2v}$-symmetry for the M(CO)$_3$ framework, *i.e.* the two olefinic ligands should each occupy an equatorial position in the trigonal bipyramidal complex. This structural type of complex has recently been established crystallographically for tricarbonyl($\eta^4$-1,5-dimethylene-2,6-dimethylcyclooctane)iron[4a]. In the latter case, however, the coordinated double bonds are connected *via* the eight-membered ring; as such, the geometry of the complex is severely predetermined. Structure *(3a)* represents the results of the X-ray analysis[4b] of *(3)*. The complex has, as also expected for the analogous iron compound[1a,5], trigonal bipyramidal geometry, in which the olefinic ligands occupy equatorial positions with their C=C axes in the trigonal plane.



*(3a)*

The $^1$H-NMR spectrum of *(3)* (Fig. 1), recorded at 20 °C, shows two sets of signals of approximately equal intensity for the methyl acrylate ligands. The obvious suspicion that the asymmetrical structure *(3a)*, found in the solid state, is retained in solution, is, however, not correct as shown by the spectral changes occurring upon cooling. The signals broaden and, at still lower temperatures, sharpen up again to some extent. The broadening of the resonances, denoted by H(1′)—H(4′), commences prior to that of H(1″)—H(4″). The resulting relative assignments have been confirmed for the protons of both vinyl groups by double resonance experiments. Apparently, two fluxional systems are present. Of the six realistic structures that can be envisaged for *(3)* (without enantiomers) three — *(3a)*—*(3c)* and *(3d)*—*(3f)* —are interconverted by rotation around the metal-olefin bonds (Z = CO$_2$CH$_3$). Each of these processes induces (on the NMR time scale) a symmetry element ($C_2$ and $C_s$ respectively). As a result only one set of signals for each of the two systems in the fast exchange range at ambient temperature is observed. Conclusions regarding the exchange steps and the relative concentrations of the participating species cannot yet be drawn, as the spectral changes are not completed at the lowest temperatures (down to −90 °C





at 270 MHz) accessible to us. The temperature dependent changes in the $^{13}C$-NMR spectrum, which are in accord with the observations in the $^{1}H$-NMR spectrum, however, offer no additional information. An isomerization of the two systems requires the cleavage of a metal-olefin bond. Such a process should lead to coalescence of the two sets of resonances present at room temperature if it occurs sufficiently fast. This, however, is not observed up to 50 °C; above this temperature, the sample starts to decompose irreversibly. On the other hand, a slow isomerization of this type, as observed for the analogous iron compound at *ca.* 0 °C[1a], cannot be excluded.

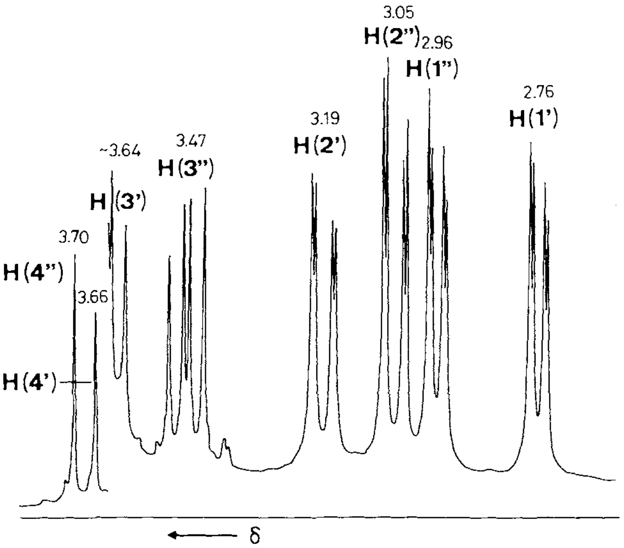
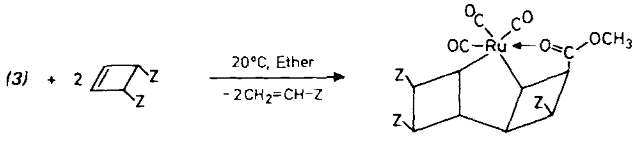


Fig. 1. 270 MHz $^{1}H$-NMR spectrum of *(3)* in $CD_2Cl_2$ at 20 °C.

There is no indication as yet for a linkage of the methyl acrylate ligands in *(3)* to form a carbonylruthenacyclopentane derivative, which should occur at the unsubstituted β-C atoms[5]. However, if *(3)* is allowed to react with excess dimethyl 3-cyclobutene-*cis*-1,2-dicarboxylate, both methyl acrylate ligands are displaced and the tricarbonyl-6-ruthenatricyclo[5.2.0.0$^{2,5}$]nonane complex *(4)* is obtained[6], by linkage of the newly entered olefins. The structural analogy between *(4)* and the corresponding iron complex[1b] has been ascertained by X-ray structure analysis[7a]. The vibration typical of an "end-on" coordinated ester group[1b] appears at 1629 $cm^{-1}$ in the infrared spectrum[6] of *(4)*.



*(4)* ($Z = CO_2CH_3$)

$(CH_2{=}CH{-}CO_2CH_3)[(C_6H_5)_3P]Ru(CO)_3$ *(5)*

*(3)* reacts with triphenylphosphane at 0 °C to yield ($\eta^2$-methyl acrylate)tricarbonyl(triphenylphosphane)ruthenium *(5)*[6]; some tricarbonylbis(triphenylphosphane)ruthenium is also formed as a by-product, the relative amount of which increases with rising temperature. Thus, the n-donor ligand displaces methyl acrylate instead of inducing—as intended—the linkage to a ruthenacyclopentane complex. It is inferred from the IR spectrum[6] of *(5)* that several (presumably three) distinct species are present in solution. The olefin should occupy an equatorial position in the trigonal bipyramid; as found for related iron complexes, the phosphane ligand could be coordinated either axially[1a,7b,7c] or equatorially[7c]. Variable temperature $^{1}H$-NMR spectra[3b] point toward a fluxional behavior of *(5)*, effected by olefin rotation (cf. [8]) and/or axial-equatorial site exchange of the phosphane ligand (cf. [7c]). These results still, however, require completion and confirmation by the corresponding $^{13}C$- and $^{31}P$-NMR spectra.

Tricarbonylbis($\eta^2$-dimethyl fumarate)ruthenium[3b] is the second complex of this type whose structure has been determined crystallographically[9]. The structure corresponds to that of *(3)*, allowing for the presence of the two additional ester groups.

### *Procedure*

*(2)* (1.95 g, 3.05 mmol) and methyl acrylate (7.87 g, 91.5 mmol) in 250 $cm^3$ pentane, under argon, are irradiated in an immersion lamp apparatus (Solidex glass, $\lambda \gtrsim 280$ nm) at ~10 °C with a high-pressure mercury Philips HPK 125 W lamp. After *(2)* has dissolved completely and the orange color of the solution has disappeared (1–2 h), the irradiation is continued for *ca.* 6 h. If necessary, the solution is filtered and concentrated to about half the original volume. At −80 °C *(3)* precipitates as white crystals, which are separated from the mother liquor by inverse filtration and dried *in vacuo* at −30 °C. Yield 1.99 g *(3)* (61%). M.p. 36–38 °C.

Received: August 28, 1980 [Z 755 IE]
German version: Angew. Chem. *93*, 475 ( 1981)

CAS Registry numbers:
*(2)*, 15243-33-1; *(3)*, 77495-49-9; *(4)*, 77507-03-0; *(5)*, 77495-50-2;

---

[1] a) *F.-W. Grevels, D. Schulz, E. Koerner von Gustorf,* Angew. Chem. *86*, 558 (1974); Angew. Chem. Int. Ed. Engl. *13*, 534 (1974); b) *B. E. Foulger, F.-W. Grevels, D. Hess, E. A. Koerner von Gustorf, J. Leitich,* J. Chem. Soc., Dalton Trans. *1979*, 1451.

[2] a) *F.-W. Grevels, J. G. A. Reuvers, J. Takats,* J. Am. Chem. Soc., in press; b) *B. F. G. Johnson, J. Lewis, M. V. Twigg,* J. Organomet. Chem. *67*, C75 (1974); c) *L. Kruczynski, J. L. Martin, J. Takats, ibid. 80*, C9 (1974).

[3] a) *R. G. Austin, R. S. Paonessa, P. J. Giordano, M. S. Wrighton,* Adv. Chem. Ser. *168*, 189 (1978); b) *F.-W. Grevels, J. G. A. Reuvers, J. Takats,* unpublished results.

[4] a) *F.-W. Grevels, K. Schneider, C. Krüger, R. Goddard,* Z. Naturforsch. *B 35*, 360 (1980); b) *L.-K. Liu, C. Krüger,* in press.

[5] *A. Stockis, R. Hoffmann,* J. Am. Chem. Soc. *102*, 2952 (1980).

[6] *(4)*: m.p. 126–130 °C (dec.). IR (*n*-hexane): metal carbonyl region, $\tilde{\nu}=2080, 2015, 1980.5$ $cm^{-1}$; ester carbonyl region, $\tilde{\nu}=1749, 1736.5, 1629$ $cm^{-1}$. $^{1}H$-NMR ($C_6D_6$): $\delta=3.19, 3.28, 3.40, 3.42$ ($4CH_3$), 2.8–3.8 (8H). The mass spectrum shows the molecular ion and the successive loss of 3CO (*m/e* = 526, 498, 470, 442; $^{102}Ru$). *(5)*: m.p. 107–109 °C (dec.). IR (*n*-hexane): metal carbonyl region, $\tilde{\nu}=2083$ m, 2067 m, 2058 w, 2007 sst, 1968 st, br $cm^{-1}$; ester carbonyl region, $\tilde{\nu}=1714$–1702 br $cm^{-1}$.

[7] a) *C. Krüger, Y.-H. Tsay,* personal communication; b) Cryst. Struct. Commun. *5*, 219 (1976); c) *J. A. Osborn, J. Takats et al.,* unpublished results.

[8] a) *L. Kruczynski, L. K. K. LiShingMan, J. Takats,* J. Am. Chem. Soc. *96*, 4006 (1974); b) *S. T. Wilson, N. J. Coville, J. R. Shapley, J. A. Osborn, ibid. 96*, 4038 (1974).

[9] *C. Krüger, G. Wolmershäuser,* personal communication.

## Charge Transfer Interactions between the Ligands of a Ternary ATP-$Cu^{2+}$-Phenanthroline Complex

By *William S. Sheldrick*[*]

Ternary complexes of metal ions play a significant role in biological processes, *e.g.* as enzyme-metal ion-substrate

---

[*] Priv.-Doz. Dr. W. S. Sheldrick
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

complexes. Although the enzymatic phosphate transfer requires, in most cases, a divalent metal ion $M^{2+}$—under physiological conditions $Mg^{2+}$—and ternary enzyme-$M^{2+}$-ATP complexes are involved in this reaction, no structure of a ternary ATP complex has previously been determined. Furthermore, no X-ray structural analysis has been carried out on a binary metal ion-ATP complex. On the basis of $^1H$-NMR studies[1] on the model systems $Cu(ATP)(bpy)^{2-}$ [bpy = 2,2′-bipyridyl] and $M(ATP)(phen)^{2-}$ [$M^{2+} = Mg^{2+}$, $Zn^{2+}$; phen = 1,10-phenanthroline], which are significantly more stable than the corresponding binary complexes $M(ATP)^{2-}$, it has been suggested that these adducts may display a metal ion-bridged conformation, which allows a charge transfer interaction between the 2,2′-bipyridyl or 1,10-phenanthroline ligands and the adenine base. In this proposed structure, the metal ion coordinates both the β- and γ-phosphate oxygens of the ATP. We have now isolated the ternary complex $[Cu(ATP)(phen)]_2 \cdot 7H_2O$ *(1)* at pH = 2.8 and report here its molecular structure (Fig. 1)[2]. At this pH, N1 of the adenine is protonated[3].

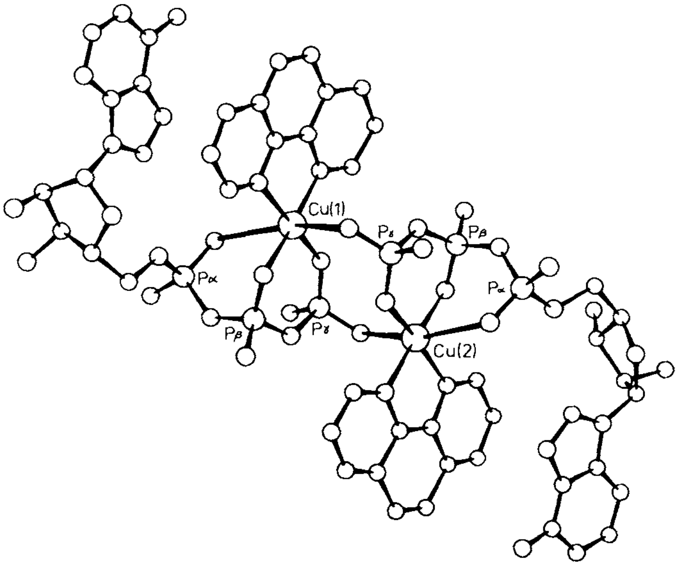


Fig. 1. Molecular structure of $[Cu(ATP)(phen)]_2$.

Both independent Cu atoms in *(1)* display a strongly distorted [4 + 2]-octahedral coordination. In each case α-, β- and γ-phosphate oxygens of an ATP are coordinated by the same $Cu^{2+}$ ion. The two phenanthroline N atoms, one ATP β- and one ATP γ-phosphate oxygen provide the equatorial ligands. The following distances were determined: Cu—$O_β$ 194.2(9) and 197.7(9); Cu—$O_γ$ 192.5(8) and 191.9(8); ($O_β$—)Cu—N 198.9(10) and 205.0(12); ($O_γ$—)Cu—N 201.3(10) and 199.3(11) pm. The coordination sphere is completed by one α-phosphate oxygen of the same ATP and one γ-phosphate oxygen of the other ATP. However, the axial Cu—$O_α$(—H) interaction is weak [Cu...$O_α$(—H) = 287.8(9) and 273.0(8) pm]. In contrast, the axial Cu—$O_γ$ distances are 228.4(8) and 227.3(9) pm respectively. As a result of the weak Cu—$O_α$(—H) interaction, the coordination of the Cu atoms is distorted somewhat in the direction of a square pyramidal geometry. Cu1 is displaced 4.4 pm from the best equatorial plane in the direction of the Cu—$O_γ$ axial bond and Cu2 by 4.3 pm. Both adenosine moieties display similar nucleotide configurations; the observed values lie in the typical regions for purine nucleotides. The conformations at the glycosidic C1′—N9 bond are *anti* ($\chi_{CN}$ = 32.3 and 5.7°), those at the C4′—C5′ bond *gauche-gauche* ($\psi_{OC}$ = 59.6 and 50.1°)[4]. The ribose moieties display the C3′-*endo*-conformation. Similar conformations are observed for both independent ATP molecules in the crystal lattice of $ATPNa_2 \cdot 3H_2O$ ($\chi_{CN}$ = 69 and 39°, $\psi_{OC}$ = 66.3 and 48.6°), whereas one ribose moiety adopts a C3′-*endo*-, the other a C2′-*endo*-conformation[5].

The crystal structure of *(1)* is stabilized by both *intra*- and intermolecular interactions between adenine and phenanthroline systems. The shortest intramolecular distances to the atoms of a phenanthroline system are observed for C8 of the first adenine [331.7 pm] and C5 of the second adenine [348.5 pm]. The base planes are not quite parallel to one another [angles = 6.7 and 5.8°]. This structure demonstrates that base stacking may be observed in ternary ATP complexes together with the involvement of all three phosphate functions in the metal coordination (the α-function albeit to a lesser extent) without the nucleotide being forced to take up an unusual conformation. In accordance with the observed structures of ternary complexes of nucleotide monophosphates[6], the adenine bases are not involved in coordination to the metal ions. It can, therefore, be assumed with some degree of certainty that metal ions preferentially coordinate the phosphate oxygens in enzyme-metal ion-ATP complexes.

1,10-Phenanthroline may be regarded as a simple model for an enzyme which binds $M(ATP)^{2-}$ more strongly than $M^{2+}$ or $ATP^{4-}$ alone, *e.g.* the system arginine kinase/$Mn(ATP)^{2-}$[7]. The present results then suggest that charge transfer interactions may play an important role in the increased stability of enzyme-$M^{2+}$-ATP complexes.

## *Experimental*

0.28 g (0.5 mmol) $ATPNa_2$ in 3 $cm^3$ $H_2O$ is added with stirring to a solution of 0.10 g (0.5 mmol) $Cu(NO_3)_2$ and 0.10 g (0.5 mmol) 1,10-phenanthroline in 6 $cm^3$ $H_2O$ at 80°C. The pH value is adjusted to 2.8 and the temperature held at 80°C for 30 min. Blue-green prismatic crystals precipitate upon slow cooling. *(1)*, which is obtained in quantitative yield, is filtered off and washed with water and methanol.

Received: September 1, 1980 [Z 756 IE]
German version: Angew. Chem. *93*, 473 (1981)

CAS Registry numbers
*(1)*, 77507-04-1

---

[1] *C. F. Naumann, H. Sigel,* J. Am. Chem. Soc. *96*, 2750 (1974); *P. R. Mitchel, H. Sigel, ibid. 100*, 1564 (1978).

[2] *(1)*, $C_{44}H_{44}N_{14}O_{26}P_6Cu_2 \cdot 7H_2O$, crystallizes monoclinic, $P2_1$, with $a = 1180.7(3)$, $b = 2482.4(5)$, $c = 1069.3(2)$ pm, $\beta = 94.98(3)°$, $Z = 2$, $\rho_{calc} = 1.73$ g $cm^{-3}$. The structure was refined to $R = 0.069$, $R_w = 0.067$ for 3649 independent reflexions ($2\theta \leqslant 120°$, Cu$K_\alpha$-radiation, $F^2 \geqslant 2.0\sigma(F^2)$). Cu, P and O atoms received anisotropic temperature factors. Of the 7 crystal water molecules, 4 are disordered.

[3] *C. F. Naumann, B. Prijs, H. Sigel,* Eur. J. Biochem. *41*, 209 (1974).

[4] Definitions of $\chi_{CN}$ and $\psi_{OC}$ are given in *M. Sundaralingam,* Ann. N. Y. Acad. Sci. *255*, 3 (1975).

[5] *O. Kennard, N. W. Isaacs, W. D. S. Motherwell, J. C. Coppola, D. L. Wampler, A. C. Larson, D. G. Watson,* Proc. R. Soc. (London) *A 325*, 401 (1972).

[6] *Chaiau-Yu Wei, B. E. Fischer, R. Bau,* J. Chem. Soc. Chem. Commun. *1978*, 1053; *K. Aoki,* J. Am. Chem. Soc. *100*, 7106 (1978).

[7] *D. H. Buttlaire, M. Cohn,* J. Biol. Chem. *249*, 5733, 5741 (1974).

# Insertion of —CN into the Metal-Carbene Carbon Bond: A Route to Methyleneaminocarbene Complexes

By *Helmut Fischer* and *Ulrich Schubert*[*]

Owing to the polarity of the CN-bond, azomethines $R^1$—N═$CR^2R^3$ react with a wide variety of substrates[1]. Complexes formed by replacement of one of the substituents ($R^1$, $R^2$ or $R^3$) are therefore especially suited for stu-

---

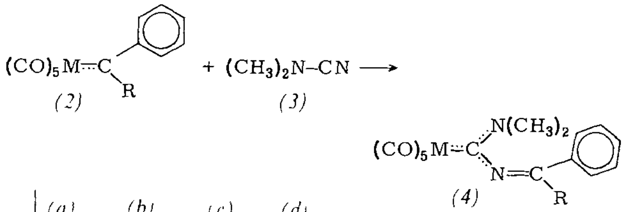
[*] Dr. H. Fischer, Dr. U. Schubert
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

dies on the influence of metal-organic fragments on the reactivity of organic functional groups. In the case of the methyleneaminocarbene complexes

$(CO)_5M{-}C(R)N{=}CR^2R^3$ *(1)*

an additional polarization and thus activation of the N=C bond could be expected, owing to the large deficiency of electrons at the carbene-carbon atom.

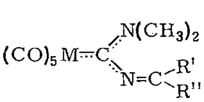
Compounds of type *(1)* are now readily accessible by reaction of arylcarbene(pentacarbonyl)chromium(0) and -tungsten(0) *(2)* with cyanamides. The complexes *(2)* react with dimethylcyanamide *(3)* almost quantitatively in polar or non-polar solvents, even at room temperature, with insertion of the CN-group into the metal-carbene carbon bond to give pentacarbonyl[dimethylamino(methyleneamino)carbene]chromium(0) and -tungsten(0) *(4)*[2].



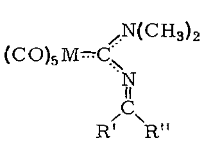
| | *(a)* | *(b)* | *(c)* | *(d)* |
|---|---|---|---|---|
| M | Cr | W | W | W |
| R | $OCH_3$ | $OCH_3$ | $C_6H_5$ | $p$-$CH_3C_6H_4$ |

The new yellow crystalline products *(4)*, which are stable under nitrogen at room temperature, are readily soluble in polar solvents, and only moderately soluble in non-polar solvents. The position of the $\nu_{CO}$ bands hardly changes on varying R, whereas the C=N stretching vibration (KBr mull) is more influenced: 1680 *(4a)*, 1677 *(4b)*, 1644 *(4c)*, and 1636 *(4d)* $cm^{-1}$; cf. 1666 $cm^{-1}$ ($H_5C_6{-}N{=}C(C_6H_5)OCH_3$) and 1611 $cm^{-1}$ ($H_5C_6{-}N{=}C(C_6H_5)_2$)[3].

The two singlets observed for the $N{-}CH_3$ protons in the $^1H$-NMR spectra indicate partial double bond character of the $C_{carb}{-}N(CH_3)$-bond. Moreover, it follows from the $^1H$-NMR spectra that only one isomer *(A, B, C, D* or *E)* is formed.



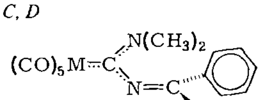
*A, B*



*C, D*

*A, C*: R' = $C_6H_5$, R'' = R

*B, D*: R' = R , R'' = $C_6H_5$



*E*

In all four isomers with parallel π-systems *(A—D)* considerable steric interactions are to be expected, either with the carbonylmetal moiety or, with the amino groups coplanar to the carbene plane in aminocarbene complexes. An X-ray structure analysis showed the presence of the isomer *E* (torsional angle N1—C1—N2—C2: 100.6°); indication of this was already provided by the yellow color of *(4)*, since in the case of *A—D* the first absorption maximum would have been expected at distinctly higher wavelengths. The equal lengths of the C1—N1 and C1—N2 bonds (see Fig. 1) prove that there is, nevertheless, π-interaction between the two nitrogen atoms and the carbene-carbon. On the basis of the observed geometry a most unusual $n_\pi$-$p_\pi$ bonding must be assumed for C1—N2. The contribution of the carbonylmetal fragment to the electronic stabilization of the carbene-carbon is small, owing to the contribution of the two organic substituents, as is evidenced by the very long Cr—C1 bond—whose unusual length is only seldom met with, even in aminocarbene complexes[5].

The $^1H$-NMR spectrum of *(4d)* (in hexachlorobutadiene) does not alter until decomposition of *(4d)* takes place, with concomitant change in color to brown. An isomerization of *E* to *A* and/or *B* or to *C* and/or *D* can therefore not be detected.

The formation of *(4)* from *(2)* and *(3)* is a second-order reaction. The rate constants *k* of a series of diphenylcarbene(pentacarbonyl)tungsten complexes, in which one of the two parahydrogen atoms is replaced by a donor group, or by an acceptor group, show a good positive correlation with the Hammett σ-constants[6]. This suggests a nucleophilic attack of the negatively polarized nitrogen of the CN group of *(3)* at the $\delta^+$-polarized carbene-carbon of *(2)* in the first reaction step. Subsequently, insertion into the $M{-}C_{carb}$ bond takes place—most likely with intermediary formation of a metallacycle. A similar mechanism was also deduced from the results of kinetic studies on the insertion of ynamines into the metal-carbene carbon bond of carbene complexes[7a], and presumed for the insertion of ethoxyacetylene in the same compounds[7b]. Complexes of type *(1)* were previously only accessible by reaction of pentacarbonyl[methoxy(methyl)carbene]chromium(0) with oximes or diphenylmethaneimine[8a] and of pentacarbonyl[methoxy(phenyl)carbene]chromium(0) with 1-aminoethanol[8b]. An investigation of the reactivity of these compounds however, was not carried out, mainly owing to the poor yields (5.7 to 21%). In addition, two complexes amino-substituted on the methylene group [$R^2 = N(C_2H_5)_2$, $R^3 = C_2H_5$] could be obtained by addition of amino(methyl)carbene- or amino(phenyl)carbene(pentacarbonyl)chromium(0) to *N,N*-diethyl-1-propynylamine[9].

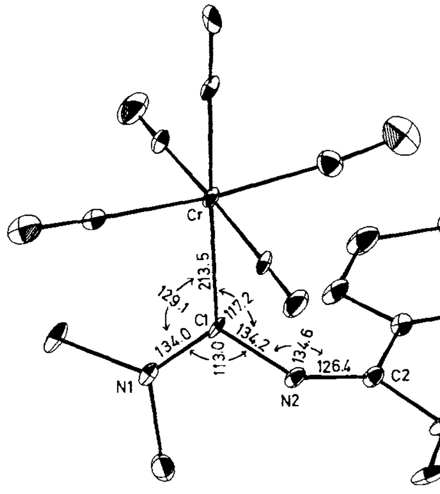


Fig. 1. Structure of complex *(4a)*. The hydrogen atoms are not shown. Standard deviations: 0.4—0.7 pm, and 0.3—0.4°.

### *Procedure*

A solution of *(2)* (1.0 mmol) and *(3)* (1.05 to 1.10 mmol) in ether (3 $cm^3$) is stirred at room temperature for one [*(2c)*] to ten hours [*(2a)*]. The initial deep-red solution turns bright yellow. After removal of solvent in a water-jet vacuum the residue is washed with $3 \times 5$ cm$^3$ of pentane; the pentane is then decanted off. After several hours' drying in a water-jet vacuum one obtains analytically pure *(4)*. *(4a)*—*(4d)*: m.p. = 69, 79, 130 (dec.), 106 °C; yields 85, 75, 80, 81%.

Received: March 17, 1980 [Z 718a IE]
German version: Angew. Chem. *93*, 482 (1981)

---

[1] Cf. also *S. Patai*: The Chemistry of the Carbon-Nitrogen Double Bond, Interscience, London 1980.

[2] The structure of *(4)* is confirmed by IR, $^1$H-NMR and mass spectra, elemental analysis, and an X-ray structure analysis [of *(4a)*].

[3] *J. Fabian, M. Legrand, P. Poirier*, Bull. Soc. Chim. Fr. *1956*, 1499.

[4] *(4a)*, triclinic, space group $P\bar{1}$ ($Z=2$), $a=837.8(6)$, $b=944.4(10)$, $c=1230.2(11)$ pm, $\alpha=86.16(8)$, $\beta=107.24(6)$, $\gamma=103.37(6)°$, $V=904\times10^6$ pm$^3$; $\rho_{calc}=1.404$ g/cm$^3$, 3159 independent reflections ($2° \leq 2\theta \leq 50°$, Mo$_{K\alpha}$, graphite monochromator, $\lambda=71.069$ pm); 2391 structural factors ($F_0 \geq 4.2\sigma(F_0)$), $R=0.057$; Syntex $P2_1$/XTL.

[5] *E. O. Fischer, R. B. A. Pardy, U. Schubert*, J. Organomet. Chem. *181*, 37 (1979), and references cited therein.

[6] *H. Fischer*, J. Organomet. Chem. *197*, 303 (1980).

[7] a) *H. Fischer, K. H. Dötz*, Chem. Ber. *113*, 193 (1980); b) *C. P. Casey, S. W. Polichnowski, A. J. Shusterman, C. R. Jones*, J. Am. Chem. Soc. *101*, 7282 (1979).

[8] a) *L. Knauss, E. O. Fischer*, Chem. Ber. *103*, 3744 (1970); b) J. Organomet. Chem. *31*, C68 (1971).

[9] *K. H. Dötz*, J. Organomet. Chem. *118*, C13 (1976).

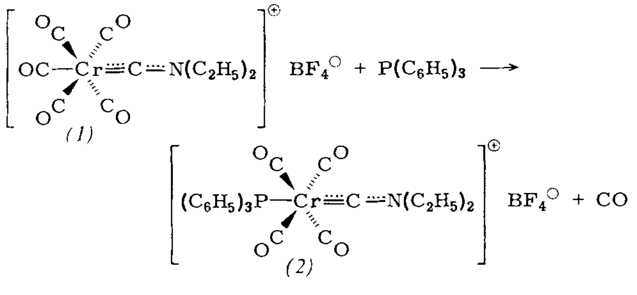
---

## Ligand Mobility in Carbyne Complexes[**]

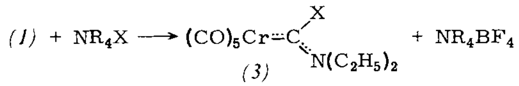
By *Helmut Fischer, Andreas Motsch, Ulrich Schubert,*
and *Dietmar Neugebauer*[*]

Pentacarbonyl(halocarbene)metal complexes are of particular interest as potential intermediates in the synthesis of halo(tetracarbonyl)carbynemetal complexes from carbene complexes and trihalides of main group III elements[1]. Thus, pentacarbonyl[diethylamino(halo)carbene]chromium(0), $(CO)_5Cr[C(X)NEt_2]$ *(3)*, X = Cl, Br, I, spontaneously rearranges in solution with loss of CO to give *trans*-$X(CO)_4CrCNEt_2$ *(5)*[2]. Replacement of the *trans*-CO group by another neutral ligand should afford valuable information on the course of this rearrangement of a carbene complex into a carbyne complex.

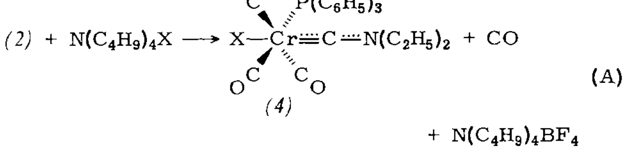
Pentacarbonyl(diethylaminocarbyne)chromium tetrafluoroborate *(1)*[3] reacts with triphenylphosphane in a first-order reaction (half-life 68 s in 1,1,2-trichloroethane at 25 °C) to give *trans*-tetracarbonyl(diethylaminocarbyne)triphenylphosphanechromium tetrafluoroborate *(2)* (red-brown crystals, decomposition above 120 °C)[4].



The *cis*-isomer of *(2)* could not be detected. In the reaction of *(2)* with $N(C_4H_9)_4X$ analogous to the preparation of *(3)* from *(1)* and tetraalkylammonium halides, however, we did not obtain *trans*-tetracarbonyl[diethylamino(halo)carbene]triphenylphosphanechromium(0), but, surprisingly, *mer*-tricarbonyl(diethylaminocarbyne)halo(triphenylphosphane)chromium *(4)*[4].

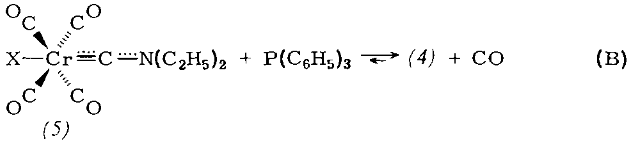


X = F, Cl, Br, I



*(a)*, X = Cl; *(b)*, X = Br; *(c)*, X = I

In *(4)* the groups originally *trans* oriented in *(2)* are in the *cis*-position, while the entering ligand ($X^-$) takes up the *trans*-position to the carbyne group. No indication could be found of the formation of *trans*-tetracarbonyl[diethylamino(halo)carbene]triphenylphosphanechromium or other isomers of *(4)*. *(4)* is also accessible from *trans*-tetracarbonyl(diethylaminocarbyne)halochromium *(5)* by CO/PPh$_3$ exchange (first-order reaction, half-life for *(5b)*→*(4b)* 129 s in 1,1,2-trichloroethane at 25 °C).



*(a)*, X = Cl; *(b)*, X = Br; *(c)*, X = I

X-ray structure analyses were carried out on *(2)* and *(4b)* (Fig. 1)[4]. Comparison with the structures of the analogous methylcarbyne complexes

[*trans*-$Me_3P(CO)_4Cr{\equiv}CMe]BCl_4$ *(6)* [5]
and *mer*-$Br(Me_3P)(CO)_3Cr{\equiv}CMe$ *(7)* [6]

showed, first of all, that the amino group could be in resonance with the metal-carbon bond[7]. As a result, the electron density at the metal in the aminocarbyne complexes is greater than in the corresponding methylcarbyne complexes. This manifests itself almost exclusively in a shortening of the metal-ligand bond length of the group *trans* to the aminocarbyne moiety (Cr—Br in *(4b)*: 257.2 pm, in *(7)*: 260.3 pm; Cr—P in *(2)*: 246.4 pm, in *(6)*: 247.4 pm; it should be remembered that metal-PMe$_3$ bond lengths are shorter than metal-PPh$_3$ bond lengths in comparable complexes).

Although the reactions *(2)*→*(4)* and *(5)*→*(4)* (at least in the case of X = Br) proceed almost equally rapidly, formation of *(4)* *via* the reaction sequence

$$(2) + X^- \rightarrow (5) + PPh_3 \rightarrow (4) + CO$$

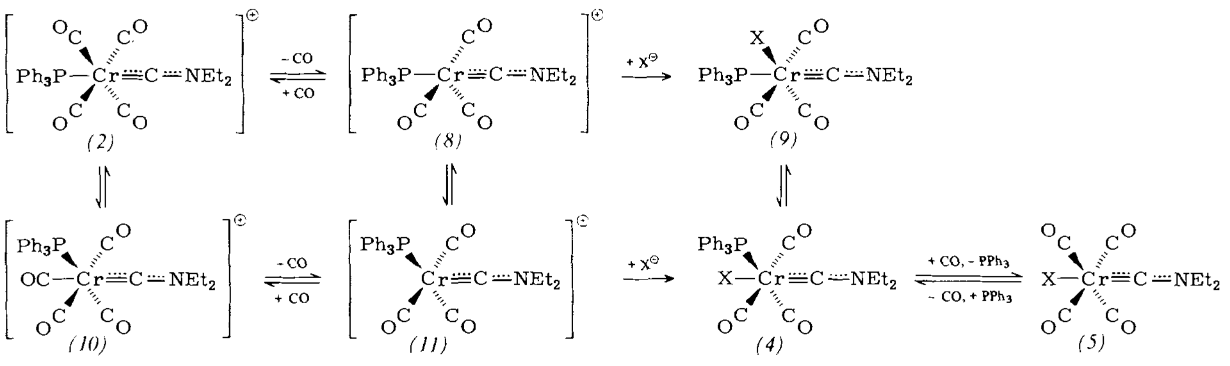
can be ruled out, since PPh$_3$ is not exchanged in *(2)* in the presence of excess free triisopropylphosphane but CO is

---

[*] Dr. H. Fischer [+], Dipl.-Chem. A. Motsch, Dr. U. Schubert,
Dr. D. Neugebauer
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[+] Author to whom correspondence should be addressed.

[**] Kinetic and Mechanistic Investigations of Transition Metal-Complex Reactions, Part 7.—Part 6: *H. Fischer*, J. Organomet. Chem. *197*, 303 (1980).



Scheme 1. Anions of *(2)*, *(8)*, *(10)* and *(11)* are not shown.

replaced by this phosphane in a slow reaction with formation of $[PPh_3PiPr_3(CO)_3CrCNEt_2]BF_4$.

*(2)* reacts almost quantitatively with $Br^-$ and $I^-$ (reaction A) under pseudo-first-order conditions and with rapid removal of the extruded carbon monoxide (purging of the solution with $N_2$); on the other hand, *(4b)* and *(4c)* react further with free CO to give *(5b)* and *(5c)*, respectively, in the closed cuvette or under CO as protecting gas (back reaction of B). This back reaction can be avoided by addition of $PPh_3$ in large excess[8]. This would suggest the reaction sequence shown in Scheme 1.

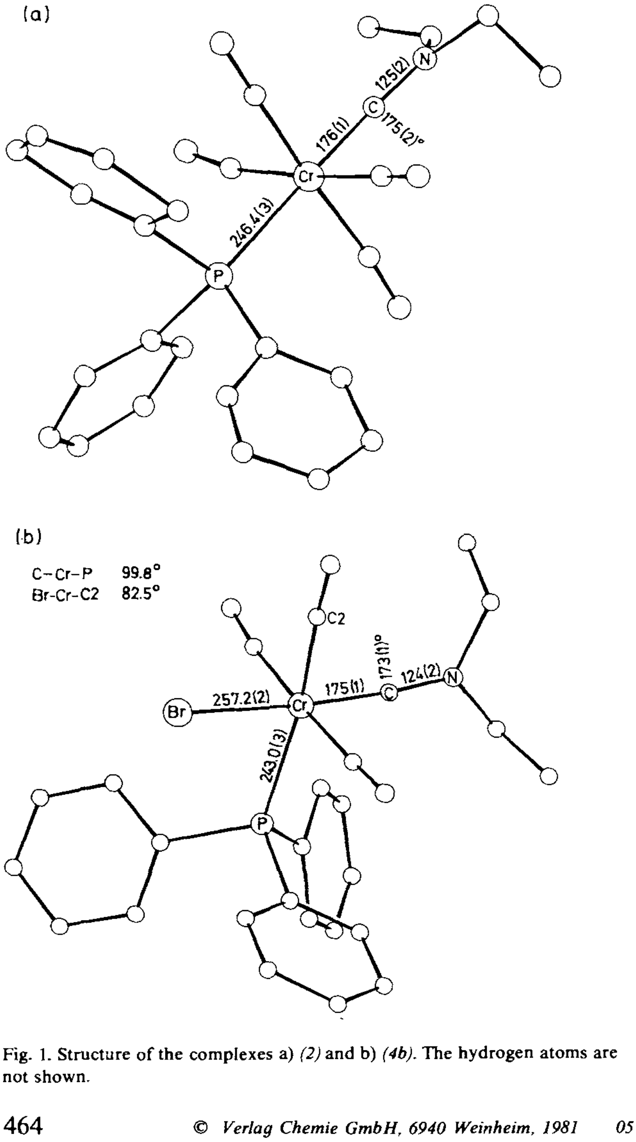


Fig. 1. Structure of the complexes a) *(2)* and b) *(4b)*. The hydrogen atoms are not shown.

Although the sequence *(2)*→*(8)*→*(11)*→*(4)* is most likely, and although neither *(9)* nor *(10)* could be hitherto detected, the sequences *(2)*→*(10)*→*(11)*→*(4)* and *(2)*→*(8)*→*(9)*→*(4)* cannot be ruled out with certainty.

The reason for the marked difference in the reaction of *(1)* and *(2)* with halides could be explained in terms of the different charge distribution in these compounds, which is also reflected in the bond lengths. The $C_{carbyne}$—N bond lengths in *(1)* (125.6(12) pm)[9] and in *(2)* (125.2(16) pm) are actually about the same size, but the Cr—$C_{carbyne}$ bond length in *(1)* (179.7(9) pm)[9] is distinctly greater than that in *(2)* (175.7(11) pm). Whereas the substantial localization of the positive charge in *(1)* at the carbyne-carbon leads very rapidly to *(3)* (with assumption of a second-order reaction $k$ can be estimated as > 1000 $dm^3\ mol^{-1}\ s^{-1}$ for X = Br in 1,1,2-trichloroethane at −30 °C), with *(2)* (here the charge is predominantly localized in the $PPh_3$—$Cr(CO)_4$ moiety) one obtains *(4)* in a substantially slower reaction primarily by a dissociative mechanism with substitution and rearrangement.

Received: July 23, 1980 [Z 718b IE]
German version: Angew. Chem. *93*, 483 (1981)

---

[1] Cf. also a) *E. O. Fischer*, Angew. Chem. *86*, 651 (1974); b) *E. O. Fischer, U. Schubert*, J. Organomet. Chem. *100*, 59 (1975).

[2] a) *E. O. Fischer, W. Kleine, F. R. Kreissl*, J. Organomet. Chem. *107*, C23 (1976); b) *E. O. Fischer, W. Kleine, F. R. Kreissl, H. Fischer, P. Friedrich, G. Huttner, ibid. 128*, C49 (1977); c) *H. Fischer, A. Motsch, W. Kleine*, Angew. Chem. *90*, 914 (1978); Angew. Chem. Int. Ed. Engl. *17*, 842 (1978).

[3] *E. O. Fischer, W. Kleine, F. R. Kreissl*, Angew. Chem. *88*, 646 (1976); Angew. Chem. Int. Ed. Engl. *15*, 616 (1976).

[4] a) The structure of *(2)* and *(4a—c)* is confirmed by IR and $^1H$-NMR spectra, elemental analysis, and, in the case of *(2)* and *(4b)*, by X-ray structure analysis; b) *(2)*: orthorhombic, $Pna2_1$ ($Z=4$), $a=2164.2(16)$, $b=790.1(6)$, $c=1647.7(8)$ pm; 1531 structure factors ($F_0 \geqq 4.5\sigma$, $2° \leqq 2\theta \leqq 50°$), $R=0.074$.—*(4b)*: monoclinic, $P2_1/c$ ($Z=4$), $a=1286.9(6)$, $b=1009.0(3)$, $c=2036(1)$ pm, $\beta=98.22(4)°$; 2340 structure factors ($F_0 \geqq 4.0\sigma$, $2° \leqq 2\theta \leqq 48°$), $R=0.086$. Syntex $P2_1$/XTL, $Mo_{K\alpha}$ radiation (graphite monochromator, $\lambda=71.069$ pm), measuring temperature *ca.* −20 °C.

[5] *G. Huttner, A. Frank, E. O. Fischer*, Isr. J. Chem. *15*, 133 (1976/77).

[6] *G. Huttner, H. Lorenz, W. Gartzke*, Angew. Chem. *86*, 667 (1974); Angew. Chem. Int. Ed. Engl. *13*, 609 (1974).

[7] *E. O. Fischer, G. Huttner, W. Kleine, A. Frank*, Angew. Chem. *87*, 781 (1975); Angew. Chem. Int. Ed. Engl. *14*, 760 (1975).

[8] The reaction of *(2)* with $Cl^-$ does not come to equilibrium, since *(4a)* and *(5a)* decompose with cleavage of CO.

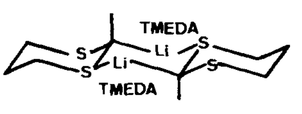
[9] a) *U. Schubert, E. O. Fischer, D. Wittmann*, Angew. Chem. *92*, 662 (1980); Angew. Chem. Int. Ed. Engl. *19*, 643 (1980); b) *U. Schubert, D. Neugebauer, H. Fischer, A. Motsch, P. Hofmann, B. E. R. Schilling*, Chem. Ber., in press; the bond lengths quoted here and in [9b] for *(1)* differ somewhat from those quoted in [9a] because of a further refinement.

# Crystal Structure of 2-Lithio-2-phenyl-1,3-dithiane-Tetrahydrofuran-Tetramethylethylenediamine (1/1/1); Electron-Density Difference Maps for Lithio-methyl- and Lithio-phenyl-dithiane

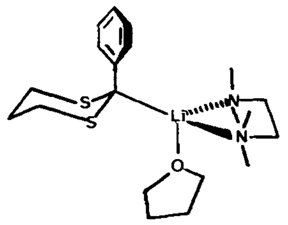
By *René Amstutz, Jack D. Dunitz,* and *Dieter Seebach*[*]

*Dedicated to Professor Edgar Heilbronner on the occasion of his 60th birthday*

The nature of the Li—C bond and of the stabilization of carbanionoid centers by adjacent third- and higher-row atoms are both still matters of debate[1]. "..., the mechanism of anion stabilization by third and higher row elements remains an unsettled and important problem. Operational criteria to distinguish charge transfer from polarization effects are difficult to devise, particularly with the limitations of working with real compounds[1c]". The main features of electron-density difference maps obtained by X-ray analysis are often identifiable, at least qualitatively, with concepts (bonding density, lone-pair electrons, π-bonds) that chemists use in discussing the electronic structure of molecules[2]. In this paper we describe evidence from such maps[2] for the existence of two different types of Li—C bond in closely related sulfur-α-substituted organolithium compounds, namely dimeric 2-lithio-2-methyl-1,3-dithianetetramethylethylenediamine (TMEDA) *(1)*[3] and the title compound *(2)*[4].

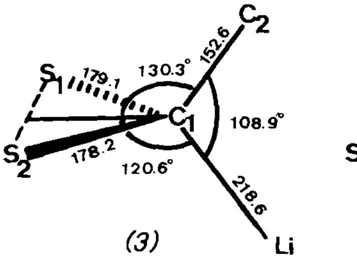


*(1)*

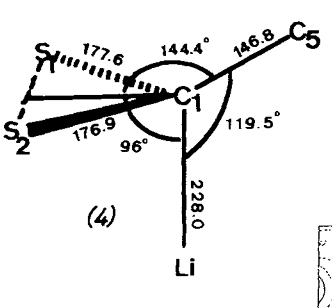


*(2)*

Crystalline *(2)* was obtained by deprotonation of phenyldithiane [0.25 M solution in hexane/tetrahydrofuran (THF) 3 : 1] with butyllithium in the presence of TMEDA (0.33 M) at −15 °C, followed by cooling to −78 °C. X-ray analysis[5] of *(2)* led to the structure depicted in Figure 1. The surroundings of the carbanionoid centers in *(1)* and *(2)* are shown in *(3)* and *(4)*, respectively.



*(3)*



*(4)*

Several features of the structure of the metalated phenyldithiane *(2)* are noteworthy. In order to achieve its usual coordination number 4, the lithium atom is bonded to the oxygen atom of a THF molecule in addition to the dithiane carbon C1 and the two nitrogen atoms of TMEDA; thus, in contrast to *(1)*, the complex *(2)* is monomeric. The phenyl group in unmetalated 2-phenyldithiane is equatorial[6] but in *(2)* is axial[7] and its plane is rotated by 90° with respect to the unmetalated compound to achieve an orientation that allows conjugative stabilization. Although the C1—C5 bond length of 147 pm indicates considerable double-bond character, the carbanionoid C1 is still far from planar (see Fig. 1). On passing from *(1)* to *(2)*, the Li—C bond length increases by 10 pm and the angle between this bond and the S1—C1—S2 bisector decreases from 121° to 96° [cf. *(3)* and *(4)*]. While these changes indicate a shift towards a π-complex type of structure in *(2)* (cf. the structure of benzyllithium-TMEDA[8]), they may appear small when considerd against the differences in reactivity between the two compounds, for example, with α,β-unsaturated carbonyl compounds[9], or against the difference of 8 units between the p$K_s$'s of the conjugate acids[1c].

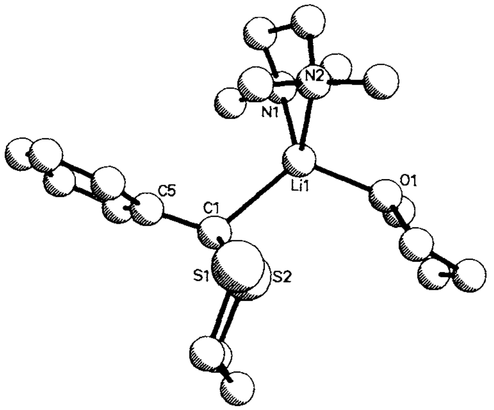


Fig. 1. Structure of complex *(2)* with H-atoms excluded (drawn by Program PLUTO, Cambridge Crystallographic Data Centre). Crystal data: Space group $P\bar{1}$; $Z=2$, $a=900.56$, $b=980.32$, $c=1295.55$ pm, $\alpha=96.28$, $\beta=97.15$, $\gamma=101.55°$, $\rho_{calc}=1.178$ g/cm³. Bond lengths [pm, $\sigma \leqslant 0.5$ pm] Li1—O1 197.0, Li1—N1 214.8, Li1—N2 211.0; angle [°, $\sigma \leqslant 0.10°$] O1—Li1—N1 105.8, O1—Li1—N2 108.8, O1—Li1—C1 117.2, C1—Li1—N1 119.8, C1—Li1—N2 114.1, N1—Li1—N2 86.9.

Electron-density difference maps ($\Delta\rho = \Delta\rho_{exp} - \Delta\rho_{calc}$) calculated for *(1)* and *(2)* show, on the whole, similar bonding density for corresponding C—C, C—N, and C—S bonds in the two structures together with lone-pair peaks in the expected directions, close to the N, O and S atoms. By far the greatest difference between the two maps occurs at the Li atoms. Figure 2 shows sections of $\Delta\rho$ for *(1)* and *(2)* in the plane of C1, Li and an N atom of TMEDA. The diffuse peaks along the bond directions may be identified as bonding or lone-pair density. At the Li atoms, $\Delta\rho$ is

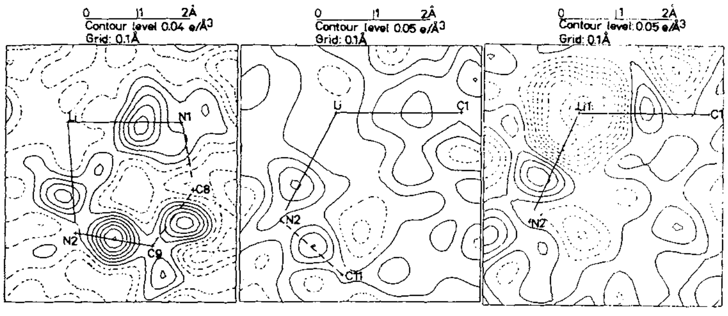


Fig. 2. Electron-density difference-maps in the planes: N1—Li—N2 and C1—Li—N2 of *(1)* and C1—Li—N2 of *(2)*. Contours at intervals of 0.05 eÅ⁻³ (negative contours dotted).

---

[*] Prof. Dr. D. Seebach, Dipl.-Chem. R. Amstutz, Prof. Dr. J. D. Dunitz
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

*0570-0833/81/0505-465* $ *02.50/0*

close to zero in *(1)* but strongly negative in *(2)*. By integration, the electron-density deficit on the Li atom in *(2)* is estimated to be about 0.5—0.6 electrons. Thus, from the electron-density difference maps, 2-lithio-2-methyldithiane would seem to have a covalent, at most polarized, Li—C bond, whereas 2-lithio-2-phenyldithiane can be regarded as an example of a contact ion-pair complex.

Received: January 9, 1981 [Z 762 IE]
German version: Angew. Chem. *93*, 487 (1981)

---

[1] a) *E. Buncel, T. Durst:* Comprehensive Carbanion Chemistry, Elsevier, Amsterdam 1980; b) *T. Clark, J. Chandrasekhar, P. v. R. Schleyer*, J. Chem. Soc. Chem. Commun. *1980*, 672; c) *S. A. Streitwieser Jr., E. Juaristi, L. L. Nebenzahl*, in [1a], Chpt. 7.

[2] *P. Coppens*, Angew. Chem. *89*, 33 (1977); Angew. Chem. Int. Ed. Engl. *16*, 32 (1977); *J. D. Dunitz:* X-Ray Analysis and the Structure of Organic Molecules, Chpt. 8, Cornell University Press, 1979.

[3] *R. Amstutz, D. Seebach, P. Seiler, B. Schweizer, J. D. Dunitz*, Angew. Chem. *92*, 59 (1980); Angew. Chem. Int. Ed. Engl. *19*, 53 (1980).

[4] *D. Seebach*, Synthesis *1969*, 17; *D. Seebach, E. J. Corey*, J. Org. Chem. *40*, 231 (1975); *B.-Th. Gröbel, D. Seebach*, Synthesis *1977*, 357.

[5] A single crystal of *(2)* was enclosed in a thin-walled quartz capillary in a dry argon atmosphere using tetradecane as adhesive and transferred to a Enraf-Nonius-CAD4 diffractometer with graphite-monochromator ($Mo_{K\alpha}$-radiation) and low-temperature device. Data collection at −180 °C gave 3976 measured reflections (2314 with $I > 3\sigma_I$); out to $\theta = 27°$. Least-squares refinement with anisotropic vibration parameters for non-hydrogen atoms, isotropic for hydrogens gave $R = 0.038$ ($R_w = (\sum w||F_o| - |F_c||/\sum w|F_o|) = 0.045$, $w = \sigma^{-2}(F)\exp(A\sin^2\theta/\lambda^2)$ with $A = 3.2$ Å$^2$. Cf. *P. Seiler, J. D. Dunitz*, Acta Cryst. *B 29*, 589 (1973). Similar refinement of *(1)* gave $R_w = 0.033$ with $A = 4.2$ Å$^2$. $\Delta\rho = \rho_{exp} - \rho_{calc}$ maps were calculated with standard scattering factors for neutral atoms (International Tables for X-Ray Crystallography, Vol. 4, pp. 72—75.

[6] *M. T. Kalff, C. Romers*, Acta Crystallogr. *20*, 490 (1966).

[7] In agreement with conclusions from captive experiments: *A. G. Abatjoglou, E. L. Eliel, L. F. Kuyper*, J. Am. Chem. Soc. *99*, 8262 (1977).

[8] *S. Pattermann, I. L. Karle, G. D. Stucky*, J. Am. Chem. Soc. *92*, 1150 (1970).

[9] *P. C. Ostrowski, V. V. Kane*, Tetrahedron Lett. *1977*, 3549; *A. Yamaichi, C. A. Brown*, J. Chem. Soc. Chem. Commun. *1979*, 100; *M. El-Bouz, L. Wartski*, Tetrahedron Lett. *1980*, 2897.

---

## $Ca_3AlAs_3$—An Intermetallic Analogue of the Chain Silicates[**]

By *Gerhard Cordier* and *Herbert Schäfer*[*]

*Dedicated to Professor Karl Heinrich Lieser on the occasion of his 60th birthday*

Salts with complex anions gain metallic bonding character if the nonmetallic components in their anionic moieties are replaced by semimetals—there result Zintl phases with complex anions. This transition in bond character was recently demonstrated for compounds having $Ba_4Si(Ge)As_4$ structure, in which $Si(Ge)As_4^{8-}$-tetrahedra occur, corresponding to the isosteric $Si(Ge)O_4^{4-}$ tetrahedra in the *ortho*-silicates and germanates[1]. We have now succeeded in preparing $Ca_3AlAs_3$ having $(AlAs_3)_n^{6-}$-chain anions which are isosterically and structurally completely analogous to the polysilicate(germanate) anions $(SiO_3)_n^{2-}$ and $(GeO_3)_n^{2-}$. As shown in Figure 1[2] the structure contains "*Einer-einfachketten*" (nomenclature after *Liebau*) of $AlAs_4$ tetrahedra. The Al—As atomic distances of 250.2, 250.3, 253.9 pm (2 ×) correspond to the sum of the covalent radii of these elements as quoted by *Pauling* (≙ 244 pm); they are significantly shorter than the sum of the metal (≙ 291 pm) or ionic radii (≙ 272 pm). The bond angles at the central Al atom are 102.4, 112.4 (2 ×), 108.8 (2 ×), 111.6°. These results demonstrate for the first time that chains of corner-linked tetrahedra, which are already known as basic structural units in the salts of isopolyacids of the main group elements, *e.g.* of silicon or phosphorus, can also occur in intermetallic compounds of the Zintl type.

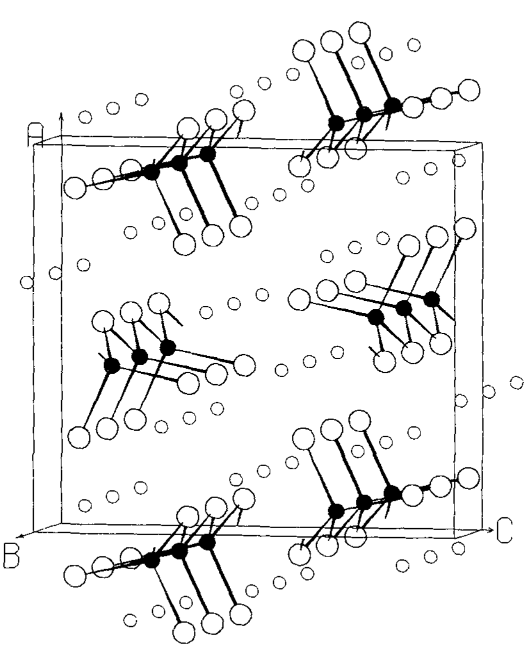


Fig. 1. Structure of $CaAlAs_3$. Small open circles ≙ Ca atoms, large open circles ≙ As atoms, small closed circles ≙ Al atoms [2].

*Experimental*

Stoichiometric amounts of the elements were heated under argon at 1200 K in corrundum crucibles contained in quartz bombs. After cooling, the reaction product was homogenized, re-heated to 1200 K, and annealed for 24 h at 900 K. The metallic-like regulus thus obtained was optically and X-ray crystallographically uniform. $Ca_3AlAs_4$ is relatively stable, but shows distinct signs of decomposition on exposure to moist atmosphere for a few days; the shiny metallic-like surfaces become dull and covered with a gray layer of unknown composition.

Received: October 31, 1980 [Z 760 IE]
German version: Angew. Chem. *93*, 474 (1981)

---

[1] *B. Eisenmann, H. Jordan, H. Schäfer*, Angew. Chem. *93*, 211 (1981); Angew. Chem. Int. Ed. Engl. *20*, 197 (1981); Z. Anorg. Allg. Chem., in press.

[2] $Ca_3AlAs_3$, orthorhombic, space group Pnma, $Z = 4$, $a = 1221.2(3)$, $b = 420.1(2)$, $c = 1343(4)$ pm, automatic two-circle diffractometer Stoe Stadi II ($Mo_{K\alpha}$, graphite monochromator, ω-scan), $R = 0.093$ (1074 independent reflections). Solution of structure by statistical phase-determination methods; SHEL-X program system, *G. M. Sheldrick*, University of Cambridge, England (1976).

[*] Prof. Dr. H. Schäfer, Dr. G. Cordier
Abteilung II für Anorganische Chemie im
Eduard-Zintl-Institut der Technischen Hochschule
Hochschulstr. 4, D-6100 Darmstadt (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

---

## Macrotricyclic Quaternary Ammonium Salts: Enzyme-Analogous Activity[**]

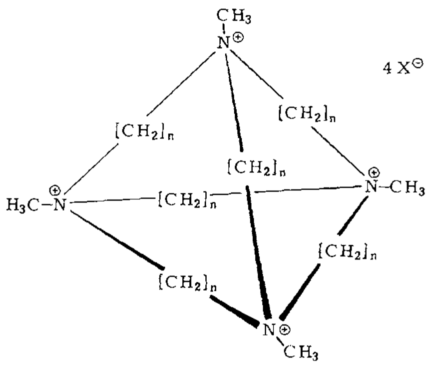
By *Franz P. Schmidtchen*[*]

Natural enzymes achieve their extraordinary specificity and catalytic activity by binding of the substrates in an en-

[*] Dr. F. P. Schmidtchen
Lehrstuhl für Organische Chemie und Biochemie
der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] Part 3: This work was supported by the Deutsche Forschungsgemeinschaft.—Part 2: [4].

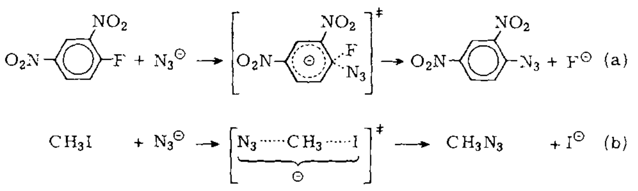
zyme pocket (active center), which is furnished with a functionality that is complementary to the rate determining transition state and therefore stabilizing. Electrostatic (salt-bridges) and hydrophobic interactions play a prominent role[1]. A great deal of attention is currently being paid to the synthesis of model enzymes—predominantly semisynthetic molecules[2] such as cyclodextrins. The fully synthetic macrotricyclic ammonium salts *(1)* and *(2)*[3] harbor a series of properties which are required of an enzyme model: they are equipped with a cavity of definite size in which a strong electropositive potential prevails, while the alkylene chains provide a hydrophobic environment. In contrast to detergents which form micelles, *(1)* and *(2)* (*e.g.* as fluorides or glucuronates) are molecular-dispersively soluble in $H_2O$ in the required concentration range (<0.1 M). The specific binding of anions[4] would lead one to expect that anionic transition states could also be bound and thus stabilized, and the accompanying reactions accelerated. We report here the influence of *(1)* and *(2)* on the reactions described in eqs. (a)—(c).



*(1)*, n = 6, $X^{\ominus} = CH_3C_6H_4SO_3^{\ominus}$
*(2)*, n = 8, $X^{\ominus} = F^{\ominus}$

While addition of *(1)* clearly inhibits the reaction of azide anions with fluoro(dinitro)benzene (FDNB) [eq. (a)], *(2)* accelerates all three reactions, in part considerably (Table 1). The catalyzed reactions (a) and (b) show saturation kinetics typical of enzymes (Fig. 1), so that a general salt effect cannot explain the observed changes in rate. The opposite influence in the reaction according to eq. (a) on addition of *(1)* or *(2)* points rather more to a specific interaction[4]. *(1)* complexes "hard" anions of suitable size about one hundred times more strongly than *(2)*. On the other hand, *(2)* is better suited for stabilizing readily polarizable anions. *(1)* and *(2)* bind azide ions in their molecular cavities ($K_D[N_3^{\ominus}\subset$ *(1)*$] = 2\times10^{-3}$ M; $K_D[N_3^{\ominus}\subset$ *(2)*$] = 1.2\times10^{-2}$ M) and thus stabilize—albeit to different extents—the educts of reaction (a). The transition state is characterized by marked electron delocalization and therefore high polarizability, so it is stabilized much better by *(2)* than by *(1)*. Also the activation entropy of the reaction (a)—owing to the larger molecular cavity and better accessibility, the activated complex in *(2)* should be easier to obtain than in *(1)*—ought to be greater in the reaction catalyzed by *(2)* than in that catalyzed by *(1)*. Indeed, the free energy of activation of the spontaneous reaction lies between that of the more rapid—addition of *(2)*—and that of the slower—addition of *(1)*.

The acceleration of enzyme-catalyzed substitutions arises in considerable part from the change in mechanism: the spontaneous reaction proceeds bimolecularly, the enzyme-catalyzed reaction monomolecularly[1]. As example in which the entropy effect does not arise, we investigated the monomolecular decomposition of *erythro*-2,3-dibromo-3-phenyl propionate (DBPP) [eq. (c)][5]. In aqueous methanol, DBPP decomposes in two ways (A and B) to the isomeric β-bromostyrenes: whereas the synchronous fragmentation gives exclusively the *Z*-isomer, monomolecular dissociation at the benzyl position affords a carbenium ion,



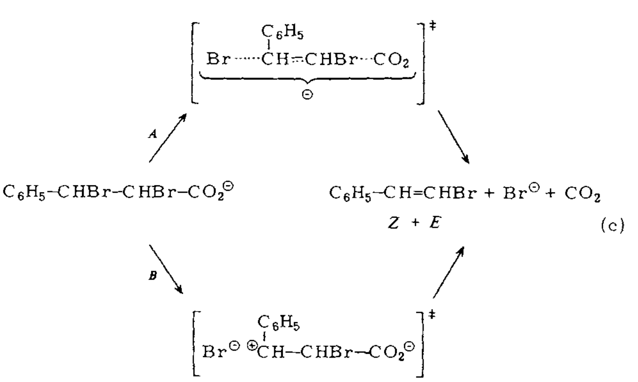


Table 1. Catalysis of the reactions (a)—(c) in 25% methanol by *(1)* and *(2)*; abbreviations, see text.

| Reaction | Concentration [M] Substrate | Catalyst | $T$ [°C] | $\frac{v_{catal.}}{v_{spont.}}$ |
|---|---|---|---|---|
| (a) | $[N_3^{\ominus}] = 10^{-2}$; $[DNFB] = 10^{-4}$ | [*(1)*] $= 10^{-2}$ | 4 | 0.5 [a] |
| (a) | $[N_3^{\ominus}] = 10^{-2}$; $[DNFB] = 10^{-4}$ | [*(2)*] $= 10^{-2}$ | 4 | 20 [a] |
| (b) | $[N_3^{\ominus}] = 6\times10^{-3}$; $[CH_3I] = 10^{-2}$ | [*(2)*] $= 10^{-2}$ | 27 | 37 [a] |
| (c) | $[DBPP] = 2\times10^{-2}$ | [*(2)*] $= 4\times10^{-2}$ | 27 | 1.8 [b]<br>$E/Z = 0.48$ |
| (c) | $[DBPP] = 2\times10^{-2}$ | — | 27 | —<br>$E/Z = 1.64$ |

[a] Initial rates. [b] Average rates after 200 min.

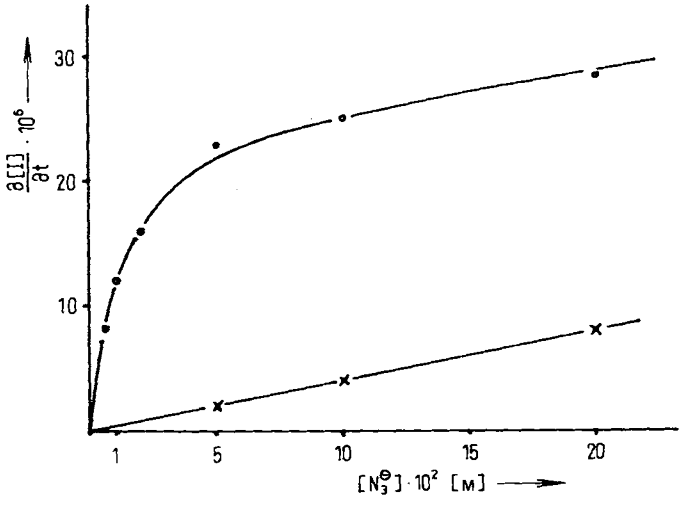


Fig. 1. Kinetics (initial rates mol/dm³·min) of the reaction (b) in 25% methanol at 27 °C without (×) and with (o) *(2)* ($10^{-2}$ M); $[CH_3I] = 10^{-2}$ M.

which is converted by cleavage of $CO_2$ into the products in a thermodynamic *E/Z* ratio ($E/Z = 9/1$).

In the spontaneous reaction ($[DBPP] = 2 \times 10^{-2}$ M; $T = 27\,°C$) we obtained 20% conversion after 200 min and an *E/Z* ratio of the bromostyrenes of 1.64. On addition of $4 \times 10^{-2}$ mol of *(2)*, the same reaction gave a 36% conversion in 200 min and an *E/Z* ratio of 0.48. This shows that *(2)* preferably—if not exclusively—catalyzes the formation of the *Z*-bromostyrene. Yet a further enzyme-analogous property of the host molecule *(2)* should be outlined here: Of the two modes of reaction of the substrate, the one which proceeds *via* the easily polarizable anionic transition state is specifically accelerated. Reaction (c) proves that the increases in rates in the catalysis by *(2)* cannot be ascribed solely to the change of molecularity of the reaction (proximity effect, reactions (a) and (b)).

The observed change in rates of the reactions (a), (b) and (c) can be qualitatively correctly predicted by means of the Hughes-Ingold rules, if *(1)* and *(2)* are regarded as dipolar aprotic "solvents". The acceleration of anionic reactions by *(2)* on going from a protic to an aprotic medium is not, however, due to destabilization of the ground state[6] but to stabilization of the transition state.

The synthetic macrotricyclic ammonium salt *(2)* takes up substrates in a molecular cavity and accelerates reactions in the inclusion complex by lowering the energy of the transition state. It has saturation kinetics and shows substrate-specificity as well as reaction-specificity, but owing to the highly symmetric molecular disposition does not show stereospecificity. On the basis of this very close analogy to the biocatalysts we propose for *(2)* the designation "artificial enzyme".

Received: October 24, 1980 [Z 748 IE]
German version: Angew. Chem. *93*, 469 (1980)

CAS registry numbers
*(1)*, 76939-55-4; *(2)*, 76939-54-3; 1-fluoro-2,3-dinitrobenzene 70-34-8; 1-azido-2,4-dinitrobenzene 4096-88-2; iodomethane 74-88-4; azidomethane 624-90-8; *erythro*-2,3-dibromo-3-phenylpropionic acid 31357-31-0; (*E*)-B-bromostyrenes 588-72-7; (*Z*)-B-bromostyrenes 588-73-8;

---

[1] *A. R. Fersht:* Enzyme Structure and Mechanism, Freeman, San Francisco 1977.

[2] *J. H. Fendler, E. J. Fendler:* Catalysis in Micellar and Macromolecular Systems, Academic Press, London 1975. *J. R. Knowles, J. Boger,* J. Am. Chem. Soc. *101*, 7631 (1979); *R. Breslow, M. F. Czarniecki, J. Emert, H. Hamaguchi, ibid. 102*, 762 (1980); *I. Tabushi, Y. Kuroda, A. Mochizuki, ibid. 102*, 1152 (1980).

[3] *F. P. Schmidtchen,* Angew. Chem. *89*, 751 (1977); Angew. Chem. Int. Ed. Engl. *16*, 720 (1977); *F. P. Schmidtchen,* Chem. Ber. *113*, 864 (1980).

[4] *F. P. Schmidtchen,* Chem. Ber. *114*, 597 (1981).

[5] *E. Grovenstein Jr., D. E. Lee,* J. Am. Chem. Soc. *75*, 2639 (1953).

[6] *A. J. Parker,* Chem. Rev. *69*, 1 (1969).

---

# Tetracyclo[4.1.0.0$^{2,4}$.0$^{3,5}$]heptanes from 7,8-Diazatetracyclo[4.3.0.0$^{2,4}$.0$^{3,5}$]non-7-enes[**]

By *Manfred Christl* and *Erich Brunn*[*]

*Dedicated to Professor Alfred Roedig on the occasion of his 70th birthday*

We recently reported the first available method for the synthesis of the tetracyclo[4.1.0.0$^{2,4}$.0$^{3,5}$]heptane skeleton[1] by addition of halocarbenes to benzvalene *(1)*. The parent compound *(3a)* is formed by reduction of the 7,7-dichloro- and 7,7-dibromo-derivative. We now report on an entry to the 7-methyl- and 7-aryl-derivatives *(3b)*—*(3h)*, thus enabling this tetracyclic system to be investigated in much better detail.

The addition of diazomethane to benzvalene *(1)*[1a] affords *(2a)* in 83% yield; the reaction can also be carried out with diazoethane and 2-diazopropane (*ca.* 15 h at 20 °C in ether) as well as with phenyl- and diphenyldiazomethane and with diazofluorene (8 d at 20 °C in ether), whereupon the 1-pyrazoline derivatives *(2b)*—*(2h)*[4] (Table 1) are formed. In contrast, ethyl diazoacetate does not react with *(1)*[2].

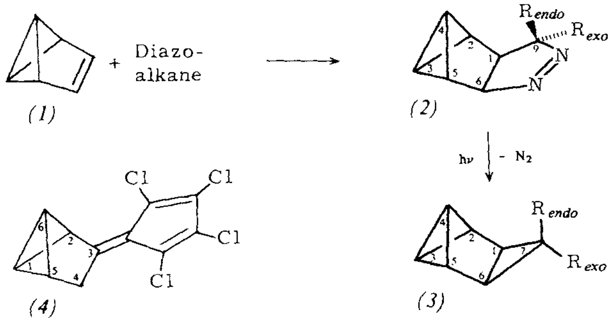


Table 1. Yields, ratios of isomers, and boiling and melting points of compounds *(2)* and *(3)*.

| $R_{exo}$ | $R_{endo}$ | Cpd. | Yield [%] | $\left(\frac{exo}{endo}\right)$ | B.p. or M.p. [°C/torr] and [°C] | Cpd. | Yield [%] | $\left(\frac{exo}{endo}\right)$ | B.p. or M.p. [°C/torr] and [°C] |
|---|---|---|---|---|---|---|---|---|---|
| H | H | *(2a)* | 83 | (—) | 55—60 (bath)/$10^{-1}$ | *(3a)* | 27 | (—) | 104/730 |
| $CH_3$ | H | *(2b)* | 58 | (1.7) | 40—50 (bath)/$10^{-3}$ | *(3b)* | 78 | (1.8) | 62—65/90—100 |
| H | $CH_3$ | *(2c)* | | | | *(3c)* | | | |
| $CH_3$ | $CH_3$ | *(2d)* | 100 | (—) | 60 (bath)/$10^{-3}$<br>35 | *(3d)* | 39 | (—) | 50-60 (bath)/15 |
| $C_6H_5$ | H | *(2e)* | 59 | (1.3) | 80—100 (bath)/$10^{-3}$ | *(3e)* | 81 | (1.5) | 40—70 (bath)/$10^{-2}$ |
| H | $C_6H_5$ | *(2f)* | | | 80—87 | *(3f)* | | | |
| $C_6H_5$ | $C_6H_5$ | *(2g)* | 72 | (—) | 152 | *(3g)* | 73 | (—) | 73—75 |
| Biphenylene | | *(2h)* | 79 | (—) | 126—128 | *(3h)* | 97 | (—) | 78—85 |

Irradiation of the 1-pyrazolines or 1-pyrazoline mixtures *(2)* in benzene solution with a high-pressure mercury lamp through Duran leads to elimination of nitrogen and formation of the tetracyclo[4.1.0.0$^{2,4}$.0$^{3,5}$]heptane derivatives *(3)*[4] (Table 1).

As molecular models clearly show, strong steric hindrance occurs between the *endo*-substituents and 4-H in the 7-*endo* substituted compounds *(3c)*, *(3d)*, *(3f)*, *(3g)* and, especially, *(3h)*, which influences the reactivity. Thus, the *endo*-isomers *(3c)* and *(3f)* of the *(3b)/(3c)*- and *(3e)/(3f)*-

---

[*] Prof. Dr. M. Christl, Dipl.-Chem. E. Brunn
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

mixtures rearrange into 7-methyl- and 7-phenylcycloheptatriene, respectively, even at room temperature in $CDCl_3$, probably in a process catalyzed by traces of acid, whereas the *exo*-isomers remain unchanged.

On reaction of *(1)* with tetrachlorodiazocyclopentadiene we did not observe a pyrazoline of type *(2)*. Yellow crystals with m.p. 148 °C are obtained in 11% yield, which we assign the fulvene structure *(4)*[5].

Received: June 23, 1980 [Z 749 IE]
Supplemented: October 20, 1981
German version: Angew. Chem. *93*, 474 (1981)

---

[1] a) *M. Christl*, Angew. Chem. *85*, 666 (1973); Angew. Chem. Int. Ed. Engl. *12*, 660 (1973); b) *M. Christl, G. Freitag, G. Brüntrup*, Chem. Ber. *111*, 2307 (1978).

[2] Reaction of methyl 2-diazopropionate with *(1)*, on the other hand, affords two 1-pyrazolines, which on irradiation are converted into the two methyl 7-methyltetracyclo[$4.1.0.0^{2,4}.0^{3,5}$]heptane-7-carboxylates. We thank Prof. *F.-G. Klärner*, Ruhr-Universität Bochum, for communicating these results prior to publication.

[3] *M. Christl*, Chem. Ber. *108*, 2781 (1975).

[4] The spectroscopic properties of *(2b)*—*(2h)* and *(3b)*—*(3h)* are in accord with those of the parent systems *(2a)* [1a, 3] and *(3a)* [1b, 3]. The data for the diphenyl derivatives *(2g)* and *(3g)* are representative. *(2g)*: IR (KBr): $\nu = 1544\ \mathrm{cm}^{-1}$ (N═N); UV (ethanol): $\lambda = 336$ nm ($\varepsilon = 310$, N═N); $^1$H-NMR ($CDCl_3$): $\delta = 1.38$ (dq, 2-H, $J_{1,2} = 1.7$, $J_{2,3} \approx J_{2,4} \approx 1.8$, $J_{2,5} = 5.1$ Hz), 1.70 (dqi, 4-H, $J_{1,4} \approx J_{4,6} \approx 1.5$, $J_{3,4} = 9.0$, $J_{4,5} \approx 1.8$ Hz), 2.00 (dt, 3-H, $J_{3,5} \approx 1.8$ Hz), 2.87 (dq, 5-H, $J_{5,6} = 1.8$ Hz), 2.98 (br. d, 1-H, $J_{1,6} = 6.3$ Hz), 5.35 (br. d, 6-H), 7.30 (m, $C_6H_5$); $^{13}$C-NMR ($CDCl_3$): $\delta = 2.3$ (d, $J = 217$ Hz, C-4), 6.4 (d, $J = 217$ Hz, C-3), 36.1 (d, $J = 168$ Hz, C-2), 38.3 (d, $J = 171$ Hz, C-5), 46.6 (d, $J = 140$ Hz, C-1), 97.9 (s, C-9), 99.5 (d, $J = 150$ Hz, C-6), 126.4—128.4 (d, C-2′—C-6′, C-2″—C-6″), 142.9 (s, C-1′,1″). *(3g)*: $^1$H-NMR ($CDCl_3$): $\delta = 1.06$ (dtt, 4-H, $J_{1,4} = 0.6$, $J_{2,4} = 2.6$, $J_{3,4} = 8.7$ Hz), 1.92 (br. s, 1,6-H), 2.06 (m, 2,5-H), 2.58 (dt, 3-H, $J_{2,3} = 0.9$ Hz), 6.9—7.5 (m, $C_6H_5$). $^{13}$C-NMR ($CDCl_3$): $\delta = 4.8$ (d, $J = 218$ Hz, C-4), 25.8 (d, $J = 212$ Hz, C-3), 34.6 (d, $J = 170$ Hz, C-1,6), 35.1 (d, $J = 166$ Hz, C-2,5), 51.0 (s, C-7), 125.3, 125.6 (d, C-4′,4″); 127.0, 127.9, 128.1, 131.2 (d, C-2′,3′,5′,6′,2″,3″,5″,6″), 142.4, 146.4 (s, C-1′,1″).

[5] $^1$H-NMR ($CDCl_3$): $\delta = 2.33$ (m, 5-H), 2.80 (m, 4-$H_2$), 2.90 (m, 1,6-H), 4.10 (dt, 2-H, $J_{1,2} = 1.8$, $J_{2,5} = 4.8$ Hz); UV ($CHCl_3$): $\lambda = 304$ s ($\varepsilon = 28\,700$), 309 (30 700), 323 s (19 700), 390 s nm (900).

---

## Chemiluminescence of Tricarbonyl(chloro)(1,10-phenanthroline)rhenium(I) during the Catalytic Decomposition of Tetralinyl Hydroperoxide[**]

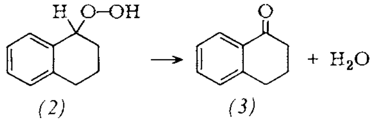
By *Arnd Vogler* and *Horst Kunkely*[*]

The thermal decomposition of organic peroxides[1a] or of hydrogen peroxide[1b] is catalyzed by transition metal complexes. This reaction is also of great importance in biological systems. In the past few years it has been shown, particularly by *Schuster et al.*, that even organic compounds are capable of catalyzing peroxide decomposition[2]. The energy liberated in this decomposition is sufficient to generate the catalyst in an electronically excited state; as a result a chemiluminescence can be observed. It is therefore necessary that the catalyst is oxidized by the peroxide in the first step. The electronic excitation takes place in the last step by reduction of the oxidized catalyst. It now seemed worthwhile checking whether this mechanism also applies to catalyses with transition metal complexes.

[Re(phen)(CO)$_3$Cl] *(1)*

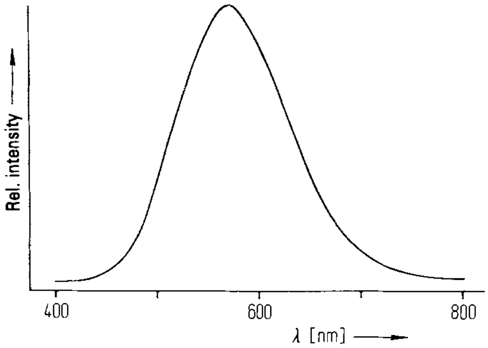
appeared to us to be a suitable candidate for such investigations, since this complex can not only be reversibly oxidized electrochemically (+1.3 V *vs.* SCE) but also undergoes an electrogenerated luminescence[3]. Moreover, it was considered essential that an attempt should be made to extend our knowledge of the chemiluminescence of transition metal complexes, about which only very little is known so far[4].

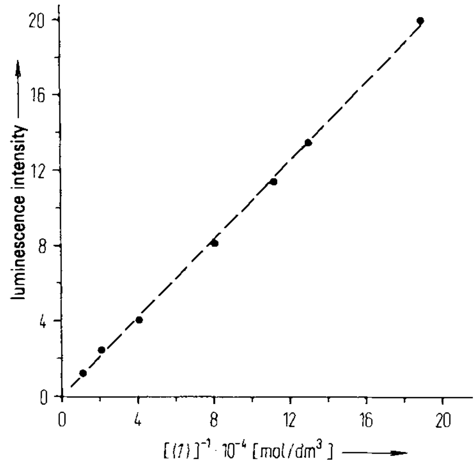
Tetralinyl hydroperoxide *(2)* decomposes only slowly in boiling tetralin, whereas on addition of the complex *(1)* an emission of bright light with concomitant rapid decomposition of *(2)* takes place producing α-tetralone *(3)* and water[5].



*(2)* *(3)*

The spectrum of this chemiluminescence (Fig. 1) is identical with that of the photoluminescence of pure *(1)*[6]. As follows from the linear dependence of the reciprocal of the intensity of chemiluminescence on the reciprocal of the concentration of the complex[7] (Fig. 2), the electronically excited rhenium complex is formed immediately as a result of a bimolecular reaction. The catalysis must therefore proceed according to the Schuster mechanism:





$$
\begin{aligned}
(1) + (2) &\rightarrow (1)^{\oplus}(2)^{\ominus}\\
(1)^{\oplus}(2)^{\ominus} &\rightarrow (1)^{\oplus}(3)^{\ominus} + H_2O\\
(1)^{\oplus}(3)^{\ominus} &\rightarrow (1)^{*} + (3)\\
(1)^{*} &\rightarrow (1) + \text{light}
\end{aligned}
$$

---

[*] Prof. Dr. A. Vogler, Dr. H. Kunkely
Institut für Anorganische Chemie der Universität
Postfach, D-8400 Regensburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Although further investigations must be carried out to confirm this mechanism[8], it should be pointed out that our observation is most likely of fundamental importance for an understanding of the catalytic decomposition of peroxides by transition metal complexes. Many complexes fulfill the prerequisite that they can be reversibly oxidized and have energetically low-lying excitation states which can take up the decomposition energy of the peroxides. The occurrence of a luminescence is not necessary. Under suitable conditions a reversal of this hydroperoxide decomposition, *i.e.* the photochemically catalyzed addition of water to a ketone, could be achieved[5b]; this would constitute a possible way of chemically storing light energy.

Received: October 7, 1980 [Z 750 IE]
German version: Angew. Chem. *93*, 470 (1981)

---

[1] a) Review: *D. Swern:* Organic Peroxides, Vol. I—III, Wiley-Interscience, New York 1969, 1971 and 1972. b) *A. C. Melnyk, N. K. Kildahl, A. R. Rendina, D. H. Busch,* J. Am. Chem. Soc. *101*, 3232 (1979); *H. Sigel, K. Wyss, B. E. Fischer, B. Prijs,* Inorg. Chem. *18*, 1354 (1979), and references cited therein.

[2] Review: *G. B. Schuster,* Acc. Chem. Res. *12*, 366 (1979).

[3] *J. C. Luong, L. Nadjo, M. S. Wrighton,* J. Am. Chem. Soc. *100*, 5790 (1978).

[4] a) *F. E. Lyttle, D. M. Hercules,* Photochem. Photobiol. *13*, 123 (1971); *H. D. Gafney, A. W. Adamson,* J. Chem. Educ. *52*, 480 (1975); b) *A. Vogler, L. El-Sayed, R. G. Jones, J. Namnath, A. W. Adamson,* Inorg. Chim. Acta *53*, L35 (1981).

[5] The decomposition of *(2)*, catalyzed by Mg- and Zn-porphyrins involving a chemiluminescence, has already been reported: a) *J. H. Helberger, D. B. Hever,* Ber. Dtsch. Chem. Ges. *72*, 11 (1939); b) *H. Linschitz* in *McElroy, Glass:* Light and Life, John Hopkins Press, Baltimore 1961, p. 173.

[6] *M. Wrighton, D. L. Morse,* J. Am. Chem. Soc. *96*, 998 (1974).

[7] *J.-Y. Koo, G. B. Schuster,* J. Am. Chem. Soc. *99*, 6107 (1977); *100*, 4496 (1978).

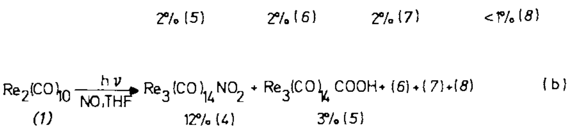
[8] $[Ru(bpy)_3]^{2+}$ also chemiluminesces, albeit only weakly, in the catalyzed decomposition of *(2)* in tetralin/dimethyl sulfoxide.

---

# Nitrogen Dioxide and the Isoelectronic COOH Group as 5-Electron Donors in Carbonylmetal Complexes; Preparation and Characterization of the First "Metallacarboxylic Acid"

By *Barbara K. Balbach, Frantisek Helus, Franz Oberdorfer,* and *Manfred L. Ziegler*[*]

Photolysis of $Re_2(CO)_{10}$ *(1)* in the presence of NO and cyclooctatriene (COT) leads, in accord with eq. (a), to formation of the products *(2)—(8)*, of which the hydrido-complexes *(6)—(8)* have already been described[1]. The species *(4)* and *(5)*, as well as *(6)—(8)*, are also formed on photolysis in the absence of COT [eq. (b)].



$$\underset{(1)}{Re_2(CO)_{10}} + COT \xrightarrow[NO, THF]{h\nu} \underset{5\%\ (2)}{Re_2(CO)_8C_4H_6} + \underset{2\%\ (3)}{Re_2(CO)_9C_3H_6} + \underset{10\%\ (4)}{Re_3(CO)_{14}NO_2}$$

$$+ \underset{2\%\ (5)}{Re_3(CO)_{14}COOH} + \underset{2\%\ (6)}{HRe_3(CO)_{14}} + \underset{2\%\ (7)}{H_3Re_3(CO)_{12}} + \underset{<1\%\ (8)}{H_4Re_4(CO)_{12}} \quad (a)$$

$$\underset{(1)}{Re_2(CO)_{10}} \xrightarrow[NO, THF]{h\nu} \underset{12\%\ (4)}{Re_3(CO)_{14}NO_2} + \underset{3\%\ (5)}{Re_3(CO)_{14}COOH} + (6) + (7) + (8) \quad (b)$$

We have been able to establish by an X-ray structure analysis that the two Re atoms in complex *(2)* are bridged by a butadiene ligand in *trans*-configuration. The butadiene complex *(2)* is isomorphic with the analogous manganese complex[2]; it can only be formed by a symmetric cleavage of COT. This could be of interest regarding the formation of COT from acetylene.

The new compounds *(4)* and *(5)* were characterized by elemental analyses, by their mass and IR spectra[3], and by X-ray structure analyses[4] (Fig. 1).

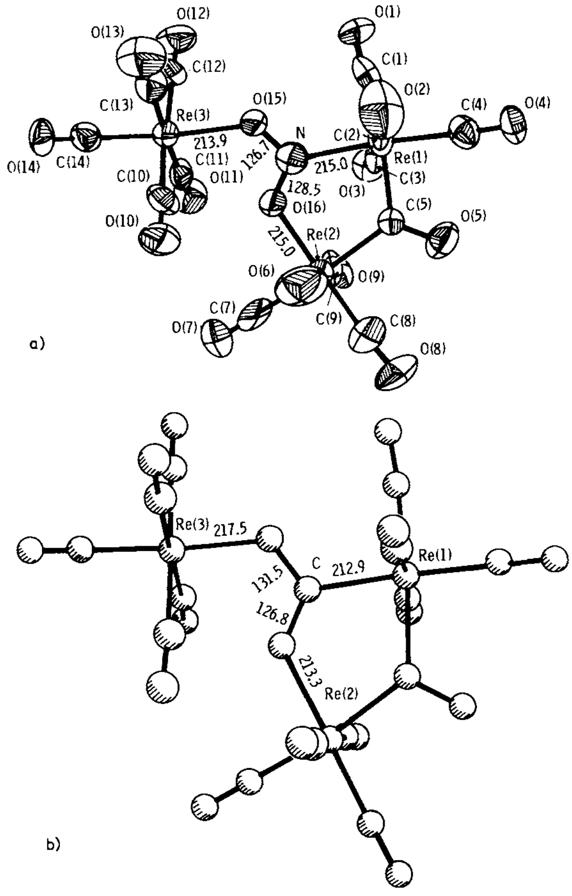


Fig. 1. a) ORTEP diagram of *(4)* projected onto the $NO_2$—Re(1) plane. b) ORTEP diagram of *(5)* projected on the COO—Re(1) plane. Bond lengths in pm.

The data obtained are consistent with a trinuclear complex without Re—Re bonding. The coherence of the species *(4)* and *(5)* is secured by a central $NO_2$ or COOH unit, both of which have 17 electrons; for the three Re atoms to uphold the 18-electron rule, these ligands must function as 5-electron donors. *(4)* and *(5)* are diamagnetic.

The IR spectrum of *(5)* contains a sharp, intense band at 3700 $cm^{-1}$, which we assign to an O—H stretching vibration; the H-atom cannot be involved in bridging. It can be replaced by deuterium by multiple dissolution of *(5)* in [D4]methanol and stirring of the solutions. As expected, the deuterated species shows a sharp band at 2700 $cm^{-1}$. Location of the H-atom in *(5)* is not possible by X-ray structure analysis. On the basis of all these experimental data, *(5)* is to be formulated as a metallacarboxylic acid in which a carbonylmetal unit corresponds to the alkyl or aryl moiety R in ROOH. Such a metallacarboxylic acid is then stable, only if both oxygen atoms of the carboxyl group are involved in coordination. The atoms of the central COO-unit and the rhenium (Re(1)) bonded to the C-atom lie,

---

[*] Prof. Dr. M. L. Ziegler [+], Dipl.-Chem. B. K. Balbach, Dipl.-Chem. F. Oberdorfer
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg (Germany)
Dr. F. Helus
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280, D-6900 Heidelberg (Germany)

[+] Author to whom correspondence should be addressed.

within the limits of accuracy, in one plane; the sum of the internal angles at C and N is 360°.

*(4)* has the same molecular geometry as *(5)*, but the species are not isomorphic.

## *Procedure*

A solution of *(1)* (1.3 g, 2 mmol) in tetrahydrofuran (THF) (300 $cm^3$) is saturated with NO and cooled to $-20\,°C$. After addition of 2 $cm^3$ of freshly distilled COT the mixture is photolyzed for 3 h; the solution, which becomes deep-red on completion of reaction, warms to about 0 °C. It was evaporated down to *ca.* 50 $cm^3$, transferred onto silica gel, and dried. The dried mass was treated with *n*-hexane and the resulting suspensoid chromatographed on a column (40×2.5 cm, 0.02—0.5 silica gel, *n*-hexane). Six zones are formed: zone 1, COT + *(1)*; zone 2, *(2)*; zone 3, *(7)*; zone 4, *(6)*; zone 5, *(3)*; zone 6, *(4)*+*(5)*. Zones 4, 5, and 6 were re-chromatographed (PSC plates, Merck, silica gel F-254, 2.5 mm, benzene), affording pure *(6)*, *(3)* and *(8)*, *(3)* as a colorless solution. A further chromatographic separation had to be carried out for the separation of *(4)* and *(5)* (Nucleosil 50-10, 300×0.4 cm, *n*-hexane, 0.05 bar, 3 $cm^3$/min, 28 °C; detector 254 nm). Fractional crystallization (room temperature to $-20\,°C$, cyclohexane/ether) afforded 40 mg of *(4)* (yield 5—6%, yellow needles) and 20 mg of *(5)* (yield 2%, yellow platelets); in each case the yields are based on *(1)*.

Received: July 14, 1980 [Z 751a IE]
German version: Angew. Chem. *93*, 479 (1981)

---

[1] *W. Fellmann, H. D. Kaesz,* Inorg. Nucl. Chem. Lett. *2*, 63 (1966); *D. K. Huggins, W. Fellmann, J. M. Smith, H. D. Kaesz,* J. Am. Chem. Soc. *86*, 4841 (1964); *R. Saillant, G. Barcelo, H. D. Kaesz, ibid. 92*, 5739 (1970).

[2] *H. E. Sasse, M. L. Ziegler,* Z. Anorg. Allg. Chem. *392*, 167 (1972).

[3] *(4)*: IR ($\nu_{CO}$; cyclohexane) 2083 m, 2040 vs, 2003 s, 1992 ms, 1980 m, 1965 ms, 1955 m. MS: $Re_3(CO)_{14}NO_2^{\oplus}$obs. 996.775, calc. 996.787. *(5)*: IR ($\nu_{CO}$; $CHCl_3$) 2080 m, 2040 vs, 2003 s, 1990 ms, 1957 ms; ($\nu_{OH}$ and $\nu_{OD}$; $CHCl_3$) 3700 s and 2700 s; 1595 m. MS: $Re_3(CO)_{14}COOH^{\oplus}$ obs. 995.799, calc. 995.792.

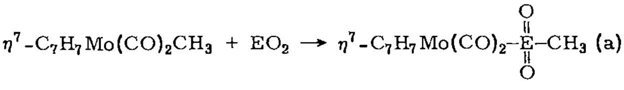
[4] *(4)*: monoclinic, space group $P2_1/a$ with $a = 1397.1(7)$, $b = 1754.8(7)$, $c = 923.0(5)$ pm, $\beta = 95.87(5)°$, $Z = 4.4265$ independent reflections other than zero, Siemens AED, 5-value method, $Mo_{K\alpha}$ radiation, $4.436 < 2\theta < 67.461$). $R = 0.087$. *(5)*: monoclinic, space group $P2_1/n$ with $a = 683.4(1)$, $b = 1776.3(4)$, $c = 1844.4(4)$ pm, $\beta = 99.33(1)$, $Z = 4$. 3995 independent reflections other than zero (P3/DATA GENERAL NOVA 3, Q-scan, $Mo_{K\alpha}$, $0 < 2\theta < 60.0$). $R = 0.049$. Reflections for $I < 2.5\sigma(I)$ were not taken into consideration in the case of *(4)* and *(5)*.

---

# Preparation of $\eta^7$-$C_7H_7Mo(CO)_2EO_2CH_3$ (E = S, Se, Te); the First Insertion of $TEO_2$ into a Metal-Carbon Bond

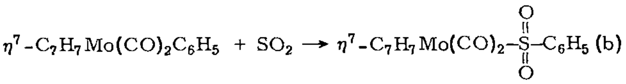
By *Winfried Dell* and *Manfred L. Ziegler*[*]

The insertion of $SO_2$ and $SeO_2$ into metal-carbon σ-bonds is already well documented[1]. The insertion of $TeO_2$ was considered as unrealizable, since the activation of a $TeO_2$ molecule appeared possible only under conditions in which the alkyl or aryl educt and/or the insertion product would no longer be stable. We have now succeeded in activating $TeO_2$ by evaporation of $TeO_2$ in a metal evaporator and condensation in an ether matrix at $-196\,°C$. The complex $\eta^7$-$C_7H_7Mo(CO)_2CH_3$ *(1)*[2], previously prepared by us, provided a species containing an extremely reactive molybdenum—methyl carbon bond suitable for an electrophilic $EO_2$ insertion (Table 1)[3]. As expected, aside from $TeO_2$, $SO_2$ and $SeO_2$ could also be inserted into the molybdenum-carbon bond [eq. (a)].



$$\eta^7\text{-}C_7H_7Mo(CO)_2CH_3 + EO_2 \longrightarrow \eta^7\text{-}C_7H_7Mo(CO)_2\text{-}\overset{O}{\underset{O}{\overset{\|}{\underset{\|}{E}}}}\text{-}CH_3 \quad (a)$$

*(1)* *(2)*, E = S; *(3)*, E = Se; *(4)*, E = Te



$$\eta^7\text{-}C_7H_7Mo(CO)_2C_6H_5 + SO_2 \longrightarrow \eta^7\text{-}C_7H_7Mo(CO)_2\text{-}\overset{O}{\underset{O}{\overset{\|}{\underset{\|}{S}}}}\text{-}C_6H_5 \quad (b)$$

*(5)* *(6)*

Analogously to the synthesis of *(1)* we were able to prepare the phenyl derivative *(5)* from $\eta^7$-$C_7H_7Mo(CO)_2Br$ and $LiC_6H_5$[2]. However, the Mo—$C_{phenyl}$ bond proved to be less reactive than the Mo—$C_{methyl}$ bond in *(1)*: with *(5)*, only the insertion of $SO_2$ could be achieved [eq. (b)].

The species *(1)*—*(6)* were characterized by elemental analysis, by their IR and $^1$H-NMR spectra and, in part, by mass spectra. The monomolecular composition of the compounds *(2)*—*(4)* followed from molecular weight determinations on *(2)* (obs. 327 (322), osmometrically, dichloroethane) and comparison of the $^1$H-NMR and IR spectra of *(2)*, *(3)*, *(4)*, and *(6)*. The phenyl derivative *(6)* had already been prepared by us by reaction of $\eta^7$-$C_7H_7Mo(CO)_2I$ with $AgSO_2C_6H_5$[4]. A characterization of the complexes *(1)*—*(6)* by X-ray structure analysis was not possible owing to their thermal instability; *(2)* can be stored for a few hours at room temperature; *(1)*, *(3)*, and *(4)* can be kept for only a few minutes.

In the $^1$H-NMR spectrum (Table 1) of *(1)*, the signal for the methyl protons appears at $\delta = -0.25$, owing to the high electron density on the methyl carbon atom; thus *(1)* is exactly predestined for such an insertion according to concepts on the mechanism of $EO_2$ insertion[3]. As expected the signals for the $CH_3$ protons in the $EO_2$-insertion products *(2)*—*(4)* appear at low field; the $\nu_{CO}$ bands of the species *(2)*—*(4)* and *(6)* are shifted to higher wave numbers compared to those of the methyl-*(1)* and of the phenyl compound *(5)*.

Table 1. Some spectroscopic data of compounds *(1)*—*(6)*.

| | IR [$cm^{-1}$] | | | $^1$H-NMR ($\delta$ values, TMS) | | |
|---|---|---|---|---|---|---|
| | $\nu_{CO}$ ($CH_2Cl_2$, vs) | $\nu_{E-C}$(vs) Nujol, KBr window | $\nu_{E-O}$(s) | $C_7H_7$ (s, 7 H) | $CH_3$ (s, 3 H) | $C_6H_5$ |
| *(1)* | 1975, 1930 | | | 5.25 | −0.25 | |
| *(2)* | 2020, 1975 | 650 | 1150, 1035, 940 | 5.70 | 2.80 | |
| *(3)* | 2000, 1940 | 565 | 1070, 887 | 5.28 | 2.32 | |
| *(4)* | 1990, 1930 | 470 | 960, 785, 750, 695 | 5.30 | 2.33 | |
| *(5)* | 1985, 1935 | | | 5.26 | | 6.88 (m, 3 H)<br>7.40 (m, 2 H) |
| *(6)* | 2030, 1990 | | 1155, 1085, 1025, 1015, 995 | 5.15 | | 7.47 (m, 3 H)<br>7.72 (m, 2 H) |

## *Procedure*

$SeO_2$ (500 mg, 4.5 mmol) was evaporated in a metal evaporator[4] at $-196\,°C$ within 2 h (20 A, 220 V) onto an ether matrix (50 $cm^3$), heated to $-78\,°C$, and then treated with a solution of *(1)* (100 mg, 0.4 mmol) in tetrahydrofuran pre-cooled to $-78\,°C$. The reaction solution was al-

---

[*] Prof. Dr. M. L. Ziegler, Dipl.-Chem. W. Dell
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg (Germany)

lowed to stand at this temperature for one week; the color of the solution turned from green to red. The mixture was subjected to low-temperature chromatography (−20 °C, Merck silica gel 60; 0.040—0.63 mm, $CHCl_3$/acetone 1 : 1, 30 × 2.5 cm). Two zones were eluted: the first (green) zone, was unreacted *(1)*, the second (red) zone was *(3)*; yield 44 mg, 30% based on *(1)*.

*(4)* is prepared analogously, but completion of reaction requires eight weeks (220 V, 70 A; yield 5—8%).

The red-brown crystals of *(3)* and of *(4)* are stable in an inert atmosphere for a few days or a few hours at −78 °C, respectively, at room temperature for a matter of a few minutes. *(3)* is soluble in $CH_2Cl_2$ and in polar solvents, *(4)* in ether and in polar solvents. The solutions of *(3)* and *(4)* decompose within a few minutes at room temperature.

Received: July 14, 1980 [Z 751 b IE]
German version: Angew. Chem. 93, 480 (1981)

CAS Registry numbers:
*(1)*, 77495-46-6; *(2)*, 77495-43-3; *(3)*, 77495-44-4; *(4)*, 77495-45-5; *(5)*, 77495-47-7; *(6)*, 59588-85-1; ($SO_2$), 7446-09-5; ($SeO_2$), 7446-08-4; ($TeO_2$), 7446-07-3

---

[1] a) *G. Vitzhum, E. Lindner*, Angew. Chem. *83*, 315 (1971); Angew. Chem. Int. Ed. Engl. *10*, 315 (1971); *A. Wojcicki*, Adv. Organomet. Chem. *12*, 32 (1974); b) *I. P. Lorenz*, Angew. Chem. *90*, 60 (1978); Angew. Chem. Int. Ed. Engl. *17*, 53 (1978).
[2] *W. Dell, M. L. Ziegler*, unpublished work.
[3] *S. E. Jacobsen, A. Wojcicki*, J. Am. Chem. Soc. *96*, 6962 (1974); Inorg. Chim. Acta *10*, 229 (1974).
[4] *D. Mohr, H. Wienand, M. L. Ziegler*, Z. Naturforsch. *B 31*, 66 (1976).

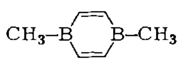
## A Triple-Decked Sandwich Complex of Rhodium with 1,4-Diborabenzene as Bridging Ligand[**]

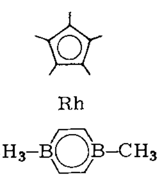
By *Gerhard E. Herberich, Bernd Hessner, Gottfried Huttner*, and *Laszlo Zsolnai*[*]

The known triple-decked complexes[1] have mainly 7-vertex *closo*-structures with pentagonal bipyramids as the basic framework. A five-membered ring functions as the central ligand and the apical positions are occupied by Mn, Fe, Co or Ni. The majority of these complexes contain 30 valence electrons (calculated *via* the noble gas formalism) and therefore adhere to the cluster rules[2]. Complexes having 29 and 31—34 valence electrons are known[3]. These do not correspond to another structural type but rather show a weakening of the cluster bonds[4].

The sandwich complex *(2)*[5], derived from the hypothetical 1,4-dimethyl-1,4-dibora-2,5-cyclohexadiene *(1)*, forms the novel pale yellow triple-decked sandwich cation *(3)*$^{2+}$ in $CF_3COOH$. The same cation is also obtained from *(2)* by stacking with $[(C_5Me_5)RhCl_2]_2/AlCl_3$ in $CH_2Cl_2$.

The 30 valence electron complex *(3)*$^{2+}$ is the first triple-decked complex derived from a diborabenzene derivative and simultaneously, the first with a heavy transition metal. Its hexagonal bipyramidal structure has not previously been observed in 8-vertex *closo*-polyhedra (Table 1)[6]. The bond lengths in the $C_4B_2$-ring are shorter in the sandwich complex $(C_5H_5)Co[MeB(C_2H_2)_2BMe]$[7] than in the triple-decked complex *(3)*$^{2+}$ (C—C 142 *vs.* 144 pm, B—C 151 *vs.* 154 pm).


*(1)*


*(2)*

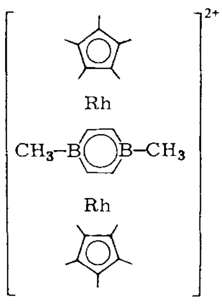

*(3)*$^{2+}$

Table 1. Structural data for *(3)*$^{2+}$.

| | | | |
|---|---|---|---|
| $C_4B_2Rh_2$-Polyhedra | | | |
| CC | 144 pm | RhC | 227 pm |
| CB | 154 pm | Rh—B | 233 pm |
| ∢CBC | 113° | Rh—Rh | 344,4 pm |
| $Rh(C_5Me_5)$ | | | |
| C—C | 143 pm | Rh—C | 216 pm |
| $C—C_{Me}$ | 149 pm | | |

Table 1. Structural data for *(3)*$^{2+}$.

Complex *(3)*$^{2+}$ can be electrochemically reduced in acetonitrile to the 31 electron cation *(3)*$^{+}$ (reversible one-electron transition at $E_{1/2} = -0.645$ V *vs.* SCE). Further reduction to the 32 electron neutral complex *(3)* (cathodic peak potential −1.18 V; reoxidation detectable at 2 $Vs^{-1}$ voltage scanning rate) is followed by fast degradation[8].

$$(3)^{2+} \rightleftharpoons (3)^{+} \rightleftharpoons (3) \rightarrow ?$$

### *Procedure*

a) *(2)*[7] (56 mg, 0.16 mmol) and $[(C_5Me_5)RhCl_2]_2$ (50 mg, 0.08 mmol) are treated with $AlCl_3$ (100 mg, 0.75 mmol) in 5 $cm^3$ $CH_2Cl_2$. After 15 min the color has change from dark red to yellow and the mixture is treated at 0 °C with 10 $cm^3$ $Et_2O$, followed by 10 $cm^3$ $H_2O$. Phase separation, precipitation with $NH_4PF_6$ (55 mg, 0.35 mmol) in 1 $cm^3$ $H_2O$ and recrystallization from acetone/$Et_2O$ gives 106 mg (76%) analytically pure *(3)*·$(PF_6)_2$, decomp. ⩾320 °C.

b) 1 $cm^3$ $CF_3COOH$ is added to a solution of *(2)*[7] (50 mg, 0.15 mmol) in 5 $cm^3$ $CH_2Cl_2$ at −80 °C and the mixture allowed to warm up to room temperature over 16 h. Work-up as described in a) gives 61 mg (93.5%) *(3)*·$(PF_6)_2$.

$^1$H-NMR ($CD_3NO_2$, int. TMS): $\delta = 0.91$ (s, 6H, BMe), 1.91 (s, 30H, $C_5Me_5$), 5.76 (s, 4H, $C_4B_2H_4$). $^{11}$B-NMR ($CD_3NO_2$, ext. $BF_3 \cdot Et_2O$): $\delta = 8$ (broad).

Received: November 10, 1980 [Z 752 IE]
German version: Angew. Chem. 93, 471 (1981)

---

[*] Prof. Dr. G. E. Herberich, Dr. B. Hessner
Institut für Anorganische Chemie der Technischen Hochschule
Professor-Pirlet-Strasse 1, D-5100 Aachen (Germany)

Prof. Dr. G. Huttner, Dipl.-Chem. L. Zsolnai
Fachbereich Chemie der Universität
D-7750 Konstanz (Germany)

[**] Triple-Decked Complexes, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 1: *G. E. Herberich, J. Hengesbach, U. Kölle, G. Huttner, A. Frank*, Angew. Chem. *88*, 450 (1976); Angew. Chem. Int. Ed. Engl. *15*, 433 (1976).

---

[1] a) *R. N. Grimes*, Coord. Chem. Rev. *28*, 47 (1979); b) *W. Siebert*, Adv. Organomet. Chem. *18*, 301 (1980).
[2] *K. Wade*, Adv. Inorg. Chem. Radiochem. *18*, 1 (1976).
[3] Examples: [1b] and *D. E. Brennan, W. E. Geiger, Jr.*, J. Am. Chem. Soc. *101*, 3399 (1979).
[4] a) Theoretical basis: *J. W. Lauher, M. Elian, R. H. Summerville, R. Hoffmann*, J. Am. Chem. Soc. *98*, 3219 (1976); b) Structural data [1b].
[5] Cf. preparation of $(C_5H_5)Co[MeB(C_2H_2)_2BMe]$ [7]; unpublished results.
[6] X-ray structure analysis of *(3)*·$(PF_6)_2$: monoclinic with $a = 878.4(7)$, $b = 1653(2)$, $c = 1183.3(8)$ pm, $\beta = 106.83(5)°$, space group $P2_{1/c}$. $Z = 2$.

1565 diffraction data (Synthex-P3), $2 \leqslant 2Q \leqslant 42°$, ω-scan, $\lambda\text{-}Mo_{K\alpha} = 71.069$ pm, graphite monochromator, $\mu = 11.7\ cm^{-1}$; solution: direct methods (Shel-XTL) refinement (Syntex-EXTL): full matrix, $R_1 = 0.046$. The cation $(3)^{2+}$ has crystallographic inversion symmetry; the best planes through the $C_5Me_5$-ring and the $C_4B_2$-ring are, within the limits of the accuracy of the determination, parallel. The $PF_6$ ions are disordered.

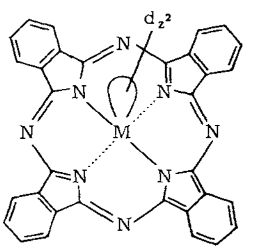
[7] *G. E. Herberich, B. Hessner, S. Beswetherick, J. A. K. Howard, P. Woodward,* J. Organomet. Chem. *192*, 421 (1980).

[8] Cyclic voltammetry in acetonitrile/0.1 M $[NBu_4]PF_6$. The electron count for the first reduction step was determined by comparison with the polarographic half-wave heights of $[Co(C_5H_5)_2]I$ at known concentrations. Priv.-Doz. Dr. *U. Kölle* is thanked for these measurements.

## Stable Metal-Phthalocyanines as Poison-Resistant Catalysts in Homogeneous Catalysis: Reduction of Organic Compounds with $NaBH_4$[**]

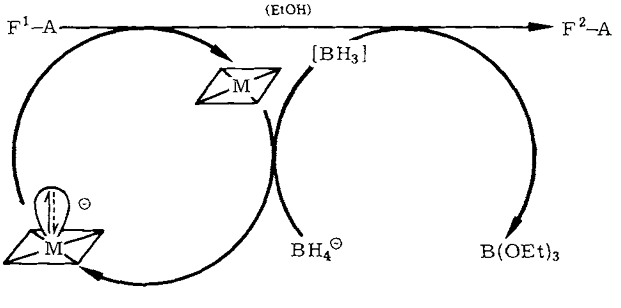
By *Heiner Eckert* and *Yvonne Kiesel*[*]

Transition metal-phthalocyanines (MPc) are extremely stable, both thermally and chemically, and hence some of them find use as fast blue dyes[1]. They can take up electrons reversibly in the $d_{z^2}$ orbital of the central atom M[2]; this predestinates them—in combination with a suitable reducing agent such as $NaBH_4$—as reduction catalysts[3].



MPc

The anions $[MPc]^{\ominus}$ of insoluble metal-phthalocyanines are soluble in polar organic solvents[2]. We recently reported on the use of the cobalt(I)-phthalocyanine anion for the selective reduction of nitro compounds[4] and for the cleavage of β-haloalkyl protecting groups[3]. $NaBH_4$ reductions[5] of nitro-[5a-c], cyano-[5a] and carbamoyl groups[5a], and of activated CC double bonds[5b,d] with addition of transition metal salts[5a,c] or catalyzed by structurally similar, but very expensive vitamin $B_{12}$[5d] or decomposable "cobaloxime"[5b,d] have also been described. Olefins and nitriles have been reduced with zinc in acidic medium in presence of vitamin $B_{12}$ as catalyst[6].



$F^1$–A and $F^2$–A see Table 1; M = VO, Mn, Fe, Co, Pd

The reduction of aliphatic and aromatic nitro- and nitroso-compounds, as well as oximes, Schiff's bases and nitriles with $NaBH_4$ under mild conditions in protic solvents (such as alcohols) at 20—25 °C to the corresponding amines can be homogeneously catalyzed with $[MPc]^{\ominus}$. CC-double bonds are hydrogenated, and halides are reduced to hydrocarbons. Arenes, aromatic halides, carboxylates and carboxamides are not attacked. The simultaneous reduction of several functional groups is also possible. The reaction rates gradually decrease along the series $C{=}C \approx Hal \approx NO_2 \approx NO > C{=}NOH \approx C{=}N{-}R > CN$; the reaction times are <30 min to 200 h. Hence, reducible groups can be successively reduced selectively under kinetic control, *e.g.* a nitronitrile to an aminonitrile or an α,β-unsaturated to a saturated nitrile (Table 1). The cata-

Table 1. $[CoPc]^{\ominus}$-catalyzed reduction of organic compounds with $NaBH_4$ in EtOH at 20 °C. Educt conc. 0.2 M; $NaBH_4$ conc. 1.4 M; CoPc conc. 0.02 M.

| Educt<br>$F^1$—A | $t$ [h] | Product<br>$F^2$—A | Yield<br>[%] |
|---|---|---|---|
| $n$-$C_3H_7$—$NO_2$ | 189 | $n$-$C_3H_7$—$NH_2$ | 76 |
| $p$-$NO_2$—$C_6H_4$—$CH_3$ | 21 | $p$-$NH_2$—$C_6H_4$—$CH_3$ | 88 |
| $p$-$NO_2$—$C_6H_4$—Cl | 2—168 | $p$-$NH_2$—$C_6H_4$—Cl | 81—96 |
| $p$-$NO_2$—$C_6H_4$—$CH_2$—CN | 6 | $p$-$NH_2$—$C_6H_4$—$CH_2$—CN | 85 |
| 2,4-$(NO_2)_2C_6H_3$—Cl | 214 | 2,4-$(NH_2)_2C_6H_3$—Cl | 79 |
| R—$NO_2$ [a] | 2.5 | R—$NH_2$ [a] | 93 |
| $p$-NO—$C_6H_4$—Cl | 94 | $p$-$NH_2$—$C_6H_4$—Cl | 95 |
| $C_6H_5$—CH=NOH | 47 | $C_6H_5$—$CH_2$—$NH_2$ | 80 |
| $C_6H_5$—$CH(CH_3)$—CH=NOH | 48 | $C_6H_5$—$CH(CH_3)$—$CH_2$—$NH_2$ | 73 |
| $c$-$C_6H_{10}$=NOH | 48 | $c$-$C_6H_{11}$—$NH_2$ | 78 |
| $C_6H_5$—CH=N—$CH(CH_3)_2$ | 72 | $C_6H_5$—$CH_2$—NH—$CH(CH_3)_2$ | 92 |
| $C_6H_5$—CN | 168 | $C_6H_5$—$CH_2$—$NH_2$ | 53 |
| $C_6H_5$—$CH_2$—CN | 137 | $C_6H_5$—$CH_2$—$CH_2$—$NH_2$ | 63 |
| NC—$(CH_2)_4$—CN | 188 | $NH_2$—$(CH_2)_6$—$NH_2$ [b] | 27 |
| $C_8H_{17}$—CH=CH—$C_7H_{14}$—$CO_2Et$ | 40 [c] | $C_{17}H_{35}$—$CO_2Et$ | 100 |
| $C_6H_5$—CH=CH—$CO_2Et$ | 0.5 | $C_6H_5$—$CH_2$—$CH_2$—$CO_2Et$ | 98 |
| $(CH_3)_2C$=CH—CO—$NH_2$ | 165 | $(CH_3)_2CH$—$CH_2$—CO—$NH_2$ | 80 |
| $C_6H_5$—CH=CH—CN | 1 | $C_6H_5$—$CH_2$—$CH_2$—CN | 82 |
| $n$-$C_{12}H_{25}$—Br | 21 | $n$-$C_{12}H_{26}$ | 97 |
| 2,4-$(CH_3)_2C_6H_3$—$CH_2Cl$ | 2 | 1,2,4-$(CH_3)_3C_6H_3$ | 63 |
| $p$-$NO_2$—$C_6H_4$—CO—$CH_3$ | 48 | $p$-$NH_2$—$C_6H_4$—CH(OH)—$CH_3$ | 79 |
| $p$-$NO_2$—$C_6H_4$—$CH_2$—CN | 156 | $p$-$NH_2$—$C_6H_4$—$CH_2$—$CH_2$—$NH_2$ | 77 |
| $p$-$NO_2$—$C_6H_4$—CH=CH—$CO_2Et$ | 120 | $p$-$NH_2$—$C_6H_4$—$CH_2$—$CH_2$—$CO_2Et$ | 64 |

[a] R = 2-acetamino-4-methoxy-5-methoxycarbonylphenyl. [b] Isolated as *N,N'*-dibenzoyl derivative. [c] 3 h at 50 °C.

---

[*] Dr. H. Eckert, Y. Kiesel
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

lysts are used in a concentration of up to 0.001 M; in the reduced soluble form $[MPc]^{\ominus}$ they change color (Table 2), thus allowing the course of the reaction to be monitored. After the reaction (in non-reducing medium), the catalyst MPc is quantitatively recovered; it can be used again for reductions without any further treatment.

Table 2. $[MPc]^{\ominus}$-catalyzed reduction of *p*-chloronitrobenzene with $NaBH_4$ in EtOH at 20—25 °C. Educt conc. 0.2 M; $NaBH_4$ conc. 1.4 M; MPc conc. 0.02 M.

| M in MPc | Color of $[MPc]^{\ominus}$ [a] | *t* [h] | Yield of *p*-$NH_2$—$C_6H_4$—Cl [%] |
|---|---|---|---|
| $V^{IV}O$ | lilac | 2 | 48 |
| $V^{IV}O$ | | 23 | 91 |
| $Mn^{II}$ | dark green | 2 | 85 |
| $Fe^{II}$ | wine red | 3 | 74 |
| $Fe^{II}$ | | 96 | 89 |
| $Co^{II}$ | deep yellow-green | 2 | 81 |
| $Co^{II}$ [b] | | 71 | 74 |
| $Co^{II}$ [c] | | 3 | 26 |
| $Co^{II}$ [c] | | 70 | 76 |
| $Pd^{II}$ | black [d] | 2 | 80 |
| $Pd^{II}$ | | 120 | 98 |
| Vitamin $B_{12b}$ | blue green [e] | 2 | 34 |
| Vitamin $B_{12b}$ | | 20 | 64 |

[a] 1—15 min after the combined addition of $NaBH_4$ and MPc in solution. [b] $NaBH_4$ conc. 0.4 M. [c] CoPc conc. 0.002 M. [d] Color of the sparingly soluble crystals. [e] Color of the vitamin $B_{12s}$ solution.

Strong catalyst poisons[7] such as divalent S-compounds (β-naphthalenethiol, 1-octanethiol), or cyanide or iodide ions in tenfold excess (referred to the catalyst; equimolar referred to the educt) do not influence the rate of the reaction, or if so only slightly. This is reflected in the almost identical yields of reduction products in reactions with or without catalyst poison (Table 3). This immunity is underscored in the case of $[MPc]^{\ominus}$ catalysts with M = Fe or Co, probably owing to maximal localization of the negative charge in the "central atomic orbitals" of these $[MPc]^{\ominus}$. This finding is consistent with the results of LCAO-MO calculations on the electron-configuration of MPc[2]. The poisoning effects of the metals with d-electrons (*e.g.* $Cu^{2+}$, $Fe^{2+}$) are deactivated by their reduction to the metals under the reaction conditions. The M—C bond in alkyl-MPc complexes, which can be formed as intermediates from $[MPc]^{\ominus}$ and alkylating agents, is likewise reductively cleaved by $NaBH_4$. Thus, an organo-MPc, such as 2-hydroxyethyl-$Co^{III}$Pc, can be used with the same effect as MPc for the catalysis of reduction.

Table 3. $[MPc]^{\ominus}$-catalyzed reduction of *p*-chloronitrobenzene with $NaBH_4$ in the presence of strong catalyst poisons. For conditions see Table 2; concentration of catalyst poison 0.2 M.

| Catalyst poison | M | *t* [h] | Yield [%] of *p*-$NH_2$—$C_6H_4$—Cl without catalyst poison | with catalyst poison |
|---|---|---|---|---|
| β-Naphthalenethiol | Co | 2 | 81 | 84 |
| *n*-$C_8H_{17}$—SH | Co | 2 | 81 | 72 |
| $CN^{\ominus}$ | Co | 2 | 81 | 58 |
| $CN^{\ominus}$ | Co | 8 | — | 83 |
| $CN^{\ominus}$ | Fe | 3 | 74 | 70 |
| $I^{\ominus}$ | Co | 2 | 81 | 77 |
| $Cu^{2+}$ | Co | 2 | 81 | 93 |
| HO—$CH_2$—$CH_2$—$Co^{III}$Pc | | 2 | 81 | 85 |
| $CN^{\ominus}$ | Vitamin $B_{12b}$ | 2 | 34 | 10 |

The reduction of a nitro group with $NaBH_4$ can also be catalyzed by the structurally related vitamin $B_{12}$, but the reaction is slower and susceptible to catalyst poisoning (Tables 2 and 3). Moreover, vitamin $B_{12}$ is not so favorable as the metal-phthalocyanines regarding stability, insolubility in the "non-active state", and price. The easily accessible "cobaloximes"[5b,d] (vitamin $B_{12}$ models) are readily decomposable in the reduced form and tend to undergo side reactions at the ligand[8]. While many metal-macrocycles, *e.g.* the metal-porphyrins[9], can be relatively easily demetalated, the metal in stable MPc is almost irreplaceable even under drastic conditions (e.g. 5 N HCl/reflux; 5 N NaOH/reflux; conc. $H_2SO_4$)[1a]. The sensitivity of the porphyrins to light, which leads to their photooxidation[9], is not observed in the case of the light-fast dyes MPc. Because of their stability the MPc's are guaranteed a very long life even under "hard" conditions.

The stable MPc's are thus a successful combination of soluble $[MPc]^{\ominus}$ catalysts during the reduction and insoluble MPc-procatalyst under non-reducing conditions.

## *Procedure*

MPc[1] (0.5 g, *ca.* 0.9 mmol) is added under $N_2$ to a solution of $NaBH_4$ (2.7 g, 70 mmol) in EtOH (50 $cm^3$). The deep-colored solution (or suspension) is treated with 10 mmol $F^1$—A (Table 1) and the water-cooled mixture stirred at 20—25 °C under constant pressure (Tables 1 and 2). The ice-cold mixture is then neutralized with 5 N HCl (5—10 min until completion of the initially vigorous evolution of gas; pH 6—7) and the deep-blue precipitate separated by centrifugation (5 min; 3000 rpm) and washed three times with MeOH; the catalyst MPc remains behind. For re-use the catalyst is washed three times with water and dried between 20 and 200 °C. The combined centrifugates are evaporated down and the residue partitioned between water and $CH_2Cl_2$. In the case of aliphatic amines the residue is partitioned with 1 N NaOH/ether. Volatile amines are isolated from the ether phase as $F^2$—A·HCl. Concentration and drying of the organic phase affords the products $F^2$—A. These are purified by filtration of a solution in hexane/ether in the case of neutral substances, and by filtration of their aqueous solutions in hydrochloric acid in the case of amines.

Received: November 26, 1980 [Z 753 IE]
German version: Angew. Chem. *93*, 477 (1981)

CAS Registry numbers:
*n*-$C_3H_7$—$NO_2$, 108-03-2; *p*-$NO_2$—$C_6H_4$—$CH_3$, 99-99-0; *p*-$NO_2$—$C_6H_4$—Cl 100-00-5; *p*-$NO_2$—$C_6H_4$—$CH_2$—CN, 555-21-5; 2,4-$(NO_2)_2C_6H_3$-Cl, 97-00-7; R-$NO_2$, 4093-41-8; *p*-NO—$C_6H_4$-Cl, 932-98-9; $C_6H_5$—CH=NOH, 932-90-1; $C_6H_5$—$CH(CH_3)$—CH=NOH, 13213-36-0; *c*-$C_6H_{10}$=NOH, 100-64-1; $C_6H_5$—CN, 100-47-0; $C_6H_5$—$CH_2$—CN, 140-29-4; NC—$(CH_2)_4$—CN, 111-69-3; β-pinene, 127-91-3; $C_6H_5$—CH=CH—$CO_2Et$, 103-36-6; $(CH_3)_2C$=CH—CO—$NH_2$, 4479-75-8; $C_6H_5$—CH=CH—CN, 4360-47-8; *n*-$C_{12}H_{25}$—Br, 143-15-7; 2,4-$(CH_3)_2C_6H_3$—$CH_2Cl$, 824-55-5; *p*-$NO_2$—$C_6H_4$—CO—$CH_3$, 100-19-6; *p*-$NO_2$—$C_6H_4$—CH=CH—$C0_2Et$, 953-26-4; $NaBH_4$, 1694-66-2; CoPc, 3317-67-7; VoPc, 13930-88-6; MnPc, 14325-24-7; FePc, 132-16-1; PdPc, 20909-39-1; Vitamin $B_{12b}$, 13422-52-1; β-naphthalenethiol, 91-60-1; *n*-$C_8H_{17}$—SH, 111-88-6; $CN^-$, 57-12-5; $I^-$, 20461-54-5; $Cu^{2+}$, 15158-11-9; Ho—$CH_2CH_2$—$Co^{III}$Pc, 62450-97-9; *n*-$C_3H_7$—$NH_2$, 107-10-8; p-$NH_2$—$C_6H_4$—$CH_3$, 106-49-0; *p*-$NH_2$—$C_6H_4$—Cl, 106-47-8; *p*-$NH_2$—$C_6H_4$—$CH_2$—CN, 3544-25-0; 2,4-$(NH_2)_2$—$C_6H_3$—Cl, 5131-60-2; R-$NH_2$, 77495-40-0; $C_6H_5$—$CH_2$—$NH_2$, 100-46-9; $C_6H_5$—$CH(CH_2)$—$CH_2$—$NH_2$, 582-22-9; *n*-$C_6H_5$—$NH_2$, 108-91-8; $C_6H_5$—$CH_2$—$CH_2$—$NH_2$, 64-04-0; $C_6H_5CONH$—$(CH_2)_6$—$CNCOC_6H_5$, 5326-21-6; pinane, 473-55-2; $C_6H_5$—$CH_2$—$CH_2CO_2Et$, 2021-28-5; $(CH_3)_2CH$—$CH_2$—CO—$NH_2$, 541-46-8; $C_6H_5CH_2$—$CH_2$—CN, 645-59-0; *n*-$C_{12}H_{26}$, 112-40-3; 1,2,4-$(CH_3)_3C_6H_3$, 95-63-6;
*p*-$NH_2$—$C_6H_4$—CH(OH)—$CH_3$, 14572-89-9;
*p*-$NH_2$—$C_6H_4$—$CH_2$—$CH_2$—$NH_2$, 13472-00-9;
*p*-$NH_2$—$C_6H_4$—$CH_2$—$CH_2$—$CO_2Et$, 7116-44-1;

---

[1] a) *A. B. P. Lever*, Adv. Inorg. Chem. Radiochem. *7*, 27 (1965); b) *F. H. Moser, A. L. Thomas:* Phthalocyanine Compounds, Reinhold Publ., New York 1963.

[2] *R. Taube*, Pure Appl. Chem. *38*, 427 (1974).

[3] *H. Eckert, Y. Kiesel,* Synthesis *1980*, 947.
[4] a) *H. Eckert,* Angew. Chem. *93*, 216 (1981); Angew. Chem. Int. Ed. Engl. *20*, 208 (1981); b) *H. Eckert, A. Schier,* Angew. Chem. *91*, 841 (1979); Angew. Chem. Int. Ed. Engl. *18*, 794 (1979).
[5] a) *T. Satoh, S. Suzuki, Y. Suzuki, Y. Miyaji, Z. Imai,* Tetrahedron Lett. *1969*, 4555; b) *Y. Ohgo, S. Takeuchi, I. Yoshimura,* Bull. Chem. Soc. Jpn. *44*, 283 (1971); c) *K. Hanaya, N. Fujita, H. Kado,* Chem. Ind. *1973*, 794; d) *M. N. Ricroch, A. Gaudemer,* J. Organomet. Chem. *67*, 119 (1974).
[6] a) *A. Fischli,* Helv. Chim. Acta *62*, 882 (1979); b) *A. Fischli, P. M. Müller, ibid. 63*, 1619 (1980).
[7] a) *F. Zymalkowski:* Katalytische Hydrierungen im Organisch-Chemischen Laboratorium, Ferdinand Enke, Stuttgart 1965; b) *P. N. Rylander:* Catalytic Hydrogenation over Platinum Metals, Academic Press, New York 1967.
[8] *R. B. Silverman, D. Dolphin,* Can. J. Chem. *54*, 1425 (1976).
[9] *K. M. Smith:* Porphyrins and Metalloporphyrins, Elsevier, Amsterdam 1975.

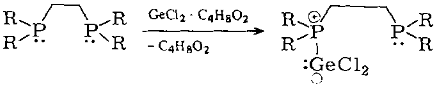
---

## *P,P,P′,P′*-Tetraphenylethylenediphosphane-dichlorogermanediyl: A Fluxional Phosphorus Ylide[**]

By *Wolf-Walther du Mont, Gero Rudolph,* and *Norbert Bruncks*[*]

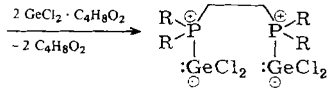
The kinetic lability of certain phosphorus ylides, phosphane chalcogenides and halogenophosphonium ions $R_3P—X$ ($X = GeCl_2$[1], $SnCl_2$[2], Te[3], $Br^+$, $I^+$[3a]) has recently been determined in the presence of non-coordinated $R_3P$. The transfer of six-electron species of heavy main group elements between phosphanes, which occurs rapidly on the $^1H$- and $^{31}P$-NMR time scales even at room temperature, can be satisfactorily described as a $P^{III}/P^{V}$ redox reaction or a "ligand exchange" process at $I^+$, $Te^0$, $Sn^{II}$ *etc.* Thus, *Scherer et al.* detected a fluxional redox system *via* transfer of tellurium in a diazadiphosphetidine derivative[3d], in which discrete $P^{III}$- and $P^{V}$-units are present in the crystal[4]. We now report the first fluxional ylide in which the "carbene analogous" dichlorogermanediyl derivative is mobile in solution at −80 °C.

*P,P,P′,P′*-tetraphenylethylenediphosphane *(1)* reacts with the $GeCl_2$-dioxane complex, depending on the stoichiometric ratio, to give the 1 : 1-complex *(2)* or the 1 : 2-complex *(3)*. Both dissolve as monomers in benzene and give $^{31}P$-$\{^1H\}$-NMR spectra consisting of *one* signal. While the $^{31}P$-singlet for *(3)* occurs at $\delta = -7$ and is consistent with a diylide structure, the considerable broadening of the $^{31}P$-NMR signal of *(2)* at $\delta = -10.2$ presents many structural possibilities. Since only one (sharp) signal appears at −80 °C in [$D_8$]toluene, apart from transfer of the ylide functionality between the phosphane groups as in *(2a)*, the chelate complex structures *(2b)* with tetragonal-pyramidal arrangement of ligands at $Ge^{II}$ or the (pseudo)-trigonal bipyramidal arrangement of ligands in *(2c)* might also be present in solution.



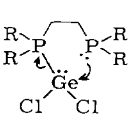
*(1)* *(2)*

*(1)*

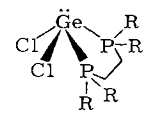


R = $C_6H_5$

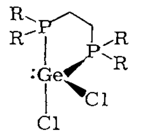
*(3)*



*(2a)*



*(2b)*



*(2c)*

In the case of *(2c)*, equilibration of the phosphane functionalities detected in the $^{31}P$-NMR spectrum implies that pseudorotation occurs at germanium. A linear Cl—Ge—Cl-arrangement is precluded on the basis of the IR-data. To clarify this problem, an X-ray structure analysis of *(2)* was therefore undertaken[5]. The data, show that the coordination sphere around the germanium in *(2c)* can be described as a distorted trigonal bipyramid, the Ge—P bond lengths are, however, very different ($Ge—P_{eq} = 251$ pm, as in $(C_6H_5)_3PGeCl_2$[6], $Ge—P_{ax} = 334$ pm, somewhat less than the van der Waals separation). Thus, the equilibration of the phosphorus atoms in solution can be satisfactorily explained by fluxion of the $\overset{\oplus}{P}—\overset{\ominus}{Ge}$-ylide *(2a)* as well as by pseudorotation of the chelate complex.

### *Procedure*

*(1)* (2.15 g, 5.4 mmol) is added to $GeCl_2$·dioxane (1.25 g, 5.4 mmol) in 30 $cm^3$ toluene. The solvent is evaporated off after 1 h, and the already pure *(2)* (2.9 g, 100%) recrystallized from toluene. Decomposition point ⩾250 °C, correct analytical data. IR (CsI/Nujol): $\nu = 270$ s, 305 vw, 335 s $cm^{-1}$ ($PGeCl_2$); $^1H$-NMR ($C_6D_6$): $\delta = 2.3$ (m); $^{31}P$-NMR ($C_6D_5CD_3$), 298 K: $\delta = -10.2$ (broad), 193 K: −10.8.

Received: July 4, 1980 [Z 754 IE]
German version: Angew. Chem. *93*, 472 (1981)

CAS Registry numbers:
*(1)*, 1663-45-2; *(2)*, 77495-41-1; *(3)*, 77495-42-2; $GeCl_2 \cdot C_4H_6O_2$, 28595-67-7

---

[*] Prof. Dr. W. W. du Mont
Fachbereich Chemie der Universität Oldenburg,
Ammerländer Heerstrasse 67—69, D-2900 Oldenburg (Germany)
Dr. G. Rudolph, Dipl.-Chem. N. Bruncks
Institut für Anorganische und Analytische Chemie
der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

[1] *W.-W. du Mont, G. Rudolph,* Chem. Ber. *109*, 3419 (1976).
[2] *W.-W. du Mont, B. Neudert,* Z. Anorg. Allg. Chem. *441*, 86 (1978).
[3] a) *W.-W. du Mont, H.-J. Kroth,* J. Organomet. Chem. *113*, C 35 (1976); b) *D. H. Brown, R. J. Cross, D. Millington, ibid. 125*, 219 (1977); c) *D. Keat, D. G. Thompson, ibid. 141*, C 13 (1977); d) *O. J. Scherer, G. Schnabl,* Angew. Chem. *89*, 500 (1977); Angew. Chem. Int. Ed. Engl. *16*, 486 (1977).
[4] *S. Pohl,* Z. Naturforsch. *B 33*, 610 (1978).
[5] *N. Bruncks, W.-W. du Mont, J. Pickardt,* Chem. Ber., in press.
[6] *N. G. Bokii, Y. T. Struchkov, S. P. Kolesnikov, I. S. Rogozhin, O. M. Nefedov,* Izv. Akad. Nauk SSSR, Ser. Khim. *1975*, 812; Chem. Abstr. *83*, 69491 s (1975).

---

## [(−)-diop]RhCl—Catalyzed Asymmetric Addition of Bromotrichloromethane to Styrene

By *Shinji Murai, Ryoji Sugise,* and *Noboru Sonoda*[*]

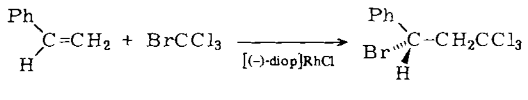
Although a number of asymmetric reactions catalyzed by transition metal complexes to form C—H, C—C, C—Si, and C—O bonds with creation of chirality have been reported[1], no reactions of this type which lead to the formation of chiral carbon-halogen bonds have been reported[2] to the best of our knowledge. We describe here the first example of an asymmetric reaction, catalyzed by a chiral transition metal complex, in which the chiral center is formed as a result of carbon-bromine bond formation.

---

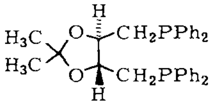
[*] Prof. Dr. S. Murai [+], R. Sugise, Prof. Dr. N. Sonoda
Department of Petroleum Chemistry, Faculty of Engineering,
Osaka University
Yamada-Kami, Suita 565, Osaka (Japan)

[+] Author to whom correspondence should be addressed.

*0570-0833/81/0505-475 $ 02.50/0*



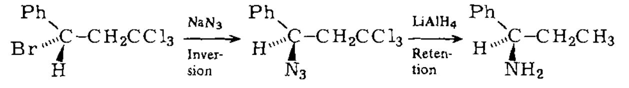
(S)-(−)-(1)



(−)-diop

The reaction of bromotrichloromethane with styrene in 2 : 1 ethanol-benzene, in the presence of an optically active phosphane-rhodium complex [(−)-diop]RhCl[3] (0.30 mmol) at 80 °C for 18 h, gave the 1 : 1-adduct *(1)* in 26% yield. The adduct *(1)* showed an optical rotation of $[\alpha]_D = -22.5$ ($c = 10.7$, $C_6H_6$) which corresponded to >32% enantiomeric excess and (*S*)-configuration.

The enantiomeric excess and the absolute configuration were determined in the following way using a sample of *(1)* with $[\alpha]_D = -11.3°$ ($c = 10.3$, $C_6H_6$) obtained in a separate run. This sample was treated with an excess of $NaN_3$ to give the azide *(2)*, which was not isolated but directly reduced with $LiAlH_4$ to (*R*)-(+)-1-phenyl-1-propylamine *(3)* which showed $[\alpha]_D = +3.43$ ($c = 8.4$, $C_6H_6$) and corresponded to an optical purity of 16%[4]. Thus, the adduct (*S*)-(−)-*(1)* with $[\alpha]_D = -22.5$ corresponds to >32% enantiomeric excess. It should be noted that the optical purity must be much higher than 32%, since $S_N2$ displacement of *(1)* with $NaN_3$ may involve partial racemization[5].



(S)-(−)-(1) (2) (R)-(+)-(3)

Since various transition metal catalysts for addition of organic halides to olefins are known[6] and a variety of chiral ligands are now available[1], the present result opens up new possibilities for asymmetric synthesis.

### *Experimental*

(*S*)-(−)-*(1)*: To a solution of styrene (9.36 g, 90 mmol) and $BrCCl_3$ (4.46 g, 22.5 mmol) in EtOH (30 $cm^3$) was added a solution of [(−)-diop]RhCl[3], prepared from $[RhCl(C_8H_{14})_2]$[7] (0.108 g, 0.30 mmol) and (−)-diop[3] (0.164 g, 0.33 mmol) in benzene (15 $cm^3$) under $N_2$. The mixture was heated under reflux for 18 h: the color of the mixture changed from green to dark brown after 30 min. Concentration and distillation gave (*S*)-(−)-*(1)* (1.78 g, 26% yield), b.p. 87–91 °C/0.6 torr[8].

Conversion *(1)*→*(3)*: A sample of *(1)* (8.51 g, 28.2 mmol) with $[\alpha]_D = -11.3$ ($c = 10.3$, $C_6H_6$), which was obtained in a separate run, was added to a solution of $NaN_3$ (4.29 g, 66 mmol) in 162 $cm^3$ of EtOH/$H_2O$ (4 : 1). The mixture was heated for 36 h at 50 °C, cooled, and treated with $H_2O$ (75 $cm^3$), $n$$Bu_2O$ (100 $cm^3$), and 40% aqueous $CaCl_2$ solution (125 $cm^3$) to separate the organic layer. The aqueous layer was extracted with $n$$Bu_2O$ (3 × 50 $cm^3$). After drying over $MgSO_4$, the combined $n$$Bu_2O$ solution containing the azide *(2)* was added dropwise to a suspension of $LiAlH_4$ (16 g, 420 mmol) in $n$$Bu_2O$ at 15 °C. The mixture was heated for 15 h at 100 °C, cooled, and made acidic with 4 N HCl. The aqueous layer was washed with $Et_2O$ (2 × 40 $cm^3$), made alkaline with conc. aqueous KOH, heated to 100 °C to dissolve the inorganic salts and after cooling extracted with $Et_2O$ (4 × 100 $cm^3$). The ethereal solution was dried over $MgSO_4$ and distilled [0.897 g, crude product (25%), b.p. ≈100° (bath temp.)/10 torr]. Redistillation afforded chemically pure (*R*)-(+)-*(3)* having $[\alpha]_D = +3.43$ ($c = 8.4$, $C_6H_6$) corresponding to 16% enantiomeric excess[4].

Received: September 8, 1980 [Z 758 IE]
German version: Angew. Chem. *93*, 481 (1981)

CAS Registry numbers:
(S)-(−)-*1*, 77495-38-6; *(2)*, 77495-39-7; (R)-(+)-*3*, 3082-64-2; PhCH=CH₂, 100-42-5; BrCCl₃, 75-62-7; [(−)-diop]RhCl, 61113-00-6

---

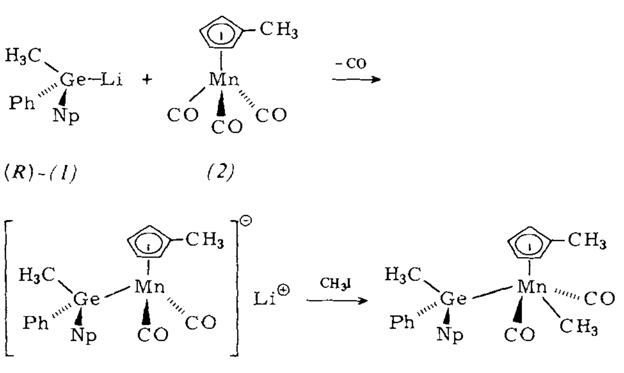
[1] *H. B. Kagan, J. C. Fiaud*, Top. Stereochem. *10*, 175 (1978).
[2] *G. Berti, A. Marsili*, Tetrahedron *25*, 4515 (1969), reported asymmetric bromination of olefins in the presence of cinchona alkaloids, which were used in almost stoichiometric amounts; *B. Boutevin, E. B. Dongla*, Tetrahedron Lett. *1977*, 4315, described $FeCl_3$-catalyzed addition of $CCl_4$ to an optically active olefin, (−)-menthyl acrylate.
[3] *H. B. Kagan, T. P. Dang*, J. Am. Chem. Soc. *94*, 6429 (1972).
[4] The highest value of optical rotation for (*R*)-(+)-*(3)* reported is $[\alpha]_D = +21.7$ ($C_6H_6$), *K. Harada, J. Oh-hashi*, Bull. Chem. Soc. Jpn. *43*, 960 (1970).
[5] Reaction of 1-chloro-1-phenylethane with $NaN_3$ in 80% EtOH has been reported to proceed with 30% racemization; *F. Hiron, E. D. Hughes*, J. Chem. Soc. *1960*, 795.
[6] *F. Minisci*, Acc. Chem. Res. *8*, 165 (1975); *J. K. Kochi:* Organometallic Mechanism and Catalysis, Academic Press, New York 1978, Ch. 6 and 8.
[7] *L. Porri, A. Lionetti, G. Allegra, A. Immirzi*, Chem. Commun. *1965*, 336.
[8] B.p. = 92 °C/0.2 torr; *M. S. Kharasch, O. Reinmuth, W. H. Urry*, J. Am. Chem. Soc. *69*, 1105 (1947).

---

## Introduction of an Optically Active Ligand into Transition Metal Complexes with Five Independent Ligands

By *Ernesto Colomer, Robert J. P. Corriu*, and *André Vioux*[*]

Recently, we reported the introduction of an optically active triorganogermyl ligand at a transition metal site, by displacement of a CO-ligand[1]. This reaction allowed us to synthesize the optically active anion *(3)*, which was isolated as the tetraethylammonium salt *(3b)* (Table 1), from the (*R*)-enantioner of the germyllithium compound *(1)* and the tricarbonylmanganese complex *(2)*. It is assumed that the reaction proceeds with retention of configuration at germanium, since optically active germyllithium compounds are known to react with retention of configuration in substitution reactions[2]. The anion *(3)* reacts with methyl iodide affording the neutral complex *(4)*, whose crystal



(R)-(1) (2)

(S)-(3) (4)

Np = 1-Naphthyl

---

[*] Prof. Dr. R. J. D. Corriu, Dr. E. Colomer, Dr. Ing. A. Vioux
Laboratoire des Organometalliques,
Equipe de Recherche associée au C.N.R.S. No. 554,
Université des Sciences et Techniques du Languedoc
Place Eugène Bataillon, F-34060 Montpellier-Cedex (France)

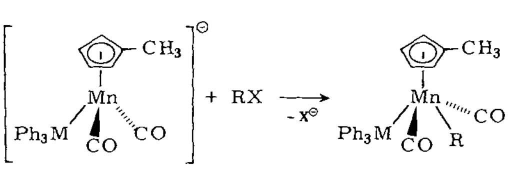
structure has not yet been determined. It is well known, however, that complexes with five ligands, one of which is a cyclopentadienyl moiety, have a square pyramidal geometry with the cyclopentadienyl moiety occupying the apical position[3]; from the IR spectrum, only the *diag-* (or *trans*) isomer—both CO-ligands are arranged *diagonally*[10a]—was obtained[4] (Table 1).

Table 1. Selected physical data of the novel complexes.

| Complex [a] | M.p. [°C] | IR [cm$^{-1}$] ($CH_2Cl_2$) $\nu_{CO}$ | $\nu_{NO}$ | $^1$H-NMR ($\delta$-values rel. to TMS) $C_5H_5$ | M–C*H* |
|---|---|---|---|---|---|
| *(3b)* [b] | 59–60<br>(53–55) [c] | 1850 s<br>1775 s | — | — [d, e] | — |
| *(4)* [f] | 112–113<br>(109–110) [c] | 1960 m<br>1905 s | — | — [g, h] | 0.99 |
| *(6a)* | 133–134 | 1970 m<br>1910 s | — | — [g, i] | 0.97 |
| *(6b)* | 96–98 | 1964 m<br>1906 s | — | — [g, i] | 3.36 |
| *(6c)* | 121–122 | 1970 m<br>1910 s | — | — [g, i] | 0.97 |
| *(6d)* | 77–79 | 1970 m<br>1911 s | — | — [g, i] | 3.40 |
| *(7)* | 172–175 | 1845 s | 1525 s | 5.00 [d] | — |
| *(8)* | 190–192 | 1835 s | 1515 s | 5.13 [d] | — |
| *(9a)* | 124–125 | 2010 s | 1645 s | 4.80 [g] | 0.74 |
| *(10a)* | 114–115 | 2005 s | 1650 s | 4.63 [g] | 2.80, 3.27 |
| *(11a)* | 141–142 | 2000 s | 1640 s | 4.77 [g] | 0.80 |

[a] All compounds gave satisfactory elemental analyses. [b] (*S*)-isomer ($[\alpha]_D^{25} = -3.9$, $CH_2Cl_2$); crystallizes with one molecule $CH_2Cl_2$. [c] Melting point of the racemate. [d] In $CD_2Cl_2$. [e] $C_5H_4$ two multiplets at $\delta = 3.87$ and 4.04; $C_5H_4CH_3$, $\delta = 1.80$; $GeCH_3$, $\delta = 0.70$. [f] (*S*)-isomer ($[\alpha]_D^{25} = +7.2$ ($C_6H_6$), +18.7 ($CH_2Cl_2$)). [g] In $C_6D_6$. [h] $C_5H_4$, two multiplets at $\delta = 3.63$ and 3.87. $C_5H_4CH_3$ and $GeCH_3$, $\delta = 1.33$. [i] $C_5H_4$, two multiplets at $\delta = 3.8$ and 4.1; $C_5H_4CH_3$, $\delta \approx 1.3$.

The triphenylgermanyl and triphenylsilyl substituted anions, *(5a)*[5] and *(5b)* respectively, were analogously alkylated with methyl iodide and benzyl bromide to the dicarbonylmanganese complexes *(6)*. The $^1$H-NMR spectrum only showed signals corresponding to the *diag*-isomer: the benzyl derivatives show a single sharp signal for the $CH_2$-group, *i.e.* the two protons—as expected for the *diag*-isomer—are magnetically equivalent (Table 1).

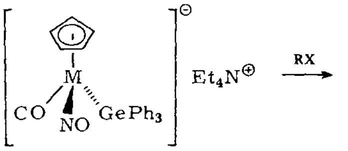


*(5a)*, M = Si
*(5b)*, M = Ge
RX = $CH_3I$, $C_6H_5CH_2Br$

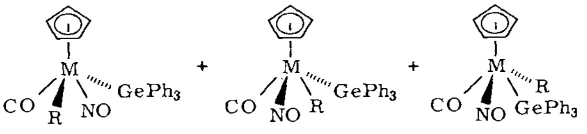
*(6a)*, M = Si, R = $CH_3$
*(6b)*, M = Si, R = $CH_2C_6H_5$
*(6c)*, M = Ge, R = $CH_3$
*(6d)*, M = Ge, R = $CH_2C_6H_5$

The alkylation of the anionic molybdenum and tungsten complexes *(7)* or *(8)*[6], respectively, can lead to the formation of three enantiomeric pairs[7]. Reaction of *(7)* with methyl iodide produced the three enantiomeric pairs *(9a)*–*(9c)* in yields of 66, 14 and 19%, respectively (determined by $^1$H-NMR spectroscopy); the pure isomer *(9a)* could be obtained in 58% yield by fractional crystallization (Table 1). Its structure was established by IR spectroscopy (Table 1). Isomers *(9b)* and *(9c)* were not isolated ($^1$H-NMR: $\delta = 4.80$ and 0.27 or 4.47 and 0.37 respectively; IR: $\nu_{CO} = 1925$ and $\nu_{NO} = 1645$ cm$^{-1}$).

In the benzyl derivative *(10a)* the $-CH_2$-protons are non-equivalent ($J = 10$ Hz) since there is a chiral center at molybdenum[8].



*(7)*, M = Mo
*(8)*, M = W
RX = $CH_3I$, $C_6H_5CH_2Br$



*(9a)* *(10a)* *(11a)*; *(9b)* *(10b)* *(11b)*; *(9c)* *(10c)* *(11c)*

*(9)*, M = Mo, R = $CH_3$; *(10)*, M = Mo, R = $C_6H_5CH_2$;
*(11)*, M = W, R = $CH_3$

These type of complexes are surprizingly—as the $^1$H-NMR spectra (in [D$_6$]dimethyl sulfoxide) show—stable up to 100 °C and no isomerization occurs (the compounds decompose first above 120 °C, but without isomerization)[9]. Complexes with five independent and different ligands are, at present, the subject of much interest[10], since they offer the possibility of synthesizing novel, stable, optically active transition metal compounds.

*Experimental*

All reactions are carried out under an $N_2$-atmosphere. In a typical experiment 326 mg (0.5 mmol) of *(7)* in 15 cm$^3$ tetrahydrofuran is treated with an excess of $CH_3I$ at room temperature. The initial brown solution becomes yellow and a precipitate of $Et_4NI$ is formed. After 15 min, the solvent is removed, the residue treated with toluene and filtered. The solution is concentrated to *ca.* 10 cm$^3$, 10 cm$^3$ hexane added and the mixture left at −20 °C. Yellow crystals of *(9a)* are obtained (157 mg, yield 58%).

Received: March 17, 1980 [Z 757a IE]
German version: Angew. Chem. *93*, 488 (1981)

---

[1] *E. Colomer, R. J. P. Corriu*, J. Chem. Soc. Chem. Commun. *1978*, 435.

[2] *A. G. Brook, G. J. D. Peddle*, J. Am. Chem. Soc. *85*, 2338 (1963); *C. Eaborn, R. E. E. Hill, P. Simpson*, J. Organomet. Chem. *15*, P1 (1968); *ibid. 37*, 267, 275 (1972); *F. Carre, R. Corriu, ibid. 65*, 349 (1974).

[3] *K. W. Barnett, D. W. Slocum*, J. Organomet. Chem. *44*, 1 (1972).

[4] *A. R. Manning*, J. Chem. Soc. *A 1967*, 1984; *W. Jetz, W. A. G. Graham*, Inorg. Chem. *10*, 1647 (1971).

[5] *E. Colomer, R. J. P. Corriu, A. Vioux*, Inorg. Chem. *18*, 695 (1979).

[6] The complexes *(7)* and *(8)* were prepared as described in [1] by treatment of ($\eta^5$-$C_5H_5$)Mo(CO)$_2$NO or ($\eta^5$-$C_5H_5$)W(CO)$_2$NO with LiGePh$_3$ at −78 °C.

[7] *H. Brunner*, Chem. Unserer Zeit 1, 157 (1977).

[8] *H. Brunner, E. Schmidt*, Angew. Chem. *81*, 570 (1969); Angew. Chem. Int. Ed. Engl. *8*, 616 (1969).

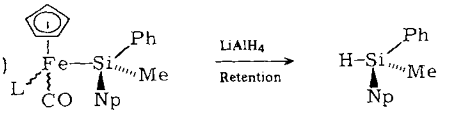
[9] Cf. *G. M. Reisner, I. Bernal, H. Brunner, M. Muschiol, B. Siebrecht*, J. Chem. Soc. Chem. Commun. *1978*, 691; *P. I. van Vliet, M. Kokkes, G. van Koten, K. Vrieze*, J. Organomet. Chem. *187*, 413 (1980); *Y. Shvo*, J. Am. Chem. Soc. *102*, 5396 (1981).

[10] a) *R. B. King, R. H. Reimann*, Inorg. Chem. *15*, 179 (1976); b) *N. J. Coville, M. O. Albers*, J. Organomet. Chem. *172*, C1 (1979); *A. G. Ginzburg, V. N. Setkina, D. N. Kursanov, ibid. 182*, C1 (1979).

# Cleavage of Silicon- and Germanium-Cobalt Bonds: Change of Stereochemistry with Different Ligands

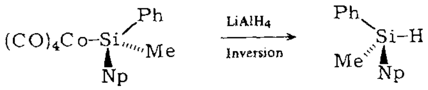
By *Geneviève Cerveau*, *Ernesto Colomer*, and *Robert J. P. Corriu*[*]

The stereochemical course of nucleophilic cleavage of Fe—Si and Co—Si bonds[1] is in good accord with the general rules for nucleophilic displacement at silicon[2]. ($\eta^5$-$C_5H_5$)(CO)LFe, a good nucleophile, is however a weakly polarizable leaving group (retention of configuration upon substitution) and $(CO)_4Co$, a poor nucleophile, a highly polarizable leaving group (inversion of configuration upon substitution)[3].



(S) (R)-(2a)

L = CO, $PPh_3$, $P(OEt)_3$; Np = 1-Naphthyl



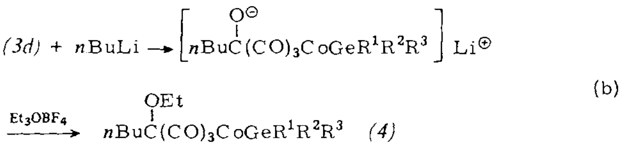
(S)-(3a) (S)-(2a)

In order to better understand the nature of Co—Si- and Co—Ge bonds, we have studied changes in the stereochemistry of the nucleophilic cleavage at silicon or germanium as a function of the electronic nature of the transition metal.

Thus, the cobalt complexes *(3a)*—*(3f)* and *(4)* (Table 1) were synthesized, under $N_2$, from the dicobalt complexes *(1)* (L = CO, $P(OPh)_3$, $PPh_3$) and the substituted silanes *(2a)* and germanes *(2b)*, respectively ($R^1$ = Me, $R^2$ = Ph, $R^3$ = 1-naphthyl [eq. (a) and (b)][4].

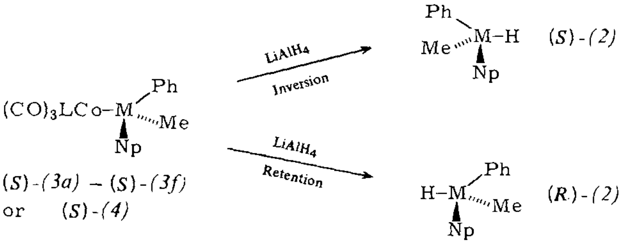
$$[(CO)_3LCo]_2 + 2R^1R^2R^3MH \longrightarrow 2\ (CO)_3LCoMR^1R^2R^3 + H_2 \quad (a)$$

*(1)* *(2a)*, M = Si *(3)*
*(2b)*, M = Ge



$$(3d) + n\text{BuLi} \longrightarrow \left[n\text{Bu}\overset{O^{\ominus}}{\overset{|}{C}}(CO)_3CoGeR^1R^2R^3\right]Li^{\oplus} \xrightarrow{Et_3OBF_4} n\text{Bu}\overset{OEt}{\overset{|}{C}}(CO)_3CoGeR^1R^2R^3 \quad (4) \qquad (b)$$

The stereochemical course of cleavage reactions with $LiAlH_4$[1b] are quite similar for silyl- and germyl-cobalt complexes and vary, depending on the ligands at cobalt, from a high degree of inversion of configuration with *(3a)* and *(3b)* or *(3d)* and *(3e)* respectively, to poor retention with *(4)* (Table 1).



(S)-(3a) – (S)-(3f) or (S)-(4) (S)-(2) (R)-(2)

The absolute configurations of the silanes[5a] and the germanes[5b], as well as that of the two tetracarbonyl complexes *(3a)* and *(3d)*[5c], were determined by X-ray structure analysis: this enabled the stereochemistry and stereoselectivity of the $LiAlH_4$-cleavage reactions to be determined unequivocally[6]. The exchange of one CO-ligand, a good π-acceptor, in the $(CO)_4Co$-residue by a good donor increases the electron density at cobalt[7] and hence reduces the nucleofugicity of the substituents. The nucleophilic cleavage of the complexes $(CO)_3LCoMR^1R^2R^3$ occurs with considerable inversion when L = CO; the degree of inversion decreases in the compounds with L = $P(OPh)_3$ and $PPh_3$. The reaction of the carbene complex *(4)*, L = C(OEt)*n*Bu, proceeds with slight retention of configuration. The σ-donor character of the ligands increases along the series (CO < $P(OPH)_3$ < $PPh_3$ < (COEt)*n*Bu). This result is in accord with the leaving group rules found in silicon chemistry[3b].

That this is only a crude analysis of the results—based on the assumption that the metal-silicon and halogen-silicon bonds are similar—is shown by the nucleophilic cleavage of $(CO)_4(NO)WGeR^1R^2R^3$[8]. In this case, a high degree of inversion of the configuration is anticipated, since the tungsten center is surrounded by five good π-acceptor ligands (NO is a better π-acceptor than CO[9]); however, a 67% retention of configuration is observed.

This inference shows that the situation is certainly more complex than can be achieved *via* a simple comparison of the properties of the Si—(or Ge)—X- and Si—(or Ge—)Co bonds. Indeed, the Ge—Co- and Ge—W-bonds are hardly comparable, since Co belongs to the first and W to the third third transition metal series.

Table 1. Some physical data and results of the stereochemical course of the reductive cleavage of complexes *(3a)*—*(3f)* and *(4)*. All novel compounds gave correct elemental analyses.

| Complex | L | M | M.p. [°C] [a] | IR $\nu_{CO}$ [cm$^{-1}$] (CHCl$_3$) [b] | $^1$H-NMR $\delta_{CH_3}$ (in $C_6D_6$/TMS) | $[\alpha]_D^{25}$ ($C_6H_6$) | Stereo-chemistry [%] [c] | $[\alpha]_D^{25}$ of $R^1R^2R^3MH$ (Pentane) [d] |
|---|---|---|---|---|---|---|---|---|
| *(3a)* | CO | Si | 93 (100) | [1b] | 1.33 | +2° [c] | 91 I | −28.3° |
| *(3b)* | $P(OPh)_3$ | Si | 124—125 (86) [f] | 2050 w, 1965 vs | 1.33 | −6.38° | 91 I | −28.3° |
| *(3c)* | $PPh_3$ | Si | 186 (161) [f] | 2030 w, 1945 vs | 1.53 | −6.48° | 68 I | −13.1° |
| *(3d)* | CO | Ge | 92.5—93 (96.5—97.5) | [1b] | 1.46 | +2.7° [e] | 87 I | −19.5° |
| *(3e)* | $P(OPh)_3$ | Ge | 123—124 (74—76) [f] | 2060 w, 1965 vs | 1.46 | −3.47° | 87 I | −19.5° |
| *(3f)* | $PPh_3$ | Ge | 198—199 (210—211.5) [f] | 2040 w, 1945 vs | 1.73 | −5.4° | 60 I | − 5.3° |
| *(4)* | — | — | oil | 2040 w, 1947 vs | 1.20 [g] | — | 55 R | + 2.5° |

[a] The melting points of the racemates are shown in brackets. [b] The complexes occur, as inferred from the IR spectra, as *trans*-isomers. An X-ray structure analysis was performed on the carbene complex *(4)* [4b]. [c] I = inversion, R = retention. [d] Maximum values of rotation: $R^1R^2R^3SiH$ $[\alpha]_D^{25}$ ±36 and $R^1R^2R^3GeH$ $[\alpha]_D^{25}$ ±26.7. [e] In pentane. [f] Decomposition. [g] In $CDCl_3$.

Received: September 11, 1980 [Z 757b IE]
German version: Angew. Chem. *93*, 489 (1981)

---

[*] Prof. Dr. R. J. P. Corriu, Dr. G. Cerveau, Dr. E. Colomer
Laboratoire de Chimie des Organométalliques
Equipe de Recherche associée au C.N.R.S. No. 554
Université des Sciences et Techniques du Languedoc
Place Eugène Bataillon, F-34060 Montpellier-Cedex (France)

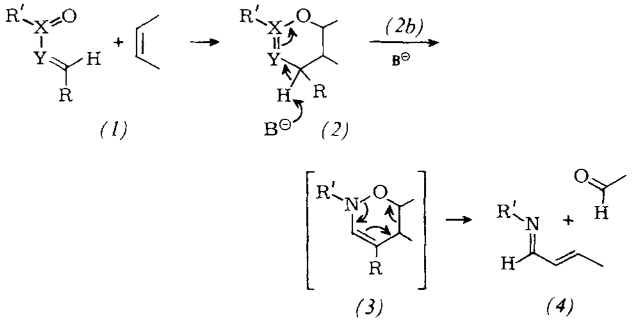
[1] a) *G. Cerveau, E. Colomer, R. J. P. Corriu, W. E. Douglas*, J. Chem. Soc. Chem. Commun. *1975*, 410; J. Organomet. Chem. *135*, 373 (1977); b) *E. Colomer, R. J. P. Corriu*, J. Chem. Soc. Chem. Commun. *1976*, 176; J. Organomet. Chem. *133*, 159 (1977).
[2] *R. J. P. Corriu*, J. Organomet. Chem. Libr. *9*, 357 (1980). *R. J. P. Corriu, C. Guérin*, J. Organomet. Chem. *198*, 231 (1980).
[3] a) *R. B. King*, Acc. Chem. Res. *3*, 417 (1970); b) *L. H. Sommer, C. L. Frye, M. C. Musolf, G. A. Parker, P. G. Rodewald, K. W. Michael, Y. Okaya, R. Pepinsky*, J. Am. Chem. Soc. *83*, 2210 (1961).
[4] The complexes *(3)* and *(4)* were prepared as described for the silyl or germanyl complexes with $R^1 = R^2 = R^3 = Ph$: a) *G. Cerveau, E. Colomer, R. J. P. Corriu, J. C. Young*, J. Organomet. Chem. *205*, 31 (1981); b) *F. Carré, G. Cerveau, E. Colomer, R. J. P. Corriu, J. C. Young, L. Ricard, R. Weiss, ibid. 179*, 215 (1979).
[5] a) *Y. Okaya, T. Ashida*, Acta Crystallogr. *20*, 461 (1966); b) *A. G. Brook*, J. Am. Chem. Soc. *85*, 3051 (1963); *A. G. Brock, G. J. D. Peddle, ibid. 85*, 1869 (1963); c) *M. Manassero*, personal communication: *F. Dahan, Y. Jeannin*, J. Organomet. Chem. *136*, 251 (1977).
[6] *L. H. Sommer, J. D. Citron, G. A. Parker*, J. Am. Chem. Soc. *91*, 4729 (1969).
[7] *M. D. Curtis*, Inorg. Chem. *11*, 802 (1972).
[8] $(CO)_4(NO)WGeR^1R^2R^3$ was prepared from $[(CO)_5WGeR^1R^2R^3]NEt_4$ (*E. Colomer, R. J. P. Corriu*, J. Chem. Soc. Chem. Commun. *1978*, 435) by treatment with $NOBF_4$: *E. E. Isaacs, W. A. G. Graham*, J. Organomet. Chem. 99, 119 (1975).
[9] *T. A. Manuel*, Adv. Organomet. Chem. *3*, 191 (1965) and references therein.

---

# "Isolated" Olefinic Double Bonds as 2π-Components in [8 + 2]-Cycloadditions

By *Martin Riediker* and *Walter Graf*[*]

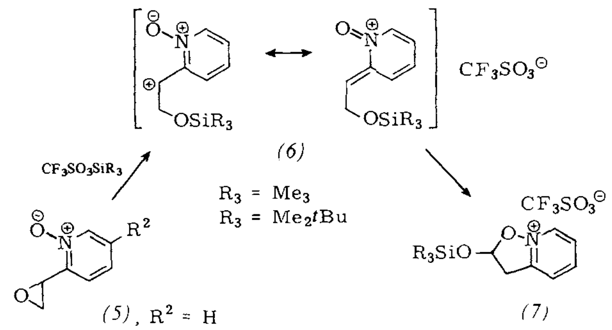
In the classical Diels-Alder reaction (D.-A. reaction with *normal* electron demand) non-activated isolated double bonds scarcely react with dienes. On the other hand, charged heterodienes such as *(1)* display excellent reactivity towards isolated olefinic double bonds even at room temperature[1-3] (D.-A. reactions with *inverse* electron demand) [cf. *(1)*→*(2)*].



*(a)*, X = C, $\overset{\oplus}{=N}$, R = H
*(b)*, $X = N^{\oplus}$, Y = CH, R = H or Alkyl
*(c)*, $X = N^{\oplus}$, Y = CH, $R = CH_2OSiR'_3$

1,2-Oxazinium salts *(2b)*[2a] enabled, *inter alia*, the cycloreversion *(3)*→*(4)*, initiated by proton abstraction *(2)*→*(3)*, to be carried out[2b].

We demonstrate here that the [8 + 2]-cycloaddition-cycloreversion sequence [cf. *(12)*→*(13)*→*(15)*] with heterocyclic *N*-oxides is a useful, and, in our opinion, potentially versatile synthetic reaction.



In the reaction of 2-oxiranylpyridine *N*-oxide *(5)* with $CF_3SO_3SiR_3$ ($R_3 = Me_3$ or $Me_2tBu$), only *(7)*, the product of a 1,2 H-shift in *(6)*, could be isolated (cf. [3]; see Table 1).

Table 1. Some physical data of the products. $^1$H-NMR in $CDCl_3$, except in the case of *(7)*, R = Me ($CD_2Cl_2$) and *(10)* ($D_2O$); δ-values, *J* in Hz; MS: *m/z*.

*(7)*, R = Me, *$^1$H-NMR: 0.18 (s, 9 H), 3.68 (d × d, J = 18, J' = 1, 1 H)*, 4.22 (d × d, *J* = 18, *J'* = 5, 1 H), 6.52 (d × d, *J* = 5, *J'* = 1, 1 H), 7.85—8.50 (m, 3 H), 8.85 (m, 1 H)

*(10)*, $^1$H-NMR: 3.08 (s, 6 H), 3.36 (s, 6 H), 6.31 (d, $J_{AB}$ = 13, 2 H), 6.66 (d, $J_{AB}$ = 13, 2 H), 8.41 (s, 4 H). On warming, a rapid change of conformation of the eight-membered ring occurs; thereby, the AB system of the methylene groups simplifies to a singlet.

*(13a)*, R = H, $^1$H-NMR: 1.00—2.50 (m, 9 H), 4.50 (d, *J* = 3, 1 H), 4.94 (m, $w_{y2}$ = 9, 1 H), 7.00—8.20 (m, 8 H), 8.73 (d × d, *J* = 6, *J'* = 1, 1 H)

*(13b)*, R = H, $^1$H-NMR: 1.43 (t, *J* = 7, 3 H), 1.25—2.50 (m, 9 H), 2.99 (d × d, $J_{AB}$ = 18, *J* = 1.6, 1 H), 3.60 (d × d, $J_{AB}$ = 18, *J* = 7, 1 H), 4.20 (q, *J* = 7, 2 H), 4.90 (m, $w_{y2}$ = 7, 1 H), 7.74 (singletoid m, 2 H), 8.90 (singletoid m, 1 H)

*(15a)*, R = H, $^1$H-NMR, *E/Z*-mixture: 1.20—1.80 (m, 4 H), 1.90—2.45 (m, 4 H), 6.75—7.80 (m, 8 H), 8.57 (m, 1 H), 9.69 (m, 1 H). Additionally for *Z*: 6.12 (t, *J* = 7, *ca.* 0.5 H), for *E*: 6.88 (t, *J* = 7, *ca.* 0.5 H); MS: 265 ($M^+$, 29%), 208 (100)

*(15a)*, R = Me, $^1$H-NMR, *E/Z*-mixture: 1.20—1.90 (m, 4 H), 2.08 (s, 3 H), 1.90—2.45 (m, 4 H), 6.95—8.00 (m, 8 H), 8.58 (m, 1 H). Additionally, for *Z*: 6.10 (t, *J* = 7, 0.6 H), for *E*: 6.84 (t, *J* = 7.5, 0.4 H); MS: 279 ($M^+$, 41%), 208 (100)

*(15b)*, R = H, $^1$H-NMR, *E/Z*-mixture (*1 : 1*): 1.20—1.80 (m, 4 H), 1.40 (t, *J* = 8, 3 H), 2.00—2.80 (m, 4 H), 4.05 (q, *J* = 8, 2 H), 7.10 (m, 2 H), 8.24 (m, 1 H), 9.72 (m, 1 H). Additionally, for *E*: 6.38 (d, *J* = 14, 1 H), 6.60 (d × t, *J* = 14, *J'* = 5, 1 H), for *Z*: 5.64 (d × t, *J* = 12, *J'* = 7, 1 H), 6.38 (d, *J* = 12, 1 H); MS: 233 ($M^+$, 28%), 176 (100)

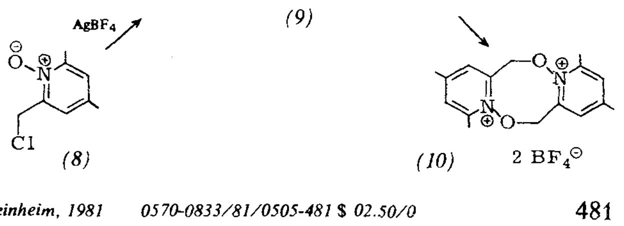
*(16a)*, R = Me, $^1$H-NMR: 1.40—2.20 (m, 8 H), superposed by 1.63 (s, 3 H), 5.98 (s, 1 H), 6.90—7.50 (m, 8 H), 8.23 (d × d, *J* = 3, *J'* = 4, 1 H); MS: 279 ($M^+$, 71%), *168 (100)*

*(17)*, $^1$H-NMR: 1.39 (t, *J* = 7, 3 H), 3.74 (s, 6 H), 3.99 (q, *J* = 7, 2 H), 4.14 (s, 2 H), 6.78 (singletoid m, 5 H), 7.99 (singletoid m, 1 H); MS: 289 ($M^+$, 24%), 272 (100)

*(18)*, $^1$H-NMR: 1.20—2.50 (m, 8 H), superposed by 1.43 (t, *J* = 7, 3 H), 4.08 (q, *J* = 7, 2 H), 4.33 (br. s, 2 H), 5.75 (br. t, *J* = 7, 1 H), 7.10 (singletoid m, 2 H), 8.20 (m, 1 H), 9.70 (m, 1 H)

The (chloromethyl)pyridine *N*-oxide derivative *(8)*, which cannot undergo such an H-shift, reacts with $AgBF_4$ to give the intermediary reactive product *(9)*, which dimerizes to *a salt of the dication (10)* (see Table 1).

The hypothetical intermediates *(6)* and *(9)* do not react with cyclohexene. However, the lifetime of the reactive in-



---

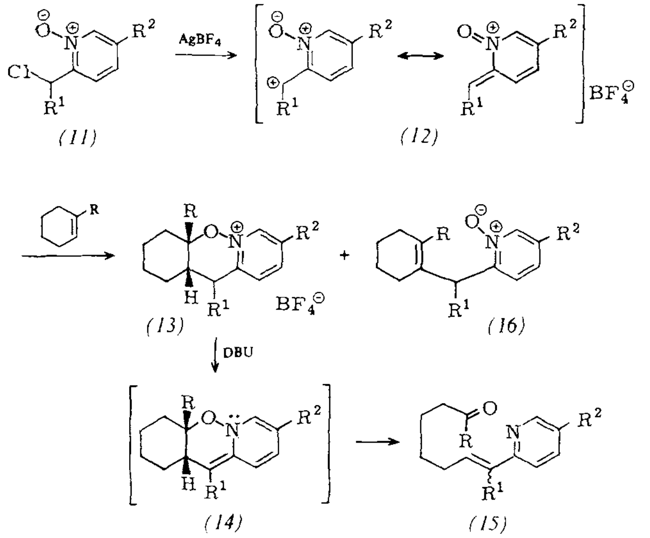
[*] Dr. W. Graf [**], Dipl.-Chem. M. Riediker
Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule
CH-8092 Zürich (Switzerland)

[**] Present address:
Fluka AG
CH-9470 Buchs/SG (Switzerland)

termediate can be prolonged by additional resonance stabilization of the positive charge of this tetraene so that a cycloaddition becomes possible. Thus, 2-(α-chlorobenzyl)pyridine *N*-oxide reacts in dichloromethane with $AgBF_4$ and cyclohexene in about 50% yield (Table 1 and 2), even at 0 °C, to give the cycloadduct *(13a)*, which was only observed by NMR spectroscopy.

Addition of 1.05 equiv. of diazabicyclo[5.4.0]undecene (DBU) led, after a brief red coloration (probably caused by *(14a)*, R = H) to formation of the cycloreversion product *(15a)*, R = H, as *E/Z* mixture (Table 1 and 2).

1-Methyl-1-cyclohexene reacts analogously with *(12a)*. As expected, on treatment with DBU we obtained, aside from the cycloreversion product *(15a)*, R = Me (*E/Z* mixture), principally the isomeric double-bond substitution products such as *(16a)*, R = Me.

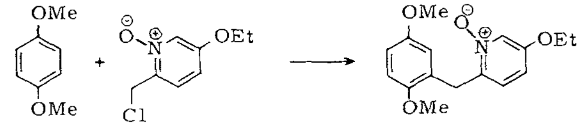


*(a)*, $R^1$ = Ph, $R^2$ = H; *(b)*, $R^1$ = H, $R^2$ = OEt

The 2-(chloromethyl)-5-ethoxypyridine *N*-oxide *(11b)* reacts with cyclohexene analogously (Table 1 and 2). A separable mixture of the substitution products *(16b)*, R = H, and the double-bond isomer with 2′-cyclohexenyl ring is obtained in *ca.* 10–20% yield.

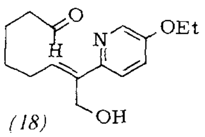
1-Methyl-1-cyclohexene, a 1,1,2-trisubstituted olefin, reacts to only a small extent with cycloaddition to give *(15b)*, R = Me; the greater part forms substitution products such as *(16b)*, R = Me, and its double-bond isomer (cf. Table 2).

In the reaction of *(11b)* with hydroquinone-dimethyl ether (1 : 1) the aromatic substitution product *(17)* is obtained in 54% yield.

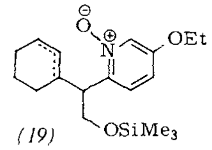


*(11b)* *(17)*

By substitution of the heteroarene ring of the reagent with a mesomeric donor, the desired cycloaddition of oxiranyl *N*-oxides such as *(5)* to isolated double bonds was also possible. Thus, *(5)*, $R^2$ = OEt, reacts with $CF_3SO_3SiMe_2tBu$ or $CF_3SO_3SiMe_3$ in $CH_2Cl_2$ in the presence of cyclohexene to give the (not isolated) cycloadduct *(13)*, R = H, $R^1 = CH_2OSiR_3$, $R^2$ = OEt, $CF_3SO_3^-$ instead of $BF_4^-$, which undergoes cycloreversion with DBU to give the compound *(18)* (Tables 1 and 2). This novel cycloaddition reaction[4] extends the palette of reactions with isolated olefinic double bonds.



*(18)*



*(19)*

### General Procedure

Cycloaddition of *(11)* to olefins: $AgBF_4$ (195 mg, 1.0 mmol) was added under Ar at room temperature to a solution of the olefin (0.5–1 mL, 5–10 mmol; distilled over Na) in dichloroethane or dichloromethane (filtered

Table 2. Results of the cycloaddition experiments [a]. Olefin, R = H: cyclohexene, R = Me: methylcyclohexene.

| Olefin | | *N*-Oxide | | Cycloadduct | | Cycloreversion product | | Substitution product [b] | | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|
| R | amount [mmol] | type | amount [mmol] | type | yield [%] | type | yield [%] | type | yield [%] | |
| H | 20 | *(11a)* | 1 | [e] | | *(15a)*, R = H | 55 | *(16a)*, R = H | 11 | [c] |
| | 2 | | 2 | [e] | | | 45 | | 10 | [d] |
| | 1 | | 2 | [e] | | | 49 | | 14 | [d] |
| Me | 20 | *(11a)* | 1 | [e] | | *(15a)*, R = Me | 22 | *(16a)*, R = Me | 51 | [c] |
| | 2 | | 2 | [e] | | | 12 | | 35 | [d] |
| | 1 | | 2 | [e] | | | 13 | | 54 | [d] |
| H | 20 | *(11b)* | 1 | *(13b)*, R = H | 53 | | — | *(16b)*, R = H [f] | 13 | [c], −10 °C |
| | 20 | | 1 | | 59 | | — | | 22 | [c], 0 °C |
| | 20 | | 1 | | 63 | *(15b)*, R = H | 57 | | 22 | [c] |
| | 20 | | 1 | | 66 | | — | | 27 | [c], 45 °C |
| | 1 | | 1 | | 50 | | 46 | | 14 | [d] |
| | 1 | | 2 | [e] | | | 45 | | 15 | [d] |
| Me | 20 | *(11b)* | 1 | *(13b)*, R = Me | 32 | *(15b)*, R = Me | 27 | *(16b)*, R = Me [f] | 57 | [c] |
| | 2 | | 2 | [e] | | | 19 | | 35 | [d] |
| | 1 | | 2 | [e] | | | 20 | | 52 | [d] |
| H | 33 | *(5)*, $R^2$ = OEt | 1.6 | [e] | | *(18)* [g] | 28 | *(19)* | 14 | [c, h] |
| | 6.9 | | 1.4 | [e] | | | 9 | | — | [c, h, j] |
| | 7.5 | | 1.5 | [e] | | | 37 | | 14 | [c, h] |
| | 10.8 | | 2.2 | [e] | | | 21 | | 6 | [c, i] |

[a] If not otherwise stated, at room temperature. [b] Total yield of the isomeric olefins. [c] Yield referred to *N*-oxide. [d] Yield referred to olefin. [e] The cycloadduct was converted *in situ*. [f] Mixture of *(16b)*, R = H, and double-bond isomer [see *(19)*]. [g] *(18)* is extremely unstable on chromatographic carrier material. [h] According to method A, cf. [3]. [i] According to method B, cf. [3]. [j] *(5)*, $R^2$ = OEt, mainly reacts with intramolecular H-shift [cf. *(7)*].

through basic Alox I). The mixture was then treated dropwise within 3 h with a solution of *(11)* (1 mmol) in 8 mL of the relevant aforementioned solvent. After filtration through celite the solution was treated with DBU (175 μL, 1.05 mmol) and then, after a further 30 min, the resulting mixture was poured into water and extracted with $CH_2Cl_2$. After separation of the aqueous phase the reaction solution was washed twice with water and once with saturated NaCl solution. The organic phase, after drying over magnesium sulfate and careful removal of solvent, gave a yellow oil, which was rapidly chromatographed on *ca.* 15 g MN-silica gel with $CH_2Cl_2/CH_3OH$ (25 : 1).

Cycloaddition of *(5)*, $R^2 = OEt$, to olefins: $CF_3SO_3SiMe_3$ (310 μL, 1.72 mmol) was added to a solution of cyclohexene (760 μL, 7.50 mmol; distilled over Na) in dichloroethane or dichloromethane. A solution of *(5)*, $R^2 = OEt$, (270 mg, 1.50 mmol) in 8 mL of one of the previously mentioned solvents was then added to the reaction mixture dropwise within 3 h. After a total of 4 h the solution was treated with DBU (260 μL, 1.75 mmol). After a further 30 min the mixture was poured into water and worked up as mentioned above. For separation, the yellow oil was rapidly chromatographed on *ca.* 40 g MN-silica gel with $CH_2/CH_3OH$, whereupon substantial amounts of *(18)* decomposed.

Received: September 26, 1980 [Z 759 IE]
German version: Angew. Chem. *93*, 491 (1981)

---

[1] *R. R. Schmidt*, Chem. Ber. *103*, 3242 (1970). The salts of *(1)*, $X = C$, $Y = N^{\oplus}H$, were prepared *in situ* from *N*-(chloromethyl)benzamides and $SnCl_4$.

[2] a) *U. M. Kempe, T. K. DasGupta, K. Blatt, P. Gygax, D. Felix, A. Eschenmoser*, Helv. Chim. Acta *55*, 2188 (1972). The salts of *(1)*, $X = N^{\oplus}$, $Y = CH_3$, were prepared from α-chloronitrones by chloride-elimination with $AgBF_4$; b) *P. Gygax, T. K. DasGupta, A. Eschenmoser, ibid. 55*, 2205 (1972).

[3] *M. Riediker, W. Graf*, Helv. Chim. Acta *62*, 205 (1979). The heterodienes *(1c)* were prepared *in situ* from epoxypropanalnitrones by $CF_3SO_3SiR_3''$-induced epoxide-opening. They show an analogous H-shift.

[4] From a mechanistic point of view it could be a stepwise [8 + 2]-Diels-Alder reaction with *inverse* electron demand; see *J. Sauer, H. Weist*, Angew. Chem. *74*, 353 (1962); Angew. Chem. Int. Ed. Engl. *1*, 269 (1962).

---

# $Mo^{IV}$ in Aqueous Solutions: The Trinuclear Cluster $[Mo^{IV}O_4F_9]^{5-}$, the First Species Isolated from Mineral Acid Solution[1]

By *Achim Müller, Andreas Ruck, Mechthild Dartmann,* and *Uta Reinsch-Vogell*[*]

Until 1973 it was assumed that acidic aqueous solutions containing $Mo^{IV}$ were not stable[2] ("The only well-known $Mo^{IV}$ species in aqueous solution is $[Mo(CN)_8]^{4-}$"[2a]). Following investigations carried out by *Souchay* (which had been overlooked until 1973; cf. [2b]) and by *Ardon* and *Pernick*[2b,4], it has now been clearly proven that $Mo^{IV}$ is stable in mineral acid solutions (the characteristic red color is caused by the absorption band: $\lambda$ *ca.* 505 nm; $\varepsilon/Mo \approx 60$ $dm^3\ mol^{-1}\ cm^{-1}$). From the results of numerous measurements using a variety of different methods, it was concluded that mono- or di-nuclear complexes are present[2-5]. It had, however, already been suggested in a review article[6] that some results were more indicative of trinuclear clusters.

A solution of $Mo^{IV}$ in aqueous HF was prepared by a normal cation exchange procedure[4]. Addition of excess $NH_4F$ allowed the isolation of deep red, in transmitted light red, crystalline needles of

$(NH_4)_5[Mo_3O_4F_9] \cdot NH_4F \cdot H_2O$ *(1)*

which was characterized by elemental analysis, IR- and VIS-spectra (characteristic band in the solid state reflection spectrum at $\lambda = 525$ nm) and by an X-ray crystal structure analysis[7]. In this way, the first successful isolation of a crystalline substance from a mineral acid solution of $Mo^{IV}$ without addition of a complexing agent was achieved. The structure of the anion corresponds to the $B_1$-type of trinuclear electron-poor transition metal clusters[6], in which the metal atoms (Mo—Mo = 2.505 Å) are surrounded by a distorted octahedron of oxygen and fluorine (Mo—F = 2.034 Å) and the central $\{Mo(\mu_3\text{-}O)(\mu_2\text{-}O)_3\}$-moiety $[Mo\text{-}(\mu_3\text{-}O) = 2.032,\ Mo\text{-}(\mu_2\text{-}O) = 1.920\ Å]$ can be considered as a distorted, incomplete cube (average bond lengths in brackets). *(1)* is isostructural with the corresponding W-compound, which notably was obtained from an aqueous solution of $W^V$ by addition of HF[8] (for an interpretation cf. [6]).

The electronic spectrum of the aqueous HF solution of *(1)* also shows the VIS-band observed in the solid state spectrum. The splitting of this band (doublet: A at ≈518, B at ≈535 nm), as well as the time-dependence of the relative intensities of A and B (following dissolution) and their dependence on the concentration of acid, indicates that several species of the type $[Mo_3O_4F_{9-x}(H_2O)_x]^{(5-x)-}$ *(2)* are probably present. The $F \rightarrow H_2O$ ligand exchange process cannot be identified significantly by a change of color, but only by a slight change in the electronic spectrum (increase in the intensity of A relative to B). These results, regarding the probable presence of $Mo^{IV}$ species with a central $Mo_3O_4$ cluster unit in mineral acid solutions, are clearly contrary to all previous results (Fig. 1). This also corresponds to our most recent understanding of $Mo^{IV}$, which shows a strong tendency to form trinuclear clusters (in accord with the $d^2$-configuration) in solutions containing no strong π-acceptor ligands[6]. We have assigned the observed VIS-bands A and B, following an EHMO calculation, to transitions in the $Mo_3$-cluster system (cf. also [6]).

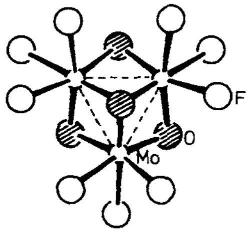


Fig. 1. Molecular structure of $[Mo_3O_4F_9]^{5-}$ in crystals of *(1)*.

## *Procedure*

A solution of $Mo^{IV}$, (from $[MoCl_6]^{3-}$ and $[MoOCl_5]^{2-}$) prepared after[4], is adsorbed on a cation exchange column (Dowex 50 WX 2) and purified with 0.5 and 1 M *p*-toluenesulfonic acid ($O_2$-free) after[4]. The exchanger is eluted with 10 $cm^3$ of a 40% aqueous solution of HF and *ca.* 20 $cm^3$ $H_2O$. $NH_4F$ (2 g) is added to the first 10 $cm^3$ of the red eluate. Dark red crystals of *(1)* precipitate (in certain cases only after slight concentration of the solution by passing nitrogen over it). Yield *ca.* 80%, relative to the Mo-content of the solution.

Received: June 30, 1980 [Z 761 IE]
supplemented: November 18, 1980
German version: Angew. Chem. *93*, 493 (1981)

---

[*] Prof. Dr. A. Müller, A. Ruck, M. Dartmann,
Dipl.-Chem. U. Reinsch-Vogell
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld (Germany)

[1] This problem was a major topic of discussion at three international conferences (Reading 1973, Oxford 1976, Ann Arbor 1979) on "The Chemistry and Uses of Molybdenum"; cf. also [2].

[2] a) *G. P. Haight, D. R. Boston* in *P. C. H. Mitchell:* Proceedings of the First International Conference on the Chemistry and Uses of Molybdenum, Climax Molybdenum Company, London 1973, p. 48; b) *M. Ardon, A. Pernick* in *P. C. H. Mitchell, A. Seaman:* Proceedings of the Second International Conference on the Chemistry and Uses of Molybdenum, Climax Molybdenum Company, London 1976, p. 206; J. Less-Common Met. *54*, 233 (1977); c) *E. I. Stiefel*, Prog. Inorg. Chem. *22*, 1 (1977); d) *M. Lamache*, J. Less-Common Met. *39*, 179 (1975); e) *F. A. Cotton, G. Wilkinson:* Advanced Inorganic Chemistry. 4th Ed., Wiley-Interscience, New York 1980; *A. Bino, F. A. Cotton, Z. Dori*, J. Am. Chem. Soc. *100*, 5252 (1978).

[3] *Th. Ramasami, R. S. Taylor, A. G. Sykes*, J. Am. Chem. Soc. *97*, 5918 (1975); *M. Ardon, A. Bino, G. Yahav, ibid. 98*, 2338 (1976).

[4] *M. Ardon, A. Pernick*, J. Am. Chem. Soc. *95*, 6871 (1973).

[5] *S. P. Cramer, H. B. Gray, Z. Dori, A. Bino*, J. Am. Chem. Soc. *101*, 2770 (1979).

[6] *A. Müller, R. Jostes, F. A. Cotton*, Angew. Chem. *92*, 921 (1980); Angew. Chem. Int. Ed. Engl. *19*, 875 (1980).

[7] Space group $P2_1/c$; $Z=4$; $a=13.662(2)$, $b=8.193(1)$, $c=15.355(2)$, $\beta=94.21(1)^\circ$; 3615 observed reflections (Syntex $P2_1$); $R=0.037$.

[8] *R. Mattes, K. Mennemann*, Z. Anorg. Allg. Chem. *437*, 175 (1977).

[9] Note added upon supplementation: Recently published results on isotopic exchange reactions ($^{16}O/^{18}O$) on $Mo^{IV}$-containing solutions, which contain $NCS^-$, also point to a trinuclear species; *R. K. Murmann, M. E. Shelton*, J. Am. Chem. Soc. *102*, 3984 (1980).

## BOOK REVIEWS

**Comprehensive Biochemistry.** Edited by *M. Florkin* (deceased), *A. Neuberger* and *L. L. M. van Deenen*. Vol. 19, Part B 1: Protein Metabolism. Elsevier Publishing Company, Amsterdam 1980. xx, 528 pages, 64 figs., bound, Dfl. 168.00.

This volume of "Comprehensive Biochemistry"[*] begins with a disarming declaration: "The Editors were faced with alternative possibilities: one either tried to deal with the major topic in a *comprehensive* manner, but this would have meant almost unavoidably a degree of superficiality which was unacceptable...". They therefore decided to give progress reports on somewhat randomly chosen but particularly topical areas of protein metabolism.

In their chapter, *V. M. Pain* and *M. J. Clemens* manage to summarize the present knowledge of the many components that take part in the protein synthesis machinery of the eukaryotic cell, to describe the mechanisms of their interactions, and to give the most important aspects of the regulation of translation. With the inclusion of more than 500 references up to 1979 and building-on on a corresponding chapter in Volume 24 (1977), this has obviously succeeded well. Just how long this information will remain new in the rapidly evolving field is a question that occurs time and again when using the whole work, which is evidently considered to be a long-term investment.

The sections by *P. J. Garlick* and *D. J. Millward* are devoted to the turnover of plasma proteins and enzymes in the flowing equilibrium of continuous synthesis and degradation in various tissues and in the whole organism. The first of these authors concentrated more on the regulation of the rates of these reactions *in vivo* and on the contribution this makes to the total nitrogen balance of an animal, the second on the various courses of degradation in the muscles and liver. In these painstaking and well coordinated articles, too, more than 500 publications have been worked into a clearly arranged and readable general presentation.

Protein metabolism and protein structure are closely entwined subjects. *A. J. Bailey* and *D. J. Etherington* were evidently of the opinion that our knowledge of general structural chemistry and of the metabolism of collagen and elastin has now reached such a state that it deserved a really detailed presentation, and convinced the sympathetic editors to allocate to them almost one-third of the book for a thorough review. In spite of dealing with more than 800 references, they still regard this review as not exhaustive. The main emphasis is placed on connective tissue biosynthesis during growth and on the mechanisms of degradation, thus providing more than just a basis for this research field equally important to medicine and the food industry.

*K. B. M. Reid* offers a stimulating and understandable résumé to the complement system, a proteolytic cascade system of a special kind. This complex defensive mechanism of higher organisms has many molecular special features, so that this chapter, too, will only be a snapshot from the year 1979.

With its extensive literature reviews and sensible presentation by the authors, who mostly come from the close circle of one of the editors, this topical book will undoubtedly prove a useful new publication for users in the fields of chemistry, biochemistry, pharmacology, and medicine. This major volume supplements a field always deliberately neglected in the main work, which has thus perhaps not always become "more comprehensible" but certainly "more comprehensive", in spite of the editors' reservations.

*L. Jaenicke* [NB 540 IE]

**Statistical Mechanics of the Liquid Surface.** By *C. A. Croxton*. John Wiley and Sons, Chichester 1980. xi, 345 pages, bound, £ 25.00.

Our understanding of the equilibrium properties of atomic fluids has increased so much in recent years with the help of statistical mechanics that a transition to complex systems appears to be realistic. The particular questions here are whether the principles of statistical mechanics can also be applied to the inhomogeneous region of the liquid-gas interface, and if the familiar thermodynamic concepts such as pressure, density, and chemical potential can be extended to the phase interface. Since many properties of the liquid surface are excess-quantities, which record the change in the liquid's properties on transition to the surface, and consequently require knowledge of the properties of the liquid, a statistical-mechanical description is difficult. Two quantities characterize the liquid-gaseous region: the density profile, which describes the change in density perpendicularly to the liquid surface, going from the density of the liquid to the density of its vapor, and the anisotropic pair distribution function, which gives the probability of finding a second particle at a defi-

---

[*] Cf. Angew. Chem. Int. Ed. Engl. *17*, 873 (1978).

nite distance from a selected reference particle. In contrast to the liquid—and this is decisive—this pair distribution function is still dependent on the distance of the selected particle from the liquid surface.

In the present work, the author—who has already written several books on the theory of the liquid state—gives the first résumé of the statistical-mechanical theories of the liquid surface. The relationships between the thermodynamic parameters of the liquid surface, among them surface tension, and the density profile and the anisotropic pair distribution function are shown very clearly in the first chapter. Since these functions are necessary for the determination of thermodynamic quantities, the second chapter—occupying almost one-fifth of the book—is devoted to the calculation of the density profile and the anisotropic pair distribution function for spherically-symmetric particles. On the one hand, a quasi-thermodynamic approximation is used, which means that in the transition zone between the liquid and the vapor the chemical potential and pressure must be constant to ensure thermodynamic and mechanical stability of the liquid surface. On the other hand, well-known integral equations from liquid-state theory, *e.g.* the Born-Green-Yvon equation, are used. The presentation is in places very compact and presupposes that the reader is well aquainted with the theories of the liquid state, *e.g.* with perturbation theory and the associated mathematical formalism, so that original literature may have to be consulted. However, this is facilitated by the wealth of literature citations.

The technique described in this chapter is then extended to liquid surfaces of nonspherical systems. In systems of this kind, the density profile is additionally dependent on the orientation of the molecules relative to the phase interface, and the resulting expressions are correspondingly complicated. With the aid of the perturbation theory, in which anisotropic interaction is interpreted as a perturbation of spherical interaction, relationships are derived for the surface tension, free energy, *etc.*; owing to the complexity of the expressions, the author cannot reproduce each calculation step and must refer to the original literature. The effects of dipole and quadrupole interactions on the density profile are discussed. In two-component systems the way in which the surface tension and the density profile depend on the composition of the mixture poses a new problem. In an infinitely sharp surface the component with the lower surface tension accumulates at the interface. In reality, according to theory, this anomaly is determined by the mean density of the liquid at the surface, also called surface adsorption, the density profile and the interaction between the particles. The way in which such density profiles can be calculated for linear molecules is also discussed in detail in Chapter 4.

Following the general theoretical part, the second part of the book is devoted to specific systems, and firstly to the surfaces of liquid metals which are formally two-component systems of mobile cations and conducting electrons. For the simplest model the density profiles of the cations and electrons are calculated, from these the surface tension and surface energy and their temperature variations, and thus the essential characteristics of the liquid metal surfaces. Detailed refinements of the models are then discussed. A chapter is added on the surface of quantum liquids, whose experimentally determined surface tension can be interpreted with quantized capillary waves known as "ripplones" or "surfones". A formal quantum-mechanical description shows that the surface tension is the excess quantity of an impulse current. The characteristic feature for water—Chapter 7—is the appearance of surface polarization. This polarization, as well as the surface tension, is calculated in detail. The result shows that the water molecules on the liquid surface are arranged with the protons facing outward.

The statistical-mechanical treatment of the conformational change of a polymeric on transition from bulk liquid to the surface is still far from being fully developed. The suppression of one degree of freedom at the phase interface implies a greater spread of the molecule on the surface. The effect of polymers on surface tension is shown within the framework of the Prigogine-Marechal theory, and the distribution of the polymer segments on the surface is deduced. The book then turns to liquid crystals. After a brief survey of the theory the excess quantity of free energy and the corresponding surface tension are calculated for perpendicular and parallel orientations of the molecules.

As practically no experimental work has been done on the determination of the density profile, computer simulation has a special relevance as a test for statistical-mechanical theories. Accordingly, in the penultimate chapter the techniques needed for the simulation of an inhomogeneous region are compared with those for the simulation of homogeneous liquids, and the results are discussed. The rapid development in the statistical mechanics of liquid surfaces is illustrated in the final chapter.

To summarize, the book gives a very clear presentation of the statistical-mechanical theory of the liquid surface. It contains many derivations and can therefore be used as an introduction to this field, assuming that the reader is familiar with the principles of statistical mechanics and with the theory of the liquid state. It gives an excellent review of the present state of the research and thus greatly facilitates access to the original literature. Unconditionally recommended.

*Helmut Bertagnolli* [NB 538 IE]

## Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Personal Computers in Chemistry.** Edited by *P. Lykos.* John Wiley & Sons, Chichester 1981. xi, 262 pp., bound, £ 14.57.—ISBN 0-471-08508-1

**Drug Design. Vol. 10. Medicinal Chemistry.** Edited by *E. J. Ariëns.* Academic Press, New York 1980. xi, 432 pp., bound, $ 49.50.—ISBN 0-12-060310-1

**Analytical Chemistry. Vol. 2. Basic Analytical Chemistry.** By *L. Pataki* and *E. Zapp.* Pergamon Press, New York 1980. xiii, 463 pp., bound, $ 55.00.—ISBN 0-08-023850-5

**Alternative Energy Sources. Part A and B.** By *J. T. Manassah.* Academic Press, New York 1981. xi, 922 pp., bound, $ 49.50 and $ 45.00.—ISBN 0-12-467101-2 and 0-12-467102-0, respectively

**General and Synthetic Methods.** Vol. 4. Senior Reporter: *G. Pattenden.* The Royal Society of Chemistry, London 1981. xiii, 376 pp., bound, £ 44.00.—ISBN 0-85186-854-1.—A volume in the series "Specialist Periodical Reports"

**Treatment of Domestic and Industrial Wastewaters in Large Plants.** Proceedings of a conference held in Vienna, Austria, September 1979. Edited by *S. H. Jenkins.* Pergamon Press, Oxford 1981. 773 pp., bound, £ 40.00.—ISBN 0-08-026033-0

**Fundamentals of Chemistry.** By *J. E. Brady* and *J. R. Holum.* John Wiley & Sons, Chichester 1981. xvii, 797 pp., bound, £ 13.75.—ISBN 0-471-05816-5

**Recent Advances in the Chemistry of β-Lactam Antibiotics.** Edited by *G. I. Gregory.* The Royal Society of Chemistry, London 1981. ix, 378 pp., bound, £ 16.00.—ISBN 0-85186-815-0

**Manager + Methoden. Band 1 und 2.** By *D. Jarsen, W. Klingelhöller,* and *E. Schönduve.* Edition Cantor, Aulendorf 1981. Vol. 1: 193 pp.; Vol. 2: 278 pp., bound, together DM 175.00.—ISBN 387-193-059-8

**Kurzes Lehrbuch der Pharmakologie und Toxikologie.** Mit einem Schlüssel zum Gegenstandskatalog. By *G. Kuschinsky* and *H. Lüllmann.* Thieme Verlag, Stuttgart 1981. 9th edit. 500 pp., bound, DM 49.80.—ISBN 3-13-368509-0

**Trace Element Analytical Chemistry in Medicine and Biology.** By *P. Brätter* and *P. Schramel.* De Gruyter, Berlin 1980. xv, 851 pp., bound, DM 180.00.—ISBN 3-11-008357-4

**Ausgangsmaterialien für die Arzneimittelherstellung.** Qualitätsanforderungen (GMP) und deren Folgen für Zulieferer und Pharma-Betriebe. Edited by *G. Hauschild.* Wissenschaftliche Verlagsgesellschaft, Stuttgart 1981. 135 pp., bound, DM 25.00.

**Chromatographic Methods.** Optimization in HPLC. By *R. E. Kaiser* and *E. Oelrich.* Hüthig Verlag, Heidelberg 1981. 278 pp., bound, DM 66.00.—ISBN 3-7785-0657-9

**Chromatographic Methods.** Recent Advances in Capillary Gas Chromatography. By *W. Bertsch, W. G. Jennings,* and *R. E. Kaiser.* Hüthig Verlag, Heidelberg 1981. 592 pp., bound, DM 75.00.—ISBN 3-7785-0711-7

**Chromatographic Methods.** Theory and Mathematics of Chromatography. By *A. S. Said.* Hüthig Verlag, Heidelberg 1981. 210 pp., bound, DM 75.00.—ISBN 3-7785-0616-1

**Chromatographic Methods.** Chromatographic Methods in Inorganic Analysis. By *G. Schwedt.* Hüthig Verlag, Heidelberg 1981. 226 pp., bound, DM 75.00.—ISBN 3-7785-0690-0

**Plastics Technical Dictionary.** Part 1: English-German. By *A. M. Wittfoht.* Hanser Verlag, München 1981. 550 pp., bound, DM 140.00.

**Einführung in die Geologie der Bundesrepublik Deutschland.** By *D. Henningsen.* Enke Verlag, Stuttgart 1981. 2nd edit. 152 pp., bound, DM 10.80.—ISBN 3-432-88512-1

**Konstitution und Vorkommen der organischen Pflanzenstoffe.** Suppl. Vol. 2, Part 1. By *W. Karrer.* Birkhäuser Verlag, Basel 1980. 960 pp., bound, SFr. 348.00.—ISBN 3-7643-0857-5

**Gmelin Handbuch der Anorganischen Chemie.** Springer-Verlag, Berlin 1981. 8th edit. B—Boron Compounds. 1st Supplement, Vol. 3: Boron and Chalcogens. Carboranes. Formula Index for 1st Supplement, Vol. 1—3. xv, 397 pp., bound, DM 799.00.—ISBN 3-540-93427-8

**Verfahrenstechnik.** Anlagentechnik I. By *R. Schulze.* VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1981. 3rd edit. 186 pp., bound, DM 22.00

**Glycidol.** Properties, Reactions, Applications. By *A. Kleemann* and *R. M. Wagner.* Hüthig Verlag, Heidelberg 1981. 186 pp., bound, DM 65.00.—ISBN 3-7785-0709-5

**Allgemeine Mikrobiologie.** By *H. G. Schlegel.* Thieme Verlag, Stuttgart 1981. 5th edit. xiv, 559 pp., bound, DM 29.80.—ISBN 3-13-444605-7

**Pharmazeutische Analytik.** By *H. J. Roth* and *G. Blaschke.* Thieme Verlag, Stuttgart 1981. 2nd edit. 448 pp., bound, DM 35.00.—ISBN 3-13-548002-X

---

**Editorial office:** Boschstrasse 12, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

**Editor:** *O. Smrekar,* **Translation Editors:** *I. G. Neil* and *A. Stimson.*

**Publishers:** Verlag Chemie GmbH. (Managing Director *Dr. Helmut Grünewald*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany. Telephone Weinheim (06201) 14031 (602-1), Telex 465516 vchwh d.

ANGEWANDTE
CHEMIE
International Edition in English

Volume 20 · Number 6/7
June/July 1981
Pages 487-616

# The Kinetics of Intramolecular Reactions from Relaxation Time Measurements

**New analytical methods (21)**

By Joseph B. Lambert, Ronald J. Nienhuis, and Joe W. Keepers[*]

Analysis of spin-lattice relaxation ($T_1$) provides alternatives to the standard line shape procedures for the investigation of intramolecular reactions; furthermore it expands the NMR range at both the high and the low energy barrier limits. Dipole-dipole- and quadrupole-relaxation times are sensitive to very rapid processes such as methyl rotation. Analysis of relaxation in the rotating frame ($T_{1\rho}$) provides kinetics for many sorts of processes, particularly those in the dynamic range that is too rapid for line shape methods. Saturation transfer and the coalescence of relaxation times at high temperatures can be used to measure high energy barriers. The scope and limitations of these methods are described.

## 1. Introduction

The intimate association of nuclear magnetic resonance (NMR) spectroscopy with the measurement of the kinetics and energy barriers for intramolecular rate processes dates back to the early 1950's[1]. Coalescence temperature determination and complete line shape analysis methods became routine during the 1960's[2]. The problems and limitations of these methods, all of which are connected *via* the observation of the coalescence of chemical shifts or coupling constants, have been critically, examined in a recent review[3]. The range of energy barriers available to coalescence methods is approximately 4.5—27 kcal/mol. The range of amenable rate constants lies approximately between $10-10^4$ $s^{-1}$, corresponding approximately to the chemical shift range in Hz. Below this range, intramolecular processes occur too rapidly on the NMR time scale. Very low barrier processes have been studied only by alternative and usually more laborious techniques such as microwave or infrared methods. Above this range, classical methods of racemization or epimerization can be used.

One of the by-products of the revolutionary Fourier transform technique in NMR spectroscopy was the wide availability of instrumentation with which relaxation times could be measured accurately and routinely. Because relaxation times depend for the most part on molecular motion, they provide an alternative to line shape coalescence as a source of kinetic information. Depending on the mode of analysis, both the low and high ends of the NMR energy barrier range can be expanded. Applications, however, are still not numerous, so that the limits of these relaxation methods for determining energy barriers have not been fully explored.

In this review, we will examine a number of these relaxation methods. We will limit ourselves to measurements on the liquid phase. Although many interesting applications

---

[*] Prof. J. B. Lambert, Dr. R. J. Nienhuis, J. W. Keepers
Department of Chemistry, Northwestern University
Evanston, Illinois 60201 (USA)

0570-0833/81/0707-487 $ 02.50/0

to the solid state have been made, the processes and problems are somewhat different. Those relaxation methods that give quantitative kinetics will be emphasized. Relaxation times also can provide qualitative analyses of complex processes such as segmental motion and intramolecular steric effects[4], particularly in biochemical systems.

## 2. Low Energy Barriers

Line shape decoalescence has never been observed for exchanging systems with barriers below *ca.* 4.5 kcal/mol. This limit is fixed by the boiling point of the gaseous coolant used in low temperature experiments (nitrogen, b. p. = – 196 °C, but the limit in practice is *ca.* – 180 °C) and by the solubility and freezing properties of most solutions. The range is being extended by the use of increasingly higher superconducting magnetic fields. Modern methods (rotation at the magic angle = MAS = "magic angle spinning") also permit high resolution NMR-spectra of solids to be recorded and may eventually make lower temperatures and hence lower barriers available[5]. For the purposes of this section, we define low barriers as those below the present limit of classical line shape techniques. The rates are in the range $10^8$—$10^{12}$ $s^{-1}$.

### 2.1 The *Woessner* Method for Dipolar Relaxation

For a nucleus with spin 1/2, attached directly to another nucleus having the same spin, dipole-dipole relaxation [$T_1$(DD)] usually provides the dominant mechanism of spin-lattice relaxation. Smaller molecules may have spin-rotation contributions [$T_1$(SR)] and higher fields may produce chemical shift anisotropy contributions [$T_1$(CSA)]. The molecular motional processes in which we are interested, however, influence dipole-dipole relaxation, so that this contribution must be isolated from the others. The frequency of these motions is of the order of, or larger than, the resonance frequency ($\gamma B_0 \approx 10^8$ $s^{-1}$).

The overall spin-lattice relaxation time $T_1$ is given by the sum of the reciprocals of the individual terms [eq. (1)].

$$\frac{1}{T_1} = \frac{1}{T_1\,(\mathrm{DD})} + \frac{1}{T_1\,(\mathrm{other})} \tag{1}$$

in which $T_1$ (DD) is the dipole-dipole relaxation time and $T_1$ (other) represents all other contributions. The dependence of the nuclear Overhauser enhancement ($\eta$ = NOE-1) on dipole-dipole relaxation permits a direct determination of $T_1$ (DD) from the observed $T_1$ and $\eta$ [eq. (2), in which the maximal $\eta$ is 1.988 for $^{13}$C-nuclei relaxed by protons].

$$T_1\,(\mathrm{DD}) = T_1\,\frac{\eta\,(\max)}{\eta} = T_1\,\frac{1.988}{\eta} \quad (\text{for } ^{13}\text{C-H}) \tag{2}$$

Dipole-dipole relaxation results from the time-dependent reorientation of magnetic dipoles. The molecular motion that gives rise to this type of relaxation is described by an overall correlation time $\tau_c$ (the time for the molecule to rotate in solution through 1 rad). For a complex molecule, overall rotation is superimposed on internal motions within it, so that $\tau_c$ is really a composite correlation time. If the effect of a specific type of motion, such as methyl rotation, can be isolated, then it becomes possible to measure the kinetic properties of that process. In 1962, *Woessner* provided the mathematical framework for isolating methyl rotation from overall motion in certain cases[6]. It was almost a decade before the advent of Fourier transform instrumentation made possible the common application of *Woessner's* theory.

For most cases, methyl rotation has been studied by $^{13}$C-relaxation. In the extreme narrowing limit, the dipole-dipole relaxation time for a $^{13}$C nucleus is related to the effective correlation time by eq. (3):

$$1/T_1(\mathrm{DD}) = n\gamma_C^2\gamma_H^2\hbar^2 r_{CH}^{-6}\tau_c \tag{3}$$

in which $n$ is the number of protons attached to the relaxing $^{13}$C-nucleus, $\gamma_C$ and $\gamma_H$ are the $^{13}$C- and $^1$H-gyromagnetic ratios, $\hbar$ is Planck's constant divided by $2\pi$, and $r_{CH}$ is the C—H bond distance. If the molecule as a whole undergoes isotropic rotational diffusion without internal rotation, the correlation time is related to an overall diffusion coefficient $D$ by eq. (4):

$$\tau_c = 1/6\,D \tag{4}$$

In the most complex case, anisotropic motion can be described in terms of an ellipsoid tumbling about three axes at different rates ($D_1 \neq D_2 \neq D_3$). To date, all applications, however, have had to simplify the analysis by assuming that motion about two of the ellipsoidal axes occurs at the same rate ($D_1 \neq D_2 = D_3$). In this case, the dipole-dipole relaxation is given by eq. (5),

$$\frac{1}{T_1(\mathrm{DD})} = n\gamma_C^2\gamma_H^2\hbar^2 r_{CH}^{-6}\left[\frac{A}{6\,D_2} + \frac{B}{D_1 + 5\,D_2} + \frac{C}{4\,D_1 + 2\,D_2}\right] \tag{5}$$

in which $A$, $B$, and $C$ are geometric factors determined by the angle $\Delta$ between the vector connecting the dipoles (normally the C—H bond) and the internal rotation axis (C—$CH_3$), which coincides with the major axis of the molecular ellipsoid. The angles to the other ellipsoidal axes drop out when $D_2 = D_3$. The geometric constants are given by eqs. (6a)—(6c)

$$A = 1/4(3\cos^2\Delta - 1)^2 \tag{6a}$$

$$B = 3/4\sin^2 2\Delta = 3\sin^2\Delta\cos^2\Delta \tag{6b}$$

$$C = 3/4\sin^4\Delta \tag{6c}$$

We will endeavor, throughout this article, to adhere as closely as possible to the notation used by *Woessner*[6], since confusion has arisen in applications because of changes in notation. The only alterations we have made in eq. (5) from *Woessner's* eq. (45) are the use of $D$ rather than $R$ for diffusion constants (to avoid confusion with the relaxation rate $R$) and the use of two different nuclei ($^{13}$C and $^1$H). *Woessner* used a pair of identical nuclei, and hence had $\gamma^4$ and $n = 3/2$ rather than $\gamma_C^2\gamma_H^2$ and $n$ = number of attached protons. The quantity in brackets [...] in eq. (5) is the correlation time $\tau_c$ for the anisotropic motion of the molecule. When $D_1 = D_2$, the motion is isotropic, and the quantity within the brackets becomes $1/6\,D$ (since $A + B + C = 1.0$), in agreement with eq. (4).

Internal rotation of a component, *e.g.* a methyl group within a molecule, alters the effective correlation time $\tau_c$, while maintaining the internuclear (C—H) distance constant. If the internal motion is independent of the overall motion and the internal rotation occurs about the major axis of the ellipsoid, it is only necessary to add an additional diffusion term $D_i$ (*Woessner* uses $R'_1$) to the diffusion constant $D_1$ about the major axis. The exact mechanics of the addition depend on the assumed mechanism of the methyl reorientation. If the mechanism is stochastic diffusion (all rotational orientations having equal probability), then $D_1$ in eq. (5) is replaced by $(D_1 + D_i)$, in which $D_i$ is the internal methyl diffusion rate in rad/s. If the methyl group undergoes rapid jumps from one position to another, the contribution of $D_i$ to the denominator of the $C$ term is reduced by 1/4. The $D_i$ is now the jump rate in jumps/s and must be multiplied by a statistical factor $a$ ($a = 3/2$ for 120° jumps in a threefold barrier; $a = 3$ for 60° jumps in a sixfold barrier; $a = 1$ for the stochastic process). The modification of eq. (5) to include internal rotation is given in eq. (7):

$$\frac{1}{T_1^{\mathrm{CH_3}}(\mathrm{DD})} = n\hbar^2 \gamma_{\mathrm{C}}^2 \gamma_{\mathrm{H}}^2 r_{\mathrm{CH}}^{-6} \left[\frac{A}{6\,D_2} + \frac{B}{D_1 + 5\,D_2 + a\,D_i} + \frac{C}{4\,D_1 + 2\,D_2 + a\,m\,D_i}\right] \tag{7}$$

in which for the stochastic process $n = 3$ (for $CH_3$), $m = 4$, $a = 1$, and for an $r$-fold methyl jump process $n = 3$ (for $CH_3$), $m = 1$, and $a = r/2$.

The axis of internal rotation (C—$CH_3$) may not necessarily coincide with the axis of symmetry of the ellipsoid. In a later paper, *Woessner et al.*[7] introduced the appropriate allowance for any arbitrary angle $\alpha$ between these axes. A much more complex expression for $T_1$(DD) resulted as shown in eq. (8)

$$\begin{aligned}\frac{1}{T_1^{\mathrm{CH_3}}(\mathrm{DD})} = n \gamma_{\mathrm{C}}^2 \gamma_{\mathrm{H}}^2 \hbar^2 r_{\mathrm{CH}}^{-6} \Bigg[\frac{1}{2}\Bigg(&\frac{A_1}{6\,D_2} + \frac{A_2}{6\,D_2 + a\,D_i} + \frac{A_3}{6\,D_2 + a\,m\,D_i} \\ &+ \frac{B_1}{D_1 + 5\,D_2} + \frac{B2}{D_1 + 5\,D_2 + a\,D_i} + \frac{B3}{D_1 + 5\,D_2 + a\,m\,D_i} \\ &+ \frac{C1}{4\,D_1 + 2\,D_2} + \frac{C2}{4\,D_1 + 2\,D_2 + a\,D_i} + \frac{C3}{4\,D_1 + 2\,D_2 + a\,m\,D_i}\Bigg)\Bigg]\end{aligned} \tag{8}$$

in which $n = 3$ for $CH_3$ and the nine constants are given by eq. (9).

$$\begin{aligned} A1 &= 1/8(1 - 3\cos^2\alpha)^2 (3\cos^2\Delta - 1)^2 \\ A2 &= 9/16 \sin^2 2\alpha \sin^2 2\Delta \\ A3 &= 9/16 \sin^4\Delta \sin^4\alpha \\ B1 &= 3/8 \sin^2 2\alpha (3\cos^2\Delta - 1)^2 \\ B2 &= 3/4(\cos^2 2\alpha + \cos^2\alpha)\sin^2 2\Delta \\ B3 &= 3/4(\sin^2\alpha + 1/4\sin^2 2\alpha)\sin^4\Delta \\ C1 &= 3/8\sin^4\alpha(3\cos^2\Delta - 1)^2 \\ C2 &= 3/4(\sin^2\alpha + 1/4\sin^2 2\alpha)\sin^2 2\Delta \\ C3 &= 3/16[(1 + \cos^2\alpha)^2 + 4\cos^2\alpha]\sin^4\Delta \end{aligned} \tag{9}$$

When $\alpha = 0$, the coefficients $A2$, $A3$, $B1$, $B3$, $C1$, and $C2$ are zero, and the remaining three coefficients $A1$, $B2$, and $C3$, respectively, become $2A$, $2B$, and $2C$ of eq. (7). The factor of 2 difference between the two sets of coefficients in equations (7) and (8) stems from the factor 1/2 inside the square brackets in eq. (8). As in all other such expressions in this paper, the figures within the brackets represent the effective correlation time $\tau_c$. In the isotropic approximation ($D_1 = D_2$), the denominators of each fraction in the correlation time expression of eq. (8) contain $6\,D$ instead of the combination of $D_1$ and $D_2$.

To date, except in a few applications[8,9], the isotropic approximation has been utilized. Applications also normally assume that $\alpha = 0$. There has been no concensus as to whether the stochastic or the methyl jump mechanism is appropriate. Various groups have used either approach, and some groups have used both[10,11]. Because the approximations of $D_1 = D_2$ and $\alpha = 0$ are so common, it is useful to write out the specific equations that embody them. For the threefold methyl jump mechanism, $a = 3/2$ and $m = 1$, as in eq. (10a),

$$\frac{1}{T_1^{\mathrm{CH_3}}(\mathrm{DD})} = 3 \gamma_{\mathrm{C}}^2 \gamma_{\mathrm{H}}^2 \hbar^2 r_{\mathrm{CH}}^{-6} \left[\frac{A}{6\,D} + \frac{B + C}{6\,D + 3/2\,D_i}\right] \tag{10a}$$

in which $D_i$ is the methyl jump rate. For the stochastic diffusion mechanism, $a = 1$ and $m = 4$, as in eq. (10b),

$$\frac{1}{T_1^{\mathrm{CH_3}}(\mathrm{DD})} = 3 \gamma_{\mathrm{C}}^2 \gamma_{\mathrm{H}}^2 \hbar^2 r_{\mathrm{CH}}^{-6} \left[\frac{A}{6\,D} + \frac{B}{6\,D + D_i} + \frac{C}{6\,D + 4\,D_i}\right] \tag{10b}$$

in which $D_i$ is the methyl diffusion rate.

In the few cases in which the overall diffusion coefficient $D$ is known, all the quantities in eqs. (10a) and (10b) are known, except $D_i$, which can consequently be determined. Normally, $D$ is determined from eqs. (3) and (4) using $T_1$(DD) for a rigid carbon atom within the molecule, whose correlation time corresponds to the overall diffusional correlation time for the entire molecule. Consequently, the complete procedure is to measure two dipole-dipole relaxation times, one that is determined only by the overall molecular diffusion $D$ and one that is determined by the superposition of overall diffusion and internal methyl rotation $D_i$. The latter motion is extracted by the application of the *Woessner* equation, *e.g.* (10a) or (10b).

When $\alpha \neq 0$, its value must be obtained by analysis of the actual geometry of the molecule. One approach is to optimize $\alpha$ to fit the experimental relaxation times[8]. In a similar fashion, anisotropic overall motion may be taken into account[8]. In this case, there are three diffusional unknowns in eqs. (7) and (8), $D_1$, $D_2$, and $D_i$. In the *Platzer* approach, $D_2$ and the ratio $\sigma = D_1/D_2$ are optimized to fit the experimental relaxation times of rigid carbons: $D_i$ is then obtained from eq. (7). In the two existing studies of anisotropic motion, the barriers to methyl rotation are not appreciably different from those calculated according to the isotropic assumption[8,9]. Thus the isotropic analysis used by other authors seems justified.

In order to convert $D_i$ to a barrier to methyl rotation, $V_0$, the magnitude of this quantity must be measured as a function of temperature. An Arrhenius plot of the type shown in eq. (11)

$$D_i = D_{i0}\exp(-V_0/RT) \tag{11}$$

then gives $V_0$ from the slope. To date, few of the applications have measured relaxation times as a function of temperature in order to apply this equation[13]. The relaxation time and nuclear Overhauser enhancement (NOE) measurements are extremely time consuming, and at least three temperatures are necessary for a reasonable Arrhenius plot. The barrier, $V_0$, can be calculated directly by eq. (11) from $D_i$ at only one temperature if $D_{i0}$ is known[12]. This quantity is the jump rate or diffusion rate of a freely rotating methyl group ($V_0 = 0$), given by eq. (12),

$$D_{i0} = (kT/I)^{1/2} = 0.89 \times 10^{13}\ \mathrm{s}^{-1}\ (40\,^{\circ}\mathrm{C}) \tag{12}$$

in which $I$ is the moment of inertia of the methyl group.

## 2.2. Applications of the *Woessner* Method

Although *Woessner* described his theory for superimposing methyl motion on overall motion in 1962, quantitative applications did not start appearing until the early 1970's. *Grant et al.* have provided most of the foundation for these applications, in a series of papers that surveyed a large number of molecular types. In one of the earliest publications[14], they examined *o*-xylene and measured its methyl rotation barrier to be about 1.4 kcal/mol. In a more detailed comparison with literature barriers, *Grant et al.* examined relatively common materials such as acetone, dimethyl sulfoxide, methyl acetate, and *tert*-butyl chloride[14]. Finally, they investigated larger series of aromatic[12, 15] and olefinic[16] systems. The derived barriers are set out in Table 1.

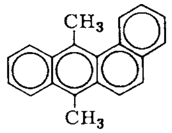
Table 1. Barriers (kcal/mol) to methyl rotation by the Woessner dipolar method.

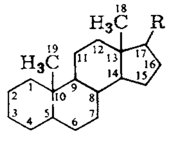
| Compound | $V_0$ [a] | $V_0$ [b] | Ref. |
|---|---|---|---|
| *Aromatic systems* | | | |
| *o*-xylene | 1.4 | | [13] |
| hemimellitene (1,2,3-trimethylbenzene) | | | [15] |
| 1,3-methyl | 1.45 | | |
| 2-methyl | free | | |
| isodurene (1,2,3,5-tetramethylbenzene) | | | [15] |
| 1,3-methyl | 1.55 | | |
| 2-methyl | free | | |
| 1-methylnaphthalene | 2.1 | | [12] |
| 1,4-dimethylnaphthalene | 2.2 | | [12] |
| 1,8-dimethylnaphthalene | 2.8 | | [12] |
| 7,12-dimethylbenzo[a]anthracene | | | [12] |
| 7-methyl | < 0.4 | | |
| 12-methyl | > 4.4 | | |
| *p*-X-toluene | | | [19] |
| $X = NO_2$ | 1.1 | 0.9 | |
| $X = (CO)CH_3$ | 1.0 | 0.9 | |
| $X = Cl$ | 1.1 | 1.0 | |
| $X = H$ | 0.5 [c] | 0.4 [c] | |
| $X = OCH_3$ | 0.9 | 0.75 | |
| $X = NH_2$ | 0.9 | 0.7 | |
| $X = H$ | 0.0 [d] | | [9] |
| perfluorotoluene | 1.4 [e] | 1.3 [e] | [24] |
| benzofuran [f] | | | [8] |
| 2-methyl | | 2.0 [c], 1.8 [d] | |
| 3-methyl | | 1.6 | |
| 4-methyl | | 0.7 | |
| 5-methyl | | free | |
| 6-methyl | | 0.9 | |
| 7-methyl | | 0.8 | |
| *Carbonyl systems* | | | |
| $CH_3(CO)CH_3$ | 0.9 | | [14] |
| $CH_3CO_2CH_3$ | 0.7 | | [14] |
| $CH_3(SO)CH_3$ | 2.2 | | [14] |
| *Olefins* | | | |
| *trans*-2-butene | 1.7 | | [16] |
| | 1.9 | 1.6 | [19] |
| *cis*-2-butene | 0.6 | | [16] |
| | 0.7 | 0.55 | [19] |
| 2-methylpropene | 1.9 | | [16] |
| 2-methylbutene | | | [16] |
| 1-methyl | 1.9 | | |
| 2a-methyl | 1.4 | | |
| 4-methyl | 0.7 | | |
| 2,3-dimethylbutene | 2.1 | | [16] |
| *trans*-1-X-propene [g] | | | [19] |
| $X = NO_2$ | 1.9 (1.4) | 1.8 (1.3) | |
| $X = CN$ | 2.3 (1.7) | 1.9 (1.6) | |
| $X = SCH_3$ | 1.8 (1.1) | 1.7 (1.0) | |
| $X = OCH_3$ | 2.0 (0.9) | 1.9 (0.8) | |
| $X = N(CH_3)_2$ | 1.5 (0.9) | 1.4 (0.75) | |
| *Saturated systems* | | | |
| $CH_3CCl_3$ | 2.9 | | [14] |
| $(CH_3)_3CCl$ | 3.5 | | [14] |
| $CH_3O(CO)CH_3$ | 1.1 | | [14] |
| *(3)* | >4.5 | | [11] |
| *(4)* $CH_3$—A | 1.7 | 1.8 | [11] |
| $CH_3$—B | free | free | [11] |
| *(5)* $CH_3$—A | 2.5 | 2.7 | [11] |
| $CH_3$—B | free | free | [11] |
| cholesteryl chloride, C-19 | 2.6 [h] | | [10, 18] |
| cholesteryl acetate, C-19 | 3.0 [h] | | [10] |
| androstanes [i] | | | [17] |
| 2-β-OH, C-18 | | 2.8 | |
| C-19 | | 2.7 | |
| 2-C=O, C-18 | | 2.8 | |
| C-19 | | 2.6 | |
| 3-β-OH, C-18 | | 2.7 | |
| C-19 | | 2.0 | |
| 3-α-OH, C-18 | | 2.8 | |
| C-19 | | 2.1 | |
| 3-C=O, C-18 | | 2.7 | |
| C-19 | | 2.3 | |
| camphor [j] | | | [13] |
| 8 methyl | 2.7 [e], 2.8 [k] | | |
| 9 methyl | 2.6 [e], 2.6 [k] | | |
| 10 methyl | 2.3 [e], 2.7 [k] | | |
| camphor | | | [20] |
| 8 methyl | 2.6 [d] | | |
| 9 methyl | 2.4 [d] | | |
| 10 methyl | 2.5 [d] | | |
| *(6)* [m] | | | [21] |
| 7 methyl | | 2.1 | |
| 8 methyl | | 2.6 | |
| 9 methyl | | 2.6 | |

[a] Methyl jump model. [b] Stochastic diffusion model. [c] Isotropic calculation. [d] Anisotropic calculation [e] $E_a$, calculated from an Arrhenius plot. [f] Di-, tri- and tetramethylbenzofurans, see [8]. [g] The values in brackets are for the *cis*-derivatives. [h] Model not specified. [i] Calculated from the lifetimes ($\tau_i = 1/6\,D_i$) by the formulas $\tau_i^{-1} = 6\,D_{i0}e^{-V_0/RT}$, $D_{i0} = 0.89 \cdot 10^{13}\ \mathrm{s}^{-1}$. For $V_0$ values of other androstane derivatives, as well of cholesterol, *trans*-5α- and *cis*-5β-cholesterol see [17]. [j] $V_0$-values were also determined for borneol, α-pinene, isopinocampheol, isoborneol, fenchone and β-fenchol; see [13] and [20]. [k] $V_0$, calculated from eqs. (11) and (12). [l] For $V_0$-values of other methylsubstituted adamantane derivatives, see [20]. [m] For $V_0$-values of analogues methylencarbonyl and dicarbonyl compounds, see [21].

These authors found an interesting steric effect that is imposed by symmetry. In 7,12-dimethylbenzo[a]anthracene *(1)*, the higher steric congestion at the 12-position raises the barrier above the range of the *Woessner* method. The 7-methyl group has nearly identical symmetry on either side and approaches a free rotor.

(1)



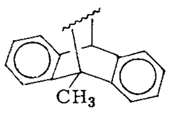


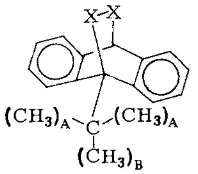
(2)

The study of saturated systems began with a comprehensive examination of steroids by *ApSimon et al.*[17]. Although they reported only lifetimes (the reciprocal of the diffusion rates multipled by six), these figures may easily be converted to barriers by application of eqs. (4), (11), and (12). Isolated values from earlier studies can be similarly treated[18]. Most of the methyl barriers in steroids *(2)* are close to 2.8 kcal/mol. The barrier is sensitive to the steric environment of the methyl group. The differences between the C-18 and C-19 barriers can be accounted for in terms of the number of *syn*-axial $CH_3$—H interactions. Replacement of a $CH_2$-group involved in a methyl *syn*-axial interaction by a CO group has a strong influence on the rotational barrier[17].

*Axelson* and *Holloway*[11] carried out a series of studies on the 9,10 adducts of 9-methyl- and 9-*tert*-butylanthracenes *(3)*, *(4)*, and *(5)*. The barrier to 9-methyl rotation was uniformly above the upper limit to the *Woessner* method in compounds of type *(3)* so that only lower limits could be set, *e.g.*, >4.5 kcal/mol. The *tert*-butyl groups in *(4)* and *(5)* contain two distinct methyl species. The unique methyl group ($CH_3$-B) gave, in each case, a barrier below the lower limit of the *Woessner* method, so that their rotation was termed free. In some cases (see Table 1), the barriers for the remaining pair of equivalent methyl groups were measured to be in the vicinity of 2.0 kcal/mol.

(3)



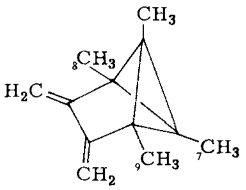


*(4)*, X = C=CH₂
*(5)*, X = C(CN)₂

In a study already alluded to, *Platzer* measured the barriers in an extensive series of methyl-substituted benzofurans[8]. The major contribution of this study, however, was the introduction of a practical method for carrying out anisotropic analyses.

We examined the rotational barriers in a large number of *p*-toluenes and *cis*- and *trans*-substituted propenes[19]. The major thrust of this work was an analysis of the factors controlling rotation of methyl groups attached to a trigonal carbon. A poor correlation of the barriers with $\sigma_R$ eliminated resonance-based phenomena such as hyperconjugation. The major controlling factor appeared to be the polar nature of the substituent, measured by $\sigma_I$. Steric effects were also present in *cis*-propene derivatives.

Two groups have reported barriers for methyl-substituted compounds related to norbornane and adamantane derivatives[13,20]. Almost all these barriers are in the range 2.2–3.1 kcal/mol (Table 1). A similar range was found for the methyl barriers in substituted tricyclo[3.1.0.0$^{2,6}$]hexanes such as *(6)*[21].



(6)

The *Woessner* method provides the most practical approach available today for the measurement of barriers in rapidly rotating methyl groups. Its upper limit is not far from the lower limit of NMR line shape coalescence methods, so the two procedures are complementary. Although lacking the accuracy of barriers determined by microwave spectroscopy, the *Woessner* barriers are easily accessible and reasonably reliable. The energy barriers in *extremely rapidly* rotating groups approaching the free rotor, still elude NMR methods based on dipolar relaxation.

To date, the only quantitative application of the *Woessner* method to rotational barriers for groups other than methyl is to the rotational barriers of the $CF_3$-group in perfluorotoluene[22]. One qualitative study of phenyl rotation in diphenyl disulfide and its Group VIb congeners has appeared[23]. The reported lifetimes can be converted to barriers of *ca.* 6.5 kcal/mol, which seemingly lie above the upper limit of the method. The authors note that internal phenyl reorientation and the overall molecular diffusion have similar lifetimes, particularly for diphenyl disulfide.

### 2.3. Notational Confusion

So far as we have been able to determine, no two papers have used the same notation for reporting the *Woessner* equation. One of the objectives of the current review is to recommend a standard notation that is as close as possible to the original introduced by *Woessner*[6].

One of the most confusing aspects of notation is the coefficient $n$ that appears in eqs. (3), (5), (7), and (8). In various places, it has appeared as 3, 3/2, or 3/4. *Woessner*'s original coefficient was 3/2[6], because his derivation was for a pair of equivalent nuclides[2]. The quantity $\gamma^4$ therefore replaced $\gamma_C^2\gamma_H^2$ in his expressions. For a single $^{13}C$ nucleus relaxed by protons, the appropriate coefficient is the number of directly attached protons that dominate the dipole-dipole relaxation, *e.g.* $n=3$ for $CH_3$. Nonetheless, we find few studies that use "3" for this coefficient along with the standard definition of the *Woessner* geometrical factors [eqs. (6) and (9)][8,9,13,17,19-22]. One set of investigators[10] modified *Woessner*'s definition of $A$, $B$, and $C$ [eq. (6)] by a factor of 4, so that, for example, $A=(3\cos^2\Delta-1)^2$. The factor of 4 was moved to the denominator of the coefficient at the front of the *Woessner* expression, so that it appears that $n=3/4$. Another set of workers made this same change in the definition of $A$, $B$, and $C$, but multiplied each of these factors by 1/4 within the expression for $\tau_c$ to compensate, so that the net result was again $n=3$[12]. Although the resulting $n$ is correct, we would still recommend retaining *Woessner*'s definition of $A$, $B$, and $C$.

For studies that include $\alpha \neq 0$, allowance has to be made for the fact that the *Woessner* $A1$ and $A$ coefficients are not comparable. As defined by *Woessner*, $A1$ becomes $2A$ when $\alpha = 0$. Some workers simply chose to redefine the $A1$ set of coefficients by a factor of 1/2 [eq. (9)], so that $n=3$[15,16]. Two groups, however, retained *Woessner*'s definitions and brought the factor of 1/2 out to the front of the expression, so that $n$ appears to be $3/2$[11,14]. This result, however, mixes geometrical factors with the proton count. In order to retain *Woessner*'s definitions and to retain the factor $n$ as the number of attached protons, we include the compensating factor of 1/2 inside the expression for $\tau_c$ within the brackets of eq. (8). Finally, one report with $\alpha \neq 0$ and $n=3/4$ is probably in error[23], since *Woessner*'s definitions are adhered to. The overall factor should be 3/2, to allow for the number of protons and the difference in definition between $A$ and $A1$. In this same report, the expression when $\alpha = 0$, uses $n=3/2$ rather than 3, so the error is consistent. It probably arose from the change in definition required when the two nuclei are different nuclides.

Because of the differences in notation for the *Woessner* geometric factors, none of the reported papers can be read casually. Detailed examination of the exact notation must be made in order to understand the meaning of $n$. We strongly recommend that $n$ be reserved for the number of attached protons, and that all other factors be relegated to the expression for $\tau_c$. Furthermore, for consistency we recommend that workers retain *Woessner*'s definitions of the geometrical factors $A$, $A1$, *etc.*

There is similar nonconformity in the notation for the methyl jump or diffusion rate. Various workers have used $D$[7,23], $R$[7,12,20], $R'$[8], $R'_1$[6], $\nu$[12], $\rho$ or $\rho_D$[15,16], $\tau_i$ (which is 1/6 of the reciprocal of the methyl diffusion rate)[17], $K$[11,21], $K'$[11], $D_i$[10,19], and $D'_i$[10,13,22]. We recommend that the usual letter for diffusion, $D$, be used, both for the overall diffusion $D$ and for the internal methyl diffusion $D_i$. The letter $\rho$ is not appropriate, because many workers use it for the ratio of the nonequivalent diffusion rates ($D_1/D_2$) in the anisotropic model (others use $\sigma$ for this ratio). We prefer to avoid $R$ (and $R_1$ in particular) because of confusion with the now standard notation for nuclear relaxation rate.

A further point of confusion is the multiplicity of representations for the differences between the methyl jump rate and the stochastic diffusion rate. Most workers have defined $D_i$ (in their notation) to be the stochastic diffusion rate or 3/2 times the jump rate. To distinguish between the two quantities, workers have used $R$ and $D$[7,13,22], $K$ and $K'$[11], or $D_i$ and $D'_i$[10], each differing by a factor of 3/2. Usage, however has not been consistent (*Woessner*'s methyl jump $D$ is *Baldo*'s stochastic $D$). In each case the preexponential $D_{i0}$ (or $K_0$, $\nu_0$, *etc.*) must also differ by a factor of 3/2 for the two mechanisms. Thus, for the stochastic diffusion model, the factor of $(kT/I)^{1/2} = 0.89 \times 10^{13}\ \mathrm{s}^{-1}$ [eq. (12)], but for the threefold methyl jump model, it is $(3/2)(kT/I)^{1/2} = 1.33 \times 10^{13}\ \mathrm{s}^{-1}$. *Ladner, Dalling,* and *Grant*[12] pointed to a resolution of this problem by taking the factor of 3/2 out of the expression for $D_i$ (they used $\nu$). To eliminate this duality of definition between the methyl jump and the stochastic diffusion models, we recommend adopting the usage of *Ladner et al.* Thus, in our eqs. (7) and (8) the symbol $D_i$ is used for the jump or diffusion rate, and the difference in definition is accounted for by the coefficient $a$ (1.0 for stochastic diffusion, $r/2$ for an $r$-fold methyl jump). This usage has the advantage of not implicitly requiring that the methyl jump mechanism always be threefold, as does the inclusion of a factor of 3/2 in the definition of the jump rate. With this notation, the preexponential $D_{i0}$ will always be $0.89 \times 10^{13}\ \mathrm{s}^{-1}$ at 40 °C, as defined in eq. (12).

After this discussion, one might naturally expect that each worker has used a different notation for the barrier to rotation. Fortunately, however, the symbol $V$ ($V_r$ or $V_0$) has wide acceptance.

### 2.4. Limitations of the *Woessner* Method

The two experimental quantities needed for derivation of a methyl rotation barrier by the *Woessner* method are the $^{13}$C-relaxation time and the nuclear Overhauser enhancement (NOE). Under optimal conditions we have found that an error, at the 90% confidence level, of 3% for the spin-lattice relaxation time and 2% for the NOE can be achieved by averaging four or five experimental runs[19]. These errors propagate through the *Woessner* calculation and result in an error at the 90% confidence level of about 10% on the final barrier, or about 0.15—0.2 kcal/mol. The percentage error is larger for barriers below 1 kcal/mol.

Several sources of systematic error have already been mentioned. The assumption of isotropic motion may not always be justified. The effect of such an assumption on the derived barrier, however, is not at all clear. The two studies that carried out both isotropic and anisotropic calculations[8,9] did not find large differences between the two approaches. The barrier from the anisotropic calculation was lower than that from the isotropic calculation in both studies (see Table 1)[8,9]. One case should be noted. Different groups measured the isotropic barrier in $C_6H_5$—$CH_3$ (0.35—0.5 kcal/mol)[19], $C_6D_5$—$CD_3$ (0.8—0.9 kcal/mol)[24], and $C_6F_5$—$CF_3$ (1.3—1.4 kcal/mol)[22], which are all well above the microwave barrier of 0.014 kcal/mol. For $C_6H_5CH_3$, however, $D_1/D_2$ [see eq. (15)] was found to be 2.2[9]. Inclusion of this factor lowered the barrier from 0.35 to 0.0 kcal/mol, in agreement with the microwave result[9].

The assumption that the methyl rotation axis coincides with the molecular symmetry axis ($\alpha = 0$) almost certainly does not hold in a number of cases. One systematic study has been carried out on the importance of this assumption[20].

The choice between the methyl jump model and the stochastic diffusion model has almost become moot. Most recently, workers have carried out calculations with both procedures[10,11,19,22], without finding systematic differences in trends within a series. The differences of about 0.2 kcal/mol are close to the experimental error. The two models respond in nearly identical fashion to substituent effects in toluenes and propenes[19]. *Blunt* and *Stothers*[10] have quoted a useful line of demarcation at 1.4 kcal/mol, with the stochastic model preferred below this figure and the methyl jump model above it. Many of the methyl rotation barriers of interest, however, fall in the 1—2 kcal/mol region and hence offer no certain choice. *Axelson* and *Holloway*[11] have reported that the methyl jump model is most accurate (±10—15%) in the region of 2—6 kcal/mol. Although the upper end of this range seems optimistic, the error these authors quote is very similar to what we described above. At the lower barrier end, as the methyl group approaches the free rotor, the dipole-dipole mechanism of relaxation becomes increasingly less important and the entire approach becomes inapplicable. An exact lower limit below which calculations are unreliable has not been reported. Most workers simply term these systems "free rotors" (Table 1). No barriers below 0.4 kcal/mol have been reported (Table 1), so that we can probably take this value as the currently accepted lower limit.

Most methyl rotation barriers are threefold, on grounds of symmetry. In toluenes, 9-methylanthracenes, and other such aromatic systems, however, the barrier may be sixfold. The parameter $a$ in eqs. (7) and (8) depends on the angle of jump ($a=r/2$ for an $r$-fold rotation). To date, calculations for $CH_3$ have assumed threefold symmetry in the methyl jump model. In the specific case of toluene, two authors have preferred the threefold model[19,24]. A sixfold barrier was used for perfluorotoluene[22]. The effect of altering the $a$ factor in eqs. (7) and (8) has not been studied.

Cross-correlation of nuclear spins has been examined very thoroughly[26]. In particular, for the protons in a methyl group this can result in nonexponential decay in the normal graphical plot for the determination of spin-lattice relaxation times[26]. The nonexponential behavior is the result of the sum of two exponentials, because the doublet and quartet methyl magnetizations can have distinct relaxation times. *Haslinger* and *Lynden-Bell*[27] have been able to determine these distinct relaxation times and to analyze them in terms of overall motion and internal methyl rotation for uroporphyrin(II) octamethyl ester. Their correlation times could be converted into barriers. These authors feel that their method may be applicable only to relatively large molecules. The use of cross-correlation effects on the $^1$H-NMR spectrum has not yet been fully exploited, and hence further advances in the determination of methyl rotation barriers in this area can be expected. The *Woessner* method uses the $^{13}$C relaxation time, and cross-correlation can also occur in the $AB_3$ system ($^{13}CH_3$)[25]. So long as the internal diffusion rate is no more than about 20 times the overall rate ($D_i/D<20$), cross correlation effects are not important[12,24]. All quantitative *Woessner* studies to date have neglected cross-correlation effects, but at very rapid relative methyl rotation rates this could lead to problems.

Because many experimentalists have not carried out relaxation time measurements as a function of temperature in these studies, another systematic error has been introduced with regard to the value of $D_{i0}$ in the Arrhenius expression in eq. (11). This error is systematically propagated in all the calculations. Although the absolute value of the barriers may be affected by the choice of value given in eq. (12), the error has no effect on the relative values within a series. Consequently, internal comparisons of barriers within a given study do not suffer from this error. Two studies[13,22] have measured $T_1$(DD) as a function of temperature, so that the Arrhenius equation could be used. The resulting values of $E_a$ showed small systematic differences from $V_0$ [eqs. (11) and (12)]. The variable temperature approach should be preferred.

All authors have used the tetrahedral value for the angle $\Delta$(H—C—C). As *Blunt* and *Stothers* have pointed out[10], this assumption can result in considerable error in the barrier. These authors found that the rotational barrier of the C-19 methyl group in cholesteryl chloride is calculated to be 0.0±2.2 kcal/mol when the tetrahedral angle is assumed, but 2.6±0.3 kcal/mol for $\Delta=113.5°$. Unfortunately, there is no reliable method of determining the value of $\Delta$. By calculation, *Blunt* and *Stothers* suggested that the ratio $T_1^{CH_3}(DD)/T_1^{CH}(DD)$ be used as a guideline. When this ratio is in the range 0.4 to 2.4, the calculated barriers are relatively independent of small changes in the magnitude of $\Delta$. In the cholesteryl chloride case, the observed ratio of 3.0 is outside this range. The ratio 3.0 has been associated with "free rotation"[18], just as 0.333 has been associated with completely hindered rotation. Non-tetrahedral values of $\Delta$, however, can bring about values of the ratio above 3.0. The vast majority of the systems recorded in Table 1 possess relaxation time ratios within the safe range. This condition must be checked for every case.

It is common practice to apply eqs. (10a) and (10b) by dividing the expression for $CH_3$ by that for a CH carbon in the rigid framework. The division eliminates the coefficients in front of the correlation time (after allowance for the different number of attached protons) and produces a simpler calculation[8,10,19]. Eq. (*13a*) gives the resulting expression for the methyl jump model, and eq. (*13b*) that for the stochastic diffusion model.

$$\frac{T_1^{CH}(DD)}{T_1^{CH_3}(DD)} = 18\left(\frac{A}{6}+\frac{B+C}{6+D_i/D}\right) \tag{13a}$$

$$\frac{T_1^{CH}(DD)}{T_1^{CH_3}(DD)} = 18\left(\frac{A}{6}+\frac{B}{6+D_i/D}+\frac{C}{6+4\,D_i/D}\right) \tag{13b}$$

Such an approach removes some systematic error in the absolute value of $r_{CH}$. Recent studies have shown that small changes in $r_{CH}$ (*e.g.* from the commonly accepted 1.09 Å to say 1.13 Å) can alter the calculation of the overall correlation time [and hence alter $D$ in eq. (4)] by up to a factor of two[28]. The division process in eqs. (*13a*) and (*13b*) removes this source of systematic error, only if $r_{CH}$ is the same for the $CH_3$ and CH carbons. In unstrained, saturated systems, this condition is probably met. For a methyl group attached to a trigonal carbon, the situation is less clear. The structure of propene determined by microwave spectroscopy is consistent with a difference of only 0.02 Å between the bond lengths for $CH_3$ (1.09 Å) and for the trigonal CH (1.07 Å). Such a difference can lead to an error in the barrier of *ca.* 15%. Such an error is comparable to the experimental error but might become more important in unusual structural situations.

From this discussion of experimental and systematic errors, it should be clear that the *Woessner* method produces, at best, semiquantitative barriers for methyl rotation. For a series of compounds, many of the systematic errors cancel or are held constant, so that comparisons within the series probably yield relatively reliable results.

## 2.5. The *Woessner* Method for Quadrupolar Relaxation

A nucleus possessing a quadrupole moment, such as $^2$H, $^{14}$N, or $^{17}$O, can relax very efficiently by interacting with the unsymmetrical electric field of the surrounding electrons[29]. Just as for dipole-dipole relaxation, the quadrupole-electric field relaxation requires tumbling of the molecule for effective coupling of the two components (relaxing nucleus and quadrupolar nucleus). If the quadrupolar nucleus is located within a portion of the molecule that is capable of internal rotation, then the total motion of the nucleus is a superposition of the internal rotation and the overall molecular motion. The geometrical analysis for anisotropic motion parallels the analysis for dipole-dipole relaxation, with changes in the coefficients that precede the expression for the correlation time. *Woessner*[7,30] has derived the appropriate relationship between $T_1$(Q) and the correlation time, which we give for both anisotropic motion [eq. (14a)] and isotropic motion [eq. (14b)].

$$\frac{1}{T_1(\mathrm{Q})} = 3/2\,\pi^2(1+1/3\,\eta^3)(e^2 q Q h^{-1})^2 \left[\frac{A}{6\,D_2} + \frac{B}{D_1+5\,D_2+a\,D_i} + \frac{C}{4\,D_1+2\,D_2+a\,m\,D_i}\right] \qquad (14a)$$

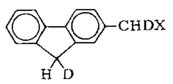
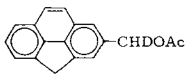
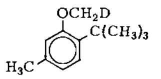
$$\frac{1}{T_1(\mathrm{Q})} = 3/2\,\pi^2(1+1/3\,\eta^3)(e^2 q Q h^{-1})^2 \left[\frac{A}{6\,D} + \frac{B}{6\,D+a\,D_i} + \frac{C}{6\,D+a\,m\,D_i}\right] \qquad (14b)$$

The asymmetry parameter $\eta$ has always been taken to be zero in this context. At least for deuterium, this ought to be a good assumption. As in the parallel expression for dipole-dipole relaxation [eqs. (7) and (10)], $a=1$ and $m=4$ for the stochastic diffusion mechanism for methyl rotation and $a=r/2$ and $m=1$ for an $r$-fold jump mechanism.

The only differences between eq. (14a) and eq. (7) are found in the constants that precede the correlation time. The factor $n$ (number of attached protons) has no relevance in a mechanism involving the relaxing nucleus and its surrounding electron cloud, and is therefore absent. The distance factor $r_{\mathrm{CH}}$ and the gyromagnetic ratios have been replaced by the quadrupole coupling constant, $(e^2 q Q h^{-1})$, in which $e$ is the charge of the electron, $eq$ the electric field gradient, and $eQ$ the nuclear quadrupole moment. Some authors replace $3/2\pi^2(e^2 q Q h^{-1})^2$ by $3/8(e^2 q Q h^{-1})^2$. The geometrical factors $A$, $B$, and $C$ have the same meaning as defined in eq. (6).

It is interesting that most reported applications of this approach have measured $T_1$(Q) as a function of temperature, so that no assumption must be made about the value of $D_{i0}$ in eq. (12). The barriers are obtained by an Arrhenius plot of the methyl jump or diffusion rate *vs.* reciprocal temperature. The experiment is somewhat easier than for the dipole-dipole method, since the NOE is not measured. It is assumed that the observed relaxation time is dominated by $T_1$(Q). Studies using this technique include examination of toluene ($^2$H relaxation)[21], dimethylformamide ($^2$H, $^{14}$N, $^{17}$O)[31], the methyl-substituted benzyl cyanides (tolylacetonitriles) ($^{14}$N)[32], and various aromatic systems ($^2$H)[33]. Related studies have provided values of $\tau_i$ by this method but did not report barriers[34-36]. The reported barriers are given in Table 2.

Table 2. Barriers (kcal/mol) to rotation from the *Woessner* quadrupolar approach.

| Compound | Bond | $V_0$ [a] | $V_0$ [b] | Ref. |
|---|---|---|---|---|
| dimethylformamide | N—$CH_3$ | | 1.4 | [31] |
| *m*-tolylacetonitrile | C—$CH_2CN$ | | 1.5 | [32] |
| *p*-tolylacetonitrile | C—$CH_2CN$ | | 1.5 | [32] |
| toluene | C—$CD_3$ | 0.93 | 0.83 | [21] |
|  | C—$CH_2D$<br>C—CHDOH<br>C—CHDOAc<br>C—CHDCl | free<br>2.7<br>2.8<br>2.9 | | [33] |
|  | C—CHDOAc | 3.3 | | [33] |
|  | O—$CH_2D$ | 1.9 | | [33] |

[a] Methyl jump model. [b] Stochastic diffusion model.

Comparison of $V_0$ for toluene measured by the $T_1$(DD) and $T_1$(Q) methods shows a difference of about 0.4 kcal/mol. These barriers are well removed from the microwave value of 0.014 kcal/mol[37]. *Woessner* and *Snowden*[21] emphasize that even a qualitative interpretation of their data demands that the methyl group in toluene is not a "free rotor", which is at variance with the microwave results. This variance may be the result of use of the isotropic approximation in the NMR measurement[9].

*Wallach*[32] studied rotation about the $CH_2CN$ group in the tolylacetonitriles. In the *o*-tolyl derivative, he found $CH_2CN$ rotation to be hindered, *i.e.*, it was above the barrier limit to the *Woessner* method. Consequently, he used this system to provide the overall diffusion rate $D$ for the determination of the internal rate $D_i$ in the *m*- and *p*-tolyl compounds. *Lehn et al.*[33] examined several C—CHDX and O—CHDX systems. By transferring the rotational rates to other molecules, they were able to report barriers for a much larger number of systems than is presented in Table 2.

Examination of the quadrupolar relaxation provides a useful alternative to the dipole-dipole procedure. The more readily obtainable data encourage the measurement of the rotational rates as a function of temperature. The study of $^2$H relaxation in $CD_3$ is probably not a viable alternative to the investigation of $^{13}$C relaxation in $^{13}CH_3$ in all cases, because of the necessity of synthesizing the deuterated derivatives. The study of $^2H$ relaxation in CHDX (X$\neq$hydrogen), however, provides an opportunity for the measurement of rotational barriers for groups that lack threefold symmetry. Applications of the quadrupolar approach for systems containing $^{14}N$, $^{17}O$, $^{11}B$, and other quadrupolar nuclei should provide continued variety in the types of systems able to be studied.

### 2.6. The *Ellis* Method for Spin-Rotation Relaxation

Quite often, the $^{13}C$ spin-lattice relaxation of a methyl group has a very large contribution from spin-rotation, $T_1$(SR), which can be evaluated from eq. (1). $T_1$(DD) is calculated from the nuclear Overhauser enhancement, and $T_1$(other) is assumed to arise entirely from spin rotation ($T_1$(SR)). *Zens* and *Ellis*[38] reasoned that the barrier to rotation of the methyl-group should be related in some way to the rotational angular momentum and hence to $T_1$(SR).

$$1/T_1(\mathrm{SR}) = 8/3\,\pi^2\hbar^{-2}\,k\,T\,C_{\parallel}^2\,I_{\parallel}[\tau_{\mathrm{SR}}] \qquad (15)$$

Eq. (15) expresses the relationship between the spin-rotation relaxation time and the temperature $T$, the Boltzmann constant $k$, the spin-rotation interaction coupling constant $C_{\parallel}$, the moment of inertia $I_{\parallel}$ about the axis of rotation, and the correlation time for angular momentum reorganization $\tau_{SR}$. It must be assumed that rotational motion about the parallel axis is much faster than motion about the perpendicular axis or of the molecule as a whole. It is unlikely that the perpendicular axis will have a significant contribution, and the overall spin-rotation can be evaluated from $T_1$(SR) for a $^{13}C$ atom not involved in the internal rotation. The dominance of internal spin-rotation has been documented for nitrite rotation in *n*-butyl nitrite (*n*-$C_4H_9$—ONO)[39].

By replacing the thermal energy term $kT$ by the expression ($kT+V_0$), *Zens* and *Ellis*[38] were able to take quenching of angular momentum by the barrier to rotation $V_0$ into account. From eleven known values of $V_0$ and measurements of $T_1$(SR), they found a semiempirical relationship [eq. (16)].

$$V_0 = (T_1(\mathrm{SR}) - 25.61)/9.783 \qquad (16)$$

This relationship, derived for 38 °C, provides a straightforward procedure for measuring barriers from spin-rotation relaxation times. These authors calculated the barriers to methyl rotation in camphor to be 3.05 kcal/mol for 8-$CH_3$, 3.26 for 9-$CH_3$, and 3.08 for 10-$CH_3$[38]. They also enumerated a number of limitations to this procedure: eq. (16) is only valid at 38 °C; it was assumed that the internal spin rotation is more dominant than the total spin-rotation, and that protons (not $^{19}F$, *etc.*) must be attached to carbon in order to calculate $T_1$(SR) by reciprocal subtraction of $T_1$(DD) (from NOE measurements!) from $T_1$ in eq. (1).

Subsequent applications of the *Zens-Ellis* equation have not been entirely successful. In particular, two studies obtained negative barriers to rotation[40,41], and a third[42] claimed that the approach is theoretically unsound. Further examination of the *Zens-Ellis* data demonstrated that the linearity of eq. (16) was false and had been caused by systematic errors in the measurement of the nuclear Overhauser effects[43]. The actual plot of $T_1$(SR) *vs.* $V_0$ has considerable curvature. *Ellis, Poole, et al.*[43] were able to fit the curve by a modification of eq. (15) that separated the correlation time into distinct overall and internal components: curves for 10° and 38 °C were presented.

The relationship between $V_0$ and $T_1$(SR) is not linear and hence barriers must be obtained from a plot. The method has not yet been thoroughly explored, so that the extent of its limitations remain unplumbed. The specification of a single temperature is a minor limitation. The range of applicable barriers has not been determined and the dominance of internal spin-rotation over overall spin-rotation has not been systematically demonstrated. One group used differences between the *Ellis* and *Woessner* barriers to determine the H—C—C angle[20]. Finally, the influence of experimental error associated with $T_1$ (observed) and NOE measurements on the accuracy of the barriers $V_0$ has not yet been examined quantitatively. Nonetheless, the method remains a useful alternative to the *Woessner* approach.

## 3. Intermediate Energy Barriers

By "intermediate barriers", we refer to those corresponding approximately to the range for line shape coalescence, *i.e. ca.* 4.5 to 27 kcal/mol. At the lower end of this range, one of the first applications of relaxation phenomenon to dynamic problems was the use of spin-echo techniques[44]. The primary aim of these experiments was to increase the dynamic range of kinetic measurements and hence to improve the accuracy of the derived barriers. The method probably does not improve significantly on lowering the barrier limit observable by NMR line shape methods. Most of these experiments preceded the Fourier transform era. Similar, if not expanded, objectives can now be attained by the $T_{1\rho}$ method, which is simpler to carry out and is available on commercial equipment. For these reasons, we will direct our attention to $T_{1\rho}$ and not attempt to further the existing review of spin-echo techniques[45].

### 3.1. Rotating Frame Relaxation ($T_{1\rho}$)

As mentioned in Section 2.1 the spin-lattice relaxation time $T_1$ is sensitive to motional processes which have rates in the vicinity of the resonance frequency, $\gamma B_0$ (*ca.* $10^8$ $s^{-1}$). Lower rates can be achieved by measuring relaxation times in the $B_1$ field, whose frequency is lower than the $B_0$ field. The measurement can be carried out by a two-pulse sequence. The magnetization is first placed in the xy plane by a 90° pulse. Then, instead of measuring the growth of magnetization in the z direction ($T_1$), the magnetization is locked in the xy plane by a continuously applied 90° phase-shifted pulse. During this pulse, the nuclear vectors rotate with the weaker $B_1$ field (precess around the rotating $B_1$ with angular frequency $\omega_1 = \gamma B_1$), rather than with the $B_0$ field (angular frequency $\omega_0 = \gamma B_0$). At the end of the lock pulse, the rate of decay of magnetization in the xy plane is measured (time constant $T_{1\rho}$). Extrapolation of the spin-locking power to zero would give $T_2$. Despite its relationship to the xy plane, the rotating frame relaxation time is called $T_{1\rho}$ (not $T_{2\rho}$) because of the similar function of the $B_0$ and $B_1$ fields for $T_1$ and $T_{1\rho}$. $T_{1\rho}$ can be defined as the time constant for decay of magnetization along the rf field $B_1$, which is rotating in the xy plane perpendicular to the direction of $B_0$. If decoupling is required, it is gated-off during the spin-locking pulse.

*Meiboom* first carried out $T_{1\rho}$ experiments[46], and *Deverell et al.*[47] demonstrated their applicability to kinetics. The latter authors pointed out that dipole-dipole, spin-rotation, *etc.*, contributions should be similar for $T_1$ and $T_{1\rho}$. Because of different frequency sensitivities, however, the two relaxation times differ in contributions from exchange processes, $T_{1\rho}$ being sensitive to slower rates. The net $T_{1\rho}$ (exchange) due to the rate process is obtained by reciprocal subtraction of $T_1$ from $T_{1\rho}$ (observed) [eq. (17)].

$$\frac{1}{T_{1\rho}(\text{exch.})} = \frac{1}{T_{1\rho}(\text{obs.})} - \frac{1}{T_1} \tag{17}$$

For exchange between two sites with equal population, the net $T_{1\rho}$(exch.) is related to the spin-locking frequency $\omega_1$, the mean lifetime $\tau = 1/k$ ($k$ is the rate constant for the exchange process), and the chemical shift difference between the exchanging sites $\Delta\nu$ (in Hz) by eq. (18).

$$\frac{1}{T_{1\rho}(\text{exch.})} = \pi^2(\Delta\nu)^2 \frac{\tau}{1+\omega_1^2\tau^2} \tag{18}$$

The desired quantity in eq. (18) is $\tau$, the reciprocal of the exchange rate, from which the barrier $\Delta G^{+}$ can be calculated. Measurement of $\tau$ as a function of temperature of course gives $\Delta H^{+}$ (or $E_a$) and $\Delta S^{+}$ (or $\log A$). If the slow exchange $\Delta\nu$ is known, then $\tau$ can be obtained directly from eq. (18). Such an experiment would be equivalent to the study of decoalescence in the slow exchange limit. Decoalescence cannot normally be studied unless that limit is achieved and $\Delta\nu$ is measured[*]. The $T_{1\rho}$ method, however, does not require achieving the slow exchange limit and measuring $\Delta\nu$. A plot of $T_{1\rho}$(exch.) as a function of $\omega_1^2$ will give $\tau$ and $\Delta\nu$ from the slope and intercept. Thus, the $T_{1\rho}$ method offers the considerable advantage of determining fast kinetics without necessarily achieving the slow exchange line shape limit. The practical kinetic range for the method is about $10^2$—$10^6$ s$^{-1}$. Thus it overlaps with, and slightly expands upon, the lower limit of line shape methods.

Although a number of applications of $T_{1\rho}$ to the solid state have been reported, applications to kinetics in solution are only just being carried out. *Stilbs* and *Moseley*[48] obtained the barrier to amide rotation in urea ($^1$H measurements, $\Delta G^{+} = 10.8$ kcal/mol) and in tetramethylurea ($^{13}$C measurements, 6.1 kcal/mol) from $T_{1\rho}$. By variation of $\omega_1$, they were able to measure $\Delta\nu$ well above the coalescence temperature. Thus for tetramethylurea, the measurements were at −115 and −120 °C, while the coalescence temperature is close to −150 °C. These authors also carried out a Monte Carlo error analysis on their data.

*Doddrell et al.* measured the rotational barrier to C—C bond rotation between the aldehyde group and the phenyl moiety from the $^{13}$C $T_{1\rho}$ in benzaldehyde ($\Delta H^{+} = 7.3$ kcal/mol) and *p*-methoxybenzaldehyde (8.7 kcal/mol)[49]. These measurements were made 100—120 °C above the known coalescence temperatures. The same group[49] has measured the ring reversal barrier in 1,1-dimethylpiperidinium iodide ($\Delta H^{+} = 10.5$ kcal/mol, $\Delta G^{+}(-3\,°\text{C}) = 10.0$ kcal/mol) from $T_{1\rho}$ of the methyl carbons. From $\Delta G^{+}$, the coalescence temperature was calculated to be about −50 °C, well below the freezing point of the aqueous solution needed to dissolve this salt. The ring reversal barrier in *cis*-decalin has also been measured from $T_{1\rho}$[50], and applications to conformational operations in polypeptides have appeared[51].

The $T_{1\rho}$ method suffers from few of the systematic errors associated with the *Woessner* method, but it cannot treat the very rapid rotational processes that the *Woessner* method can. The method is not restricted by the symmetry of the exchanging entities — as the *Woessner* method is — to CH$_3$ and CH$_2$X groups. As yet, the $T_{1\rho}$ procedure has not been extended to exchange between sites with unequal populations. The commercial availability of spectrometers that now can measure $T_{1\rho}$ certainly should encourage applications of the method. Because of its high accuracy and its applicability to fast kinetics without the necessity of obtaining the slow exchange $\Delta\nu$, rotating frame relaxation methods should achieve broad acceptance in the future.

## 4. High Energy Barriers

The methods discussed in this Section provide slower rates than those that line shape techniques could provide on the same system. The barriers are at the upper end of, or above the line shape coalescence range.

### 4.1. Saturation Transfer or the *Forsén-Hoffman* Method

Although the modification of the Bloch equations for chemical exchange processes had been achieved by *McConnell* in 1958[52], it remained for *Forsén* and *Hoffman*[53] to exploit the theory and provide an alternative line shape analysis. In a two spin system, saturation of one resonance (B) causes transfer of magnetization to another resonance (A) that is in chemical exchange with it. *Forsén* and *Hoffman* showed how the analysis of the peak perturbations at A can provide both relaxation times and the rate constants for exchange. The method may be used qualitatively to demonstrate the identity of specific spins undergoing the exchange process. Many of the qualitative applications have been discussed in a review[54].

The Bloch expression for the change in magnetization ($M_z^A$) at site A is made up of one decay term in $T_{1A}$ for normal relaxation to equilibrium ($M_0^A$) and a second decay term in $\tau_A$ (the reciprocal of the A→B rate constant) for transfer of spin from A to B *via* the exchange process [eq. (19)]. There is no term in $\tau_B$ because of the saturation condition.

$$-\frac{\mathrm{d}M_z^A(t)}{\mathrm{d}t} = \frac{(M_z^A(t) - M_z^A(0))}{T_{1A}} + \frac{M_z^A(t)}{\tau_A} \tag{19}$$

---

[*] Note: In the simplest case considered here, $\Delta\nu$ can also be obtained from the "half-width" at the coalescence point.

Equation (19) is normally rewritten in terms of a total lifetime $\tau_{1A}$ [eq. (20)]

$$\frac{1}{\tau_{1A}} = \frac{1}{\tau_A} + \frac{1}{T_{1A}} \tag{20}$$

that includes both spin-lattice relaxation and exchange [eq. (21)].

$$\frac{dM_z^A(t)}{dt} = \frac{M_z^A(0)}{T_{1A}} - \frac{M_z^A(t)}{\tau_{1A}} \tag{21}$$

The solution to this differential equation is given by eq. (22).

$$M_z^A(t) = M_z^A(0)\left[\frac{\tau_{1A}}{\tau_A}\exp^{(-t/\tau_{1A})} + \frac{\tau_{1A}}{T_{1A}}\right] \tag{22}$$

Peak heights are taken as a valid measure of $M_z(t)$. When $t$ approaches infinity, eq. (22) can be rearranged to give eq. (23).

$$\frac{M_z^A(\infty)}{M_z^A(0)} = \frac{\tau_{1A}}{T_{1A}} \tag{23}$$

Thus, measurement of $M_z(0)$ and $M_z(\infty)$ gives the ratio of $T_{1A}$ to $\tau_{1A}$. If $T_{1A}$ can be measured independently, then $\tau_{1A}$ and hence $\tau_A$ can be obtained. Alternatively, one can plot $\log[M_z^A(t) - M_z^A(\infty)]$ *vs.* $t$ [from eq. (22)] to give a straight line with slope $\tau_{1A}$, whence $T_{1A}$ and $\tau_A$. A similar set of experiments in which A is saturated and B is observed would give $T_{1B}$ and $\tau_B$.

Despite the attractiveness of this approach, very few quantitative applications appeared prior to the Fourier transform era. As *Mann*[55] pointed out, the method described by *Forsén* and *Hoffman* requires repetitive scanning through the resonance at least once a second, in order to provide an independent measure of $T_{1A}$. A few spectrometers were set up to carry out such experiments (the old Sanborn recorder was particularly good for this purpose).

*Anet* and *Bourne* examined [D$_{11}$]cyclohexane by the original *Forsén-Hoffman* method[56]. Saturation of the axial or equatorial proton in the temperature range −97 to −117 °C, when coupled with line shape analysis from the range −24 to −82 °C, provided very accurate parameters for the barrier to ring reversal ($\Delta G^{+} = 10.22$ kcal/mol, $\Delta H^{+} = 10.8$ kcal/mol, and $\Delta S^{+} = 2.8$ eu). The fact that the exchanging axial and equatorial protons are in different molecules avoids another problem. Irradiation at the resonance frequency of a nucleus can cause nuclear Overhauser polarization effects on and removal of coupling to other nuclei within the same molecule. These effects can confuse analysis of saturation transfer. In another early application, *Kabakoff* and *Namanworth*[57] obtained the activation energy to rotation around the cyclopropyl-C$^{\oplus}$ bond in the cyclopropyldimethylcarbenium ion ($E_a = 13.7$ kcal/mol, $\log A = 12.2$).

The advent of pulsed Fourier transform $^{13}$C techniques obviated most of the drawbacks to the *Forsén-Hoffman* method. Use of a dilute (natural abundance) $^{13}$C spin means that the irradiated and observed nuclei are almost certainly not in the same molecule, so that decoupling and Overhauser effects no longer confuse the analysis. Possibly more important, pulsed Fourier transform operation provides an independent measure of $T_1$, so that rapid, repetitive scanning is not necessary. Instead of saturating the B nucleus, the Fourier transform procedure normally inverts B selectively with a 180° pulse, followed by a 90° observation pulse. Because of exchange effects between $T_{1A}$ and $T_{1B}$ (Section 4.2), however, this method gives a valid $T_1$ only when $T_{1A} = T_{1B}$[55]. *Boekelheide et al.*[58] measured the barrier to ring reversal in [2.2]metaparacyclophanes from $^1$H-NMR spectra, assuming equal relaxation times, as $\Delta H^{+} = 17.0$, $\Delta S^{+} = -8.8$ eu. *Mann*[55] reported the first $^{13}$C (dilute spin) application of the *Forsén-Hoffman* method, for ring reversal in *cis*-decalin, with independent measurement of $T_1$ and the assumption that $T_1^A = T_1^B$. His *Forsén-Hoffman* studies between −70 and −45 °C were supplemented by line shape kinetics up to about +40 °C. With CD$_2$Cl$_2$ as solvent, he obtained $\Delta H^{+} = 12.35$ kcal/mol, $\Delta S^{+} = 0.15$ eu, $E_a = 12.85$ kcal/mol, $\log A = 12.85$, and $\Delta G^{+}(27\,°\mathrm{C}) = 12.30$ kcal/mol. The figures for CD$_3$C$_6$H$_5$ were $\Delta H^{+} = 12.47$ kcal/mol, $\Delta S^{+} = 0.06$ eu, $E_a = 12.97$ kcal/mol, $\log A = 12.97$, $\Delta G^{+}(27\,°\mathrm{C}) = 12.45$ kcal/mol. In a later study, *Mann*[59] presented a method applying his procedure to systems in which $T_{1A} \neq T_{1B}$. For dimethylformamide, he combined the *Forsén-Hoffman* method (40.5 to 59 °C) with a line shape analysis (100 to 160 °C) to give $\Delta H^{+} = 20.39$ kcal/mol and $\Delta S^{+} = -1.49$ eu. In addition to these multi-temperature studies, there have been other Fourier transform investigations at only a single temperature that reported rate constants but not activation parameters[60]. Saturation transfer involving $^{13}$C nuclei has also been used to study ligand migration mechanisms[61].

The *Forsén-Hoffman* method provides a very useful procedure for studying kinetics at the upper end of the barrier range for line shape methods. To date, most of the studies, however, have relied upon a combination of *Forsén-Hoffman* and line shape methods in order to produce the largest possible dynamic range of rate constants. It should nonetheless be possible to use saturation transfer to provide kinetics for systems that do not attain the fast exchange line shape extreme. For most Fourier transform applications, however, the *Forsén-Hoffman* method requires that $T_{1A} = T_{1B}$, since the independent measurement of $T_1$ only yields a true value under these conditions (Section 4.2). Also, many NMR-spectrometers are not designed to deliver selective irradiation of a single $^{13}$C resonance under Fourier transform conditions: they provide selective $^1$H irradiation but nonselective $^{13}$C irradiation. This drawback should disappear with future development of instrumentation. For the upper end of the barrier range, the *Forsén-Hoffman* approach is the method of choice for exchanging spins of equal spin-lattice relaxation time. It ought to be used not only to expand line shape kinetics but also to study non-coalescing systems.

### 4.2. The Coalescence of Relaxation Times

Saturation of one of the component resonances in an exchanging system leads to simplification of the differential equation [eq. (19)] for the change in magnetization and hence to a simple exponential solution [eq. (22)]. If saturation is nonselective, there must be a term (in the case of the A magnetization) both for loss of magnetization by A and gain from B [eq. (24)].

$$-\frac{dM_z^A(t)}{dt} = \frac{(M_z^A(t) - M_z^A(0))}{T_1^A} + \frac{M_z^A(t)}{\tau_A} - \frac{M_z^B(t)}{\tau_B} \tag{24}$$

The solution to this equation takes the form of eq. (25).

$$M_z^A(t) = M_z^A(0) + C_1 \exp(-t/T_I) + C_2 \exp(-t/T_{II}) \tag{25}$$

The constants in this expression have been defined elsewhere[62-65].

The major difference between this solution and that for the more restrictive *Forsén-Hoffman* conditions is the double exponential that is present in eq. (25). In contrast, *Forsén-Hoffman* data are controlled by a single time constant $\tau_{1A}$ (the reciprocal sum of $T_{1A}$ and $\tau_A$). In a normal spin-lattice relaxation measurement (inversion or saturation recovery) for a non-exchanging system, the data are also controlled by a single time constant $T_1$. The double exponential form of eq. (25) means that exchanging systems gives rise to nonlinear behavior in the usual magnetization plot ($\ln M_z$ *vs.* $t$), similar to the behavior of systems exhibiting cross-correlation[25].

The physical interpretation of the pair of time constants [$T_I$ and $T_{II}$ in eq. (25)] depends on the relative values of the lifetimes and relaxation times. We can consider three kinetic regions. At the slow exchange limit (low temperatures, long lifetimes compared to relaxation times), $T_I$ corresponds to $T_{1B}$ and $T_{II}$ to $T_{1A}$. The values of the coefficients are such that the $C_1$ term drops out for A-magnetization and the $C_2$ term drops out for B-magnetization. Thus, each resonance line gives single exponential decay (or growth) of magnetization, and the time constants are the true relaxation times[62,65].

At the fast exchange limit (high temperatures, short lifetimes compared to relaxation times), the first term (with time constant $T_I$) goes to zero. The result is single exponential decay or growth of magnetization, and the reciprocal of the time constant $T_{II}$ is the weighted average of the reciprocals of the true relaxation times, $T_{II}^{-1} = 0.5(T_{1A}^{-1} + T_{1B}^{-1})$ for equal population or $T_{II}^{-1} = p_A T_{1A}^{-1} + p_B T_{1B}^{-1}$ in general. Thus, under conditions of rapid exchange, the usual inversion recovery experiment for $T_1$ does not give a true relaxation time, but a weighted average for the various sites[65]. It should be emphasized that "slow exchange" and "fast exchange" in the present context do not have the same meaning as for line shape analysis. In the latter context, the terms refer to the presence or absence of line collapse. In the present context, they refer to the relative values of the lifetimes and the relaxation times. At the beginning of the fast exchange limit, in terms of relaxation, distinct resonances still appear for the two exchanging species. Thus, fast exchange for relaxation ($T_1$ coalescence) is still slow exchange for line shapes ($\Delta\nu$ decoalescence). At higher temperatures line shape coalescence would eventually take place. In the region of fast relaxation exchange and slow line shape exchange, relaxation times can be measured for both the A and the B resonances. The result would apparently be equal relaxation times, but the numbers are averaged ($T_{II}$) rather than true ($T_{1A}$, $T_{1B}$) relaxation times. We refer to this phenomenon as relaxation time coalescence, which precedes line shape coalescence as the temperature is raised[65].

The coalescence of relaxation times occurs in the intermediate kinetic region between fast and slow relaxation exchange, when the lifetimes and relaxation times have comparable values. In this region, the magnetization exhibits double exponential (nonlinear) behavior, and the time constants $T_I$ and $T_{II}$ correspond to a complex mixture of the lifetimes ($\tau_A$ and $\tau_B$) and the true relaxation times ($T_{1A}$ and $T_{1B}$) (see eq. (5) in [65]). Single exponential analysis of inversion recovery data in this region will give false values for the relaxation times.

There have been two approaches to exploit relaxation behavior in the coalescence region in order to obtain exchange lifetimes (reciprocal first order rate constants). *Strehlow* and *Frahm*[64] obtained closed solutions when $T_{1B} \ll T_{1A}$ (in a ratio of at least 1:5). They applied this method to the exchange of water between the inner hydration sphere of nickel ions and the bulk solution. A large inequality between the two relaxation times might be expected to occur if paramagnetic relaxation has a greater influence on one of the relaxation times, if there is a large difference in the size of A and B, or if relaxation is quadrupolar-determined and the two species have considerably different symmetries. Thus, this approach is severely limited by the necessity of unequal relaxation times.

In the second approach to exploiting relaxation time coalescence to study kinetics, we developed a nonlinear regression analysis to solve the complete differential equation[65]. This approach gives the mean lifetimes ($\tau_A$ and $\tau_B$) and the true relaxation times ($T_{1A}$ and $T_{1B}$) in the intermediate (coalescing) region. Applied to amide rotation in dimethylformamide, this method gives lifetimes (and hence barriers) very close to those from extrapolated line shape analysis. Regression analysis of the nonlinear change in magnetization has the main advantage over other high barrier techniques that it is not constrained by the relative values of the true relaxation times. They need not be equal or very unequal. It offers the most general approach, but its accuracy must be further tested.

## 5. Final Comments

Measurement of spin-lattice relaxation times can expand both the high and the low extremes of the barrier range available to line shape experiments (see the summary in Figure 1; the limits are tentative).

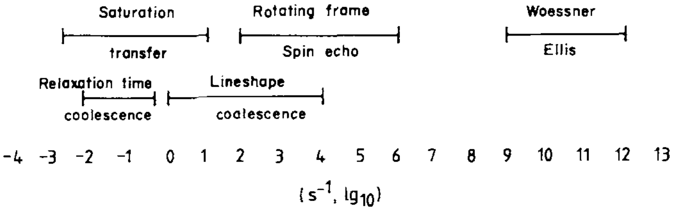


Figure 1. The dynamic range of rate constants ($s^{-1}$ on a logarithmic scale of base 10) for NMR methods.

For very fast rotational processes, the *Woessner* method provides the semiquantitative determination of barriers in systems whose relaxation is dominated by dipole-dipole or quadrupole relaxation. The method has numerous systematic errors, but relative rates within an homologous series appear to be reliable. For systems whose relaxation is dominated by spin rotation, the *Ellis* procedure offers an alternative to the *Woessner* method. This procedure is highly parametrized and as yet has not been applied to very many undetermined cases. Both of these methods are presently restricted to $CH_3$ or $CH_2X$ rotation. For slightly higher barriers, the $T_{1\rho}$ method can be applied to systems that fail to decoalesce at very low temperatures, without restriction on the symmetry of the exchanging species. It is less prone to systematic errors than the *Woessner* method, and offers outstanding promise for measurements of the kinetics in systems with low-to-intermediate barriers. Saturation transfer (the *Forsén-Hoffman* method) similarly offers outstanding promise in the intermediate-to-high barrier region. The lifetimes and relaxation times for the exchanging sites A and B can be measured regardless of the relative values of $T_{1A}$ and $T_{1B}$, provided that the spectroscopist has equipment for selective irradiation and rapid repetitive scans. Otherwise, the relaxation time is measured independently, and the result is only valid when $T_{1A} = T_{1B}$. Exchange rates in the high barrier region can be measured by the analysis of relaxation time coalescence. The usual inversion recovery method for determining $T_{1A} \neq T_{1B}$ gives false values when the lifetimes and relaxation times have comparable magnitudes. For nonselective irradiation without saturation transfer, rates can be measured relatively easily if the true relaxation times are considerably different in magnitude ($T_{1B} \leqslant T_{1A}$). Regression analysis within the region of relaxation time coalescence can give the lifetimes and true relaxation times, regardless of the relative magnitudes of the true relaxation times. This last method has not been tested in a variety of situations, although potentially it offers a general approach to the measurement of barriers that are near or above the limit to line shape coalescence.

Relaxation time methods span the barrier range from close to 0 kcal/mol to possibly above 30 kcal/mol, corresponding to a dynamic range of 15 orders of magnitude in the rates (Figure 1). They offer both alternatives to and extensions of the classical line shape coalescence/decoalescence approaches. The field is still rapidly developing, so that new methods, new restrictions, and new expansions can be expected.

*The authors wish to thank the National Science Foundation and the National Institutes of Health for support of this work. We are indebted to Dr. Donald E. Woessner and to Professor Horst Kessler for valuable comments.*

Received: March 4, 1980 [A 369 IE]
German version: Angew. Chem. *93*, 553 (1981)

---

[1] *H. S. Gutowsky, D. W. McCall, C. P. Slichter,* J. Chem. Phys. *21*, 279 (1953); *J. A. Pople, W. G. Schneider, H. J. Bernstein:* High-resolution Nuclear Magnetic Resonance, McGraw-Hill, New York 1959, Chapter 10.

[2] *J. B. Lambert, H. F. Shurvell, L. Verbit, R. G. Cooks, G. H. Stout:* Organic Structural Analysis, Part 1, Macmillan, New York 1976, Chapter 6.

[3] *G. Binsch, H. Kessler,* Angew. Chem. *92*, 445 (1980); Angew. Chem. Int. Ed. Engl. *19*, 411 (1980).

[4] *E. Breitmaier, K.-H. Spohn, S. Berger,* Angew. Chem. *87*, 152 (1975); Angew. Chem. Int. Ed. Engl. *14*, 144 (1975).

[5] *J. R. Lyerla, C. S. Yannoni, D. Bruck, C. A. Fyfe,* J. Am. Chem. Soc. *101*, 4770 (1979).

[6] *D. E. Woessner,* J. Chem. Phys. *37*, 647 (1962).

[7] *D. E. Woessner, B. S. Snowden, Jr., G. H. Meyer,* J. Chem. Phys. *50*, 719 (1969).

[8] *N. Platzer,* Org. Magn. Reson. *11*, 350 (1978).

[9] *J. B. Lambert, R. J. Nienhuis, R. B. Finzel,* J. Phys. Chem. *85*, 1170 (1981).

[10] *J. W. Blunt, J. B. Stothers,* J. Magn. Reson. *27*, 515 (1977).

[11] *D. E. Axelson, C. E. Holloway,* Can. J. Chem. *54*, 2820 (1976).

[12] *K. H. Ladner, D. K. Dalling, D. M. Grant,* J. Phys. Chem. *80*, 1783 (1976).

[13] *A. Ericsson, J. Kowalewski, T. Liljefors, P. Stilbs,* J. Magn. Reson. *38*, 9 (1980).

[14] *K. F. Kuhlmann, D. M. Grant,* J. Chem. Phys. *55*, 2998 (1971); *J. R. Lyerla, Jr., D. M. Grant,* J. Phys. Chem. *76*, 3213 (1972).

[15] *T. D. Alger, D. M. Grant, R. K. Harris,* J. Phys. Chem. *76*, 281 (1972).

[16] *S. W. Collins, T. D. Alger, D. M. Grant, K. F. Kuhlmann, J. C. Smith,* J. Phys. Chem. *79*, 2031 (1975).

[17] *J. W. ApSimon, H. Beierbeck, J. K. Saunders,* Can. J. Chem. *53*, 338 (1975).

[18] *A. Allerhand, D. Doddrell, R. Komoroski,* J. Chem. Phys. *55*, 189 (1971).

[19] *J. B. Lambert, R. J. Nienhuis,* J. Am. Chem. Soc. *102*, 6659 (1980).

[20] *H. Beierbeck, R. Martino, J. K. Saunders,* Can. J. Chem. *58*, 102 (1980).

[21] *W. A. Mellink, R. Kaptein,* Org. Magn. Reson. *13*, 279 (1980).

[22] *J. Kowalewski, A. Ericsson,* J. Phys. Chem. *83*, 2644 (1979).

[23] *M. Baldo, A. Forchioni, K. J. Irgolic, G. C. Pappalardo,* J. Am. Chem. Soc. *100*, 97 (1978).

[24] *D. E. Woessner, B. S. Snowden, Jr.,* Adv. Mol. Relax. Proc. *3*, 181 (1972).

[25] *L. G. Werbelow, D. M. Grant,* Can. J. Chem. *55*, 1558 (1977); Adv. Magn. Reson. *9*, 189 (1977); J. Chem. Phys. *63*, 4742 (1975).

[26] *J. D. Cutnell, J. A. Glasel,* J. Am. Chem. Soc. *98*, 264 (1976).

[27] *E. Haslinger, R. M. Lynden-Bell,* J. Magn. Reson. *31*, 33 (1978).

[28] *K. Dill, A. Allerhand,* J. Am. Chem. Soc. *101*, 4376 (1979).

[29] See [2], pp. 138-139.

[30] *D. E. Woessner,* J. Chem. Phys. *42*, 1855 (1965).

[31] *D. Wallach, W. T. Huntress, Jr.,* J. Chem. Phys. *50*, 1219 (1969).

[32] *D. Wallach,* J. Phys. Chem. *73*, 307 (1969).

[33] *C. Brevard, J. P. Kintzinger, J. M. Lehn,* Tetrahedron *28*, 2447 (1972).

[34] *R. A. Assink, J. Jonas,* J. Chem. Phys. *53*, 1710 (1970).

[35] *M. D. Zeidler,* Ber. Bunsenges. Phys. Chem. *69*, 659 (1965).

[36] *E. v. Goldammer, M. D. Zeidler,* Ber. Bunsenges. Phys. Chem. *73*, 4 (1969).

[37] *H. D. Rudolph, A. Jaeschke, P. Wendling,* Ber. Bunsenges. Phys. Chem. *70*, 1172 (1966); *H. D. Rudolph, H. Dreizler, A. Jaeschke, P. Wendling,* Z. Naturforsch. *A 22*, 940 (1967).

[38] *A. P. Zens, P. D. Ellis,* J. Am. Chem. Soc. *97*, 5685 (1975).

[39] *J. B. Lambert, D. A. Netzel,* J. Magn. Reson. *20*, 575 (1975).

[40] *J. B. Lambert, R. J. Nienhuis,* unpublished results on *p*-substituted toluenes and *cis* and *trans*-substituted propenes.

[41] *R. F. Jordan, J. R. Norton,* J. Am. Chem. Soc. *101*, 4853 (1979).

[42] *D. M. Doddrell, M. R. Bendall, A. J. O'Connor, D. T. Pegg,* Austral. J. Chem. *30*, 943 (1977).

[43] *A. Tancredo, P. S. Pizani, C. Mendonca, H. A. Farach, C. P. Poole, Jr., P. D. Ellis, R. A. Byrd,* J. Magn. Reson. *32*, 227 (1978).

[44] *A. Allerhand, F.-M. Chen, H. S. Gutowsky,* J. Chem. Phys. *42*, 3040 (1965).

[45] *L. W. Reeves* in *L. M. Jackman and F. A. Cotton:* Dynamic Nuclear Magnetic Resonance Spectroscopy, Academic Press, New York 1975, Chapter 4.

[46] *S. Meiboom,* J. Chem. Phys. *34*, 375 (1961).

[47] *C. Deverell, R. E. Morgan, J. H. Strange,* Mol. Phys. *18*, 553 (1970).

[48] *P. Stilbs, M. E. Moseley,* J. Magn. Reson. *31*, 55 (1978).

[49] *D. M. Doddrell, M. R. Bendall, P. F. Barron, D. T. Pegg,* J. Chem. Soc. Chem. Commun. *1979*, 77; *D. M. Doddrell, P. F. Barron, J. Field,* Org. Magn. Reson. *13*, 119 (1980).

[50] *M. Ohuchi, T. Fujito, M. Imanari,* J. Magn. Reson. *35*, 415 (1979).

[51] *H. E. Bleich, A. R. Day, R. J. Freer, J. A. Glasel,* Biochem. Biophys. Res. Commun. *87*, 1146 (1979).

[52] *H. M. McConnell,* J. Chem. Phys. *28*, 430 (1958).

[53] *S. Forsén, R. A. Hoffman,* J. Chem. Phys. *39*, 2892 (1963).

[54] *J. W. Faller,* Determination Org. Struct. Phys. Methods *5*, 75 (1973).

[55] *B. E. Mann,* J. Magn. Reson. *21*, 17 (1976).

[56] *F. A. L. Anet, A. J. R. Bourn,* J. Am. Chem. Soc. *89,* 760 (1967).
[57] *D. S. Kabakoff, E. Namanworth,* J. Am. Chem. Soc. *92,* 3234 (1970).
[58] *S. A. Sherrod, V. Boekelheide,* J. Am. Chem. Soc. *94,* 5513 (1972); *S. A. Sherrod, R. L. daCosta, R. A. Barnes, V. Boekelheide, ibid. 96,* 1565 (1974).
[59] *B. E. Mann,* J. Magn. Reson. *25,* 91 (1977).
[60] *F. W. Dahlquist, K. J. Longmuir, R. B. DuVernet,* J. Magn. Reson. *17,* 406 (1975); *I. D. Campbell, C. M. Dobson, R. G. Ratcliffe, R. J. P. Williams, ibid. 29,* 397 (1978).
[61] *M. Feigel, H. Kessler, D. Leibfritz, A. Walter,* J. Am. Chem. Soc. *101,* 1943 (1979).
[62] *J. S. Leigh, Jr.,* J. Magn. Reson. *4,* 308 (1971).
[63] *A. C. McLaughlin, J. S. Leigh, Jr.,* J. Magn. Reson. *9,* 296 (1973).
[64] *H. Strehlow, J. Frahm,* Ber. Bunsenges. Phys. Chem. *79,* 57 (1975).
[65] *J. B. Lambert, J. W. Keepers,* J. Magn. Reson. *38,* 233 (1980).

---

# Molecular Self-Organization and the Origin of Life[**]

## By Hans Kuhn and Jürg Waser[*]

The sequence of many small physically and chemically plausible steps that lead to self-organization of matter are considered. These are governed by periodic temperature changes and a multi-faceted spatial environment, both of which occurred in suitable locations on the primordial planet. The specific model described reveals the logical framework of this process, the nature and locations of fundamental difficulties as well as the means by which they might be overcome. The barriers that must be surmounted are mostly related to an accumulation of copying errors. An early stagnation barrier was hurdled by aggregate formation, by means of which erroneous copies are rejected; a further barrier was overcome by the evolution of machinery capable of synthesizing "cellular" envelopes which confine the building components. A system evolved which produced a primitive "replicase" that stabilized a rudimentary genetic code. A later stagnation phase ended when the functional system was reorganized by the evolution of separate machinery for replication and for translation of genetic information. - The purpose of this account is to stimulate experiments and theoretical efforts towards the improvement, refinement, and expansion of the model described. It also demonstrates the fruitfulness of the present style of approach that leads to assertions about the prerequisites, logical framework, and organizational structure of evolutionary processes.

## 1. The Genetic Blueprint and its Translation

A feature of all living systems is their ability to produce copies of themselves. They consist of macromolecules functioning together as an entity in a similar way to the interacting parts of a machine. Living individuals contain their own blueprint along a nucleic acid strand, in the form of a specific sequence of four kinds of nucleotides. During multiplication of an individual this information is copied by replication of the nucleic acid strand. The blueprint can be translated into proteins, that is, linear sequences of twenty kinds of amino acids. This step is accomplished by means of *adapter* or *transfer ribonucleic acid* molecules. For every amino acid $a_1, a_2, a_3 \ldots$ at least one specific molecule of this type, to which it can become attached exists, which also carries a specific *anticodon* nucleotide triplet. Adapter molecules can in turn couple by complementary base pairing to a nucleic acid strand that contains the blueprint for the protein in question *(messenger ribonucleic acid).* Attachment of the base triplet of an adapter molecule to a base triplet on a messenger nucleic acid strand can only occur if corresponding base pairs are *complementary.* The four bases G (guanine), C (cytosine), A (adenine), and U (uracil) are pairwise complementary; bases G and C can readily form three hydrogen bonds with each other, while bases A and U can readily form two hydrogen bonds with each other. Put more simply, if there is a C on the messenger strand there must be a G in the corresponding place on the adapter molecule, *etc.*; for example, the first *codon* triplet ACU on the messenger strand (read in the 5'3'-direction) must correspond to an adapter molecule with the *anticodon* triplet UGA (read in the 3'5'-direction), which carries *e.g.* the amino acid $a_1$ (Fig. 1). Amino acids

---

[*] Prof. Dr. H. Kuhn
Max-Planck-Institut für Biophysikalische Chemie
Am Fassberg, D-3400 Göttingen-Nikolausberg (Germany)
Prof. Dr. J. Waser
La Jolla, California (USA)
formerly California Institute of Technology, Pasadena, California (USA)

[**] Based on a lecture presented at the III. Versammlung der Gesellschaft Deutscher Naturforscher und Ärzte in Hamburg, September 23, 1980

*0570-0833/81/0707-0500 $ 02.50/0*

are therefore linked into protein chains with an amino acid sequence that is determined by the blueprint. These proteins then form the functional structure of the organism.

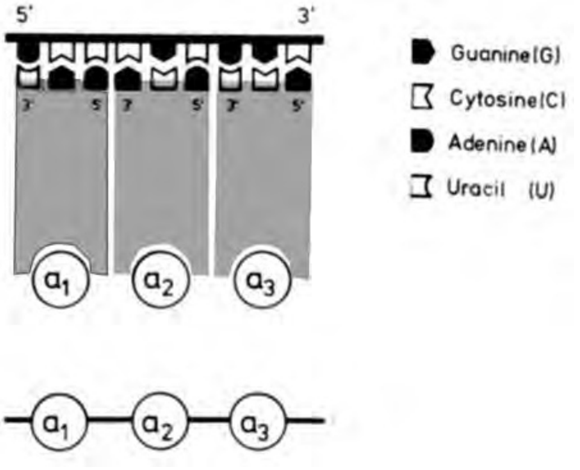


Fig. 1. Simplified version of present-day protein synthesis, guided by a blueprint nucleic acid strand (top), to which adapter molecules carrying the amino acids $a_1$, $a_2$, $a_3$ are attached. Once in favorable juxtaposition the amino acids can form polypeptide bonds (bottom).

Errors during the copying of the blueprint may cause changes in the proteins. Such errors are usually disadvantageous, but in rare cases lead to improved survival chances of the changed individuals. Individuals survive that are best adapted to the environment. Such progressive adaptation to the environment represents a process of *"learning"* for the system that requires many generations.

## 2. The Method of Model Paths

How could simple systems of this kind, that learn by evolution arise? How could machinery for the translation of genetic information that contains proteins as essential translation products arise? How can this chicken-and-egg problem, be solved? Can the laws of physics be applied towards its understanding?

The appearance of the first system capable of learning represented a jump in quality, in which a fundamental property of matter suddenly manifested itself. Systems began to be carriers of information, of a meaningful message, with a content capable of growing as the learning process advanced. Prior to this not even the faintest trace of this property existed, but once the breakthrough had occurred, the process of learning went on inexorably *via* the continued confrontation of evolving systems with their surroundings and their adjustment to environmental changes by multiplication, mutation and selection.

Experimental data capable of directly showing how this manifestation—the sudden appearance of learning machines and the slow evolutionary process leading to the genetic apparatus of present-day biological systems could have come about—is not available. The search for such model paths is important not only as an aid in recognizing these astonishing phenomena as a consequence of plausible physical processes, but also to indicate particularly important steps and in this way to stimulate experiments that might be fruitful. The task of indicating promising experiments is an important aspect of the ideas discussed here, and it is therefore of value to describe the models in a concrete and specific manner.

In more general considerations of self-organization it is easy to overlook the crucial difficulties, and the detailed consideration of an imaginable path constitutes a method of avoiding this problem. However, it cannot be expected that the model steps considered furnish an accurate description of the events that actually occurred.

It is also important not to lose sight of the logical relationship between the different steps, a relationship that is easily buried in the necessarily cumbersome details required for an adequate description of the steps. Each step only leads to the next, and so the overall logical structure of the model is not apparent until the very end (see Section 14, Fig. 24). It is this overall structure that represents the essence of the model, a structure that is not affected, even if some of the details in the steps may have to be changed.

The methodological program for recognizing and understanding the grand connections in the process of self-organization, which we describe here, therefore involves consideration of specific paths consisting of many simple steps[1,2]. A good illustration is the description of how a translation apparatus might have arisen. The presentation is kept simple in order to point out decisive relationships in the clearest possible way.

A machine is constructed by fitting its parts together *via* external directed action. In a similar way, molecular functional cooperatives can be produced artificially, and this is the aim of the Abteilung für Molekularen Systemaufbau in the Max-Planck-Institut für Biophysikalische Chemie. Molecules are forced together in a planned way by directed external action. For example, if suitable molecules on the surface of liquids are pushed together, the monomolecular layers thus formed aggregate, to produce the functional cooperative[3]. On the primordial planet the role of the experimentalist is replaced, in a way, by the enormous variety of environmental influences.

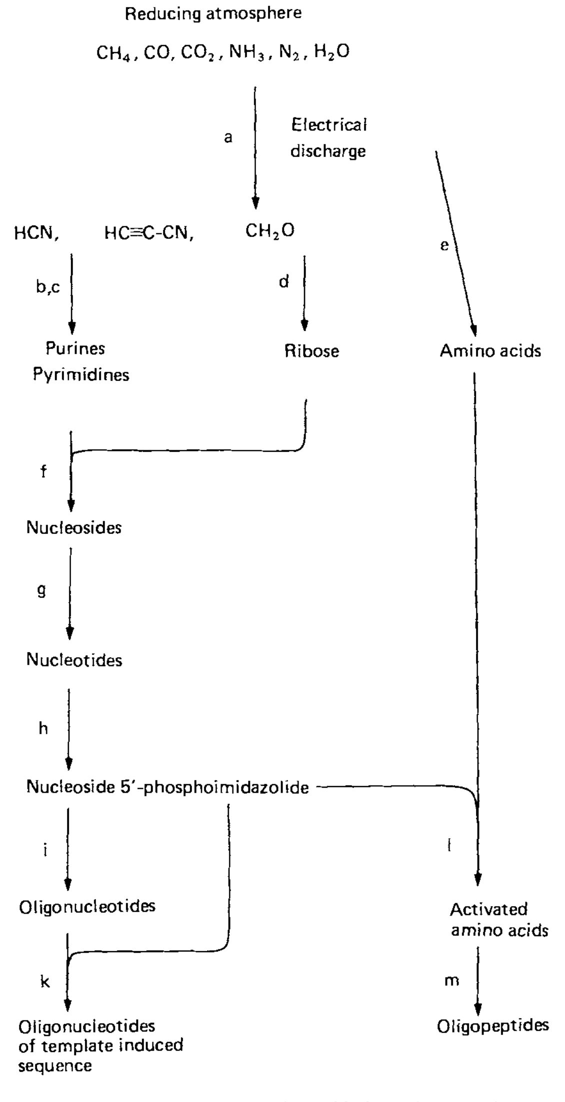
## 3. Some Results of Prebiotic Chemistry

The most important components of our model for the origin and the earliest steps of life are amino acids, ribose, and the nucleotide bases G, C, A, and U. These substances were presumably present on the primordial planet and might have accumulated in particular regions by natural concentration processes, such as evaporation of an aqueous solution and redissolution of the residue, or by adsorption and desorption. Using simulations of conditions thought to have existed on prebiotic earth, many researchers[4-28] have been able to obtain nucleotide bases, sugars, and amino acids from the gases $CH_4$, $CO_2$, $H_2O$, $N_2$, and $NH_3$ which presumably formed the reducing atmosphere of the planet[*]. It has also been possible to demonstrate that these compounds can be made to yield nucleotides

---

[*] It is also quite possible that meteorites, known to contain nucleobases and amino acids, were the initial sources of these building blocks [26—31]. They could have accumulated in particular locations by adsorption and desorption [32].

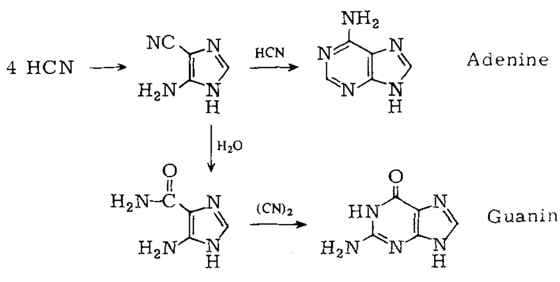
and oligonucleotides, on the one hand, and activated forms of amino acids on the other, under conditions believed to be realistic. Moreover, *Orgel*[21] has recently succeeded in the enzyme-free polymerization of nucleotides on nucleic acid templates, more than 90% of the nucleotides of the replicate strands being complementary to those on the template strands. Some important results of this work are summarized in Scheme 1, in steps a—m.



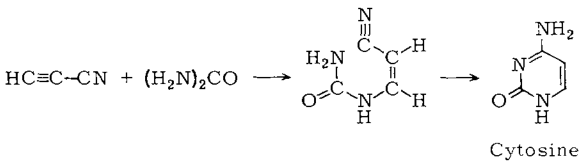
Scheme 1. Possible processes on the prebiotic earth. a) to m) see text.

a) Electrical discharges in mixtures of these gases have led to HCN, $H_2$, $CH_2O$, propynenitrile, and hydrocarbons[4-6].

b) Adenine and guanine have been obtained by cyclic oligomerization of HCN and hydrolysis[7-9].

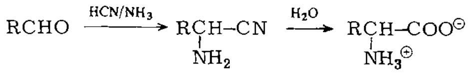


c) Cytosine has been prepared by the reaction of propynenitrile and urea[10].



d) Ribose has been obtained from formaldehyde in the presence of alumina and kaolinite[11].

e) 14 of the 20 amino acids that are protein components could be obtained by electrical discharge and Fischer-Tropsch synthesis in the presence of solid catalysts (nickel-iron, magnetite, clays), and by Strecker synthesis[12-13].

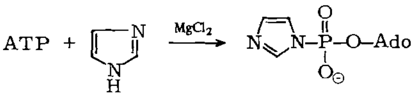


$$\mathrm{RCHO} \xrightarrow{\mathrm{HCN/NH_3}} \mathrm{R\underset{NH_2}{C}H{-}CN} \xrightarrow{\mathrm{H_2O}} \mathrm{R\underset{NH_3^{\oplus}}{C}H{-}COO^{\ominus}}$$

f) Nucleosides have been prepared by the evaporation of aqueous solutions of purines and ribose (or 2-deoxyribose) containing magnesium chloride[14].

g) Heating nucleosides with inorganic phosphates and urea, in the presence of magnesium salts, has yielded mononucleotides (5′-triphosphates). In the absence of $Mg^{2+}$ a mixture of 5′-, 3′-, and 2′-phosphates was produced[15].

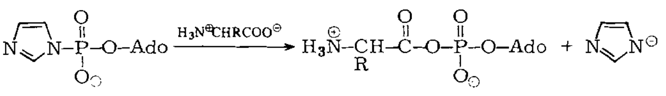
h) Adenosine-(Ado-)oligophosphates such as ATP could be converted into nucleoside 5′-phosphoimidazolides by the evaporation of aqueous solutions containing $MgCl_2$[16].



i) Adenosine and uridine 5′-phosphoimidazolides have been shown to form oligonucleotides with five and more chain members in a reaction catalyzed by $Pb^{2+}$ ions[17].

k) Several cases of template-induced polymerizations of nucleotide derivatives have been observed. Of particular interest are those of nucleoside 5′-phosphoimidazolides, presumed to be available under prebiotic conditions (see h). Guanosine 5′-phosphoimidazolide (ImpG) has been polymerized on a polycytidylic acid template in the presence of $Zn^{2+}$, forming chains of 30-40 members that are predominantly connected in the 3′-, 5′-positions, in an analogous way to the bonding in biological nucleic acids.
When a mixture of ImpC and ImpG and a polycytidylic acid template are used, ImpG (that is, the compound containing the base complementary to the base in the template) is incorporated with high selectivity into the growing strand[18-21].

l) Adenosine(Ado-) 5′-phosphoimidazolide has been demonstrated to form aminocyl adenylates[16].



m) Aminoacyl adenylates have been polymerized in aqueous solution in the presence of specific clays[23-25].

The results in Scheme 1 support the assumption that short strands are able to replicate under special conditions, and it therefore seems promising to search for such conditions. Attempts to achieve template-induced polymerization using deoxyribose instead of ribose were unsuccessful[21], a result that supports the assumed model *i.e.* that the first carrier of genetic information was RNA and that DNA came into the picture at a later stage, when a genetic apparatus for producing enzymes became available.

The results demonstrate that prebiotic synthesis of energy-rich nucleotide derivatives, oligonucleotides, and activated amino acid derivatives required solid-state reactions as well as reactions in aqueous solution and in the gas phase. It is plausible that such substances could have accumulated on primeval earth only in particular locations where a multitude of special conditions were fulfilled, that allowed a succession of very different reactions to occur, requiring highly diversified and structured regions.

## 4. First Steps in the Origin of Life

Chain molecules consisting of two kinds of complementary monomers in a random sequence are considered here as examples of very simple systems with the property of producing copies of themselves. Suppose that such strands may have arisen occasionally by the accidental condensation of monomers. Such strands can then replicate by serving as templates (Fig. 2). Monomers in the solution can attach themselves to complementary monomers along the given strand. The monomers become interlinked and form a second strand, the replicate or (−)-strand. The two strands separate; on the new strand a new replicate forms that is identical with the original or (+)-strand. Repeated strand replication can, of course, take place only with suitable kinds of monomers and requires appropriate conditions, such as highly specific periodic temperature changes. Since the primordial planet exhibited an immense variety of environmental conditions, it is almost certain that the required temperature variations existed in small localized regions.

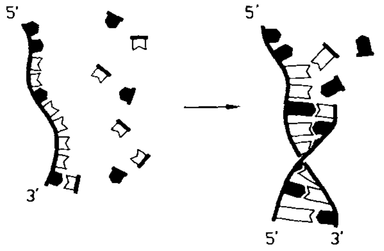


Fig. 2. Replication along a template strand. The template strand and its replicate form a double helix.

We may thus imagine a short nucleic acid strand on primordial earth containing the two complementary bases guanine and cytosine that are anchored together in the strand by ribose and phosphate groups and are capable of interlinking by three hydrogen bonds. It is further supposed that this short strand has diffused into one of the special regions mentioned, after having been formed elsewhere by accidental condensation during the drying of a solution of monomers. In this strand, all of the monomers are presumed to be linked in such a way that the strand can serve as a precise template for replication, the chain members being associated by 3′5′-linkages. During replication, a double helix is formed, as in all nucleic acids present in biosystems. The special aspects of such a template strand are that its monomers are spatially situated in a way that is appropriate for the attachment of replicate monomers, which are then in a favorable position to interlink into the daughter strand. A helical arrangement favors rapidity and precision of chain replication, because the environment of each new building block that is to be attached is the same as that of the preceding block, resembling the situation of a sequence of steps in a spiral stairway. The bases of neighboring nucleotides along the template and growing daughter strands are stacked, increasing with each added nucleotide the energetic stability of the growing double helix that involves interaction between solvent molecules as well as the stacked bases. The template-directed polymerization runs along the 3′5′-direction of the template strand, while the direction of the daughter strand is in the opposite sense, its 5′-end being at the 3′-end of the template strand.

All of this requires monomers of the same chirality. It is accidental which chirality the original strand has, since the process would work just as well if the mirror images of all monomers were used. However, the appearance of an appropriate template strand is decisive for the chirality of all subsequent daughter strands. Hence, it is not surprising that the chirality of the building blocks in all living systems of a given kind is the same.

By considering a solution of the different monomers that may have existed on earth at the location considered (see[2] Section 18.1.4.1.), it is possible to estimate the probability with which the very special original template strand can be formed through accidentally correct condensation. In this way, the plausibility of such a step can be justified for strands containing, for example, ten monomeric units. There should be one correct strand in approx. 0.1 mmol of strands of randomly condensed monomers, *i.e.* in one of $10^{20}$ strands (cf. also Section 17). For longer strands the probability that all monomers are linked in the correct way is much smaller, so that model considerations must begin with short strands.

The probability of the spontaneous appearance of a correct strand of 10 monomers may be compared with that of obtaining an unbroken sequence of 26 sixes when throwing dice. The latter probability is $(1/6)^{26}$ or also about $10^{-20}$. The example may clarify the proposition that by trying one's luck with a sufficient number of dice even such an exceedingly improbable event can be made to occur with near certainty. Thus, when $10\times6^{26}=10^{21}$ dice are used simultaneously the event is expected to occur for about $10^{-20}10^{21}=10$ dice. It can therefore be assumed with a probability close to unity that at least one of the dice used shows a six in each of 26 successive throws (more exactly with a probability of $1-[1-(1/6)^{26}]^{10\cdot 6^{26}} \simeq 1-(1/e)^{10} \simeq 0.99995$).

By continued replication many such strands are formed, once an appropriate template strand has arisen and has accidentally diffused into a favorable location in which the conditions required for replication prevail. Disregarding processes of loss there should be 2 strands after one generation, $4=2^2$ strands after 2, and $2^n$ strands after n generations. Eventually, a stationary state is reached in which as many strands are created by replication as disappear by losses *e.g.* by strand diffusion from the favorable region.

## 5. Barrier Caused by Too Many Errors

Every so often, strands become lengthened by the accidental condensation of two short strands. This can readily occur, in contrast to the spontaneous formation of a longer strand by the direct linkage of monomers. Longer strands diffuse more slowly and thus have better chances to stay in the favorable region than short ones. As time passes, ever longer strands are made and the shorter ones disappear. However, with growing strand length the probability increases that, during replication, a monomer is built into a "lethal" daughter strand, preventing renewed replication of the new strand, *e.g.* because some monomer contains an incorrect sugar. Hence there is an upper limit to feasible chain length extension and as shown by quantitative considerations this is reached with about 50 monomers (see [2], Section 18.1.4.1. therein).

It can also happen that a non-complementary nucleotide (*e.g.* G instead of C) is incorporated as monomer during replication. The new strand can still be used as a template for replication, but its nucleotide sequence is different from that of the parent strand. In time, strands with all possible sequences are therefore formed.

Strands may fold into specific conformations by internal pairing of complementary bases, provided the base sequence is appropriate[*]. Such conformations can confer selective advantages upon existing *forms*, as the common aspects of similar strands will be called. Some conformations make strands resistant against chemical attack, for example, by the mutual protection of adjoining regions. However, any given conformation, such as that of a partial hairpin (Fig. 3), is tied to an exact sequence of nucleotides and is therefore lost by almost any new error. If a favorable folding conformation has arisen, by accident, it is soon lost because of the high level of replication errors with 50 monomers, the approximate number for any reasonable sophisticated folding conformation.

The model thus leads to difficulties at this point. An insurmountable limit of the amount of information that can be transferred by replication appears to have been reached. It is hard to see how an accumulation of errors can be avoided in such first self-reproducing systems, how a form does not "forget" what it has "learned".

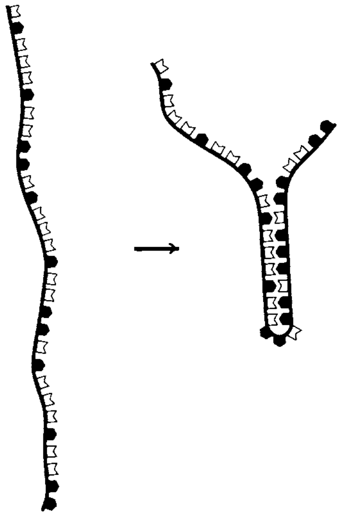


Fig. 3. Nucleotide sequence that permits a partial hairpin conformation.

## 6. Faulty Replicates Rejected During Aggregate Formation

This barrier can, however, be surmounted by a very simple mechanism that nonetheless has far-reaching consequences within the model. Consider a strand, that is capable of assuming the conformation of a hairpin along its entire length, with the hairpin bend at the middle of the strand because of an appropriate sequence of nucleotides (Fig. 4). A strand that arises by the template replication of

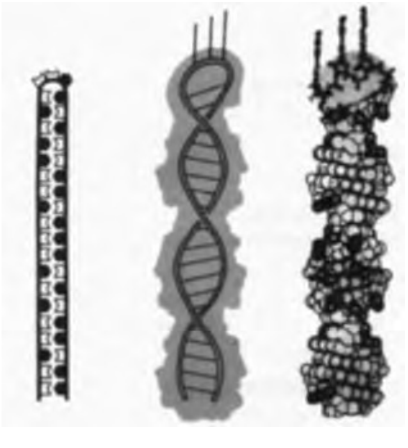
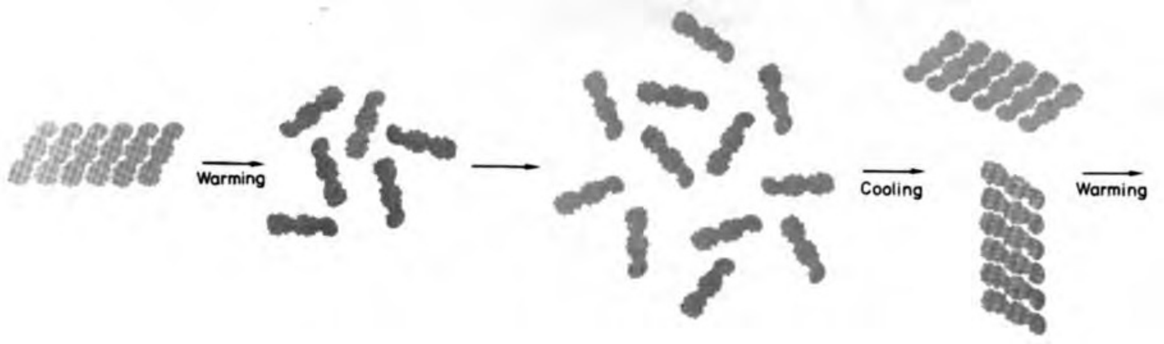


Fig. 4. Left: Possible arrangement of bases G and C that permits a hairpin conformation along the entire strand. The supposition that early strands contained, mainly or exclusively, just these two nucleotides is made plausible by comparative studies of nucleotide sequences of different transfer ribonucleic acids by *Eigen* and *Winkler* [41]. Middle: Schematic drawing of hairpin strand conformation in which the "legs" of the hairpin form a double helix. The outline is that expected for the van der Waals radii. Right: Molecular model of hairpin strand. For clarity the upper portion is shown as a ball- and stick model, the lower portion as a space-filling model. Double helix is left-handed as recently found by *Rich et al.* [35] and *Dickerson et al.* [36] in an X-ray crystal analysis of guanine-cytosine oligonucleotides, and by *Arnott et al.* [37] in GC DNA fibers. A left-handed double helix had been discussed by *Pohl* and *Jovin* [38] as the result of a phase transition at high salt concentration.

---

[*] For transfer RNA, such conformations have been established by X-ray structure determinations [33]. The melting of different regions of single strands, upon temperature increase, has been investigated by examining high-resolution $^1$H-NMR spectra that reveal gradual transitions from folded to unfolded conformations [34]. Upon cooling, the original folding conformations establish themselves error-free. The change between the unfolded single-stranded and the double-stranded forms of nucleic acids occurs between about 30 and 100 °C, and one may count on the existence of such temperatures on prebiotic earth.



a hairpin is automatically capable of again assuming a hairpin conformation (cf. Fig. 13). From detailed examinations of space-filling models it turns out that in a suitable medium, such hairpin strands can form aggregates with amazing precision (Fig. 5). The precision of aggregation is such that faulty hairpins are rejected during aggregate formation, so that in this way an all-important error-filtering mechanism is brought into being. The aggregates may be stabilized by suitable bivalent cations, such as $Ca^{2+}$ ions, that hold together negatively charged phosphatidyl groups on the outside of neighboring hairpin strands. The number of monomers considered to comprise such hairpin strands roughly corresponds to that of today's transfer ribonucleic acids (70—80 monomers), a point that is significant and to which we will return.

Fig. 5. Aggregation of two convoluted hairpin strands.

The survival chances of strands in an aggregate are increased by their mutual protection against chemical attack, or because it may be less easy for aggregated strands to leave the favorable region. Aggregates may undergo self-reproduction. Suitable temperature and other environmental changes may cause their disassembly into component strands. The individual strands may replicate and again assume folded conformations. They are thus able to diffuse and again aggregate through favorable accidental collisions, hence, increasing the number of aggregates. All of this requires a very specific and highly detailed program of temperature changes that must be periodically repeated for repetition of the process described. Convolution of strands and aggregation are favored by cooling, disassemblage of aggregates and deconvolution of strands by warming. However, a myriad of cyclic temperature programs existed on the primordial planet (Fig. 6), and it is almost certain that an appropriate program was realized at least once, in a region that need not have been larger than about 1 mm across (see [2], Section 18.1.4.2).

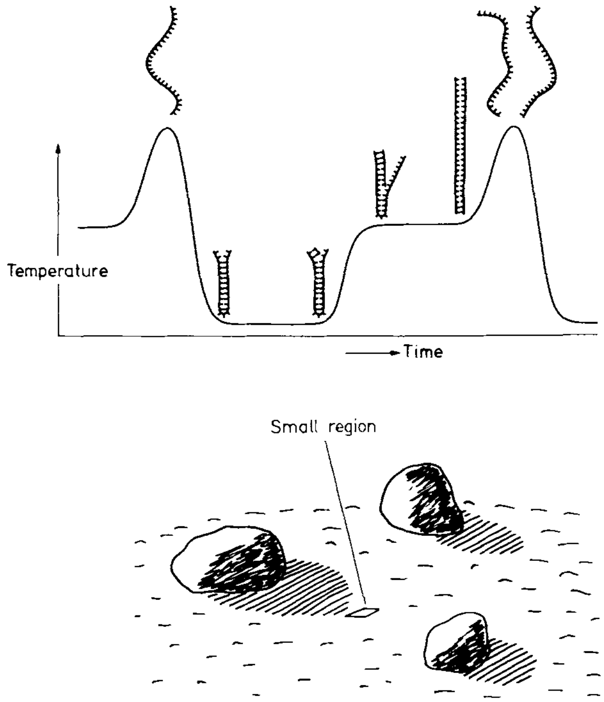


Fig. 6. a) Multiplication of aggregates by disassembly into strands, replication of the strands, and reaggregation. b) Schematic temperature variation required for strand replication. At the highest temperatures the strands are uncoiled. As the temperature decreases, internal base-pairing occurs and the strands convolute, taking up *e.g.* the conformation of a hairpin. In this conformation, replication could only start at an end of the hairpin and progressed from there as the temperature rose and internal base pairing began to weaken. The aggregation of convoluted strands and the later disassembly of aggregates requires an additional superimposed cyclic temperature variation. c) Realization of periodic changes in temperature by shadow-casting rocks in a region of small linear dimensions (*e.g.* 1 mm). The rocks are immersed in a broth of energy-rich monomers.

It is of importance that the component strands do not diffuse too far from each other during the multiplication phase, because they would be lost and reaggregation could no longer occur. The phenomena discussed must therefore have taken place in a confined space, such as in small pores of a rock formation. The pore walls kept the strands together during their diffusion, so they were able to locate each other again and could form new aggregates. The rock formation is presumed to be inundated by a solution of suitable energy-rich monomers that could easily diffuse through the pore channels, while the strands formed were largely retained by them (Fig. 7). Neighboring pores are invaded by strands, and the descendents of the aggregates formed in the original pore slowly spread through the porous material. Detailed considerations lead to a pore diameter of about 500 *nm* or 5000 Å (see [2], Section 18.1.4.2d). For purposes of comparison, this is of the order of magnitude of a bacterium.

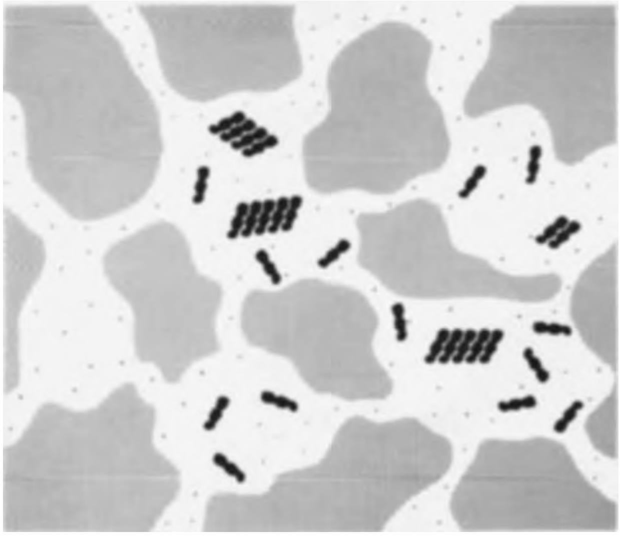


Fig. 7. Pores with channels, into which monomers can readily diffuse while strands capable of forming aggregates and serving as templates for replication are mostly held back.

Aggregates such as those described, offer crucial selective advantages because they are capable of invading larger pores than single strands. Additionally such advantages would result from machinery that facilitated the assembly of convoluted strands into aggregates. Both the disassembly of aggregates and their later reassembly must have come about easily and quickly. Linear aggregates consisting of essentially identical component parts are especially favored by these requirements, because they can fall apart suddenly (as would not be the case for three-dimensional aggregates), and any one of the component parts can reaggregate with any other one. The requirements would be met by the aggregates of hairpin strands just discussed.

## 7. The Assembler

A large selective advantage would be inherent in machinery that speeds the assembly of convoluted hairpin strands. A model of a simple mechanism, that would serve this purpose, consists of an extra unfolded strand that has become attached to one of the hairpin strands (Fig. 8, left). The extra strand is assumed to be capable of acting as a *collector strand* that guides other hairpin strands to the location of growth of the aggregate; in essence, the collector strand converts the spatial diffusion of folded strands to be aggregated into a one-dimensional diffusion along the open strand (Fig. 8, middle). They may, for example, migrate from one place of attachment on the collector strand to the next. The carrier of the collector strand acts as an initial *nucleation site* in the formation of the picket fence-like aggregate, serving also as its endpost (Fig. 8, right). The orientation of the hairpin strand forming this endpost is opposite to that of the other hairpin components of the aggregate.

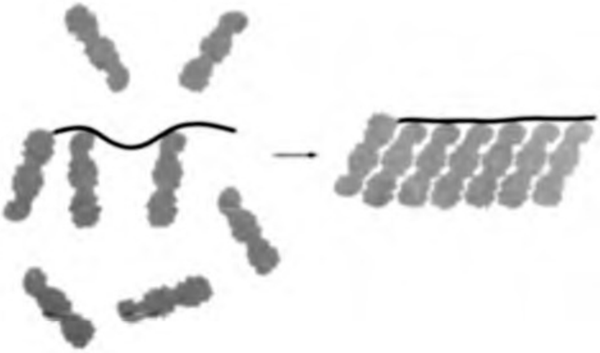


Fig. 8. Mechanism facilitating the aggregation of hairpin strands. Left: The hairpin strand on the far left is turned upside down and has an unfolded strand attached to it that can function as collector strand. Right: Picket fence-like aggregate formed in this way.

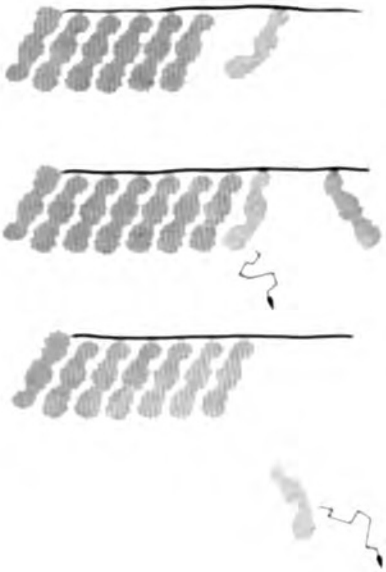


Fig. 9. Mechanism facilitating aggregation acts as an error filter. Top: Strand with error that convolutes to faulty hairpin which diffuses along the collector strand. Middle: Faulty hairpin does not fit into the aggregate and is rejected, a correct copy taking its place (bottom).

Figure 9 shows, in detail, how the aggregate formation by the *assembler* just described causes the all-important rejection of erroneous copies and in this way prevents the accumulation of replication errors. The consequence of this error-filtering action is that the hairpin components of an aggregate are essentially error-free. Without it, a hairpin formed by accident would lose the information "hairpin" within a few generations. The components of an aggregate "co-exist" in this sense; they form a functional cooperative that survives or dies as a whole and that evolves as an entity.

In the proposed *molecular* model the hairpin strands are attached to the collector strand by base-pairing of triplets of complementary nucleotide pairs, as shown schematically (Fig. 10). The model exhibits an astonishingly precise fit between neighboring hairpin strands (Fig. 11 and 12).

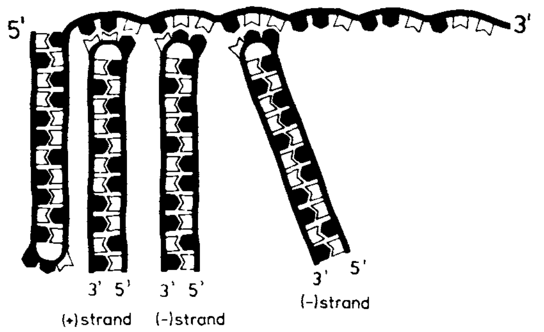


Fig. 10. Details of base pairing in aggregate being formed. Note attachment of hairpin strands to collector strand by triplets of complementary bases.

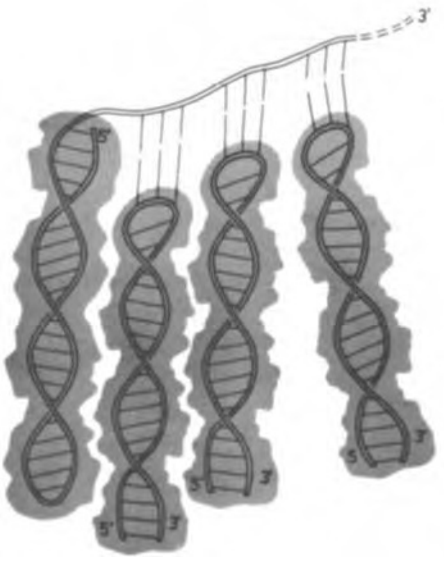


Fig. 11. Spatial arrangement of strands shown in Fig. 10. Hairpin "legs" are twisted into double helices and outlines are as expected for van der Waals contacts.

Equally precise is the fit among the stacked bases in the triplets of complementary base pairs just mentioned. The excellent fit shown in the figures appears to be ruined in models in which the hairpin strands are attached by more than three bases to complementary bases on the collector strand. On the other hand, at least three nucleotides are needed to form the 180° bend of a hairpin. Finally, there is an excellent fit between the hairpin strand of opposite orientation at the beginning of the aggregate and the first hairpin strand adjoining it. All fits appear to require that the 3'5'-strand directions are as indicated in Figure 10.

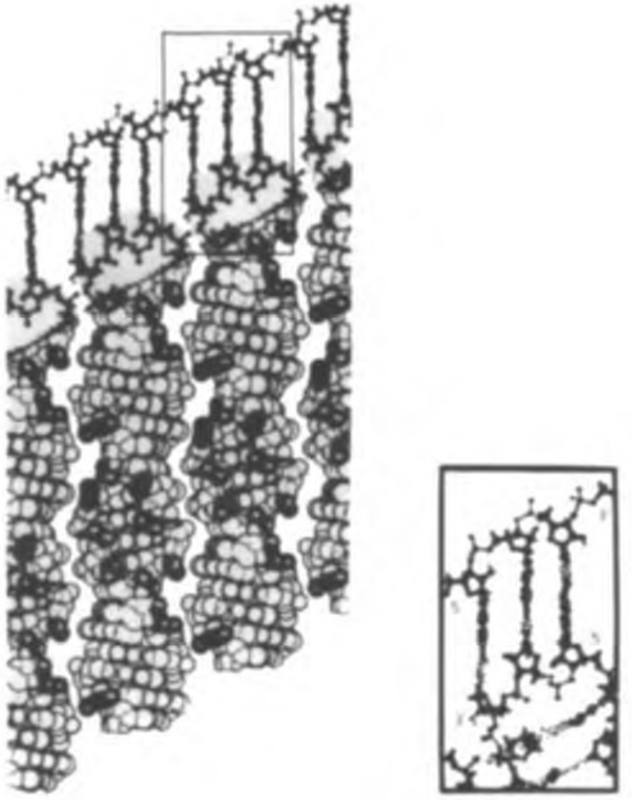


Fig. 12. Details of the excellent fit between the different hairpin strands in a picket fence-like aggregate and between the base triplets at the hairpin bends and complementary triplets along the collector strand (inset). No equally good fits seem to be possible with hairpin strands in the usual right-handed helical conformation.

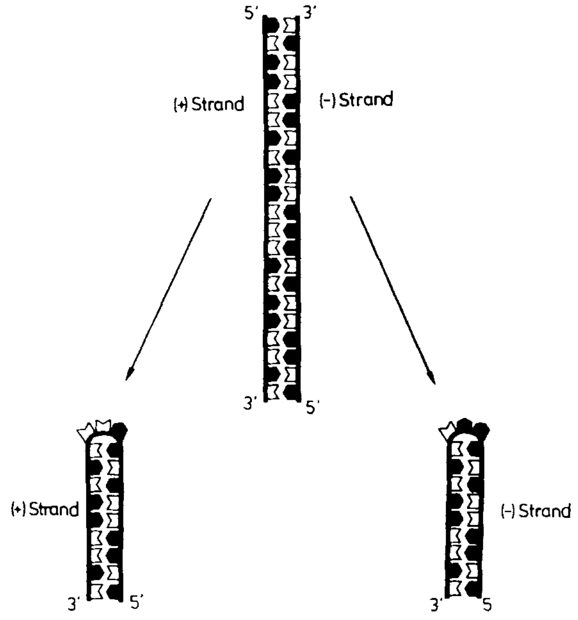


Fig. 13. (+)- and (−)-hairpin strands. Middle: Upon completion of replication, with bases paired. Left: (+)-Strand in hairpin conformation. Right: (−)-Strand in hairpin conformation.

An important feature of this model is that both (+)- and (−)-strands can be used as components. This feature permits great economy in the use of strand material and in the assembly of aggregates. Except for the bases in the middle, which are complementary to each other, the (+)- and (−)-strands are identical (Fig. 13).

The nucleotide in the first position of the triplet at the hairpin bend could, for example, be C in (+)-, as well as, (−)-strands; in the third position it then has to be G in both strand types. At the corresponding first positions of the collector strand there would then always have to be G and at the third positions C. The midpositions can be randomly occupied by G or C. If a midposition of the collector strand contains G, then a (+)-strand can attach itself, and in the other situation a (−)-strand. In this way, a simple "reading frame" would be established. A "word" on the collector strand would always begin with G and end with C.

The bonding energies of base pairing are insufficient at room temperature to establish stable bonding between two triplets of bases. It is therefore reasonable to imagine that a hairpin strand is first attached only very loosely to the collector strand. Each newly acquired hairpin strand can then move back and forth along the collector strand until it reaches the growth region of the aggregate, where its attachment is stabilized by close fit to the hairpin strand preceding it on the aggregate. The model therefore permits the postulated one-dimensional diffusion along the collector strand. The new hairpin strand is firmly incorporated if its triplet contains the appropriate bases that must be complementary to the corresponding bases on the collector strand; it is discarded if this is not the case. Each newly incorporated hairpin strand provides additional stabilization to the portion of the aggregate that already exists. If this mechanism is to function as described, the binding energy for the lateral interactions between a newly incorporated hairpin strand and the one preceding it must be approximately equal to the binding energy of its base triplet and the corresponding triplet on the collector strand. If this energy were smaller, there would be no firm incorporation at room temperature. If it were larger, any hairpin strand would be firmly incorporated regardless of whether its base triplet were complementary to the corresponding triplet on the collector strand or not.

The direction in which the triplets are read along the collector strand is the same 5′3′-direction in which today's genetic blueprint, the strand of messenger ribonucleic acid, is read. Similarly, the triplets of the hairpin strands of the aggregate are in the opposite 3′5′-direction, as are the anticodon triplets of today's transfer ribonucleic acids. It is quite striking that the excellent fit of the hairpin strands in the aggregate is just as one would wish from the model, and it is therefore easy to imagine that the collector strand is the primordial form of today's messenger ribonucleic acid. The hairpin strands would be the primordial forms of the adapter or transfer ribonucleic acid molecules mentioned at the beginning. As mentioned earlier, they would contain about the right number of nucleotides. The aggregates would represent the primordial forms of the translation apparatus.

The experimental realization of such aggregates is of considerable importance, and the search for conditions (high ionic strength or suitable solvent) that would favor the folding of strands of GC ribonucleic acid into the hairpin conformation of our model, the *Arnott-Rich-Dickerson* left-handed double helix would be of interest[*]. The conditions (strand length and medium) must be chosen in such a way that stabilization by the lateral fit of neighboring hairpin strands would be of exactly the correct magnitude. Under these circumstances formation of the described aggregates is predicted[**]. It can also be imagined that the interlocking of just two hairpin strands and their attachment to the collector strand results in an aggregate of sufficient stability to facilitate further aggregation. The nucleation center at the end of the collector strand would then be unnecessary and could be omitted. Such systems would also represent fruitful research targets.

The view that the collector strand is the primordial form of the carrier of genetic information is supported by sequence analyses of the DNA of viruses, procaryotes, and eucaryotes by *Shepherd*[40]. The clear periodic correlation found, indicates that the reading frame PuNPy (Pu = purine, like G; Py = pyrimidine, like C; N = purine or pyrimidine) originally existed, vestiges of which are still in evidence.

The concept that the hairpin strands are the primordial forms of transfer ribonucleic acids is supported by the most recent studies of *Eigen* and *Winkler*[41], who have found a great similarity in the sequences of the different transfer nucleic acids they compared. These findings led them to an *ancestral* sequence that is therefore derived from empirical data. It exhibits a certain symmetry in the sense that it permits a strand with this sequence to convolute into a hairpin conformation (or into the cloverleaf conformation considered by *Eigen*). This result makes the model so far described even more attractive, but the question still remains as to how the machinery described could undergo the astonishing transformation into an apparatus capable of translating nucleic acid sequences into amino acid sequences or proteins.

## 8. Catalytic Activity of Aggregates

Let us proceed to develop the model further and see where our considerations lead. How could the aggregates

---

[*] Recently, *J. H. von De Sande* and *T. M. Jovin* of the Max-Planck-Institut für Biophysikalische Chemie, Göttingen, have found evidence of a conformational change in GC ribonucleic acids, that suggests a transition to a left-handed helix, as postulated. In an aqueous solution of GC-RNA, containing $NaClO_4$ and 20% ethanol, a concentration increase of the salt from 4.8 mol liter$^{-1}$ to 6 mol liter$^{-1}$ causes a change in the sign of the circular dichroism (DC) maximum at 284 nm (from + to −), while the maximum is shifted to 294 nm. The CD spectrum of GC-RNA at the higher salt concentration is very similar to the spectrum of the left-handed *Arnott-Rich-Dickerson* form of GC-DNA. The change in conformation is associated with a marked increase in tendency towards aggregation just as would be expected on the basis of our model (personal communication). In the methylated polynucleotide (poly(dG-m$^5$ dC) the transition into the left-handed helix conformation can be induced at a $Mg^{2+}$ concentration three orders of magnitude lower than that required for the unmethylated polymer, *i.e.* close to usual physiological conditions (*M. Behe* and *G. Felsenfeld*, Proc. Natl. Acad. Sci. USA *78*, 1619 (1981)).

[**] Current views of possible DNA and RNA double helix conformations and their dependence on the nucleotide sequences are still in considerable flux and further stable conformations may well be found (cf. *e.g.* the DNA conformation recently proposed by *Hopkins* [39]). What is of importance to our model is the close fit of neighboring hairpin strands, and it makes no difference whether a good fit can be achieved by left-handed or right-handed double helices or by yet another conformation.

consisting of collector strand and hairpin strands develop catalytic properties for use in protein synthesis?

It was noted earlier that errors in the nucleotide sequence of a hairpin strand can affect its conformation and in this way prevent it becoming part of an aggregate (cf. Fig. 9). However, not all errors are important in this regard, only those that affect lateral contacts between neighboring strands in an aggregate. Errors at the hairpin ends are of little or no consequence with regard to aggregation, and these ends can easily open-up when replication errors disturb the pairing of the first and last two bases (Fig. 14).

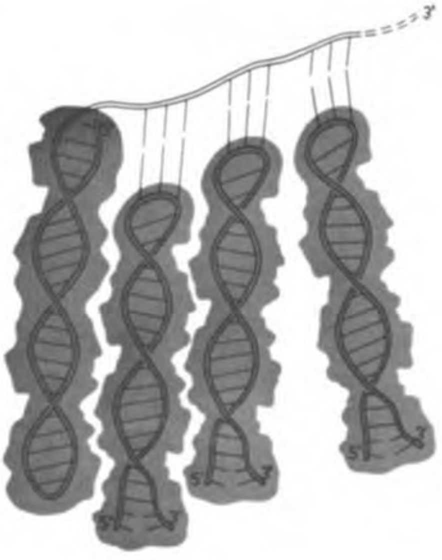


Fig. 14. Hairpin strands in which the last few bases at the strand ends are not complementary and for this reason are not paired. The open hairpin ends do not affect the precision with which the hairpin strands fit together in the aggregate.

In fact, even in the earliest hairpin strands these ends could have remained open: Open ends would only be of help in permitting the start of replication at a strand end (cf. Fig. 6b), and would impart selective advantages upon such strands by preventing the confusion that would arise if strand replication began simultaneously in several locations.

We now postulate that amino acids, linked to appropriate activating groups, became attached to these open ends. The existence of amino acids on the primordial planet can readily be assumed, because they are easily obtained in simulations of prebiotic conditions (Section 3). Once attached to the hairpin ends of an aggregate these amino acids are assumed to readily form mutual polypeptide bonds, being held in close proximity by the hairpin ends and satisfying other steric conditions. The polypeptide chains formed are then released and the entire process repeated (Fig. 15).

In our model, polypeptides consisting of glycine and alanine, the two amino acids that are produced in the largest amounts in prebiotic simulations, bestow great advantages upon forms producing them: Being hydrophobic and capable of agglomeration they formed impediments in pore channels and in this way slowed down diffusion, making possible the colonization of pores with wider channels

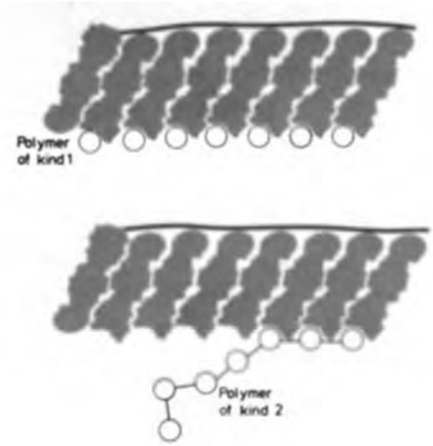


Fig. 15. Catalysis of polypeptide formation. Top: Hairpin ends exhibit an affinity towards activated amino acids that, once attached, can form polypeptide bonds. Bottom: The completed polymer is released.

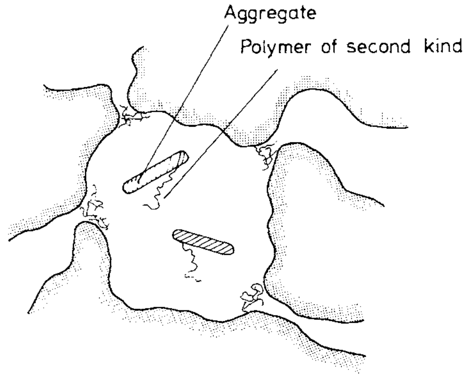


Fig. 16. Polypeptides serving as impediments to diffusion in pore channels.

than before (Fig. 16). At a later stage, they coalesced into some sort of "cellular" envelopes that again furthered the propagation of forms producing them (Fig. 17). The envelopes presumably acted as nets, allowing mononucleotides to enter and preventing nucleic acid strands from leaving[*]. This requirement can be fulfilled by agglomerated polypeptides, but not by lipids, which therefore are expected to be useful and to become cell membrane constituents only at the time a specific semipermeability is required[**].

---

[*] The significant function of a polymer envelope as a barrier against diffusion has already been recognized by *Oparin* [42], who investigated coacervates. Coacervates form a pre-existing structure, as is the case for the porous rocks in the present model. Note, however, that in our model the polymer envelopes have the function of liberating the evolving system from the pre-existing porous structure. Their position in the logical framework of our model is thus completely different from that of the coacervates in *Oparin*'s picture. If one assumes (together with *Oparin*) that polypeptide envelopes were available even at the beginning, then no selective advantages would have accrued in aggregates that might have accidentally arisen with catalytic properties towards the formation of envelope components. No selective pressure in the direction of envelope producing systems would have existed in such a situation.

[**] The polypeptide envelope could also be endowed with certain catalytic properties towards the hydrolysis of nucleic acid strands, accelerating the degradation of erroneous copies that are not included in aggregates. The liberated mononucleotides would be available for strand synthesis and selective advantages would be gained.

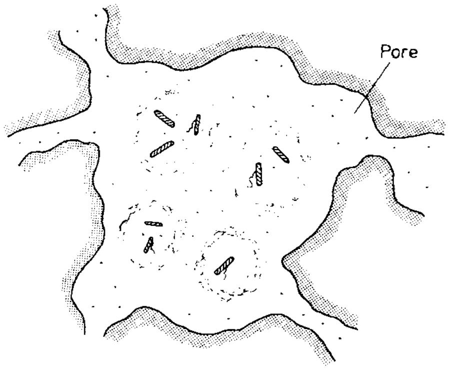


Fig. 17. Polypeptides serving as "cellular" envelopes.

Note that the formation of stable structures such as impediments and envelopes requires monomers, such as amino acids, with properties that differ from those of the monomers that make up the strands. The reason is that these structures must remain intact during the environmental changes that drive the replication of aggregates and strands.

Any change that permits a liberation from the region of small pores, increases the possibilities for multiplication because the changed form does not face competition in the new region. This effect, the advantage of the more complex form in the colonization of new domains, leads to continued evolution in the direction of more complex forms. The increase in refinement of evolving forms is a necessary consequence of the variety and the multi-faceted wealth of environmental conditions. Without such variety, no selective gradients would have existed and there would have been no evolution.

## 9. The Translation Apparatus

The evolution of polypeptides, that serve as impediments and later as envelopes of increasing complexity, leads to another important development. To see this, it should be remembered that both (+)- and (−)-hairpin strands, both of which are always present, can be built into the aggregate side by side. The two strand types are identical except that they have complementary bases in the midposition and in corresponding positions at the ends of the strands (Figs. 13 and 18). If the ends of a (+)-strand are occupied by the bases G, for example, then there must be bases C at the ends of a (−)-strand. The two kinds of strands could then have different affinities for two kinds of activated amino acids. At the same time, the two kinds of strands have different bases in the midposition in the middle of their anticodon triplets. In this way an automatic correlation would exist between amino acids and bases in the middle of the anticodon triplet, and as a consequence of this, a correlation between the sequence of nucleotides on the collector strand and that of amino acids in the polypeptide. The hairpin strands would serve the function of adapter molecules.

A possible explanation of how a specific linkage of an amino acid to a nucleotide could have arisen is illustrated for (+)-strands at the very bottom of Figure 18. The amino acid $a_1$ is activated by a purine nucleotide (G) (cf. Scheme 1, step 1). Intercalation and complementary base pairing would then mediate specific linkage and place the amino acid in such a position that reaction with the 2′-OH group of the ribose of the terminal nucleotide of the strand could occur. Our molecular model shows that the whole sequence of steps described would be sterically quite plausible, permitting reaction with the 2′- as well as the 3′-OH

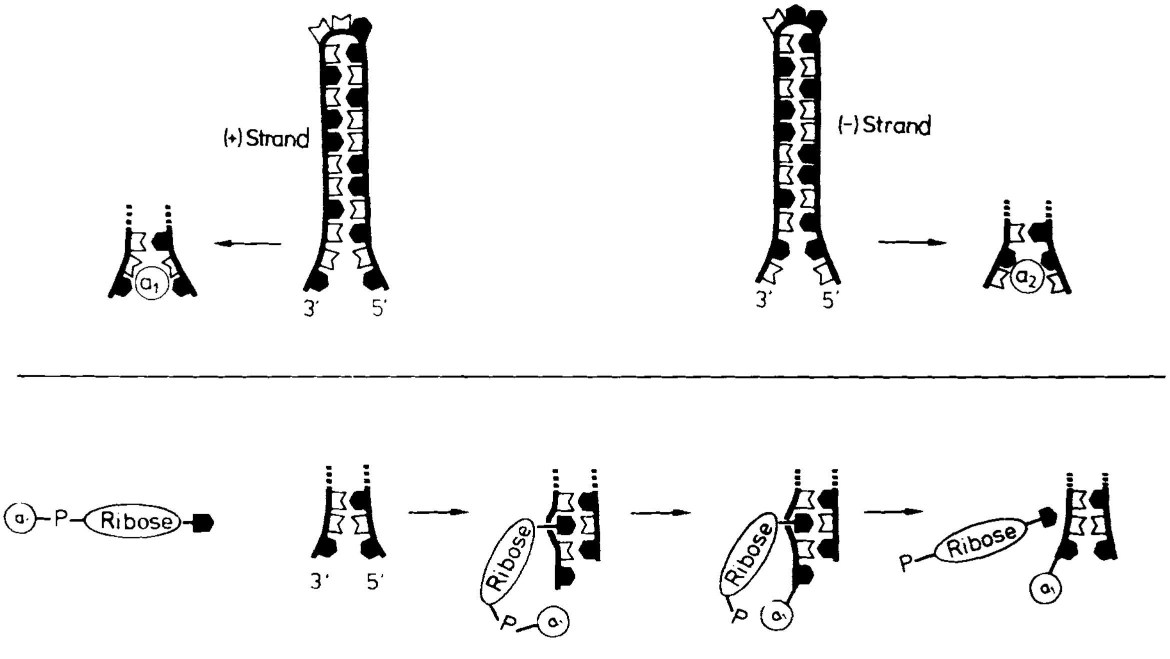


Fig. 18. (+)- and (−)-hairpin strands as adapters for amino acids $a_1$ and $a_2$. Note that the two strands are identical expect for the nucleotides in the middle and the ends of each strand. Top (left and right): Attachment of amino acids in highly schematic view. Bottom: possible mode of attachment of an amino acid $a_1$ that has been activated by a purine nucleotide to the end of a (+)-strand.

group of the ribose in question. This would correspond to the same linkage that is found in today's charged tRNA. Amino acid $a_2$ could be activated in a corresponding way by a pyrimidine nucleotide (C) and then linked to the terminus of a (−)-strand. A specific enrichment in activated amino acids in special locations of the prebiotic planet can readily be imagined[*].

The nucleotide sequence on the collector strand changes slowly with time, and periodically a sequence can occur that corresponds to a polypeptide exhibiting traces of enzymatic properties, which acts as a primitive *"replicase"*, *i.e.* as an enzyme that accelerates replication and reduces the number of replication errors. This primitive replicase would have to decrease the frequency of these errors sufficiently, so that the information coding for it would not be lost during the number of generations required to fix it by selection. Without replication, improvements of this kind would be "forgotten" by the form within a few generations.

A quantitative estimate shows that these conditions can be achieved even by quite weak enzymatic activity. For example, if the survival rate is increased by just 10% by the advent of a "replicase" consisting of ten amino acids, a reduction of the replication error rate per base from 1/100 to 1/300 is sufficient for fixation by selection (see [2], Section 18.1.4.3).

It can be imagined that such replicase activity can be achieved, for example, by a short polypeptide that fits into a notch of a double helix which exists in the region where the new strand is formed during strand replication, and which slips along in the notch, remaining in the region of replication as the new strand is lengthened[**]. Its presence would stabilize the double helix conformation during replication and improve the contact between the two strands in that region. Replication would be accelerated and there would be fewer errors in base pairing during replication.

If the conditions for the formation of the aggregates described were known, attempts could be made to produce the postulated polypeptides from activated glycine and alanine or perhaps from two other amino acids. Once the circumstances of aggregation and template-directed strand synthesis are understood, they could be used to formulate an appropriate periodic temperature program that could be used to direct the reproduction of aggregates, with a view to the gradual appearance of a replicase.

The attainment of a replicase represents a major breakthrough; the development of machinery for reading and translating a code. It permits the evolution of systems with further enzymes. Progress could now proceed at a rapid pace. Additional bases and positions in the codon triplet became incorporated into the code and the code translator became more sophisticated. No difficulties arose in this regard in computer simulations in which codes first for two, and later for up to six amino acids were allowed to evolve[44]. Cooperation develops between the different components inside the envelope, and the whole grows into a functional cooperative. The evolution of ever more refined replicases permits the genetic transmission of ever larger amounts of information between parent and daughter systems.

This, in principle, is the answer to the question posed originally of how a translation apparatus, that consists of translation products, could arise. In our model a very simple process is decisive; the astonishingly precise fitting together of building blocks consisting of a nucleation unit, a collector strand, and hairpin adapter strands.

## 10. Further Details of the Primordial Translation Process

Even the earliest concept of the present model of a translation apparatus[1] at first featured the middle position of the nucleotide triplet used in the attachment of the collector strand as the only position employed for coding. If it is further assumed that, in the beginning, only the bases G and C were used in strand nucleotides, then the first and third bases of the anticodon triplets mentioned would always be G and C, respectively, or reversed C and G (because of the symmetry properties of (+)- and (−)-hairpin strands discussed earlier). These two positions would thus, at first only have been used to fix the "reading frame" for code triplets. The actual code words for amino acids would then either have been CCG and CGG, or GGC and GCC. *Eigen* and *Schuster*[45] have opted for the second possibility, since GGC codes for glycine in all biological organisms, and GCC for alanine, the two most prominent amino acids of prebiotic chemistry. A reading frame of the form PuNPy is also favored by *Shepherd*'s results mentioned in Section 7[40]. After the invasion of the midposition by A and U, the triplets GAC and GUC became available. These triplets code for aspartic acid and valine, respectively, also among the most abundant amino acids in simulations of prebiotic terrestrial conditions. Aspartic acid is hydrophilic and it can well be imagined that with its availability the development of polypeptides with enzymatic activity became possible.

*Crick, Brenner, Klug,* and *Pieczenik*[46] have developed a model of an early primordial translation apparatus, that also consists of a strand of messenger RNA and adapters; however, they have not indicated how such an apparatus might have evolved. The difficulty that three base pairs are insufficient for stable attachment of adapters to a messen-

---

[*] Aside from chemical differences that may cause one kind of amino acid to be activated by a purine nucleotide and another by a pyrimidine nucleotide, physical differences between the activated molecules may also exist. It is conceivable, for example, that there is little difference between the two modes of activation of a given amino acid at the site at which activation takes place, but that separation of different species occurs by a physical effect, *e.g.* by differences in chromatographic properties. It can readily be imagined that a mixture of activated amino acids is adsorbed on a substrate such as montmorillonite clay and then eluted by an aqueous solution of inorganic salts, separate zones being formed with $a_1$-G in one location, $a_1$-C in another, *etc.*; the zones serving as physically separated reservoirs of activated species. The pores in which the crucial action takes place would then be in the vicinity of suitable reservoirs, so that *e.g.* $a_1$-C and $a_2$-G would be able to trickle into the porous region. It is easy to separate nucleotides in cationic as well as anionic exchange columns, using aqueous salt solutions as eluants [32].

[**] Investigations of specific binding of proteins on nucleic acids have shown that a section in a polypeptide of, say, ten amino acids can form a two-stranded antiparallel β-sheet that fits into the groove of a double helix [43]. It would be of great interest to search for Gly-Ala-polypeptides with, for example ten amino acids that facilitate a template-directed polymerization of nucleic acid strands and act as primitive replicases in this fashion.

ger strand is overcome in their model by postulating that five base pairs are used in the bonding and are, moreover, involved in a flip-flop mechanism actuated by the state of bonding into a polypeptide of the attached amino acids. (This model was discussed and modified by *Eigen* and *Schuster*[45].) There is no evidence that a similar mechanism is involved in present-day ribosomes[47]. The difficulty that three base pairs are insufficient for stable attachment is overcome in our model by the inter-linkage of neighboring adapters in the picket fence-like aggregate; an interlinkage that contributes decisively to the stability of this cooperative system of close-fitting components (cf. Section 7).

## 11. Ancestral and Primordial Sequences

The important results of *Eigen* and *Winkler*[41] on the sequence analysis of known tRNA's were used in Section 7 to support our model considerations. Their analysis established a probable common *ancestral sequence* of all transfer ribonucleic acids (Fig. 19). Two nucleotides U in positions 60 and 65 and one of the three nucleotides C in positions 61—63 were deleted here to improve the complementary base pairing in the hairpin conformation (*Eigen* and *Winkler* preferred to delete the C triplet, just mentioned, as having probably been added at a later time). *Eigen* and *Winkler*[41] attempted to derive an even earlier *primordial sequence* from this ancestral sequence by assuming that the template coding for the very first polypeptide was identical with the original adapter subunit, the primordial transfer ribonucleic acid. They thus obtained their primordial sequence by changing the ancestral sequence in such a way that along the entire strand, read in the 5′3′-direction, there is a sequence of guanine-N-cytosine triplets (where N denotes any one of the four bases). In Figure 19, these triplets are indicated by brackets; purines (G or A) are shown by filled, pyrimidines (C or U) by open symbols (cf. Fig. 1). Positions in which there is agreement between ancestral and primordial sequences are marked by (+) symbols while (−) symbols indicate disagreement. No distinction was made between different purines or between different pyrimidines.

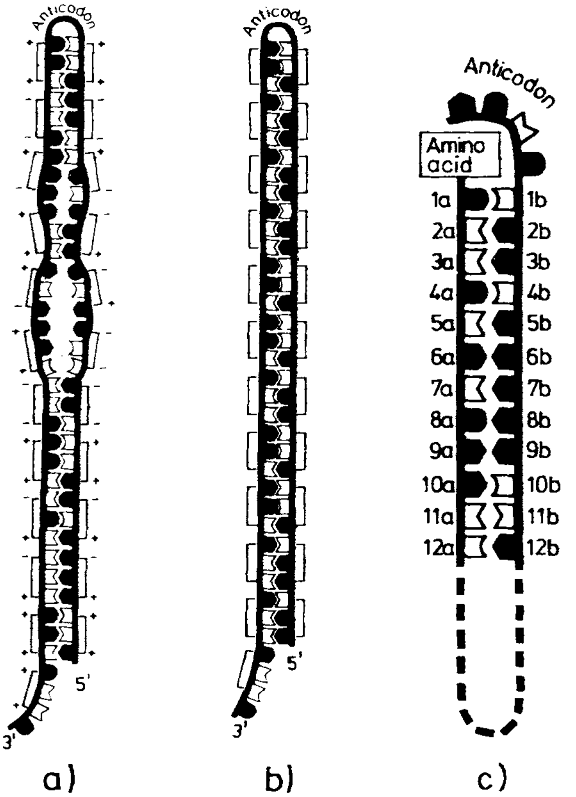


Fig. 19. Ancestral and primordial tRNA sequences. a) Ancestral sequence derived by *Eigen* and *Winkler* from a consideration of known nucleotide sequences of tRNA, shown in hairpin conformation. Three nucleotides, in positions 60, 61 and 65 have been deleted. b) Primordial sequence of *Eigen* and *Winkler* (after [22]). c) Primal tRNA according to *Hopfield* [48]. Nucleotide sequence is that of Val-tRNA of *E. coli*. The primal nucleotide strand contains only half of the present-day tRNA nucleotide sequence, folded in a manner that brings the 3′-terminus (charged here with an amino acid) into proximity of the anticodon triplet.

If we only distinguish between purines and pyrimidines, we find 27 agreements (at 15 "first" and 12 "third" locations) and 19 disagreements, a difference that is considered to be relevant to *Eigen*'s model. In our model a more accidental sequence of the complementary nucleotides along the "legs" of the hairpin is expected, so that the deviation from the average value should be close to that expected for a statistical fluctuation. For a random sequence, agreement would be expected in 23 cases with a standard deviation of $\pm\sqrt{23/2}=3.4$. The value of 27, therefore, does not deviate significantly from the average value. For a random distribution, the chance of finding the observed or a larger deviation from the mean is 30% $\left(2\sum_{i=27}^{46}\binom{46}{i}\Big/2^{46}\right)$.

There might nevertheless be a preference for the sequence PuNPy (where Pu = purine base and Py = pyrimidine base). To investigate this possibility, the frequencies with which the sequences PuNPy, PuNPu, PyNPy, and PyNPu should occur in a random arrangement, in which 15 of the 23 "first" locations are occupied by Pu and 12 "third" locations by Py, are calculated. The probability of the sequence PuNPy is then $15\times12/23^2$ and those of the other sequences $15\times11/23^2$, $8\times12/23^2$, and $8\times11/23^2$, respectively.

The situation, for all of the 23 triplets, is therefore as follows:

| | | | | |
|---|---|---|---|---|
| PuNPy | from Fig. 19a, b: | 9 | statistically | 8±2 |
| PuNPu | | 6 | | 7±2 |
| PyNPy | | 3 | | 4±2 |
| PyNPu | | 5 | | 4±2 |

Again there is no statistically significant difference between the experimental values and those expected in a random situation.

A comparison of the sequences of 20 known tRNA's of *E. coli*[49] that code for 14 amino acids has lead *Hopfield*[48] to another model for primal tRNA. It rests on the assumption that the strand conformation was such that the anticodon and the amino acid of the charged primal tRNA were in direct contact (Fig. 19c). The nucleotide strand of the proposed model only contains the portion of today's tRNA that runs from its acceptor terminus (to which an amino acid can be bonded) to the anticodon triplet. The conformation of the proposed primal tRNA would therefore be different from that of its supposed descendant and the nucleotides shown in juxtaposition in Figure 19c would nowadays be quite distant from each other. *Hopfield* derives support for his model from a statistical analysis of the nucleotide pairs in positions 1a, 1b to 6a, 6b. If these pairs were to exhibit more than *a priori* complementarity, this would constitute evidence in favor of the posited model.

For a random occupation of the six pairs of positions considered by the four kinds of nucleotides one would expect an average of $6 \times \frac{1}{4} = 1.5$ complementary base pairs; while observed values run as high as 5 in the example shown in Figure 19c, the average over the 20 tRNA's is 2.5. While *Hopfield* argues from a number of considerations, that the difference between the values of 2.5 and 1.5 is statistically significant, it appears that a comparison with a random sequence of nucleotides is not pertinent, because the 20 observed sequences are far from random, as can be seen from columns 2 through 5 of Table 1 based on the collection of nucleotide sequences by *Barrell* and *Clark*[49]. Thus, the three nucleotides at the 3'-terminus are always ACC, and most other values in the table differ considerably from the average value of $20/4 = 5$. It is evident that the details of these occupancies are related to different nucleotide functions in the positions in question. What are the probabilities of finding complementary nucleotides in the pairs of positions of interest? From Table 1 the probabilities of finding nucleotides A, C, U and G in position 6a are 2/20, 11/20, 0, and 7/20 respectively, while for 6b the probabilities are 1/20, 2/20, 1/20, and 16/20, respectively. The probability of finding complementarity is the sum of the probabilities for the base pairs AU, UA, GC, and CG:

$$\left(\tfrac{2}{20} \times \tfrac{1}{20}\right) + \left(0 \times \tfrac{1}{20}\right) + \left(\tfrac{7}{20} \times \tfrac{2}{20}\right) + \left(\tfrac{11}{20} \times \tfrac{16}{20}\right) = 0.48\,.$$

If an event has an *a priori* probability $p = 0.48$, then the result from 20 attempts is approximately $Np = 20 \times 0.48 = 9.6$, with a standard deviation $\pm\sqrt{Np(1-p)} = \pm 2.2$.

Table 1: Analysis of 20 tRNA's of *E. coli* [a].

| Position | Number of tRNA's with A | C | U | G | Number of base pairs observed | statistical |
|---|---|---|---|---|---|---|
| 1a | 20 | | | | 6 | |
| 1b | 12 | 2 | 6 | 0 | | |
| 2a | | 20 | | | | |
| 2b | 3 | 3 | 4 | 10 | 10 | |
| 3a | | 20 | | | 8 | |
| 3b | 0 | 11 | 1 | 8 | | |
| 4a | 10 | 1 | 2 | 7 | 8 | 6.3±2.1 |
| 4b | 3 | 8 | 6 | 3 | | |
| 5a | 3 | 14 | 3 | 0 | 7 | 8.1±2.2 |
| 5b | 5 | 3 | 2 | 10 | | |
| 6a | 2 | 11 | 0 | 7 | 10 | 9.6±2.2 |
| 6b | 1 | 2 | 1 | 16 | | |
| 7a | 2 | 10 | 3 | 5 | 5 | 5.7±2.0 |
| 7b | 3 | 5 | 5 | 7 | | |
| 8a | 4 | 10 | 3 | 3 | 4 | 7.4±2.2 |
| 8b | 4 | 0 | 4 | 12 | | |
| 9a | 0 | 11 | 3 | 6 | 5 | 6.8±2.1 |
| 9b | 3 | 1 | 5 | 11 | | |
| 10a | 4 | 7 | 2 | 7 | 8 | 5.1±2.0 |
| 10b | 0 | 6 | 12 | 1 | | |
| 11a | 2 | 13 | 5 | 0 | 1 | 1.3±1.1 |
| 11b | 2 | 16 | 1 | 1 | | |
| 12a | 0 | 6 | 9 | 5 | 11 | 5.7±2.0 |
| 12b | 3 | 4 | 2 | 11 | | |

[a] In Met-tRNA the base in position 10b is unknown, so that for the pair of positions 10, the calculations include 19 rather than 20 cases. For purposes of calculation the rare bases pseudouridine and 3-(3-amino-3-carboxypropyl)uridine were counted as U and $N^7$-methylguanine as G.

The expectation value for the number of complementary base pairs is therefore 9.6±2.2. The statistical value is close to the observed value of ten base pair complementarities. Analogous conclusions apply to positions 5a and 5b as well as 4a and 4b (columns 6 and 7 of Table 1). If there had been base complementarity in primordial tRNA in the region concerned, statistical values significantly higher than those observed would be expected. This is not the case[*].

While *Hopfield* limited his statistical considerations to the pairs of positions 1 to 6, it is of interest to include the additional pairs 7 to 12. Again approximate agreement is found between the numbers of observed complementary base pairs and the numbers based on statistical analysis just described (Table 1, columns 6 and 7). There is, however, one exception; the pairs of positions 12a, 12b for which the number of observed complementary pairs is eleven, almost double the statistical value. The reason for this discrepancy is that in eight of the eleven present-day tRNA's positions involved, 12a and 12b are actually paired, forming the beginning of loop I. Only the pairs 7a, 7b to 11a, 11b are therefore significant in this context. If *Hopfield*'s model were correct, significantly more complementary base pairs would be expected in these positions than corresponds to the calculated statistical values (Table 1, columns 6 and 7). In fact, for these five position pairs the number of observed complementary pairs is smaller also than would be expected for an *equal a priori* distribution of the four kinds of nucleotides over the ten positions. From Table 1 the total of observed complementary pairs is 23, giving an average of $23/20 = 1.15$, while the expected avarage number of complementary base pairs is $5 \times \frac{1}{4} = 1.25$. In summary, *Hopfield*'s model cannot be supported by means of the observed complementarities.

---

[*] The statistical test used here cannot be applied to the pairs of positions 1 to 3b, because positions 1a, 2a and 3a are always occupied by the same respective nucleotides in the sequence ACC. If *Hopfield*'s model were correct, one would expect positions 1b to 3b to be preferentially occupied by the sequence UGG. However, in position 1b, for example, A is found twice as often as U.

## 12. DNA Takes Over the Storage of Genetic Information

The example of the emergence of a translation apparatus illustrates the method of procedure in our model. Further important steps are considered here in a more cursory fashion. A question that is initially extremely puzzling is how and when the translation apparatus described was restructured into the genetic apparatus of today's biological systems, which have a completely different organizational structure. The methodological program used previously leads, however, to the view that a restructuring of precisely this kind almost certainly had to occur.

Systems containing translation devices invaded regions of ever larger pores and, related to these events, increased in complexity and sophistication. However, the achievable degree of complexity is limited at this level by congestion. That is, while (+)-collector strands contain the codes for useful polypeptides, the corresponding (−)-strands are either useless for the synthesis of polypeptides or, even worse, effect the production of nonsense polypeptides that add to the confusion inside the envelope and use up amino acids. These complications increase with the sophistication and variety of devices that synthesize different polypeptides. An individual can therefore manufacture only a limited number of different enzymes, and a quiescent phase of evolution is thus reached.

A possible way out is the following: The "replicase" can sustain minor changes because of erroneous base couplings, and eventually "replicases" with slightly different properties can evolve in the same envelope. Let such an enzyme $E_1$ be one that favors, to a small degree, mononucleotides containing deoxyribose rather than ribose in the synthesis of strands and $E_2$ an enzyme that in turn favors such deoxyribose-rich strands as templates in the synthesis of strands rich in ribose. By chance let enzyme $E_2$ be slightly more efficient than $E_1$ (Fig. 20). The $E_1$-catalyzed replication of a (+)-strand of RNA (denoted by $R^+$) then yields a deoxyribose-rich (−)-strand (denoted by $D^-$) that in turn can serve as template for the rapid production of a number of copies $R^+$, assisted by the efficient enzyme $E_2$. The strands $R^+$ can convolute into hairpins and aggregate into enzyme-synthesizing devices. Thus, a few $D^-$ strands now produce many $R^+$ strands. Directional selection oc-

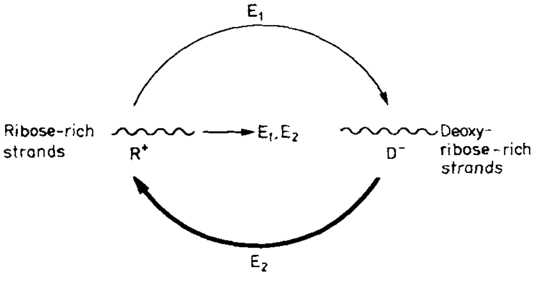


Fig. 20. Emergence of deoxyribose-rich ($D^-$)-strands. Short deoxyribose-rich (−)-strands ($D^-$) are synthesized on ribose-rich (+)-strands ($R^+$), catalyzed by enzyme $E_1$, while $E_2$ catalyzes the synthesis of $R^+$ on $D^-$. Enzyme $E_2$ is more efficient than $E_1$.

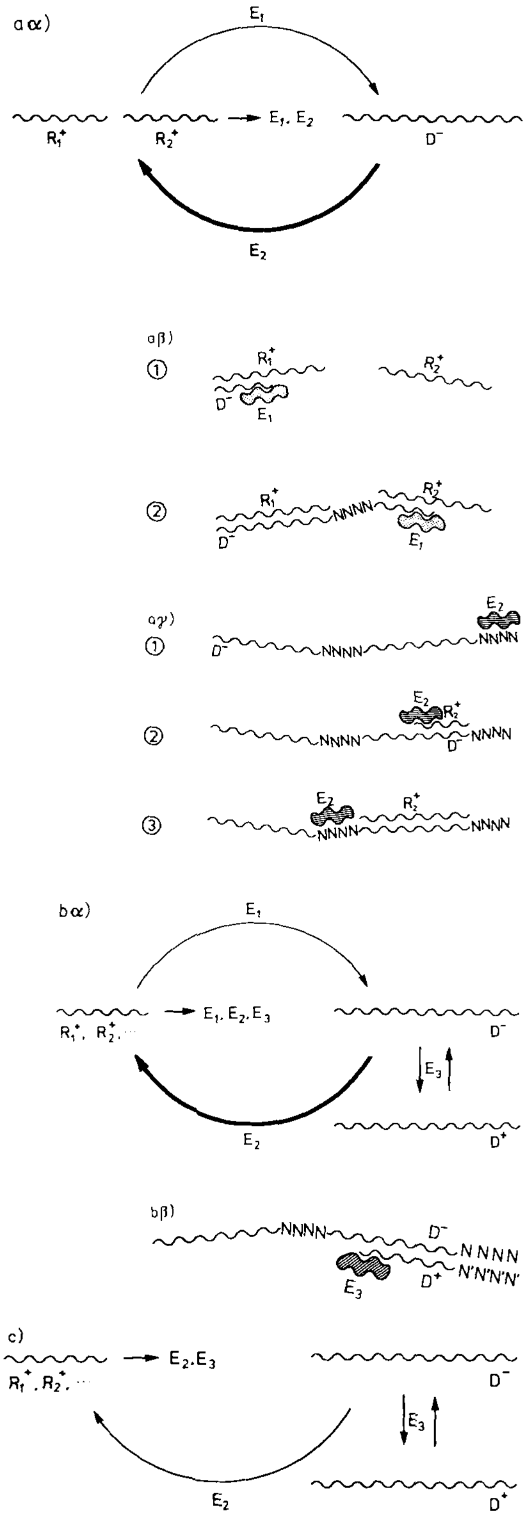


Fig. 21. Organizational structure of the processes that permit the separation of the machinery for replication and enzyme synthesis. a) $D^-$ becomes longer and serves as template for short strands $R_1^+, R_2^+, \ldots$; α) schematic representation of the catalytic action of enzymes $E_1$ and $E_2$; β) strands $R_1^+$ and $R_2^+$ serve as templates in the formation of $D^-$, catalyzed by enzyme $E_1$. The stretch NNNN is formed without the benefit of a template; γ) formation of $R_2^+$ with $D^-$ serving as template, catalyzed by enzyme $E_2$. The NNNN portions of the $D^-$ strand are not replicated but serve as recognition regions where replication is to begin ① and end ③. b) Enzyme $E_3$ catalyzes the replication of $D^+$ on $D^-$ strands and *vice versa*; α) schematic representation of the catalytic action of the enzymes $E_1$, $E_2$, and $E_3$; β) formation of $D^+$ with $D^-$ acting as template strand, catalyzed by enzyme $E_3$. The portion N'N'N'N' on $D^+$ is formed by replication of the analogous portion NNNN on $D^-$. c) Enzyme $E_1$ is no longer needed; schematic representation of the catalytic actions of the enzymes $E_2$ and $E_3$.

curs, favoring genetic machinery in which mechanisms for replication and enzyme synthesis become separate. The difficulty that arose through the accumulation of unproductive strands and of nonsense polypeptides is thus solved by a reorganization of the system, and the appearance of a third sort of polymers rich in deoxyribose nucleotides.

The cooperation of enzymes $E_1$ and $E_2$ permits, for a while, growth of the functional cooperative by the emergence of additional enzymes. However, linked to the increase in complexity of this macromolecular society, there is an increase in organizational problems, since the blueprints of the organisms are distributed over many $R^+$ strands ($R_1^+, R_2^+ \ldots$). The difficulty can be overcome by combining the complementary strands $D_1^-, D_2^- \ldots$ into fewer longer strands and eventually into just one long $D^-$ strand (Fig. 21a α) that then serves as template for new strands $R_1^+, R_2^+ \ldots$. Apart from the decrease in organizational problems thus brought about, there is also less tendency for a long strand to escape by diffusion.

The process of lengthening the $D^-$ strands would be aided by an enzyme acting as *"ligase"*. It can be imagined that enzyme $E_1$, slipping along as replication proceeds, protrudes from its slot as the end of the strand is reached. The protruding end may then assist in the occasional attachment of a second strand that happens to be nearby. The result is a $D^-$ strand, that is lengthened by the new piece, which contains the information of the two $R^+$ strands separated by a short piece of strand NNNN that was polymerized template-free (Fig. 21a β)[*].

Enzyme $E_2$, involved in the synthesis of the short strands $R_1^+, R_2^+, \ldots$, must contain recognition sites for the locations along the $D^-$ strand at which replication of $R^+$ strands must start and end. Perhaps the short pieces along $D^-$ that arose through non-template polymerization can act in a special way (Fig. 21a, γ).

A further necessary step is the modification of an earlier "replicase" into an enzyme $E_3$ (Fig. 21b, α) that catalyzes the formation of $D^+$ strands from $D^-$ templates and the converse. Since only $D^-$ should be used as template for producing strands $R_1^+, R_2^+, \ldots$, enzyme $E_2$ should be able to interact with the recognition sites of $D^-$ only, which would therefore have to be special. They might *e.g.* consist of the sequence NNNN, to which the "non-recognition" piece N′N′N′N′ on $D^+$ would correspond, where N′ is the nucleotide complementary to N (Fig. 21b β).

Such a system of enzymes would confer great selective advantages and initiate the evolution of machinery for replication operating with increased efficiency and accuracy. The mechanism would lead to a situation in which DNA strands became the carriers of information. $E_1$ would degenerate and $E_2$ evolve into *"transcriptase"* (Fig. 21c). (Since *inverse transcriptase* is endowed with the same function as $E_1$ it is conceivable that it evolved from such a precursor.)

At an early stage, another apparatus must have evolved that improved the contact between the collector strand and the hairpin adapters, suppressing "reading" errors. This surmise is strongly suggested by the fact that today's ribosomes are the only functional cell elements (enzyme systems) that are largely composed of nucleic acids and may therefore have evolved from such an apparatus.

At this stage all essential elements of the present-day genetic machinery, as known from molecular biology, have been accounted for and their evolution appears to be a necessity.

## 13. Exchange of Genetic Information

As the systems considered grew ever more complex, the information passed from one generation to the next increased. Let W be the probability that during replication an error occurs in the choice of a new base, so that the base incorporated into the daughter strand is not complementary to the corresponding base on the template strand. This probability must consequently decrease as the number, $N_{total}$, of monomers involved in information storage and transfer increases, and it can be shown that the relation $N_{total}\ W = 1$ must approximately be satisfied (cf. [2], Section 18.1.4.7). This condition theoretically assures that there is a sufficient number of error-free copies in each generation so the form does not become extinct. There is also some experimental evidence for this approximate relationship. It has, for example, been found by *Weissmann et al.*[51] that $W \simeq 1/3000$ for Qβ-bacteriophage, for which the number of nucleotides is 4500.

As $N_{total}$ increases, W must decrease, *e.g.* by the appearance of improved "replicases". However, a new difficulty arises, caused by the requirement that there must be a certain minimum error frequency to permit the continuous adaptation of the systems to an ever-changing environment, when $N_{total}$ reaches approximately $10^6$. The required approximate value of W is $10^{-6}$. Once the corresponding approximate value of $N_{total} = 10^6$ has been reached, it becomes impossible to increase $N_{total}$ further without violating one of these two limiting conditions (Fig. 22). A phase of stagnation is reached in the model and a new fundamental organizational change, a new breakthrough is required to overcome this barrier.

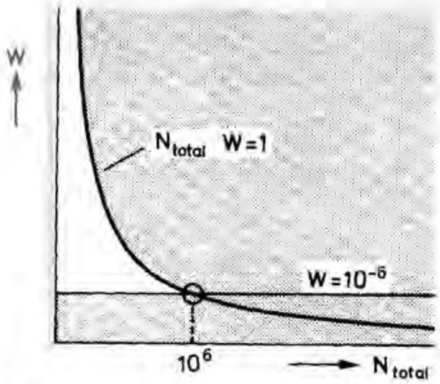


Fig. 22. Conditions for W. The value of $10^6$ on the horizontal axis represents an upper limit for $N_{total}$. Gray region is in violation of the two boundary conditions described in the text.

---

[*] It is known, that under certain conditions Qβ replicase can cause the template-free replication of strands [50].

In the model, this breakthrough consists in the exchange of genetic information between individuals. An evolution of sexual machinery that permits the mutual exchanges of pieces of strand takes place, *i.e.* there is recombination of genetic material that may confer advantages upon the recipients. The approximate requirement that $W = 10^{-6}$ is thereby relaxed, and $N_{total}$ can grow, as long as accidental improvements in the replication machinery lower W to a level at which the condition $N_{total}\ W \simeq 1$ is again satisfied. The gain in flexibility through recombination must, of course, outweigh the loss caused by the decline in the replication error rate. An improvement of the mechanism for the recombination of genetic material and a decrease in W and increase in $N_{total}$ are thus strongly coupled to each other.

The stage of information under discussion corresponds approximately to that of a bacterium, for which the total number of nucleotides in the DNA lies between $3 \times 10^6$ and $6 \times 10^6$, only a fraction of which carry information coding for proteins, *i.e.* constitutes $N_{total}$. The portion of DNA that carries such information is probably quite large in bacteria, so that a value of about $10^6$ for $N_{total}$ would seem justified. For *E. coli* it is found experimentally[52] that $W \simeq 10^{-8}$; indeed *E. coli* sometimes exchanges genetic material by conjugation.

The interchange of genetic material strongly accelerates the accumulation of genetic information and therefore determines the direction of further evolution. At the stage considered, a division into organisms that remained simple and others that became more and more complex must have occurred. Simplicity of organization (non-development of sexual machinery or limitation to very primitive such machinery) yields selective advantage in some ecological niches—the organisms remained at the stage of procaryotes.

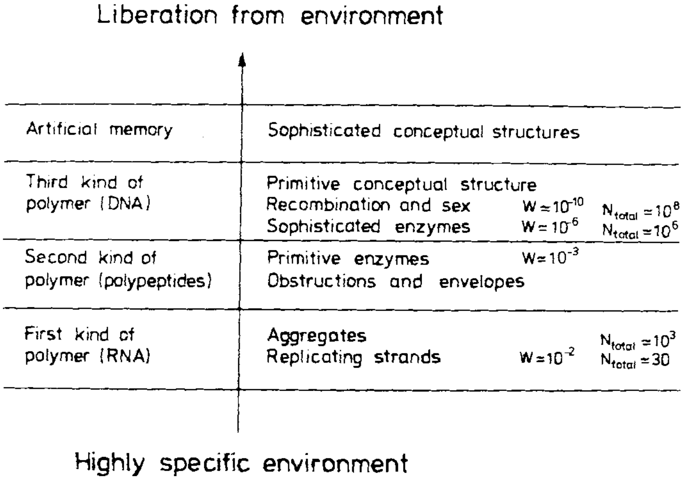
A decisive improvement in the sexual machinery presupposes an increase in complexity. The increase in sophistication caused organizational problems that could only be solved by the subdivision of the cell interior, hence improving the regulation of molecular traffic. The cell architecture became more complicated—eucaryotes evolved. In regions, in which the procurement of nutrients required the development of more and more complicated devices, only further structuring by multicellularity was left as a means of escape into new living spaces.

The question of the emergence of primitive sexual mechanisms, a necessity in the model considered, must not be confused with the question, commonly discussed by evolutionary ecologists, of the present-day selective forces maintaining sexual reproduction. Asexual reproduction must have repeatedly arisen in different evolutionary lineages as a derivation of primitive sexual reproduction.

## 14. Thermal Barriers to Information Storage and Transfer

It is not possible, however, to increase $N_{total}$ beyond a certain limit, because new difficulties arise in the model. The new barrier arises because errors caused by ever-present thermal fluctuations cannot be avoided, a fact that implies the existence of a minimum value below which W cannot be decreased.

This barrier can only be hurdled once machinery is available that uses larger than molecularly dimensioned symbols and in this manner permits the storage of much greater quantities of information than is possible by the genetic apparatus. Such machinery is available in written language, and more recently, in computers. Information in artificial memories, such as instructions for the manufacture of some device, is transmitted over many generations and modified and supplemented by material that is subject to a selection process. The revolutionary breakthrough of artificial storage systems is comparable to the revolution associated with the separation of the machinery for replication from that for protein synthesis, during which DNA became the receptacle of genetic information. As then, a change in the system of information transmission led to a huge increase in the information that could be transferred from one generation to the next.



| | | | |
|---|---|---|---|
| Artificial memory | Sophisticated conceptual structures | | |
| Third kind of polymer (DNA) | Primitive conceptual structure<br>Recombination and sex<br>Sophisticated enzymes | <br>$W \simeq 10^{-10}$<br>$W \simeq 10^{-6}$ | <br>$N_{total} \simeq 10^8$<br>$N_{total} \simeq 10^6$ |
| Second kind of polymer (polypeptides) | Primitive enzymes<br>Obstructions and envelopes | $W \simeq 10^{-3}$ | |
| First kind of polymer (RNA) | Aggregates<br>Replicating strands | <br>$W \simeq 10^{-2}$ | $N_{total} \simeq 10^3$<br>$N_{total} \simeq 30$ |

Fig. 23. Increased complexity of information storage led to increased independence from specific environments.

Some of the breakthrough phases described are summarized in Figure 23. This depicts, in our view, the main line of evolution—a sequence of many minute steps that lead to an ever-increasing liberation from an environment that was, in the beginning, very special. This development is related to a large increase in complexity, of which $N_{total}$ is a measure, and to a decrease in the probability W of replication errors. At first only one kind of polymer, ribonucleic acid, was of importance. Replication set in, followed by the formation of aggregates. A second kind of polymer, the polypeptides, became important. Envelopes developed and a genetic translation apparatus evolved. A third kind of polymer, deoxyribonucleic acid, permitted, the complete reorganization of the system of information transfer. A refined translation apparatus evolved and sexuality became important. Finally, artificial memory systems became carriers of information.

While individual steps can always be replaced by others that are somewhat different, without thereby destroying the logical connections between the steps, the fundamental

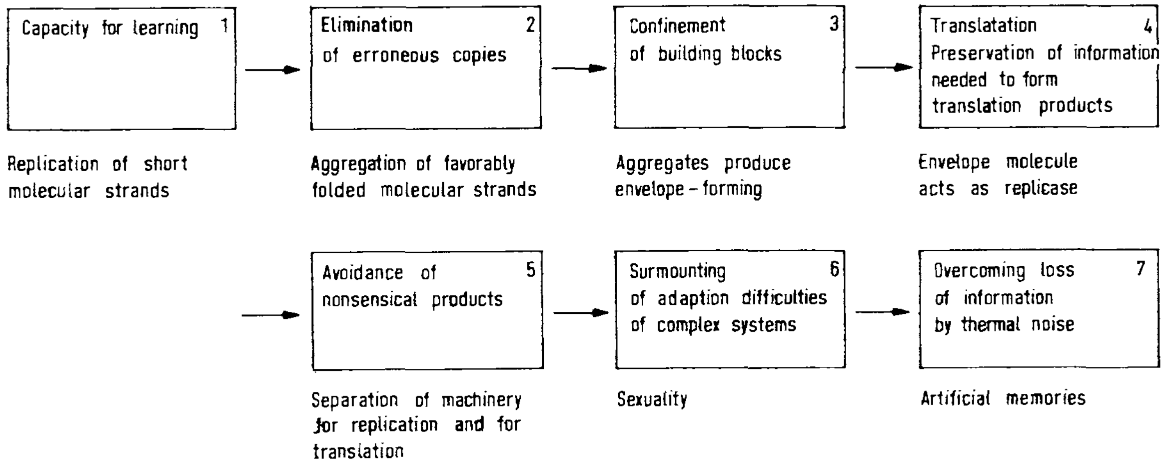


Fig. 24. Organizational framework of the evolution process. Logical requirements (boxes) and their realizations.

changes in the system structure of the explored model seem to be fixed necessities. Under appropriate circumstances, a system appears that is capable of learning (Fig. 24, step 1). The complexity increases but stagnation sets in, because of the accumulation of replication errors. To overcome it, machinery for the discarding of erroneous copies is needed and is achievable (step 2). The complexity of the systems again increases, until stagnation occurs, because they are tied to pre-existing compartmentation. To conquer this barrier machinery is needed and achievable that permits a containment of building blocks that is independent of external structure (step 3). Given appropriate conditions this machinery develops, by necessity, into machinery for code translation and machinery that permits the preservation of information needed to form translation products (step 4). This development in turn allows an increase in complexity until stagnation sets in at a certain level, because of the accumulation of nonsense products. The conquest of this hurdle (step 5) requires machinery that permits the bypassing of meaningless production and can be achieved by reorganization of the systems. Further evolution leads to increasingly complex, and thus ever more delicate systems, ending again in stagnation because of inadequate adaptability of the systems. The barrier can again be hurdled by a fundamental reorganization of the systems (step 6). This change permits the achievements of a level of complexity that cannot be raised further because of thermal noise, until another fundamental restructuring of the organization permits a conquest of this barrier (step 7).

## 15. Knowledge as a Measure of the Usefulness of Information

The process of evolution can be described as a phenomenon that, at some place and at some time in the development of any suitable planet (Fig. 25), starts with a bang. All of a sudden a strand arises that can replicate, thereby creating a system that adapts itself again and again to a changing environment, in many steps of replication and selection. This process of evolution proceeds in jumps: Nothing of importance happens for long periods, until a reorganization of the system ushers in a rapid new development. In a corresponding way there are discontinuous increases in the contents of the message of which the systems are carriers. An important function that is a measure of and increases with the degree of the evolution of the systems will be termed the *knowledge* of the systems. We roughly define this function as the information (measured in bits or yes-no decisions) contained in the totality of the blueprints that had to be rejected by necessity until the stage of evolution considered was reached (see [53] and [2], Section 18.1.5). Knowledge is a measure of the usefulness of the information accumulated during the course of evolution. (*Shannon*'s well-known measure for information[54] represents the *amount* of information, the number of bits, and not its *usefulness*.)

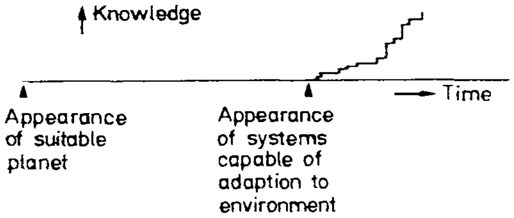


Fig. 25. Emergence of life. Learning systems suddenly appear, without prior traces of this new quality. *Knowledge* of evolving systems increases discontinuously.

## 16. Comparison with Another Approach

Our model differs in a cardinal point from an often-presented viewpoint—adhered to, for example, by *Prigogine*[55], *Eigen*[56], and others[57]—in which it is asserted that a model for the origin of life can be described in terms of the spontaneous formation of structure in a solution far from equilibrium, to which suitable reactants are supplied and reaction products removed in a steady-state situation.

In *Eigen*'s view a translation apparatus, that is, an apparatus in which tRNA molecules can attach themselves to a strand of messenger RNA, serving as adapters can spontaneously appear in a suitable solution of nucleotides, the result being the synthesis of polypeptides that can act as "replicase". Here, this apparatus must form before an effective mechanism for the removal of replication errors has become available. After *Eigen* and *Schuster* (see [45], Section XV therein), such a filtering mechanism is only formed later by the cyclic coupling of two or more reaction cycles. For example, in the case of two cycles 1 and 2 that produce the replicases $R_1$ and $R_2$, respectively, cycle 1 is catalyzed by $R_2$ and cycle 2 by $R_1$, so that cooperation between the two cycles exists in this way. The resulting *hypercycle* then dominates the solution.

In our opinion, the fundamental enigma is the mechanism that caused the emergence of a translation apparatus. The degree of intricacy is such, that a device of this kind could only have developed after the evolution of an effective mechanism for the removal of replication errors.

The only conceivable error-filtering mechanism (rejection of erroneous copies in the formation of an aggregate) requires pre-existing external spatial and temporal structure as *sine qua non* for the coming together of convoluted strands—for their aggregation, for the disassemblage of aggregates and replication of aggregate components, and for the correct reconstruction of functionally new, and at times improved, aggregates.

Our conception is in conflict with the view that a fundamental event in the origin of life was the spontaneous appearance of structure, caused by an inner instability (an occurrence that is the basis of many natural phenomena). Instead, we consider the question of how life originated *primarily* as a problem of finding the logical framework and organizational structure of evolutionary processes: By what principles can systems emerge that are capable of learning? What fundamental barriers confront such systems that can learn once they exist? What fundamental possibilities exist to overcome these barriers? *Secondly* we consider it as a problem of physical chemistry: What fundamental possibilities satisfying the organizational requirements exist in physical chemical models, that is, by remaining within the framework of physical and chemical laws? Given such a starting position questions about the thermodynamic conditions for the appearance of dissipative structures in a homogeneous solution, in a stationary state far removed from equilibrium, do not arise. Instead, pre-existing spatial and temporal structure is recognized as a fundamental requirement, and therefore a homogeneous, stationary system cannot serve as a suitable starting point. Thus, one does not ask for the conditions for the existence of a cyclic reaction sequence that must be satisfied everywhere in the solution, but for conditions that must prevail in a specific location so that aggregates consisting of a small number of macromolecules as components can appear and multiply; such aggregates have the qualities of a simplest translation apparatus, and can develop, by mutation and selection, ever more complex capabilities in their interaction with a multifaceted environment.

With this initial position, the appearance of a translation apparatus contributes the decisive breakthrough: A mechanism for the production of ever more complex enzymes has become available. A cyclic coupling of systems that produce replicases contributes nothing at this level. Cooperation arose earlier in our model, with the formation of aggregates, while in *Eigen*'s approach the first appearance of cooperation is the mutual interaction of cycles that produce replicases. As we have seen, a certain cyclic coupling between replicase-producing systems becomes important, in our model, at a later stage of evolution when deoxyribonucleic acid began to play a role. The type of coupling developing at that time is different from the one involved in *Eigen*'s hypercycle.

According to *Eigen*, hypercycles are the only possibile way of surmounting the informational crisis that arises through the proliferation of replication errors, because they simultaneously satisfy the following three conditions[58]:

1) Each replicative unit must selectively maintain its information content in competition with its own error distribution.
2) Competition between replicative units that belong to the same functional cooperative must cease to operate.
3) The functional unit as an entity must be capable of competition against alternative units.

These three conditions are, however, also satisfied by the systems, which we have considered; *i.e.* molecular strands that form aggregates (condition 1, because erroneous copies are rejected by the aggregate; condition 2, because of cooperation among the components of the aggregate; and condition 3, because of the special survival properties of the aggregate as a whole). On the other hand, this system does not constitute a hypercycle. In the case of a single kind of strand (for example, functionally equivalent (+)- and (−)-hairpin strands), autocatalytic replication of a kind of strand simply occurs, while aggregation serves to increase its viability.

The cardinal problem concerning the origin of life is how one can imagine the development of the simplest systems that could adapt to their environment—systems consisting of a few macromolecules capable of mutual cooperation. An essential requirement for this process is the existence of a spatially and temporally structured environment, which is needed to keep the potential building blocks of such systems from diffusing away from the region of importance and to drive the replication, assemblage, and disassemblage of the aggregates. The presence of structure is thus the condition for the appearance of life by molecular self-organization[*], that is, for the build-up of the information content of a learning system. How such temporal and spatial structure arose on the primordial planet is a question to be answered by planetary science.

## 17. Answers to Frequent Questions and Questionable Statements Concerning the Origin of Life

Questions and erroneous statements one often hears are the following:

---

[*] In our usage of the concept of self-organization, we exclude extra-physical influences.

1) *The geological time span available for the appearance of even the simplest forms of life was insufficient, thus requiring seeding of the planet or extra-physical phenomena to explain the emergence of life.*

Evolution up to the period at which genetic machinery appeared must have occurred rapidly, because of the large error frequency that dominated the early stages. It was most rapid at the beginning, until the frequency of errors was enormously decreased by the formation of aggregates. The development of a genetic apparatus again enormously decreased the error frequency in the correct pairing of bases. The time requirement for all steps up to the development of the genetic apparatus must therefore be small compared to the time required for the instruction of the about 1000 proteins of a bacterium. We can estimate the latter time using the assumption that proteins are inserted consecutively into the functional cooperative of the form existing at the time, and through this the DNA strand lengthened by $10^3$ nucleotides for each new protein.

The nucleotide sequence on the newly added piece of strand changes by random errors in the matching of bases, and in this way the protein adjusts to its appropriate function. For simplicity we assume that each protein is instructed by approximately 100 optimization steps, and that between each of these steps the situation must be awaited in which a random distribution of the occupancies of the non-instructed locations of amino acids, produces yet another step in the optimization. This implies $1/W = 10^6$ generations per step (one base change has occurred on the average in each position during this period) or $10^6 \times 10^2$ generations per protein, and therefore a total of $10^6 \times 10^2 = 10^8$ generations. Following this, the DNA strand is again lengthened by a piece of $10^3$ nucleotides and the process repeated. The $10^3$ proteins therefore require about $10^8 \times 10^3 = 10^{11}$ generations. This amounts to approximately $10^8$ years, assuming one day *per* generation; compared to the approximately $10^9$ years available for the process in geological history.

The reason for making this estimate is to answer the question posed and is not intended to give accurate information about the time needed for the evolution of a bacterium. It may well be an overestimate by an order of magnitude, because all proteins appear to consist of about 100 *domains* that were independently instructed and then developed further by gene duplication[59].

2) *The probability of the spontaneous emergence of the simplest systems that could develop into living organisms is much too small for a physical explanation of this phenomenon.*

Here, it is important to consider the probabilities of very many minute and detailed steps. For a small number of larger steps the probabilities soon become infinitesimally small. This can even be seen in the simple case of the spontaneous appearance of the first self-replicating strand, consisting of monomers that became accidentally linked.

Each monomer must contain the correct sugar, correctly linked to a nucleotide base and to a phosphate group. The probability of this is about 1/100, or around about $1/100)^{10} = 10^{-20}$ for a strand of ten monomers. This value is within acceptable limits, as indicated in the earlier dicussion. However, for a strand of 50 members the corresponding probability is $(1/100)^{50} = 10^{-100}$, a value so small that it would take an entire universe filled with strands, at a density of one strand per $nm^3$, so that just one of them could be assumed to be accidently correct. That is, for all practical purposes, the probability that such a strand could have spontaneously been formed is zero. Our considerations imply that in general relatively large steps do not occur.

3) *Biological systems behave in a holistic, purpose-oriented fashion that is in conflict with the way in which systems describable by physical laws behave.*

In fact, no conflict exists with the laws of physics, because the described behavior is the result of the survival of the systems considered in an environment in which survival may be difficult, while a large number of slightly less suitable systems were rejected. It is the result of the well-known mechanism of evolution: multiplication, mutation, and selection.

Replication errors are disadvantageous in most cases, but lead in rare cases to an improvement of the survival chances of the changed form. Those forms, that are better adapted to the surroundings, remain. Biological evolution leads in this way to an ever improved adaptation to the surroundings. It represents a learning process that extends over great numbers of generations. Adaptation and learning, however, are in essence holistic, purpose-directed processes that are therefore seen to be derivable from physical laws.

## 18. Concluding Remarks

The methodology followed in our approach to the origin of life is intended to overcome the mental difficulties in understanding this astonishing phenomenon on a physical basis. The many small model steps that are considered have not been devised with the hope of describing the actual path followed by nature, but rather with the intention of understanding the fundamental aspects and difficulties as tangibly as possible. It is therefore remarkable that, using this method, a successful description of the development of systems endowed with a genetic apparatus is possible, as a consequence of many small plausible steps that follow each other with an almost inescapable inner logic. Given sufficient time, all of the individual steps have probabilities near unity. Even more remarkable is that one of the results of these considerations, is a detailed description of a molecular model of this apparatus. In many details, including the possible hairpin conformation of the adapter molecules, this model is identical with that described some years ago[1], at a time when many of the experimental results used here were not as yet known.

Received: February 17, 1981;
supplemented: April 3, 1981 [A 354 IE]
German version: Angew. Chem. *93*, 495 (1981)

[1] *H. Kuhn*, Angew. Chem. *84*, 837 (1972); Angew. Chem. Int. Ed. Engl. *11*, 798 (1972).

[2] *H. Kuhn, J. Waser* in *W. Hoppe, W. Lohmann, H. Markl, H. Ziegler:* Biophysik - Ein Lehrbuch, 2nd Ed., Springer, Heidelberg 1981.

[3] *H. Kuhn, D. Möbius*, Angew. Chem. *83*, 672 (1971); Angew. Chem. Int. Ed. Engl. *10*, 620 (1971); *D. Möbius*, Acc. Chem. Res. *14*, 63 (1981).

[4] *S. L. Miller, H. C. Urey, J. Oró*, J. Mol. Evol. *9*, 59 (1976).

[5] *G. Toupance, F. Rauling, R. Buvet*, Origins Life *6*, 83 (1975).

[6] *A. W. Schwartz* in *E. K. Duursma, R. Dawson:* Marine Organic Chemistry, Elsevier, Amsterdam, cited by *A. Henderoon-Sellers, A. W. Schwartz*, Nature *287*, 526 (1980).

[7] *J. Oró*, Nature *191*, 1193 (1961).

[8] *J. P. Ferris, J. E. Kuder, A. W. Catalano*, Science *166*, 765 (1969).

[9] *J. P. Ferris, P. C. Joshi, E. H. Edelson, J. G. Lawless*, J. Mol. Evol. *11*, 293 (1978).

[10] *J. P. Ferris, R. A. Sanchez, L. E. Orgel*, J. Mol. Biol. *33*, 693 (1968).

[11] *N. W. Gabel, C. Ponnamperuma*, Nature *216*, 453 (1967).

[12] *E. Anders, R. Hayatsu, M. H. Studier*, Origins of Life *5*, 57 (1974).

[13] *S. L. Miller, L. E. Orgel:* The Origins of Life on the Earth, Prentice Hall, Englewood Cliffs 1974.

[14] *W. D. Fuller, R. A. Sanchez, L. E. Orgel*, J. Mol. Evol. *1*, 249 (1972).

[15] *L. E. Orgel, R. Lohrmann*, Acc. Chem. Res. *7*, 368 (1974).

[16] *R. Lohrmann, L. E. Orgel*, Nature *244*, 418 (1973).

[17] *H. L. Sleeper, L. E. Orgel*, J. Mol. Evol. *12*, 357 (1979).

[18] *R. Lohrmann, L. E. Orgel*, J. Mol. Evol. *12*, 237 (1979).

[19] *J. Ninio, L. E. Orgel*, J. Mol. Evol. *12*, 91 (1978).

[20] *H. L. Sleeper, R. Lohrmann, L. E. Orgel*, J. Mol. Evol. *13*, 203 (1979).

[21] *L. E. Orgel*, unpublished, citated from [22]; *R. Lohrmann, P. K. Bridson, L. E. Orgel*, Science *208*, 1464 (1980).

[22] *P. Schuster* in *H. Gutfreund:* Biochemical Evolution, Cambridge University Press, Cambridge 1980.

[23] *M. Paecht-Horowitz, J. Berger, A. Katchalsky*, Nature *228*, 636 (1970).

[24] *A. Katchalsky*, Naturwissenschaften *60*, 215 (1973).

[25] *M. Paecht-Horowitz*, J. Mol. Evol. *11*, 101 (1978).

[26] *K. Dose, H. Rauchfuss:* Chemische Evolution und der Ursprung lebender Systeme, Wissenschaftliche Verlagsgesellschaft, Stuttgart 1975.

[27] *R. W. Kaplan:* Der Ursprung des Lebens, dtv/Thieme, Stuttgart, 2nd Ed. 1980.

[28] *C. Ponnamperuma:* Exobiology, North-Holland, Amsterdam 1972.

[29] *K. A. Kvenvolden, J. G. Lawless, C. Ponnamperuma*, Proc. Natl. Acad. Sci. *68*, 486 (1971).

[30] *R. A. Kerr*, Science *210*, 42 (1980).

[31] *H. Wänke* in: Evolution der Planetenatmosphären und des Lebens, 2. Deutsche Forschungsgemeinschaft - Kolloquium über Planetenforschung, 1979, p. 198.

[32] *E. Heftmann:* Chromatography, 2nd Ed., Reinhold Publ., New York 1967, p. 636ff.; *E. Stahl:* Dünnschicht-Chromatographie, 2nd Ed., Springer, Berlin 1967, p. 758ff.

[33] *A. Rich et al.*, Science *179*, 285 (1973).

[34] *D. R. Kearns, R. G. Schulman*, Acc. Chem. Res. *7*, 33 (1974).

[35] *A. H. Wang, G. J. Quigley, F. J. Kolpak, J. L. Crawford, J. H. von Boom, G. van der Marel, A. Rich*, Nature *282*, 680 (1979).

[36] *H. Drew, T. Takano, S. Takano, K. Itakura, R. E. Dickerson*, Nature *286*, 567 (1980).

[37] *S. Arnott, R. Chadrasekaran, D. L. Birdsall, A. G. W. Leslie, R. L. Ratliff*, Nature *283*, 743 (1980).

[38] *F. M. Pohl, T. M. Jovin*, J. Mol. Biol. *67*, 375 (1972).

[39] *D. J. Patel, L. L. Canuel, F. M. Pohl*, Proc. Natl. Acad. Sci USA *76*, 2508 (1979); *R. C. Hopkins*, Science *211*, 289 (1981).

[40] *J. C. W. Shepherd*, J. Mol. Evol., in press; Proc. Natl. Acad. Sci. USA *78*, 1596 (1981).

[41] *M. Eigen*, Max-Planck-Gesellschaft, Jahrbuch 1979, Vandenhoeck & Ruprecht, Göttingen, p. 17; *M. Eigen, R. Winkler*, Naturwiss. *68*, 217 (1980).

[42] *A. I. Oparin:* The Chemical Origin of Life, Charles C. Thomas, Springfield, Ill. 1964.

[43] *C. W. Carter, J. Kraut*, Proc. Natl. Acad. Sci. USA *71*, 283 (1974); *G. M. Church, J. L. Sussmann, S. H. Kim, ibid. 74*, 1458 (1977); *W. F. Anderson, D. H. Ohlendorf, Y. Takeda, B. W. Matthews*, Nature, in press. We are grateful to Dr. *G. Eichele*, of the Biozentrum der Universität Basel (Switzerland), for drawing our attention to these references.

[44] *H. Kuhn, Ch. Kuhn*, Origin of Life *9*, 137 (1978).

[45] *M. Eigen, P. Schuster*, Naturwissenschaften *64*, 541 (1977); *65*, 7, 341 (1978); The Hypercycle, A Principle of Natural Selforganization, Springer, Berlin 1979.

[46] *F. H. Crick, S. Brenner, A. Klug, G. Pieczenik*, Origin of Life *7*, 389 (1976).

[47] *A. Malzke, A. Barta, E. Küchler:* On the Mechanism of Translocation: Relative Arrangement of tRNA and mRNA on the Ribosome, in press, cited in [22].

[48] *J. J. Hopfield*, Proc. Natl. Acad. Sci. USA *75*, 4338 (1978).

[49] *B. G. Barrell, B. F. C. Clark:* Handbook of Nucleic Acid Sequences, Joynson-Bruvvers Ltd., Oxford 1974.

[50] *M. Sumper, R. Luze*, Proc. Natl. Acad. Sci. USA *72*, 162 (1975); *B. Küppers, M. Sumper, ibid. 72*, 2630 (1975).

[51] *E. Domingo, R. A. Flavell, Ch. Weissmann*, Gene *1*, 3, 27 (1976).

[52] *E. C. Cox, C. Yanofsky*, Proc. Natl. Acad. Sci. USA *58*, 1995 (1967).

[53] *H. Kuhn*, Ber. Bunsenges. Phys. Chem. *80*, 1209 (1976); in *H. Haken:* Synergetics, a Workshop. Springer, Heidelberg 1977, p. 200.

[54] *C. E. Shannon, W. Weaver:* The Mathematical Theory of Communication, University of Illinois Press, Urbana 1949.

[55] *O. Nicolis, I. Prigogine:* Self-Organization in Nonequilibrium Systems, Wiley-Interscience, New York 1977, Chap. 7.

[56] *M. Eigen*, Naturwissenschaften *58*, 465 (1971).

[57] *R. Riedl:* Biologie der Erkenntnis, 2nd Ed., Parey, Berlin 1980.

[58] *M. Eigen*, Angew. Chem. *93*, 221 (1981); Angew. Chem. Int. Ed. Engl. *20*, 233 (1981).

[59] *G. Schulz*, Angew. Chem. *93*, 143 (1981); Angew. Chem. Int. Ed. Engl. *20*, 143 (1981).

# *N*-Methyl Inversion Barriers in Six-membered Rings[**]

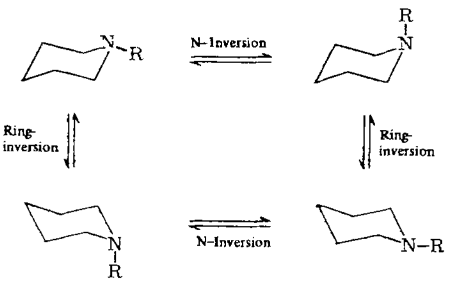
**By Alan R. Katritzky, Ranjan C. Patel, and Frank G. Riddell[*]**

Conformational conversions of *N*-methylazacyclohexanes are of particular interest: they can proceed either *via* ring- or nitrogen-inversion processes. In both procedures an equatorial *N*-methyl group is converted into an axial one, and the converse. It is appropriate to dissociate the energy barriers for *N*-methyl inversion into two "half-barriers" for the steps, axial form → transition state and equatorial form → transition state, and to report both values separately.—In this article the *N*-methyl inversion barriers of numerous methylated oligoazacyclohexanes, including species with oxygen or nitrogen atoms in the ring, are discussed.

## 1. Introduction

Since the fifties, conformational analysis has revolutionized our treatment of saturated ring systems. At first it was applied mainly to carbocyclic systems, but its influence has long been felt in saturated and partially saturated heterocyclic ring systems.

The substitution of a nitrogen or oxygen atom for a carbon atom in cyclohexane does not fundamentally change the geometry. However, a trivalent nitrogen atom displays the phenomenon of N-inversion. The *N*-substituent in a piperidine, for example, can occupy either the equatorial or axial position, and there are two possible ways of these conformations interconverting, either by ring- or N-inversion.



In the case of piperidine itself, the *position* of the equilibrium was long controversial, but this matter has now been largely cleared up and the general view accepted that the *N*-equatorial conformer predominates by a rather small factor[1]. For *N*-alkylpiperidines, it has long been accepted that the *N*-equatorial form predominates, but the *magnitude* of the N-inversion barrier in this compound and that for other *N*-alkyl groups in other azacyclohexanes has proved a fascinating and contentious problem.

The problems raised by studies of N-inversion barriers in six-membered rings such as *N*-methylpiperidine *(1)* have been a subject of dispute between the authors' laboratories[2]. Since the dates of the original communications on this subject, much further work has been carried out by each of our groups and by others and the principal points of controversy now appear to have been resolved. This review outlines our agreed assessment of the current situation.

An important basic point is that the N-inversion barrier cannot be measured by current NMR techniques for the simplest six-membered derivative *N*-methylpiperidine *(1)*. This arises because the free energy difference between the two conformations *(1e)* and *(1a)* is *ca.* 2.7 kcal/mol[3], making it impossible to record peaks from the minor conformer *(1a)* below the anticipated coalescence temperature, even with the most sophisticated modern instrumentation[*].

The only current technique that would appear to be available for the measurement of the barrier in *N*-methylpiperidine is ultrasonic relaxation; this has recently been used with success, *e.g.* in studies of rotation in ethanes[4]. An ultrasonic relaxation study on *N*-methylpiperidine by *Wyn-Jones et al.*[5] in 1975 yielded a barrier of 6.0 kcal/mol for the *ax*→*ts* barrier[**]. Although $\Delta G^0$ measured by this

---

[*] Prof. Dr. A. R. Katritzky [+], Dr. R. C. Patel
School of Chemical Sciences, University of East Anglia
Norwich, NR4 7TJ (England)
Dr. F. G. Riddell
Department of Chemistry, The University
Stirling, FK9 4LA (Scotland)

[+] Author to whom correspondence should be addressed. New address:
Deparment of Chemistry,
University of Florida,
Gainesville, Florida 32611 (USA)

[**] Conformational Analysis of Saturated Heterocycles, Part 98.—Part 97: *A. R. Katritzky, R. C. Patel, F. G. Riddell*, J. Chem. Soc. Chem. Commun. *1979*, 674.

[*] Given $\Delta G^0 = 2.7$ kcal/mol and an optimistic upper temperature limit of −150° C at which N-inversion might be frozen out, the equilibrium constant *K* is *ca.* 65000 (*i.e. ca.* $2^{16}$). Therefore, if a piece of information from the (preferred) *(1e)* completely filled one 16 bit word of store, only one bit would be recorded in a word of store containing the corresponding information from *(1a)*. Moreover these values would be superimposed on noise certainly greatly exceeding 1 bit in magnitude and would have no statistical significance. The problem is therefore beyond any 16 bit FT computer and probably beyond the dynamic range of the FT routines of all current FT computers utilizing larger word sizes.

[**] The following abbreviations are used: *ax*=axial, *eq*=equatorial, *ts*=transition state; *N*-Methyl orientation: *a*=axial, *e*=equatorial.

*0570-0833/81/0707-0521 $ 02.50/0*

technique was found to be 0.9 kcal/mol, a value much lower than that currently accepted[3], it is agreed that $\Delta H^0$ values from spectroscopic methods are more reliable than those from ultrasonic relaxation techniques, whereas $\Delta G^{+}$ determinations compare well with reliable values from other methods[4]. This suggests a $\Delta G^{+}$ value of 6.0 kcal/mol for the *ax→ts* barrier in *N*-methylpiperidine *(1)*.

## 2. Measurement of Individual Half-Barriers by NMR

A fundamental point arises in the interpretation of NMR coalescence data. The rate constant obtained from an NMR experiment is always the sum of the forward and reverse rate constants, but three cases can be distinguished:

1. If the process being observed is the freezing out of a biased equilibrium where $K$ is *e.g.* $\geq 10$, the observed rate constant is effectively the greater of the two and therefore corresponds to the conversion of the least stable conformer in the transition state. This applies in all applications of dynamic $^{13}$C-NMR line-broadening (Anet equations).

2. If there are appreciable concentrations of the two conformers of which the equilibration is being observed, the individual activation energies can be obtained from the average $\Delta G^{+}$ measured, and the $\Delta G^0$ for the system, using the equations derived by *Bovey et al.*[6].

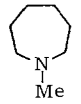
3. If the equilibrium under study is between two identical (or mirror image) conformers, then the measured rate constant is for ground state → transition state, and this applies regardless of the possible occurrence of minor amounts of other conformers along the reaction coordinate.

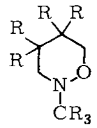
It is obviously necessary to state clearly which "half-barrier" is referred to and the neglect of this has led to much of the confusion in the literature.

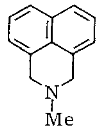
## 3. Previous Interpretation of N-Inversion Barriers

It is now clear that our viewpoints[2] can in many features be reconciled, if the work from Norwich[2a] is referred to the change axial to transition state (*ax→ts*), whereas the work from Stirling[2b] is referred to the change equatorial to transition state (*eq→ts*). This viewpoint emphasizes the fact that each nitrogen inversion barrier has to be formally regarded as made up of two half-barriers (*ax→ts* and *eq→ts*). Clearly, the difference between the two half-barriers represents the conformational energy difference of the *N*-substituent[*].

In their original preliminary communication, the Norwich group took the measured $\Delta G^{+}$ of 6.8 kcal/mol, for nitrogen inversion in the seven-membered *N*-methylhomopiperidine *(2)*[7], as a model (Table 1) to obtain empirical increments for the quantitative interpretation of changes in N-inversion barriers in terms of changes in steric and electronic factors resulting from insertion of heteroatoms in six-membered rings[2a]. It was concluded that β-heteroatoms significantly increased the atomic inversion barrier (positive β-heteroatom effect) and that α-heteroatoms had still greater barrier enhancing effects. The barrier observed for 2-methyl-1-oxa-2-azacyclohexane *(3)*, originally assigned to N-inversion[8], was suggested to be due to ring inversion because the derived empirical increments predicted the N-inversion barrier to be much lower than that observed.


*(2)*


*(3)*, R = H
*(4)*, R = D


*(5)*

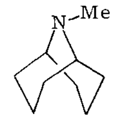

*(6)*

Table 1. Model compounds used in incremental analyses

| Compound | *(2)* | *(5)* | *(6)* | *(7)* | *(8)* |
|---|---|---|---|---|---|
| $\Delta G_c^{+}$ [kcal/mol] | 6.8 | 9.7 | 8.1 | 8.4 | 6.5 |
| Ref. | [7] | [11] | [14] | [13] | [15] |

This work was criticized by *Riddell* and *Labaziewicz*[2b], who noted that the seven-membered ring model *(2)* for N-inversion in *N*-methylpiperidine *(1)* was inadequate because it lacked the constraints imposed upon nitrogen inversion by a six-membered ring[*]. The barrier in 2-methyl-1-oxa-2-azacyclohexane *(3)* was reasserted to be due to N-inversion and this has been verified recently[9,10]. It is now clear that this barrier of *ca.* 13.7 kcal/mol (14.4 kcal/mol[10]) applies to *eq→ts*, whereas the *ax→ts* barrier is ≤ 10.0 kcal/mol, thus explaining the misassignment by the Norwich group. The Stirling workers suggested[2b] an alternative empirical analysis, which led to a barrier of 9.63 kcal/mol for the N-inversion barrier in *N*-methylpiperidine *(1)*. It was concluded that β-heteroatoms have a marked barrier decreasing effect and the N-inversion barriers reported[11,12] for compounds *(5)* and *(6)*, which at the time appeared to fall close to this derived value, were cited to support this analysis.

However, these supplementary results for *(5)* and *(6)* quoted by *Riddell et al.* can no longer be regarded as satisfactory. The N-inversion barrier of 9.7 kcal/mol in the naphthalene derivative *(5)* was considered by *Anderson* and *Oehlschlager*[11] to reflect a distorted saturated six-membered ring, for which N-inversion rates are measurable, because strain forces the C—N—C angle apart in the transition state and leads to distortion of the aromatic rings. We conclude that *(5)* represents a strained model for *eq→ts* N-inversion, with probably more strain in the *ts* than the ground state; hence, the unstrained *eq→ts* barrier

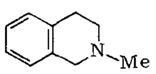
---

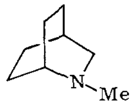
[*] In this analysis, the two observable quantities $\Delta G^0$ and $\Delta G^{+}$ are represented by three parameters. This situation would clearly be better defined if in future authors clearly specified to which direction their barriers referred. Preferably *both* half barriers should be quoted.

[*] *N*-Methyl homopiperidine *(2)* is expected to be biased to the conformation with the *N*-methyl group pseudo-equatorial.

in $N$-methylpiperidine should be significantly less than 9.7 kcal/mol. A study[13] of the tetrahydroisoquinoline *(7)* gives 8.4 kcal/mol for N-inversion. In this compound, strain that arises from opening of the C—N—C angle in the transition state is less than for *(5)*; compound *(7)*, therefore, probably provides a closer estimate of the *eq*→ *ts* barrier in *(1)* than *(5)* permits.

*(7)*





*(8)*

The barrier for the bicyclo[3.3.1]nonane derivative *(6)* has been accurately measured by *Nelsen et al.*[14] as 8.11±0.04 kcal/mol, whereas *Lehn*'s previously "unpublished" proton data for *(6)*[12] (determined at −80±10°C), $\Delta G_c^{+} = 9.5 \pm 1.0$ kcal/mol, was quoted by *Riddell* as support for his results[2b]. The variance with *Nelsen*'s $^{13}$C-NMR result was probably due to difficulties in accurately determining data from the strongly coupled proton spectra. Moreover, we now agree that *(6)* is not a good model since the methyl group is equatorial in one ring but axial in the other. The barrier in the bicyclo[2.2.2]octane *(8)* has been measured[15] by *Nelsen* to be 6.5 kcal/mol. *Nelsen* concluded that *(6)* has a higher barrier than *(8)* due to the difficulty in expanding the C—N—C angle to 120° for nitrogen inversion in *(6)* because of the rigid bicyclic system.

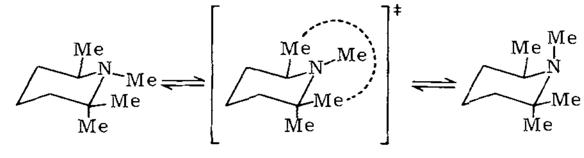
Taking the best of the available data from other workers, and considering results from our own laboratories, we suggest that the best estimations for the barriers to N-inversion in $N$-methylpiperidine are $\Delta G^{+}(ax \rightarrow ts) = 6.0$ kcal/mol and $\Delta G^{+}(eq \rightarrow ts) = 8.7$ kcal/mol. These conclusions take into account the *ca.* 2.7 kcal/mol $\Delta G^0$ in favor of the equatorial form of $N$-methylpiperidine[3].

A general but basic point, that needs consideration before discussion of the various systems, is the applicability of $\Delta G^{+}$ values from coalescence data in any comparative analysis. The barriers we are discussing range from *ca.* 6 to *ca.* 15 kcal/mol over a correspondingly large temperature range. If a nitrogen inversion process had an entropy of activation appreciably different from zero, $\Delta G^{+}$ would vary with temperature, making comparison of data obtained at different temperatures inappropriate. However, all recent carefully determined[10, 16-18] values of $\Delta S^{+}$ for nitrogen inversion processes fall in the range $0 \pm 2.5$ cal mol$^{-1}$ K$^{-1}$ rendering $\Delta G^{+}$ values a relatively good and reliable means of comparing activation energies. Finally, it was not clear that incremental schemes of the type proposed by us are at all satisfactory for the analysis of substituent effects in anything but a qualitative sense. *Riddell et al.*[19] have shown how dependent these schemes can be on one selected piece of data and that additivity of substituent effects does not hold in certain cases.

The data presently available on N-inversion barriers in $N$-methylated six-membered nitrogen-containing rings are collected in Table 2. Where possible, both *ax*→ *ts* and *eq*→ *ts* half barriers are given: there is generally an experimental error of ±0.2 kcal/mol in coalescence determinations of $\Delta G^{+}$.

## 4. Strained Piperidines

Although the equatorial conformation of 1,2,2,6-tetramethylpiperidine *(9)* is only favored by $\Delta G_c^0 = 1.9$ kcal/mol (*cf.* $\Delta G^0 \approx 2.7$ kcal/mol for $N$-methylpiperidine), both half-barriers are considerably higher than those of $N$-methylpiperidine. Destabilization of the transition state with three eclipsed methyl groups is evidently much greater than the destabilizing torsional and van der Waals interactions of the three adjacent equatorial methyl groups in the equatorial conformation (Scheme 1).



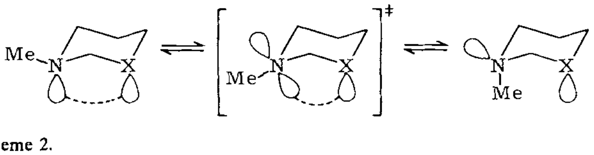
Scheme 1.

For the piperidines with fused benzene rings, [2-methyltetrahydroisoquinoline *(7)* and the naphthalene derivative *(5)*], only the *eq*→ *ts* barriers are known. Compared with 1-methylpiperidine this is marginally lower in *(7)*, but considerably raised in *(5)* by the strain involved in expanding the C—N—C bond angle to the 120° required for pyramidal N-inversion.

The bridged azabicyclononane *(6)* has its $N$-methyl group axial with respect to one ring and equatorial with respect to the other in each conformer: the measured barrier should therefore be compared to *ax*→ *ts* for piperidine, and is considerably raised by the strain in the transition state. For $N$-methyltropane *(10)* the strain is still greater in the transition state and the *ax*→ *ts* barrier is raised by 3.2 kcal/mol: however, some strain is now found in the *eq* ground state and thus *eq*→ *ts* is only raised by 1.4 kcal/mol. The barrier found for the azabicyclooctane *(8)* is near that for *ax*→ *ts* in $N$-methylpiperidine: this molecule, with boat-rings, is not strictly comparable with the others but evidently differential strains cancel in ground and transition states.

## 5. 1,4-Di- and 1,3,5-Triheteracyclohexanes

Compared with $N$-methylpiperidine, the axial conformation ground state of 1,3-heteraazacyclohexanes is stabilized by (i) removal of a β-*syn*-axial proton, (ii) the generalized anomeric effect and (iii) for the S—N-heterocycles, by further alleviation of *syn*-axial van der Waals interaction, by the greater S—N transannular distance. The equatorial conformation is destabilized by the anomeric effect and, in the case of sulfur-nitrogen heterocycles, also by torsional effects[20]. The transition state is also probably destabilized by N(p)−X(sp$^3$) lone pair—lone pair interaction (see Scheme 2).



Scheme 2.

Taken together, these interactions should increase the *ax*→*ts* barrier (positive β-heteroatom effect) but decrease the *eq*→*ts* barrier (negative β-heteroatom effect), compared to corresponding values for *N*-methylpiperidine. This conclusion amalgamates ideas from both the original analyses[2], and is amply borne out by the barriers for the three parent compounds *(11)*, *(12)* and *(13)*: *ax*→*ts* = 7.0—7.8 and *eq*→*ts* = 7.9—7.1 kcal/mol (Table 2); for 1-methylpiperidine *ax*→*ts* = 6.0 and *eq*→*ts* = 8.7 kcal/mol). A similar trend observed for 1-oxa-2-aza-4-heteracyclohexanes when compared with 2-methyl-1-oxa-2-azacyclohexane *(3)*, is discussed below.

For methylated 1,3,5-triheteracyclohexanes, the interconversion path must be defined. Two intermediates are possible: 1. the conformer with no axial methyl groups (*ee*) or 2. the conformer with two axial methyl groups (*aa*). Which intermediate is involved has no effect on the interpretation, since the measured barrier is that for *aee*→*ts* [for *(14)*] or *ae*→*ts* [for *(15)*]. However, there are also two possible transition states (Fig. 1): $t_x$ should have a higher energy than $t_y$, due to greater electronic interactions; thus pathway (2), *via* intermediate *aa*, is more likely. It follows that the measured barriers are *eq*→*ts*, and once again we clearly see the effects of the β-heteroatoms in lowering the *eq*→*ts* barriers (Table 2). The *ax*→*ts* barriers are not experimentally accessible, but they must be *lower* than those for *eq*→*ts* (see Fig. 1); however, in these cases the axial ground state has two *syn*-axial methyl groups and is hence itself of rather high energy.

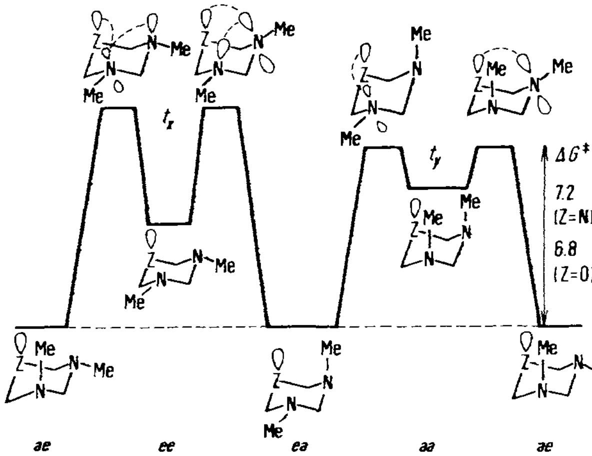
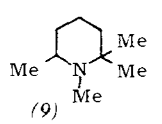
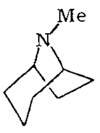
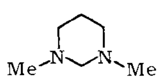


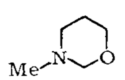
Fig. 1 Conformational equilibria of 1,3,5-trimethyl-1,3,5-triazacyclohexane *(14)* (Z = NMe) and 3,5-dimethyl-1-oxa-3,5-diazacyclohexane *(15)* (Z = O). Values in kcal/mol.

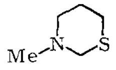
The high N-inversion barriers for *trans*-1,4,5,8-tetraazadecalin *(17)*, a '1,3-diazacyclohexane'[*], reflect additional transition state strain from (i) eclipsing methyl-methyl, (ii) p-$sp^3$ lone pair—lone pair ('passing') interactions, and (iii) rigidity of the *trans*-ring junction. Still higher barriers are found for the bicyclo[2.2.2]octylhydrazines *(26)*[15] ($\Delta G_c^{\ddagger}$ =

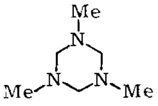

*(9)*

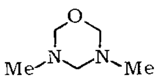

*(10)*

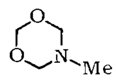

*(11)*

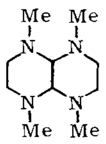

*(12)*

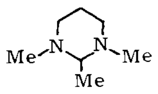

*(13)*

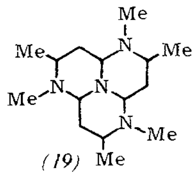

*(14)*

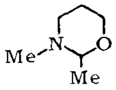

*(15)*

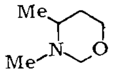

*(16)*

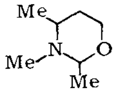

*(17)*

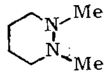

*(18)*

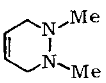

*(19)*

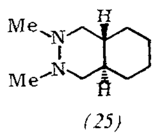

*(20)*

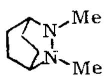

*(21)*

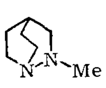

*(22)*

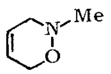

*(23)*

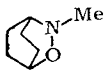

*(24)*

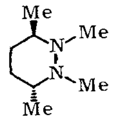

*(25)*

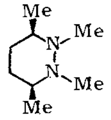

*(26)*

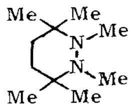

*(27)*

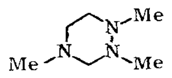

*(28)*

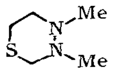

*(29)*

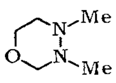

*(30)*

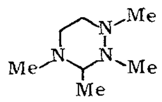

*(31)*

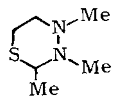

*(32)*

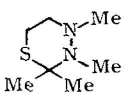

*(33)*

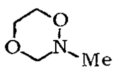

*(34)*

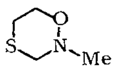

*(35)*

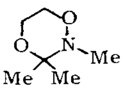

*(36)*

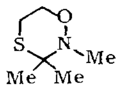

*(37)*

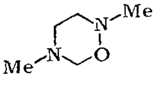

*(38)*

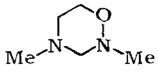

*(39)*

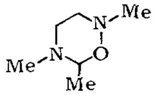

*(40)*

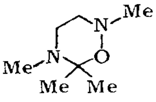

*(41)*

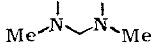

*(42)*

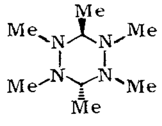

*(43)*


*(44)*


*(45)*


*(46)*


*(47)*


*(48)*

---

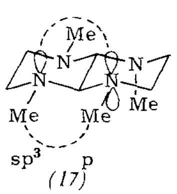
[*] Although not strictly a 1,3-diheteracyclohexane, the interactions in *(17)* are similar and are conveniently considered here. *B. Fuchs, S. Weinman, U. Schmueli, A. R. Katritzky, R. C. Patel*, unpublished results.

Table 2. Half-barriers for *N*-methyl inversion in six-membered heterocycles.

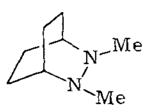
| Comp. | Ring | Subst. | DNMR-data | | | | Ref. | Half-barriers | | Foot-note |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | $T_c$ [°C] | $\Delta G_c^{+}$ [kcal/mol] | Process | $\Delta G_c^0$ [a] [kcal/mol] | | *ax-ts* | *eq-ts* [kcal/mol] | |
| *(1)* | Piperidine | 1-Me | — | — | — | 2.7 (*e*) | [3c] | 6.0 | 8.7 | |
| *(2)* | Homopiperidine | 1-Me | −125 | 6.8 | $e \rightleftharpoons e'$ | U | [7] | U | 6.8 | |
| *Strained Piperidines* | | | | | | | | | | |
| *(5)* | Dihydro-2-azaphenalene | 2-Me | −72 | 9.7 | $e \rightleftharpoons e'$ | U | [11] | U | 9.7 | |
| *(6)* | 9-Azabicyclo[3.3.1]nonane | 9-Me | −90 | 8.1 | $a \rightleftharpoons a'$ | 0.0 | [14] | 8.1 | 8.1 | |
| *(7)* | Tetrahydroisoquinoline | 2-Me | −99 | 8.4 | $e \rightleftharpoons e'$ | U | [13] | U | 8.4 | |
| *(8)* | 2-Azabicyclo[2.2.2]octane | 2-Me | −127 | 6.5 | $a \rightleftharpoons a'$ | 0.0 | [15] | 6.5 | 6.5 | |
| *(9)* | Piperidine | 1,2,2,6-$Me_4$ | −60 | 9.1 | $a \rightarrow e$ | 1.9 (*e*) | [3a] | 9.1 | 11.0 | |
| *(10)* | Nortropane | *N*-Me | −40 | 9.2 | $a \rightarrow e$ | 0.9 (*e*) | [26] | 9.2 | 10.1 | |
| *1,3-Di- and 1,3,5-Triheteracyclohexanes* | | | | | | | | | | |
| *(11)* | 1,3-Diazacyclohexane | 1,3-$Me_2$ | −120 | 7.0 | $ea \rightarrow ee$ | 0.9 (*ee*) | [27] | 7.0 | 7.9 | |
| *(12)* | 1-Oxa-3-azacyclohexane | 3-Me | −115 | 7.5 | $e \rightarrow a$ | 0.1 (*a*) | [28] | 7.6 | 7.5 | |
| *(13)* | 1-Thia-3-azacyclohexane | 3-Me | −115 | 7.1 | $e \rightarrow a$ | 0.7 (*a*) | [29] | 7.8 | 7.1 | |
| *(14)* | 1,3,5-Triazacyclohexane | 1,3,5-$Me_3$ | −120 | 7.2 | $aee \rightleftharpoons aae \rightleftharpoons aee'$ | — | [30] | < 7.2 | 7.2 | |
| *(15)* | 1-Oxa-3,5-diazacyclohexane | 3,5-$Me_2$ | −130 | 6.8 | $ae \rightleftharpoons aa \rightleftharpoons ea$ | — | [30] | < 6.8 | 6.8 | |
| *(16)* | 1,3-Dioxa-5-azacyclohexane | 5-Me | — | — | — | > 2.0 (*a*) | [30] | — | — | [b] |
| *(17)* | *trans*-1,4,5,8-Tetraazadecalin | 1,4,5,8-$Me_4$ | −71 | 9.1 | $aeae \rightleftharpoons eaea$ | 0.0 | [31] | 9.1 | 9.1 | |
| *1,3-Diheteracyclohexanes with equatorial C-methyl groups α to N-methyl groups* | | | | | | | | | | |
| *(18)* | 1,3-Diazacyclohexane | 1,2,3-$Me_3$ | *ca.* −105 | 8.0 | $eee \rightarrow aee$ | 0.9 (*aee*) | [27] | 8.0 | 7.1 | |
| *(19)* | Perhydro-1,4,7,9b-tetraazaphenalene | 1,2,4,5,7,8-$Me_6$ | −103 | 8.0 | $eaa \rightarrow aaa$ | 0.4 (*aaa*) | [27] | 8.3 | 7.9 | |
| *(20)* | 1-Oxa-3-azacyclohexane | 2,3-$Me_2$ | −110 | 7.6 | $ea \rightarrow ee$ | 0.05 (*ee*) | [28] | 7.6 | 7.65 | |
| *(21)* | 1-Oxa-3-azacyclohexane | 3,4-$Me_2$ | −105 | 7.6 | $ee \rightarrow ae$ | 0.1 (*ae*) | [28] | 7.7 | 7.6 | [c] |
| *(22)* | 1-Oxa-3-azacyclohexane | 2,3,4-$Me_3$ | −95 | 8.0 | $eee \rightarrow eae$ | 0.8 (*eae*) | [28] | 8.8 | 8.0 | [c] |
| *1,2-Diheteracyclohexanes* | | | | | | | | | | |
| *(23)* | 1,2-Diazacyclohexane | 1,2-$Me_2$ | −30 | 11.6 | $ea \rightarrow ee$ | 0.4 (*ee*) | [32] | $\geqslant$ 11.6 | $\geqslant$ 12.0 | [d] |
| | | | −88 | 7.6 | $ae \rightleftharpoons aa \rightleftharpoons ea$ | 0.0 | [24] | $\leqslant$ 6.0 | 7.6 | |
| *(24)* | 1,2-Diaza-4-cyclohexene | 1,2-$Me_2$ | −20 | 12.0 | $ea \rightarrow ee$ | U | [23, 32] | $\geqslant$ 12.0 | $\geqslant$ 12.0 | [d] |
| | | | −87 | 8.1 | $aa \rightleftharpoons ea$ | 0.0 | | $\leqslant$ 6.0 | 8.1 | |
| *(25)* | *trans*-2,3-Diazadecalin | 2,3-$Me_2$ | +2 | 12.7 | $ea \rightarrow ee$ | 0.3 (*ee*) | [24] | 12.6 | 12.9 | |
| *(26)* | 2,3-Diazabicyclo[2.2.2]octane | 2,3-$Me_2$ | −7 | 12.2 | $ae \rightleftharpoons ea$ | 0.0 | [15] | 12.2 | 12.2 | |
| *(27)* | 1,2-Diazabicyclo[2.2.2]octane | 2-Me | −113 | 7.9 | $a \rightleftharpoons a'$ | 0.0 | [15] | 7.9 | 7.9 | |
| *(3)* | 1-Oxa-2-azacyclohexane | 2-Me | *ca.* +5 | 13.7 | $e \rightleftharpoons e'$ | $\geqslant$ 3.7 (*e*) | [8] | $\leqslant$ 10.0 | 13.7 | |
| *(4)* | 4,4,5,5-Tetradeuterio-1-oxa-2-azacyclohexane | 2-$CD_3$ | +5 | 14.4 | $e \rightleftharpoons e'$ | $\geqslant$ 3.7 (*e*) | [10] | $\leqslant$ 10.7 | 14.4 | [e] |
| *(28)* | 1-Oxa-2-aza-4-cyclohexene | 2-Me | +2 | 13.5 | $e \rightleftharpoons e'$ | $\geqslant$ 3.7 | [2b] | $\leqslant$ 9.7 | 13.5 | |
| *(29)* | 2-Oxa-3-azabicyclo[2.2.2]octane | 3-Me | +22 | 14.9 | $a \rightleftharpoons a'$ | 0.0 | [10] | 14.9 | U | |
| *1,2-Diheteracyclohexanes with α-C-methyl group(s)* | | | | | | | | | | |
| *(30)* | 1,2-Diazacyclohexane | *trans*-1,2,3,6-$Me_4$ | −100 | 7.9 | $ae \rightleftharpoons aa \rightleftharpoons ea$ | 0.0 | [24] | $\leqslant$ 6.0 | 7.9 | [f] |
| *(31)* | 1,2-Diazacyclohexane | *cis*-1,2,3,6-$Me_4$ | −20 | 11.8 | $ae \rightleftharpoons ae'$ | U | [24] | U | $\geqslant$ 11.8 | [d, g] |
| *(32)* | 1,2-Diazacyclohexane | 1,2,3,3,6,6-$Me_6$ | −23 | 11.6 | $ae \rightleftharpoons ae'$ | U | [23] | U | $\geqslant$ 11.6 | [d] |
| *1,2,4-Triheteracyclohexanes with two adjacent N-methyl groups* | | | | | | | | | | |
| *(33)* | 1,2,4-Triazacyclohexane | 1,2,4-$Me_3$ | −31 | 12.0 | $ae \rightleftharpoons ae'$ | U | | U | $\geqslant$ 12.0 | [d] |
| | | | −95 | 7.5 | $ae \rightleftharpoons aa \rightleftharpoons ea$ | 1.0 (*ae*) | [25, 33] | $\leqslant$ 6.0 | 7.5 | [h, i] |
| | | | | | | | | $\leqslant$ 6.0 | 7.6 | [j, i] |
| *(34)* | 1-Thia-3,4-diazacyclohexane | 3,4-$Me_2$ | −5 | 12.4 | $ae \rightleftharpoons ae'$ | U | | U | $\geqslant$ 12.7 | [d] |
| | | | −115 | 6.8 | $ae \rightleftharpoons aa \rightleftharpoons ea$ | 1.1 (*ae*) | [20, 25, 33] | $\leqslant$ 6.0 | 6.8 | [k, i] |
| | | | | | | | | $\leqslant$ 6.0 | 7.6 | [l, i] |
| *(35)* | 1-Oxa-3,4-diazacyclohexane | 3,4-$Me_2$ | −17 | 12.6 | $ea \rightleftharpoons ea'$ | U | | U | $\geqslant$ 12.6 | |
| | | | −110 | 6.9 | $ae \rightleftharpoons aa \rightleftharpoons ea$ | 0.9 (*ae*) | [34] | $\leqslant$ 6.0 | 6.9 | [k, i] |
| | | | | | | | | $\leqslant$ 6.0 | 7.6 | [l, i] |
| *(36)* | 1,2,4-Triazacyclohexan | 1,2,3,4-$Me_4$ | −92 | 7.8 | $ae \rightleftharpoons aa \rightleftharpoons ea$ | *ca.* 1.0 (*ae*) | [25, 33] | $\leqslant$ 6.0 | 7.8 | [h] |
| | | | | | | | | $\leqslant$ 6.0 | 7.6 | [j] |
| *(37)* | 1-Thia-3,4-diazacyclohexane | 2,3,4-$Me_3$ | — | — | — | > 2 (*ae*) | [20, 25, 33] | | | [m] |
| *(38)* | 1-Thia-3,4-diazacyclohexane | 2,2,3,4-$Me_4$ | — | — | — | > 2 (*ae*) | [20, 25, 33] | | | [m] |
| *(39)* | 1,4-Dioxa-2-azacyclohexane | 2-Me | −39 | 11.4 | $e \rightleftharpoons e'$ | 0.9 (*e*) | [19, 35] | 10.5 | 11.4 | |
| *(40)* | 1-Oxa-4-thia-2-azacyclohexane | 2-Me | | 11.5 | $e \rightleftharpoons e'$ | 0.95 (*e*) | [36] | 10.6 | 11.5 | |
| *(41)* | 1,4-Dioxa-2-azacyclohexane | 2,3,3-$Me_3$ | −45 | 11.7 | $e \rightleftharpoons e'$ | 0.6 (*e*) | [19, 35] | 11.1 | 11.7 | |
| *(42)* | 1-Oxa-4-thia-2-azacyclohexane | 2,3,3-$Me_3$ | −13 | 11.9 | $e \rightleftharpoons e'$ | 0.3 (*e*) | [36] | 11.6 | 11.9 | |
| *(43)* | 1-Oxa-2,5-diazacyclohexane | 2,5-$Me_2$ | +22 | 14.6 | N-2 $e \rightleftharpoons e'$ | U | [37] | $\leqslant$ 10.9 | 14.6 | [n, o] |
| | | | −106 | 7.7 | N-5 $e \rightarrow a$ | 0.3 (N-5 *a*) | | 7.9 | 7.6 | |
| *(44)* | 1-Oxa-2,4-diazacyclohexane | 2,4-$Me_2$ | −20 | 11.1 | N-2 $a \rightarrow e$ | 1.6 (N-2 *e*) | [38] | 11.1 | 12.7 | [p] |
| | | | −112 | 7.0 | N-4 $a \rightarrow e$ | 0.8 (N-4 *e*) | | 7.0 | 7.8 | |
| *(45)* | 1-Oxa-2,5-diazacyclohexane | 2,5,6-$Me_3$ | +10 | 13.3 | N-2 $e \rightleftharpoons e'$ | *ca.* 2.0 | [37] | U | $\geqslant$ 13.3 | |
| | | | −93 | 8.2 | N-5 $a \rightarrow e$ | 0.1 (N-5 *e*) | | 8.2 | 8.3 | |
| *(46)* | 1-Oxa-2,5-diazacyclohexane | 2,5,6,6-$Me_4$ | −5 | 13.9 | N-2 $e \rightleftharpoons e'$ | U | [37] | $\leqslant$ 10.2 | 13.9 | [n] |
| | | | −103 | 7.7 | N-5 $a \rightarrow e$ | 0.5 (N-5 *e*) | | 7.7 | 8.2 | |
| *1,2,4,5-Tetraheteracyclohexanes* | | | | | | | | | | |
| *(47)* | 1,2,4,5-Tetraazacyclohexane | 1,2,4,5-$Me_4$ | −19 | 11.8 | $aaee \rightleftharpoons eeaa$ | 0.0 | [39] | $\geqslant$ 10 | $\geqslant$ 11.8 | [d] |
| *(48)* | 1,2,4,5-Tetraazacyclohexane | *trans*-1,2,3,4,5,6-$Me_6$ | −97 | 7.7 | $aeae \rightleftharpoons eaea$ | 0.0 | [40] | $\leqslant$ 6.0 | 7.7 | |

[a] U = unknown: letter in brackets denotes preferred conformer. [b] Biased to *N*-methyl axial. [c] *N*-methyl axial. [d] Process cannot be unambiguously assigned. [e] $\Delta H^{+} = 15.1 \pm 0.4$ kcal/mol; $\Delta S^{+} = 2.3 \pm 1.5$ $cal^{-1}$ $K^{-1}$. [f] 3,6-$Me_2$ diequatorial. [g] 3,6-$Me_2$ axial equatorial. [h] N-2-Inversion: N-4-methyl equatorial. [i] See Fig. 2. [j] N-1-Inversion. [k] N-3-Inversion. [l] N-4-Inversion. [m] Biased to N-3 *a*–N-4 *e*. [n] $\Delta G^0$ unknown, but probably $\geqslant 3.7$ kcal/mol in favor of N-2 *eq*; cf. *(3)*. [o] For the high energy process, $\Delta H^{+} = 14.4 \pm 0.1$ kcal/mol and $\Delta S^{+} = -1.2 \pm 0.4$ $cal^{-1}$ $K^{-1}$. [p] See Fig. 3.

12.2 kcal/mol), the intermediate methine unit in *(17)* obviously alleviates the mentioned interactions.



*(17)*



*(26)*

## 6. 1,3-Diheteracyclohexanes with Equatorial *C*-Methyl Groups in α-Position to *N*-Methyl Groups

The data in Table 2 lead to the following conclusions: (i) provided there are not more than two adjacent methyl groups, the effect of *C*-methyl on the equilibria and kinetics of *N*-methyl is small [cf. *(20)* and *(21)* with *(12)*]: (ii) three adjacent methyl groups raise *ax*→ *ts* barriers by 1.0–1.3 kcal/mol [cf. *(18)* and *(19)* with *(11)*, and *(22)* with *(12)*]: (iii) three adjacent methyl groups can considerably affect *eq*→ *ts* barriers, but the effect is variable (−0.8 to +0.5 kcal/mol for the two comparisons available).

Conclusions (ii) and (iii) can be rationalized in the following way: upon insertion of an α-equatorial *C*-methyl group leading to three adjacent methyl groups, the energy of the ground state for an equatorial *N*-methyl group is raised, as well as that for the transition state ('passing Me—Me interactions'); the effect is least for the axial *N*-methyl ground state. Comparison of the data (Table 2) for 1,3-dimethyl- *(11)* and 1,2,3-trimethyl-1,3-diazacyclohexane *(18)* shows that *ts* is raised by 1.0 and *eq* by 1.8 kcal/mol more than the *ax* ground state. A similar comparison of 3-methyl- *(12)* and 2,3,4-trimethyl-1-oxa-3-azacyclohexane *(22)* gives the *ts* and *eq* raised by 1.2 and 1.8 kcal/mol, respectively, more than the *ax* ground state. Finally, comparison of the tricyclic derivative *(19)* with *(18)* gives 0.3 and 1.3 kcal/mol respectively.

## 7. 1,2-Diazacyclohexanes

The conformational analysis of these compounds, including their N-inversion barriers, has been authoritatively reviewed by *Nelsen*[21] and only a brief account will be given here. The Norwich group originally pointed out[2a,22] that there were two different *N*-inversion barriers for these compounds and this has now been amply confirmed[21] with a distinction being made between (i) low 'non-passing' barriers for *N*-methyl inversion when the adjacent *N*-methyl group is *axial* and (ii) high 'passing' barriers when the adjacent *N*-methyl group is *equatorial*. It was originally believed[22] that the high energy of the transition state for the 'passing' barriers arose from steric methyl-methyl interactions, but later realized[2a] that the lone pair-lone pair interaction is mainly responsible (see detailed discussion in [21,23]).

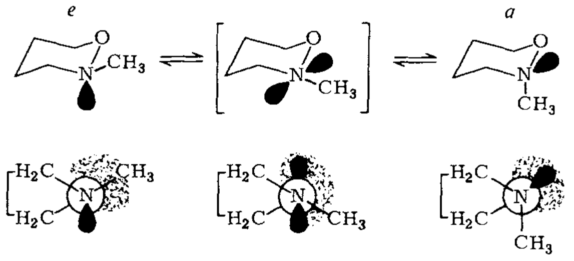
*Nelsen*'s work[24] on the bicyclic derivative *(25)*, for which ring inversion is not possible, allows accurate determination of the 'passing' *ax*→ *ts* and *eq*→ *ts* barriers as 12.6 and 12.9 kcal/mol, respectively; *i.e.* they are raised by 6.6 and 4.2 kcal/mol respectively, compared to *N*-methylpiperidine. For the parent compound *(23)*, only lower limits are available for these barriers because of ambiguity with ring inversion, but they are in good accord. For the unsaturated compound *(24)* a high passing barrier of 12.0 kcal/mol cannot be unambiguously assigned, hence the passing N-inversion barrier (*ax*→ *ts*) is ⩾12.0 kcal/mol.

The non-passing *eq*→ *ts*-barriers determined for the parent compounds *(23)* and *(24)* are, at 7.6 and 8.1 kcal/mol, respectively, significantly lower than *eq*→ *ts* for *N*-methylpiperidine; compound *(30)*, with a single adjacent *C*-methyl group, falls in the same range.

Only upper estimates for the non-passing *ax*→ *ts* barriers can be given for *(23)*, *(24)*, and *(30)*, as no signals were detected for the *aa*-conformers at low temperature: they may not be very different from *ax*→ *ts* in *N*-methyl piperidine. Only high passing N-inversion barriers are observed for *(31)* and *(32)*: the non-passing N-barrier for *(32)* is thought to be ⩽7.6 kcal/mol[23] owing to destabilization of the *ae*-ground state by axial *C*-methyl groups.

## 8. 1-Oxa-2-azacyclohexanes

We now agree that $\Delta G^{+} = 14.4$ kcal/mol found for the parent *N*-methyl compound *(3)*[2b,10] arises from N-inversion, that it should be assigned to *eq*→ *ts* (following NMR criterion (iii), see Section 2), that the $\Delta G^0$ is ⩾3.7 kcal/mol[19], and that the *ax*→ *ts* half-barrier is hence ⩽10.7 kcal/mol. Therefore, compared to *N*-methylpiperidine, the *ax*→ *ts* and *eq*→ *ts* half-barriers are raised by ⩽4.7 and 5.7 kcal/mol, respectively. Clearly, the transition state for inversion in *(3)* is raised by lone pair-lone pair interactions, which are qualitatively similar to those found for the passing N-inversion in 1,2-dimethyl-1,2-diazacyclohexane *(23)* (see Section 7) (Scheme 3).



Scheme 3.

The non-passing *N*-methyl inversion in 1,2-diazacyclohexane *(23)* has half-barrier energies not vastly different from those of *N*-methylpiperidine *(1)*: this indicates that an α-equatorial lone pair has little effect on the transition state energy. Hence, the major differences in half-barrier energies between 1,2-diazacyclohexane *(23)* and 1-oxa-2-azacyclohexane *(3)* are probably due to ground state energy variations. Quantitative comparison indicates that the equatorial ground state in *(3)* is stabilized relative to *(25)* by 1.5 kcal/mol and the axial ground state is destabilized by ⩾1.9 kcal/mol. The former effect is probably mainly steric: loss of methyl-methyl interaction. The latter is certainly due to gain in unfavorable lone pair-lone pair interactions. Barriers in the unsaturated analogue *(28)* are rather similar to those of *(3)*. Manifestations of these effects are also observed in the bicyclooctanes *(8)* and *(27)*, and *(26)* and *(29)*: lone pair-lone pair interactions and torsion effects in *(27)* lead to an increase of 1.4 kcal/mol for the barrier to *N*-methyl inversion relative to *(8)*. A similar but greater increase (+2.7 kcal/mol) is found on proceeding from *(26)* to *(29)*.

## 9. 1,2,4-Triheteracyclohexanes with Two Adjacent *N*-Methyl Groups

The 1,2,4-triheteracyclohexanes *(33)*, *(34)*, and *(35)* have high passing barriers of > 13 kcal/mol: however, the passing N-inversion barriers cannot be distinguished unambiguously from the similar energy, passing ring inversion barriers. The non-passing N-inversion barriers in these compounds have been unequivocally determined and will be discussed at length.

The relevant conformational equilibria for 1,2,4-trimethyl-1,2,4-triazacyclohexane *(33)* are shown in Figure 2[*]. The measured barrier of 7.5 kcal/mol relates to the $\Delta G^{\ddagger}$ for the conversion of conformers *ae* and *ea*, where conformer *ae* is more stable by $\Delta G^0 = 1.0$ kcal/mol (this is discussed in detail in [25]). Conformers *ae* and *ea* are interconverted *via* the still less stable conformer *aa*, and thus $\Delta G^{\ddagger}$ could either refer to *ea→aa/ea* or to *ea→ae/aa*, depending on whether *aa/ea* or *ae/aa* has the higher energy. However, we can equate the energy difference (*ae/aa* − *ae*) to the 7.6 kcal/mol barrier measured for the *N*-inversion of 1,2-dimethyl-1,2-diazacyclohexane *(23)*[21], because the γ-effect is known to be small *(vide infra)*. Hence, the observed $\Delta G^{\ddagger}$ must refer to *ea→aa/ea*, and by difference, the β-effect is calculated as a 1.1 kcal/mol *raising* of the *ax→ts* barrier *aa→aa/ea*. The barrier *aa→ae/aa* is presumably the same as in 1,2-dimethyl-1,2-diazacyclohexane, for which we only have an upper limit ≤6.0 kcal/mol. We can now calculate $\Delta G^{0\prime}$ for the minor conformer *aa* as ≥0.9 kcal/mol. Similar conclusions follow for 3,4-dimethyl-1-oxa- *(35)* and 3,4-dimethyl-1-thia-cyclohexane *(34)*. Figure 2 includes the values of $\Delta G^{\ddagger}$ and $\Delta G^0$ measured for both of these compounds. The β-effects of the O and S heteroatoms *raise* the *ax→ts* barrier *aa→aa/ea* by 1.0 and 0.5 kcal/mol respectively. $\Delta G^{0\prime}$ for the minor conformers *aa* are estimated as ≥1.1 and ≥0.7 kcal/mol, respectively. β-Effects are observed for the *N*-2- and *N*-3-inversion, respectively for *(33)*, *(34)*, *(35)*, as expected.

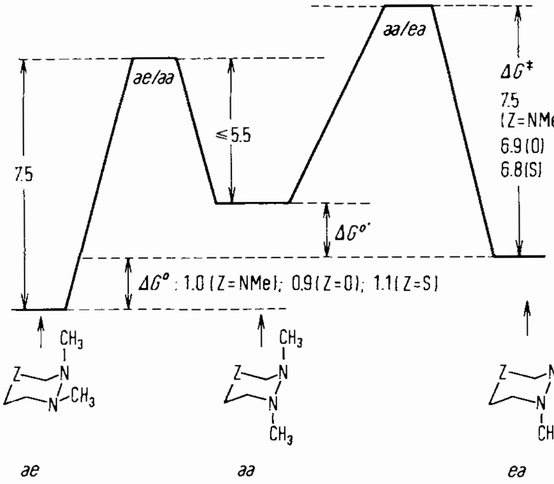


Fig. 2. Conformational equilibria for 1,2,4-trimethyl-1,2,4-triazacyclohexane *(33)* [Z=NMe (*eq*)]; 3,4-dimethyl-1-oxa-3,4-diazacyclohexane *(35)* [Z=O]; and 3,4-dimethyl-1-thia-3,4-diazacyclohexane *(34)* [Z=S]. Values in kcal/mol.

## 10. 1,2,4-Triheteracyclohexanes without Two Adjacent *N*-Methyl Groups

We consider first the compounds with a single N atom. The barriers in 2-methyl-1,4-dioxa-2-azacyclohexane *(39)* and 2-methyl-1-oxa-4-thia-2-azacyclohexane *(40)* can be compared with those of *(12)* and *(13)* to demonstrate that the effect of an α-oxygen atom is to raise the *ax→ts* and *eq→ts* barriers by 2.9 and 3.9—4.5 kcal/mol, respectively. This can be compared with the value of ≤4.7 and 5.7 kcal/mol for the effect of an α-oxygen on the barrier in *N*-methylpiperidine [cf. *(1)* and *(3)*]: additivity is evidently not maintained. A further comparison can be made with 2-methyl-1-oxa-2-azacyclohexane to determine the effect of a β-heteroatom: this is found to *lower* the *eq→ts* barrier by 3.0 and 2.9 kcal/mol for oxygen and sulfur, respectively [compare *(3)* with *(39)* and *(40)*]; corresponding effects on the *ax→ts* barrier are certainly much smaller and probably in the other direction, but cannot be calculated exactly.

The effects of adjacent geminal *C*-methyl groups on the N-inversion in *(39)* and *(40)* is shown by compounds *(41)* and *(42)* to raise *ax→ts* and *eq→ts* barriers by 0.6—1.0 and 0.3—0.4 kcal/mol, respectively.

The N-2-inversion process in 2,5-dimethyl-1-oxa-2,5-diazacyclohexane *(43)* shows that the γ-nitrogen atom has no noticeable effect: the *eq→ts* barrier is identical with that of *(3)*: in the *C*-methyl derivatives *(45)* and *(46)*, analogously high barriers are found for the N-2-inversion (13.1—13.9 kcal/mol) showing the small effect of α-C-methyl groups.

Comparison of the N-2-inversion processes in 2,4-dimethyl-1-oxa-2,4-diazacyclohexane *(44)* and 1,3-dimethyl-1,3-diazacyclohexane *(11)* shows that the α-oxygen atom increases the *ax→ts* and *eq→ts* barriers by 4.1 and 4.8 kcal/mol, respectively. Comparison with 2-methyl-1-oxa-2-azacyclohexane *(3)* indicates that the β-nitrogen atom in *(44)* raises the *ax→ts* barrier by ≥0.4 and lowers the *eq→ts* barrier by 1.7 kcal/mol (see Fig. 3).

The N-5-inversion barrier for 2,5-dimethyl-1-oxa-2,5-diazacyclohexane *(43)* and the N-4-inversion barrier for the 2,4-analogue *(44)* are, within 0.2 kcal/mol, identical to the corresponding barriers in *(12)* and *(11)*, respectively, showing that the γ-oxygen and γ-nitrogen effects are negligible. The effect of a 6-methyl group in *(45)* or 6,6-*gem* dimethyl groups in *(46)* is almost zero for the *ax→ts* barrier but raises the *eq→ts* barriers of *(43)* by 0.7 kcal/mol: the former agree, but the latter is significantly greater than those found in the corresponding pair *(12)/(20)*.

---

[*] We do not consider any conformers with an axial *N*-4-Methyl group: the lowest energy of these (1*e*2*e*4*a*)- and (1*e*2*a*4*a*)-conformers still have energies *above* both *ae* and *ea*, and will not be involved in the *ae→ea* interconversion.

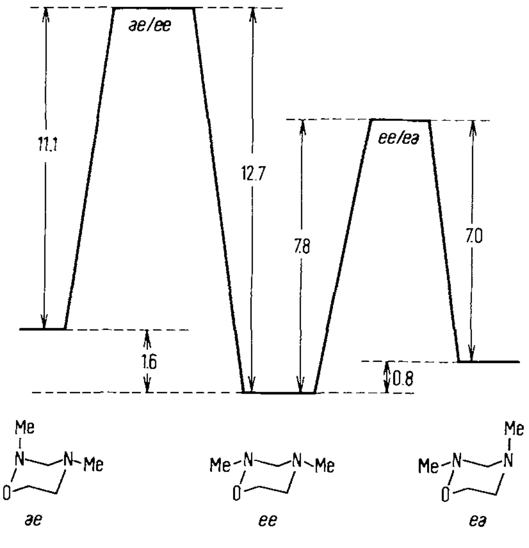
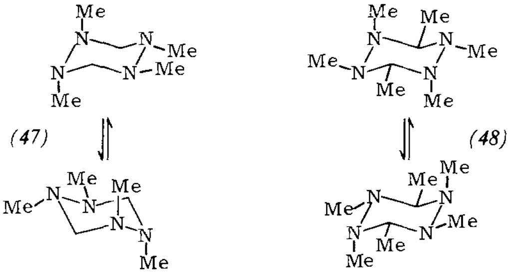


Fig. 3. Conformational equilibria and kinetics for 2,4-dimethyl-1-oxa-2,4-diazacyclohexane *(44)*. Values in kcal/mol.

## 11. Tetraheteracyclohexanes

Interconversion of the mirror image form of *sym*-tetramethyltetrazacyclohexane *(47)* (Scheme 4, left) involves either (i) passing ring inversion and non-passing N-inversion or (ii) passing N-inversion. We therefore know that the passing N-barrier *eq→ts* in *(47)* is ⩾11.8 kcal/mol. It would be expected to be similar to that for the 1,2,4-triaza-analogue *(33)* (12.0 kcal/mol).



Scheme 4.

In the hexamethyl analogue *(48)* (Scheme 4, right), the non-passing *eq→ts* barrier is 7.7 kcal/mol, almost identical to the corresponding barrier of 7.9 kcal/mol for *trans*-1,2,3,6-tetramethyl-1,2-diazacyclohexane *(30)*.

## 12. Summary

Due to substantial and variable conformational bias, N-inversion barriers in six-membered rings must be discussed in terms of the half-barriers *ax→ts* and *eq→ts*. For *N*-methylpiperidine we have decided that $\Delta G^{+}(ax\rightarrow ts)=6.0$ kcal/mol and $\Delta G^{+}$ $(eq\rightarrow ts)=8.7$ kcal/mol.

γ-Heteroatoms have negligible effects on both half-barriers (⩽0.2 kcal/mol). β-Heteroatoms *increase* the *ax→ts* (positive β-heteroatom effect), but *decrease* the eq→ts (negative β-heteroatom effect) barriers. These β-heteroatom effects are rather regular: an equatorial β-*N*-methyl group increases the *ax→ts* barrier by 1.0 kcal/mol, whereas β-oxygen and β-sulfur atoms have greater effects (+1.6 and +1.8 kcal/mol respectively). Similarly, the β-heteroatom effects on the *eq→ts* barrier are respectively −0.8, −1.2, and −1.6 kcal/mol for *eq* *N*-Me, -O and -S. The effects of α-heteroatoms are less regular: axial α-*N*-methyl groups significantly *decrease* the *eq→ts* barrier (*ca.* −1.1 kcal/mol), their effect on the *ax→ts* barrier is probably small. By contrast, equatorial α-*N*-methyl groups and α-oxygen atoms *increase* both the *ax→ts* and *eq→ts* barriers by 2.9−6.6 kcal/mol: the effect of an equatorial α-*N*-methyl group is greatest on the *ax→ts* and that of an α-oxygen is greatest on the *eq→ts* barrier.

α-*C*-methyl groups show small effects on the barriers, unless either three methyl groups on adjacent ring atoms result or a geminal dimethyl group is involved. In the former case, the *ax→ts* barriers are considerably increased, but the effect is less regular on *eq→ts*. In the latter case the reverse applies.

These effects are rationalized in terms of steric and electronic interactions.

## 13. General Significance of Results

The concept of using "half-barriers" to describe conformational changes does not appear to have been much utilized in the past, but it is clearly of general applicability. In principle, for any biased equilibrium the energy of the transition state relative to the ground state depends on which of the two (or more) ground states is considered as reference. This applies, for example, to the conformational equilibria of carbocyclic compounds, to inversion barriers for acyclic pyramidial compounds containing a chiral center, and to many rotational barriers.

Underlining the importance of realization of this concept is the fact that different experimental measurements are related to different ground states. General adoption of the quotation of equilibrium interconversions in terms of half-barriers, as described in the present paper, would be helpful in avoiding ambiguity and confusion.

Received: January 2, 1980 [A 374 IE]
German version: Angew. Chem. *93*, 567 (1981)

---

[1] *I. D. Blackburne, A. R. Katritzky, Y. Takenchi,* Acc. Chem. Res. *8,* 300 (1975).

[2] a) *I. J. Ferguson, A. R. Katritzky, D. M. Read,* J. Chem. Soc. Chem. Commun. *1975,* 255; b) *F. G. Riddell, ibid. H. Labaziewicz 1975,* 766.

[3] a) *F. A. L. Anet, I. Yavari, I. J. Ferguson, A. R. Katritzky, M. Moreno-Mañas, M. J. T. Robinson,* J. Chem. Soc. Chem. Commun. *1976,* 399; b) *D. C. Appleton, J. McKenna, J. M. McKenna, L. B. Sims, A. R. Walley,* J. Am. Chem. Soc. *98,* 292 (1976); c) *P. J. Crowley, M. J. T. Robinson, M. G. Ward,* Tetrahedron *33,* 915 (1977).

[4] *E. Wyn-Jones, R. A. Pethrick,* Top. Stereochem. *5,* 269 (1970).

[5] *V. M. Gittins, P. J. Heywood, E. Wyn-Jones,* J. Chem. Soc. Perkin Trans. 2 *1975,* 1642.

[6] *F. A. Bovey, E. W. Anderson, F. P. Hood, R. L. Kornegay,* J. Chem. Phys. *40,* 3099 (1964).

[7] *J. B. Lambert, W. L. Oliver, Jr., B. S. Packard,* J. Am. Chem. Soc. *93,* 933 (1971).

[8] *F. G. Riddell, J. M. Lehn, J. Wagner,* Chem. Commun. *1968,* 1403.
[9] *F. G. Riddell, J. E. Anderson,* J. Chem. Soc. Perkin Trans. 2 *1977,* 588.
[10] *F. G. Riddell, E. S. Turner, A. Boyd,* Tetrahedron *35,* 259 (1979).
[11] *J. E. Anderson, A. C. Oehlschlager,* Chem. Commun. *1968,* 284.
[12] *J. M. Lehn,* Fortschr. Chem. Forsch. *15,* 311 (1970).
[13] *M. Davis, H. M. Hügel, R. Lakhan, B. Ternai,* Aust. J. Chem. *29,* 1445 (1976).
[14] *S. F. Nelsen, G. R. Weisman, E. L. Clervan, V. E. Peacock,* J. Am. Chem. Soc. *98,* 6893 (1976).
[15] *S. F. Nelsen, G. R. Weisman,* J. Am. Chem. Soc. *98,* 1842 (1976).
[16] *F. G. Riddell, A. J. Kidd,* J. Chem. Soc. Perkin Trans. 2 *1977,* 1816.
[17] *D. Hofner, I. Tamir, G. Binsch,* Org. Magn. Reson. *11,* 172 (1978).
[18] *D. Hofner, S. A. Lesko, G. Binsch,* Org. Magn. Reson. *11,* 179 (1978).
[19] *F. G. Riddell, M. H. Berry, E. S. Turner,* Tetrahedron *34,* 1415 (1978).
[20] *A. R. Katritzky, R. C. Patel,* J. Chem. Soc. Perkin Trans. 2 *1980,* 279.
[21] *S. F. Nelsen,* Acc. Chem. Res. *11,* 14 (1978).
[22] *R. A. Y. Jones, A. R. Katritzky, R. Scattergood,* Chem. Commun. *1971,* 644.
[23] *G. R. Weisman, S. F. Nelsen,* J. Am. Chem. Soc. *98,* 7007 (1976).
[24] *S. F. Nelsen, G. R. Weisman,* J. Am. Chem. Soc. *98,* 3281 (1976).
[25] *A. R. Katritzky, R. C. Patel,* J. Chem. Soc. Perkin Trans. 2 *1979,* 984.
[26] *H.-J. Schneider, L. Sturm,* Angew. Chem. *88,* 574 (1976); Angew. Chem. Int. Ed. Engl. *15,* 545 (1976).
[27] *A. R. Katritzky, V. J. Baker, I. J. Ferguson, R. C. Patel,* J. Chem. Soc. Perkin Trans. 2 *1979,* 143.
[28] *A. R. Katritzky, V. J. Baker, F. M. S. Brito-Palma,* J. Chem. Soc. Perkin Trans. 2 *1980,* 1734.
[29] *A. R. Katritzky, V. J. Baker, F. M. S. Brito-Palma, I. J. Ferguson, L. Angiolini,* J. Chem. Soc. Perkin Trans. 2 *1980,* 1746.
[30] *V. J. Baker, I. J. Ferguson, A. R. Katritzky, R. Patel, S. Rahimi-Rastgo,* J. Chem. Soc. Perkin Trans. 2 *1978,* 377.
[31] *I. J. Ferguson, A. R. Katritzky, R. Patel,* J. Chem. Soc. Perkin Trans. 2 *1976,* 1564.
[32] *J. E. Anderson,* J. Am. Chem. Soc. *91,* 6374 (1969).
[33] *A. R. Katritzky, R. C. Patel, D. M. Read,* Tetrahedron Lett. *1977,* 3803.
[34] *I. J. Ferguson, A. R. Katritzky, D. M. Read,* J. Chem. Soc. Perkin Trans. 2 *1976,* 1861; *A. R. Katritzky, R. C. Patel, F. M. S. Brito-Palma, F. G. Riddell, E. S. Turner,* Isr. J. Chem. *29,* 150 (1980).
[35] *R. A. Y. Jones, A. R. Katritzky, A. R. Martin, S. Saba,* J. Chem. Soc. Perkin Trans. 2 *1974,* 1561.
[36] *A. R. Katritzky, R. C. Patel, F. G. Riddell, E. S. Turner,* unpublished results.
[37] *A. R. Katritzky, R. C. Patel,* Heterocycles 9, 263 (1978); *F. G. Riddell, E. S. Turner, ibid.* 9, 267 (1978); *A. R. Katritzky, R. C. Patel,* J. Chem. Soc. Perkin Trans. 2 *1979,* 993; *F. G. Riddell, E. S. Turner,* J. Chem. Res. (S) *1978,* 476.
[38] *F. G. Riddell, E. S. Turner,* Heterocycles 9, 267 (1978); *F. G. Riddell, E. S. Turner, A. R. Katritzky, R. C. Patel, F. M. S. Brito-Palma,* Tetrahedron *35,* 1391 (1979).
[39] *V. J. Baker, A. R. Katritzky, J.-P. Majoral, A. R. Martin, J. M. Sullivan,* J. Am. Chem. Soc. *98,* 5748 (1976).
[40] *A. R. Katritzky, I. J. Ferguson, R. C. Patel,* J. Chem. Soc. Perkin Trans. 2 *1979,* 981.

---

# Benzvalene—Properties and Synthetic Potential

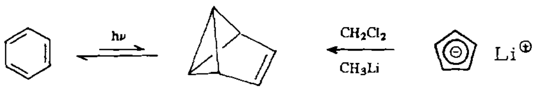
## By Manfred Christl[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

Today, thanks to the versatile synthesis developed by *Katz et al.*, benzvalene is not only the most extensively studied valence isomer of benzene but also one of the most easily synthesized bicyclo[1.1.0]butane derivatives. The double bond in this highly strained hydrocarbon is particularly reactive owing to interactions between the σ system and the double bond. Benzvalene is one of the most reactive olefins toward electron deficient substrates. Furthermore, the compound is bifunctional, since after addition to the π system the ring strain of the σ system provides the driving force for rearrangement or further addition reactions. This paper summarizes the spectroscopic properties and the reactivity of benzvalene. In order to demonstrate the importance of benzvalene and its derivatives as building blocks in organic synthesis the chemistry of compounds arising from benzvalene is also discussed. The article concludes with a summary of substituted benzvalenes.

## 1. Introduction

For the research chemist to be interested in a particular compound, three important requirements must be met: first, it must be easily accessible, it should be highly reactive, and the reaction products must show interesting properties. Cyclooctatetraene, norbornene and without doubt benzvalene *(1)* are examples of compounds satisfying these conditions.



*(1)*

The substituted derivatives *(243)*[1] and *(245)*[2] (Section 4) were already known when in 1967 *Wilzback et al.*[3] identified benzvalene *(1)* as a photoproduct of benzene. Four years later, *Katz et al.*[4,5] reported a versatile synthesis starting from lithium cyclopentadiene, dichloromethane, and methyllithium, which made it possible to obtain 20 g quantities of *(1)*. This opened up the way for intensive studies of its physical and chemical properties and also

---

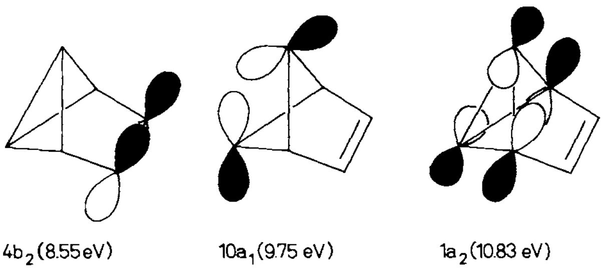
[*] Prof. Dr. M. Christl
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

0570-0833/81/0707-529 $ 02.50/0

permitted an experimental evaluation of theoretical predictions[6,7].

## 2. Spectroscopy of Benzvalene

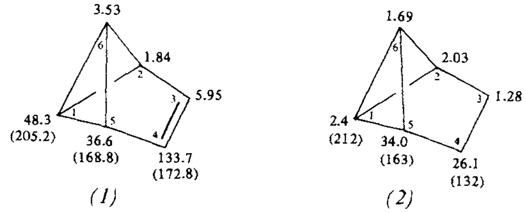
The presence in benzvalene *(1)* of two functionalities in close proximity, namely the olefinic double bond and the bicyclo[1.1.0]butane system, leads to strong interactions. This results in a UV absorption band with a maximum at $\lambda = 217$ nm ($\varepsilon \approx 2500$)[8]. In contrast, 1,2-dialkylethylenes and bicyclo[1.1.0]butane[9] show no significant absorption above 200 nm. This relatively longwave band is due, at least in part, to the increased energy of the double bond $\pi$ orbital ($4b_2$) as a result of interaction with an occupied orbital of the proper symmetry in the bicyclo[1.1.0]butane system. This follows from the photoelectron spectrum where the first ionization potential appears at 8.55 eV[10-12] (for comparison: cyclopentene 9.01, 9.18 eV[13a]; norbornene 8.97 eV[13]). Scheme 1 shows the three highest occupied orbitals of *(1)*. The ordering is based on calculations[6,10], according to which the second absorption band at 9.75 eV is due to the orbital ($10a_1$) localized almost exclusively in the central bond of the bicyclo[1.1.0]butane system. The $1a_2$ orbital (corresponding to the third ionization band at 10.83 eV) is an important contributor to the four peripheral bicyclo[1.1.0]butane bonds. The second and third ionization potentials of *(1)* are increased and decreased, respectively, in comparison with those of the unsubstituted bicyclo[1.1.0]butane (9.39 and 11.30 eV[12]). This is a consequence of the decreased angle between the two three-membered rings due to the etheno bridge[10]. It is interesting to note that in homobenzvalene *(118)* the order of the two highest occupied orbitals is interchanged: here, the HOMO is the $\sigma$ orbital of the central bicyclo[1.1.0]butane bond[12,14].



Scheme 1. The three highest occupied orbitals of benzvalene *(1)*.

The structural parameters of *(1)* were established using microwave spectroscopy[15] and electron diffraction[16]. The results are in agreement with the exception of the CH bond lengths (1.08 Å[15] and 1.14 Å[16], resp.). The dihedral angle is reduced from 121.7° in bicyclo[1.1.0]butane[17] to 106° in *(1)*. Therefore, the central bond arising from atomic orbitals possessing more than 90% p-character is shortened, from 1.497 Å in bicyclo[1.1.0]butane (C1—C3)[17] to *ca.* 1.45 Å in *(1)* (C1—C6). This trend is even more evident in the case of the bicyclo[1.1.0]butanes where the dihedral angles are even smaller[18]. The dipole moment of *(1)*, 0.88 D[19], obtained from the Stark effect in the microwave spectrum, is somewhat larger than that of bicyclo[1.1.0]butane (0.68 D)[17]. Calculations[6] show that for both molecules the negative end of the dipole is on the *endo* side of the bicyclo[1.1.0]butane system, *i.e.* in *(1)* at the site of the C=C double bond, which itself, however, contributes only 20% to the dipole moment.

The IR[20] and Raman spectra[21] of *(1)* have been thoroughly analyzed. The exceptionally low frequency (1556 cm$^{-1}$) of the C=C stretching vibration as well as the NMR spectra (Scheme 2) undoubtedly reflect the conjugation between the double bond and the strained $\sigma$ system. The signal for the allylic protons (2,5-H) appears at $\delta = 1.84$, *i.e.* at considerably higher field than the protons in the 1,6-position ($\delta = 3.53$)[3]. The unusually low field absorption of 1,6-H compared to the saturated system *(2)*[22] is also reflected in the corresponding $^{13}C$ chemical shifts: *(2)* shows signals at $\delta = 2.4$ and 34.0 which are typical values for the central and lateral hydrogen atoms in bicyclo[1.1.0]butanes[22,23]. In *(1)* the sequence is inverted. Although the position of the C2,5 signal is more or less unchanged, the C1,6 signal appearing at $\delta = 48.3$ is shifted by 45.9 ppm to lower field[24,25]. This low field shift arises from the interaction between the $\pi^*$ orbital of the double bond and the $a_2$ orbital of the bicyclo[1.1.0]butane system. This is also found in other rigid envelope-shaped cyclopentenes, the magnitude depending on the degree of ring strain[24]. Also the $^{13}C—^1H$ coupling constants in *(1)* and *(2)* show significant differences.

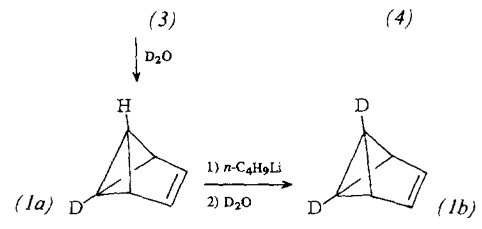


Scheme 2. $^1H$- (at positions 6,2,3) and $^{13}C$-NMR data (at positions 1,5,4, in brackets $J_{^{13}C^1H}$ in Hz) of benzvalene *(1)* and dihydrobenzvalene *(2)*. $\delta$ values, measured in $C_6H_6$ and $CDCl_3$, respectively.

## 3. Reactions of Benzvalenes

### 3.1. Metalation

As in other bicyclo[1.1.0]butanes[26] the bridgehead hydrogen atoms 1,6-H in *(1)* are comparatively acidic and therefore react easily with butyllithium to give the metalated product 1-benzvalenyllithium *(3)*[27]. This in turn reacts with methyl iodide to give 1-methylbenzvalene *(4)*[28] or with heavy water to give 1-deuteriobenzvalene *(1a)*. The



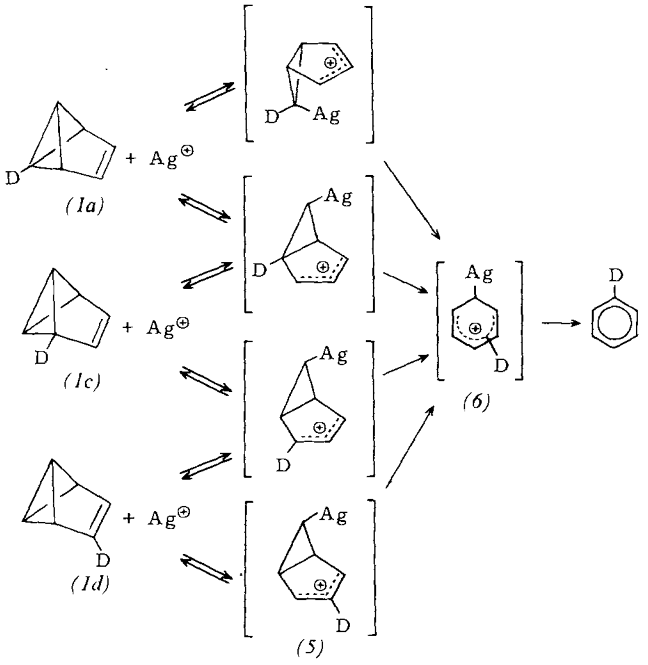
latter can undergo a further metalation, followed by treatment with $D_2O$, giving 1,6-dideuteriobenzvalene *(1b)*[27]. *(1a)*, which can also be obtained from $CD_2Cl_2$ by the Katz synthesis[29], as well as *(1b)* are highly useful in mechanistic studies.

### 3.2. Isomerization and Formation

*Hückel*[30] mentioned the formula for tricyclo[3.1.0.0$^{2,6}$]hex-3-ene already in 1937. The trivial name, benzvalene, is, however, due to *Viehe*[1,31] who wished to convey not only the relationship with benzene, but also the possibility of degenerate valence isomerism (automerization)—*e.g.* through a 1,3-shift of the C6—C2 bond. According to the principle of the conservation of orbital symmetry[32], at the time unknown, the process is thermally forbidden and also unobserved due to the migration being forced to occur suprafacially and with retention of configuration at the migrating C atom.

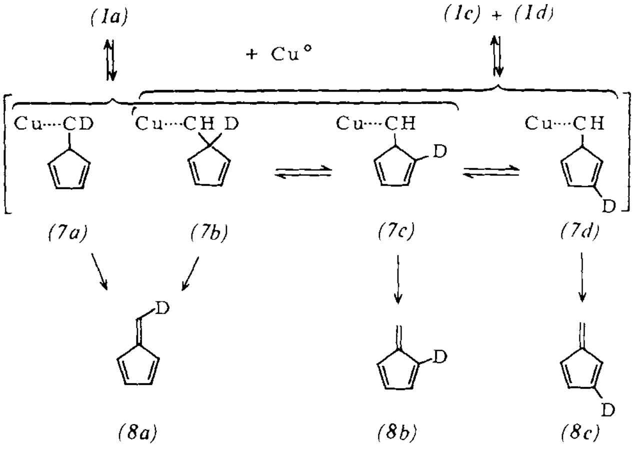
#### 3.2.1. Silver Ions and Metals

*Burger* and *Mazenod* have shown that silver(I) ions[33] and copper(0)[34] catalyze an automerization of *(1)*[25]. $Ag^{\oplus}$ ions catalyze the isomerization of *(1)* to benzene. When the isomerization of *(1a)* is interrupted after one half-life, the deuterium label is found distributed over positions 1, 2 and 3 [*(1a)*, *(1c)*, and *(1d)*]. The fact that the starting benzvalene is labeled in only *one* position means that a reversible reaction, involving *two* cations of the type *(5)*, must be involved[33]. This mechanism also explains the formation of *o*-, *m*-, and *p*-dideuteriobenzene when *(1b)* is treated with silver salts[35]. The end product of the *(1a)* isomerization reaction, deuteriobenzene, is probably formed from the cation *(5)* *via* argentobenzenium ions of the type *(6)*. The *endo* attack by $Ag^{\oplus}$ on *(1a)*, *(1c)*, and *(1d)* is analogous to protonation (see Section 3.3.1), where the stereochemical course of the reaction has been established. The $Ag^{\oplus}$-catalyzed rearrangement of tricyclo[4.1.0.0$^{2,7}$]heptane to 1,3-cycloheptadiene derivatives (the so-called α-rearrangement) is analogous to the benzvalene isomerization[36].



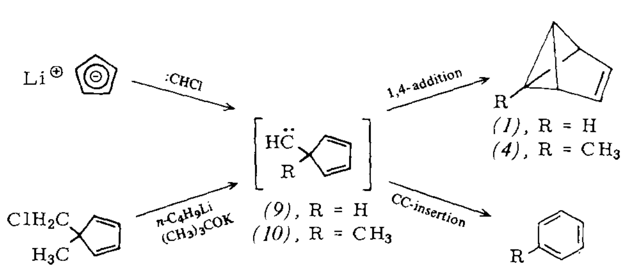
Whereas metallic silver and iron transform *(1)* into benzene, platinum, palladium, gold, nickel, and copper[3] catalyze the isomerization to fulvene *(8)*[34]. When *(1a)* reacts with copper, after *ca.* 100 sec at 25 °C, the benzvalene derivatives *(1a)*, *(1c)*, and *(1d)* are isolated in the ratio: 81 : 12 : 7. It was postulated in this case that the reaction proceeds by reversible 1,2- or 1,4-retrocarbene addition *via* the copper cyclopentadienylcarbene complexes *(7a)*–*(7c)*.

A second scrambling process must be involved because the ratio of the fulvene products *(8a)* : *(8b)* : *(8c)* (56 : 24 : 20), deviates strongly from that of *(1a)* : *(1c)* : *(1d)*. This second process must be a [1,5]-H migration leading to an equilibrium between *(7b)*, *(7c)*, and *(7d)*. The irreversible [1,2]-H shift to the exocyclic carbon atom completes the formation of the fulvene. The gas chromatography of *(1a)* on a copper column reportedly gives a quantitative yield of *(8a)*[37a].



#### 3.2.2. The Mechanism of the Katz Benzvalene Synthesis

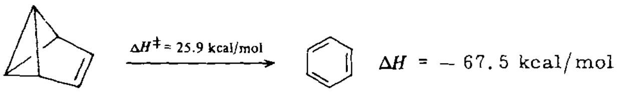
The above processes do not play a role in the Katz synthesis of *(1)* because when labeled dichloromethane is used, the resulting benzvalene is labeled in the 1-position only[29], and benzene is the only side product. A likely intermediate is the cyclopentadienylcarbene *(9)* which undergoes ring expansion to benzene, however, in the main reaction cyclizes to *(1)*, the latter process being an extremely rare 1,4-addition of a carbene.



The fact that, apart from toluene and spiro[2,4]hepta-4,6-diene only 1-methylbenzvalene *(4)* is formed in the reaction of *(10)* (formed from 5-chloromethyl-5-methylcyclopentadiene), excludes participation of the equally possible 1,2-addition as shown by *Burger* and *Gandillon*[28]. Early reports of benzvalenes labeled in all possible positions[15,37b] in the synthesis with D- or $^{13}$C-labeled dichloromethane do not, therefore, concern the synthesis itself, but rather the subsequent metal-catalyzed automerization.

### 3.2.3. Thermolysis and Thermochemical Data

The half-life of the thermal isomerization of *(1)* to benzene in ether at 30 °C is 48 h[28]. In *n*-heptane an enthalpy of activation of 25.9 kcal/mol was measured. The reaction enthalpy for the Ag$^{\oplus}$-catalyzed process is −67.5 kcal/mol[38]. Since the transformation to benzene is so exothermic, and the activation energy so low, it is not surprising that pure *(1)* is susceptible to detonation[4]. Yet, it can be safely handled in dilute solution.



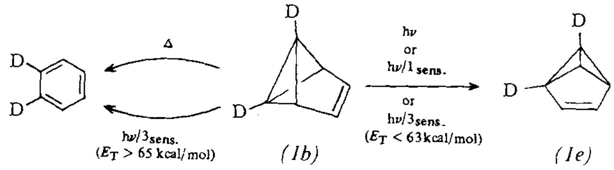
An approximate value of the heat of formation of *(1)* (87.3 kcal/mol) can be calculated from the standard heat of formation of benzene (19.8 kcal/mol)[39]. Group increments[39] yield a $\Delta H_f^0$ value of 10.4 kcal/mol for strain free *(1)*. In other words, the strain energy of *(1)* is *ca.* 77 kcal/mol, or a little higher than the sum of the strain energies of bicyclo[1.1.0]butane (67 kcal/mol) and cyclopentene (5.9 kcal/mol)[39].

According to MINDO/3 calculations the value of $\Delta H_f^0$ was at first estimated to be 114[40] and then 102 kcal/mol[10,41]. When this is compared with the MINDO/3 value of $\Delta H_f^0$ for benzene, then a reaction enthalpy which is slightly too high, *i.e.* 73 kcal/mol[41] for the transformation of *(1)* into benzene, is found. Although a one-step thermal transformation of an *endo,endo*-bridged bicyclo[1.1.0]butane into a *cis,cis*-butadiene is forbidden[32], not only MINDO/3[42], but other calculations[43,44] as well, favor a *concerted* thermal transformation of *(1)* into benzene. This is because the double bond is involved in a six-electron process. The calculated[42] activation energy of 21.5 kcal/mol is somewhat too low.

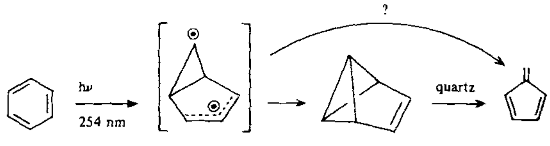
Experimental findings are also in agreement with the idea of a one-step process. Two plausible intermediates in the stepwise processes are the diradical *(11)* and Dewar benzene formed *via cis,cis,trans*-cyclohexatriene[45]. When the activation energy is compared with those of the thermal rearrangements of dihydrobenzvalene *(2)* and homobenzvalene *(118)*[46], or with the $\Delta H_f^0$ calculated for *(11)* using group increments[39], then the activation enthalpy of 25.9 kcal/mol does not seem to be large enough to generate *(11)* from *(1)*. The benzene formed in the thermolysis of Dewar benzene (by a forbidden process)[32] is chemiluminescent[47]. That formed from *(1)* is not[38], in spite of the fact that the energy liberated from the transition state (ca. 93 kcal/mol) would be more than sufficient for creation of the triplet state of benzene (*ca.* 82 kcal/mol). It follows, therefore, that Dewar benzene cannot be an intermediate in this reaction. The lack of chemiluminescence in pericyclic reactions is taken as evidence for a concerted reaction, since theory predicts the crossing of the energy surfaces for ground and triplet states and hence chemiluminescence in forbidden pericyclic reactions. As expected for a one-step reaction, the thermolysis of *(1b)* gives *o*-dideuteriobenzene[38].

### 3.2.4. Photochemistry and Photochemical Formation

In contrast to the above, direct irradiation as well as photolysis in the presence of singlet (pyrene) or triplet sensitizers (triplet energy, $E_T$, between 53 and 63 kcal/mol) leads to automerization, *i.e.* formation first of *(1e)* and then benzvalenes with two statistically scrambled deuterium atoms[48].



This is the [1,3] shift already mentioned, which *Viehe*[1,31] had in mind when naming the compound. A second benzvalene triplet state is populated using higher energy triplet sensitizers. The second triplet does not significantly decay to the first, but rather to the triplet state of benzene. The end product is *o*-dideuteriobenzene, formed with a quantum yield of *ca.* 4[48], presumably because triplet benzene sensitizes the isomerization of *(1)* to benzene[51], thereby inducing a chain process.



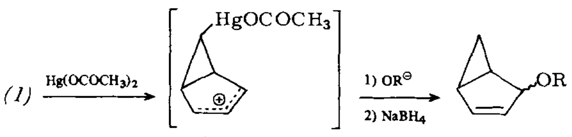
*(11)* *(1)* *(8)*

As mentioned in the introduction, *(1)* was first obtained by photolysis of benzene[3], a process in which fulvene *(8)* had already been discovered[49]. Neither of these isomers can be obtained in a yield higher than 300—500 mg per liter of pure benzene on direct irradiation at 254 nm[45]. The yields of *(1)* and *(8)* can be increased by dilution of the benzene with alkanes[3]. As common intermediate, the diradical *(11)* has been proposed[45,50]. However, *(8)* is possibly derived from *(1)* in a quartz-catalyzed reaction[45,51]. *(1)* is obtained in a measurable concentration in the direct gas-phase photolysis of benzene only in the presence of additives, which facilitate the vibrational relaxation of *(1)* and inhibit its benzene-sensitized reverse reaction[51]. The irradiation of liquid benzene at 160—200 nm gives a mixture of *(1)* and *(8)* and Dewar benzene[52].

### 3.3. Stepwise Additions to Benzvalene

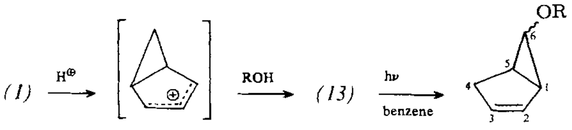
#### 3.3.1. Oxymercuration and Action of Acids

A possible intermediate in the oxymercuration[53] of *(1)* is the cation *(12)* which is analogous to the intermediate *(5)* in the Ag$^{\oplus}$-catalyzed isomerization. The cation *(12)*, however, is trapped by nucleophiles such as acetate or methanolate ions (R = CO—CH$_3$ or CH$_3$). Work-up with sodium borohydride gives low yields of the bicyclo[3.1.0]hexenyl acetates or the methyl ethers *(13)*.



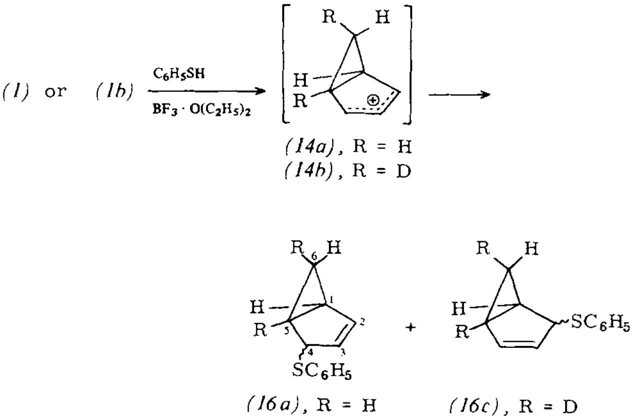
*(12)* *(13)*

Acids also react with *(1)* to give bicyclo[3.1.0]hexene derivatives. Even before the intermediate formation of *(1)* was clarified, compounds of the type *(13)* were isolated when benzene was photolyzed in acidified hydroxylated solvents (ROH = CH$_3$CO$_2$H, CF$_3$CH$_2$OH, CH$_3$OH, H$_2$O)[54]. The 6-substituted bicyclo[3.1.0]hexene derivatives *(15)* also formed originate from the benzene-sensitized vinylcyclopropane-cyclopentene rearrangement of *(13)*.



*(14)* *(15)*

Using deuterium-labeled substrates[4,54] it has been established that, in analogy to other bicyclo[1.1.0]butanes[55], a proton attacks at the bridgehead carbon, with retention, from the *endo* side. Whether or not the nucleophile ROH enters in the *exo* or *endo* position of the bicyclo[3.3.0]hexenyl cation *(14)* depends on the acidity of the medium. In a strongly acidic medium "free" *(14)* is present; thus, the nucleophiles can attack from the more sterically favorable *exo* side. On the other hand, in weakly acidic media the proton transferring, and hence *endo* oriented nucleophile has a better chance of attacking; the result is that up to 50% *endo-(13)* is formed[54].



*(14a)*, R = H
*(14b)*, R = D

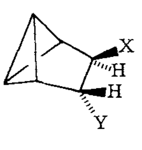
*(16a)*, R = H
*(16b)*, R = D
*(16c)*, R = D

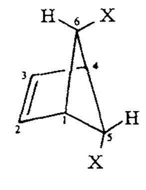
Thiophenol reacts with *(1)* in the presence of boron trifluoride etherate like an acid, giving a high yield of predominately *exo-(16a)*[56]. In agreement with the above, the use of *(1b)* as starting material leads to the specific appearance of one deuterium atom in the *exo*-6 position; the other deuterium atom is evenly distributed over positions 1 and 5, thus giving a 1 : 1 mixture of *(16b)* and *(16c)*[57]. The presence of a deuterium atom at one bridgehead carbon means that in contrast to *(14a)*, *(14b)* is unsymmetrical. Hence, there are two different but equivalent centers for attack by the sulfur nucleophile.

#### 3.3.2. Halogens

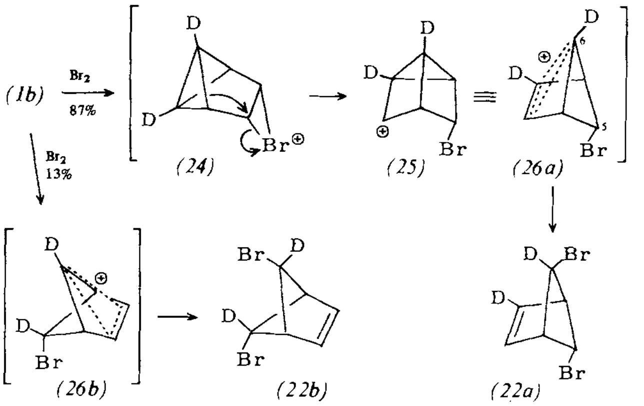
The behavior of *(1)* toward the halogens is dependent both on the nature of the halogen and the reaction conditions employed. With ether as solvent, iodine in CHCl$_3$, iodine and tetrapropylammonium bromide or tetraethylammonium chloride in acetonitrile, all react with *(1)* to give the *trans* adducts *(18)*—*(20)*[58]. Under these conditions, the initially formed iodonium ion is opened by an iodide, bromide, or chloride ion. Only a small quantity of the *trans* adduct *(17)*[58] is formed with either pyridinium hydrobromide perbromide or the dimethyl sulfide-bromine complex. The main product is the *endo,anti*-5,6-dibromobicyclo[2.1.1]hexene *(22)* which in the reaction of *(1)* with bromine in CCl$_4$ is the only product, isolated in quantitative yield[27,59,60]. Similarly, with chlorine in CCl$_4$, or iodine in acetonitrile, only the compounds *(21)*[59,60] and *(23)*[58], respectively, are isolated. Formally, the compounds *(21)*—*(23)* are adducts of the halogens to the C1—C6 bond of *(1)*. Mechanistically, however, this is only partially correct as seen in the bromination or chlorination of *(1b)*[27,60]. 87% of the bromine attacks the double bond. The resulting bromonium ion *(24)* undergoes a Wagner-Meerwein rearrangement to give *(25)* which is none other than the 6-bicyclo[2.1.1]hexenyl cation *(26a)* written in the classical form. The backside attack of a bromide ion at the C6 atom leads to *(22a)*. *(22b)* is probably formed from *(1b)* by bromine ca-

(17), X = Y = BR
(18), X = Y = I
(19), X = I, Y = BR
(20), X = I, Y = Cl





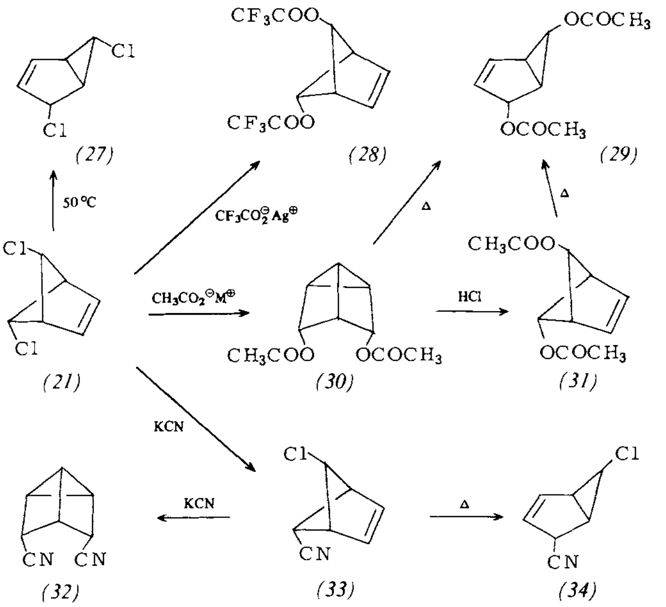
(21), X = Cl
(22), X = Br
(23), X = I



*(24)* *(25)* *(26a)*
*(26b)* *(22b)* *(22a)*

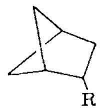
tion attack at C1. The central bond of bicyclo[1.1.0]butane is then thought to rupture through inversion to give the non-classically stabilized cation *(26b)*. The final step giving *(22b)* is analogous to that for *(26a)*→*(22a)*.

The fact that the halogen adducts are reactive is synthetically useful in the cases of *(21)* and *(22)*. Already at 50 °C, *(21)* is transformed into the bicyclo[3.1.0]hexene *(27)*. *(22)* reacts four times faster[60]. When *(21)* reacts with silver trifluoroacetate in benzene, the bistrifluoroacetate *(28)* is isolated[58]. On the other hand, with potassium acetate in acetonitrile or silver acetate in benzene, the bicyclo[2.2.0.0$^{2,6}$]hexane derivative *(30)* is formed, which can transform either into *(29)* on heating, or into *(31)* on treatment with HCl[59,60]. The bicyclo[2.1.1]hexene derivative *(31)* also rearranges thermally to *(29)*. In acetonitrile, with an excess of potassium cyanide, *(21)* gives *(32)*. When only one equivalent of potassium cyanide is used, the intermediate *(33)* is isolable; this in turn isomerizes thermally to *(34)*. The detailed study of the rearrangements of the bicyclo[2.1.1]hexene derivatives *(21)*, *(22)*, *(31)*, and *(33)* led to the discovery of a manifold of unexpected complex reaction mechanisms[60].



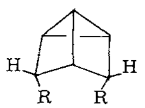
The double bond in the bicyclo[2.1.1]hexene derivative *(22)* was catalytically hydrogenated; subsequent replacement of the bromine atoms by hydrogen using triphenyltin hydride afforded bicyclo[2.1.1]hexane *(35)*[27,60].

A proof of the bicyclo[3.1.0]hexene structure was obtained when the hydrocarbon *(36)* was isolated after stepwise debromination of the bromo analog of *(27)*, first with LiAlH$_4$ and then with sodium in *tert*-butyl alcohol/tetrahydrofuran.

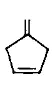


*(35)*, R = H
*(39)*, R = Br

*(36)*



*(37)*, R = H
*(37a)*, R = D



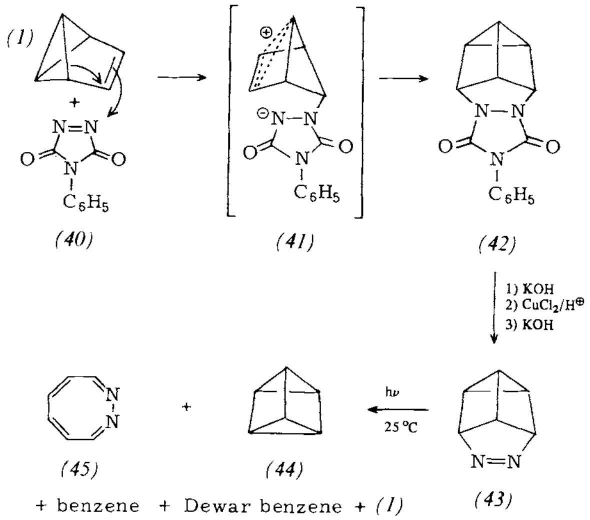
*(38)*

The reaction of *(22)* with an excess of LiAlH$_4$ afforded an economical pathway[27] to the known, but difficultly accessible C$_6$H$_8$ hydrocarbon *(37)*; *(36)* is the side product. *(37a)* is obtained when LiAlD$_4$ is used. Thus, both deuterium atoms are *endo*, which suggests the bicyclo[2.1.1]hexenyl cation as a plausible intermediate[37b]. *(22)* gives *(39)* when less than a fivefold excess of LiAlH$_4$ is used[27]. Both silver salts and [Rh(CO)$_2$Cl]$_2$ catalyze the isomerization of *(37)* to bicyclo[3.1.0]hexene *(36)* and 4-methylenecyclopentene *(38)*; with Ag$^\oplus$ formation of *(36)* is favored, with Rh(I) *(38)* is the main product.

### 3.3.3. 4-Phenyl-1,2,4-triazoline-3,5-dione *(40)* and Chlorosulfonyl Isocyanate

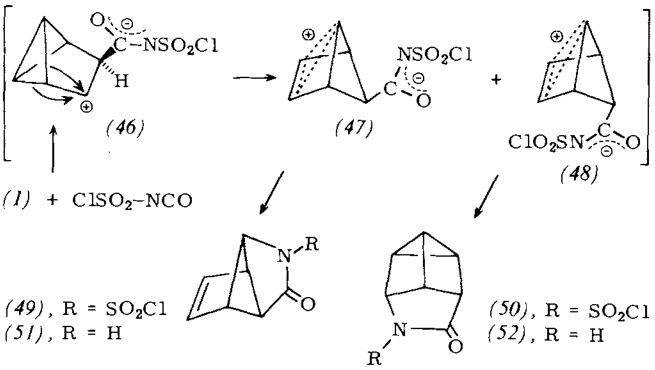
The mechanism of the addition of the triazolinedione *(40)* to benzvalene *(1)* is similar to that of the addition of bromine to *(1)*[61]. This assumption is supported by the observation made when *(40)* reacts with *(1b)*. It is possible that the non-classical zwitterion *(41)* is formed in an electrophilic addition followed by a Wagner-Meerwein rearrangement. The final step leads to *(42)*. This compound allows the preparation of the azo compound *(43)* which is also obtainable in an alternative synthesis[62]. Compound *(43)* affords only benzene on thermolysis[63a,64], but its photolysis represents the only route to the unsubstituted prismane *(44)*[61], which detonates when pure but in solution isomerizes slowly to benzene at 90 °C.

The direct irradiation of *(43)* at 25 °C gives mainly Dewar benzene and benzene, as well as small amounts of *(1)*, *(44)* and 1,8-diazacyclooctatetraene *(45)*[63a]. The low temperature photolysis, on the other hand, gives apart from benzene and *(45)*, only small amounts of *(1)* and Dewar benzene; *no (44)* is formed[64]. In the presence of the sensitizer acetophenone, *(43)* decomposes to *(45)* in 67% yield, together with benzene and nitrogen in 33% yield.



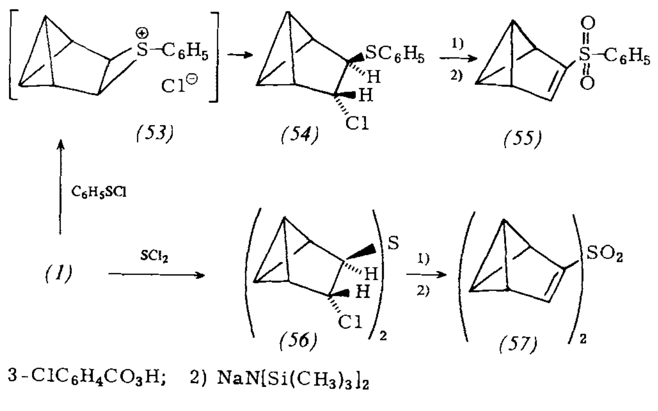
A secondary decomposition of *(45)* gives rise to the latter two products[63,65]. The synthesis and properties of *(45)* have been described in detail[65]. *(45)* is probably derived from the first triplet state of *(43)*, whereas the C$_6$H$_6$ isomers arise from the singlet state through cleavage of a C—N bond. The dependence of the product pattern on temperature and solvent observed in the direct photolysis of *(43)* is evidence for a competition between singlet-triplet transition and C—N bond cleavage; this bond breaking process requires thermal activation[63a].

Chlorosulfonyl isocyanate (CSI) attacks the strained σ bond system in bicyclo[1.1.0]butane derivatives[66], whereas it adds to the double bond in *(1)*. The reaction of *(1b)* with CSI supports the postulated mechanism[67]. The first intermediate is probably the zwitterion *(46)* containing the tricyclo[3.1.0.0$^{2,6}$]hexyl cation structure. In this intermediate both the *cis* and *trans*—with respect to the substituent—oriented bicyclo[1.1.0]butane bonds (C5—C6 and C1—C5) will migrate to the neighboring cationic center. This should give a mixture of the zwitterions *(47)* and *(48)* which cyclize to the *N*-chlorosulfonyllactams *(49)* and *(50)*. These are hydrolyzed by sodium hydroxide to the *N*-unsubstituted lactams *(51)* and *(52)*, whereas dimethylformamide transforms them into *(33)* and an isomer thereof.



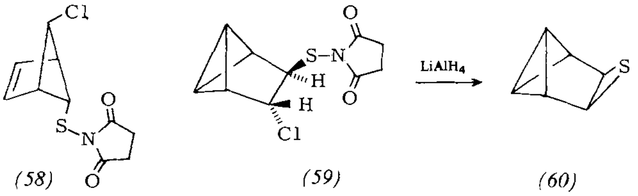
### 3.3.4. Sulfenyl Chlorides and Mercaptans

The mechanism of the addition of sulfenyl chlorides to olefinic double bonds is controversial. The participation of a free episulfonium ion such as *(53)* is not uncontested[68]. At any rate, the quantitative formation of the *trans* adduct *(54)*[67] from *(1)* and benzenesulfenyl chloride shows that rearrangement does not occur and therefore proves that an open carbocation analogous to *(46)* cannot be involved.

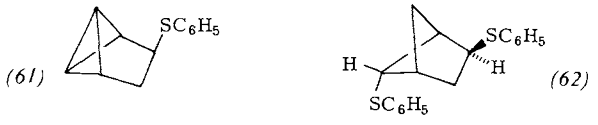


1) $3\text{-}ClC_6H_4CO_3H$; 2) $NaN[Si(CH_3)_3]_2$

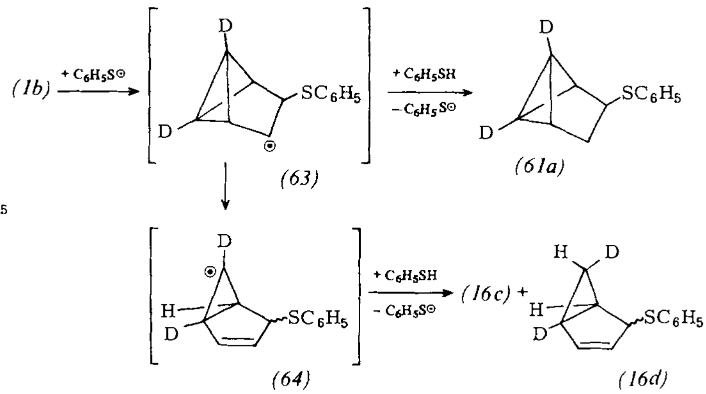
Sulfur dichloride reacts with two molecules of *(1)* to give *(56)*. *m*-Chloroperbenzoic acid oxidizes the thioethers *(54)* and *(56)* to the corresponding sulfones. From these, 3-benzvalenylphenyl sulfone *(55)*, as well as the explosive bis-3-benzvalenyl sulfone *(57)*, can be obtained by HCl elimination using sodium bis(trimethylsilyl)amide.



Benzvalenothiirane *(60)*[70] can be prepared using a new general method for the synthesis of thiiranes[69]. *N*-(chlorothio)succimide reacts with *(1)* giving a mixture of *(58)* and *(59)*. The succinimide moiety probably improves the leaving group ability of the sulfur in the intermediate episulfonium ion, thereby causing partial rearrangement to *(58)*. The main product *(59)* reacts smoothly with $LiAlH_4$ to give *(60)*, a stable isomer of the unknown parent thiepin.



The addition of thiophenol to *(1)* gives four products: *exo-* and *endo-(16a)* in a ratio of 6 : 1, together with *(61)* and *(62)*[56]. The formation of the bis-adduct *(62)* is the result of a slow secondary reaction between *(61)* and thiophenol following rapid addition of $C_6H_5SH$ to *(1)*; there is precedence for such reactions[71,72]. *(16a)* is also formed in the acid catalyzed reaction between *(1)* and $C_6H_5SH$ (see Section 3.3.1). In the uncatalyzed reaction, however, it is formed by a different mechanistic route as has been shown using *(1b)*[56,57].

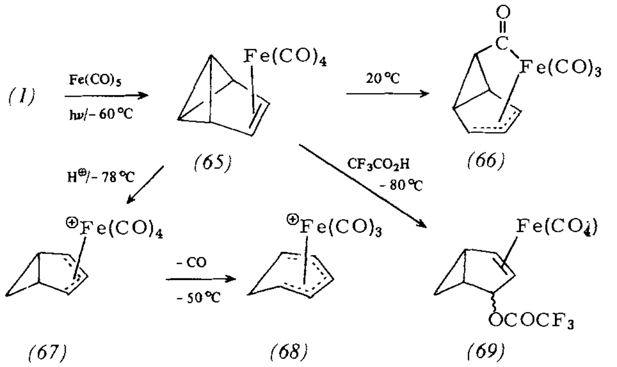


The reaction proceeds *via* a radical chain mechanism[73], in which the phenylthio radical, formed by air-oxidation of thiophenol, adds to the double bond in *(1b)*. The resulting *(63)* can react in two ways: hydrogen abstraction from thiophenol gives *(61a)*; a cyclopropylmethyl-homoallyl radical rearrangement gives *(64)*, which abstracts a hydrogen atom from thiophenol, non-stereospecifically, giving *(16c)* and

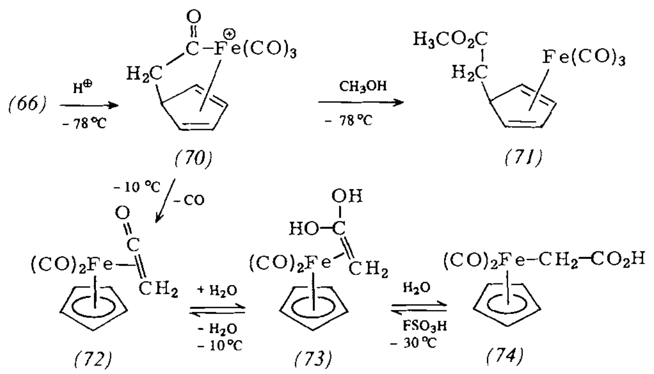
*(16d)* in the ratio 1:3[57]. The dependence of the ratio *(16a)*:*(61)* on the thiophenol concentration supports the above mechanistic scheme. This means that it is possible, starting from *(1)* with suitable choice of reaction conditions, to obtain *(16)*, *(61)* or *(62)* in essentially pure form and high yields[56]. Methylthiol reacts with *(1)* in the same way as thiophenol, giving the methyl analogs of *(16)* and *(61)*[57].

### 3.3.5. Carbonyliron Complexes

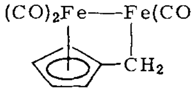
Low temperature photolysis of pentacarbonyliron in the presence of *(1)* gives the π complex *(65)*, which rapidly isomerizes to the acyl complex *(66)* above 10 °C[74]. Excess trifluoroacetic acid protonates *(65)* at −78 °C into the complexed bicyclo[3.1.0]hexenyl cation *(67)*. Above 50 °C, *(67)* looses a molecule of CO and undergoes ring expansion to the complexed cyclohexadienyl cation *(68)*.



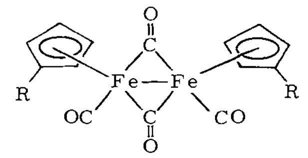
*(65)* reacts with only one equivalent of trifluoroacetic acid to give the neutral complex *(69)* with an *endo*-oriented trifluoroacetoxy group. At −10 °C an equilibrium is established between *exo*- and *endo-(69)* in which the *exo* isomer predominates. At the same time decay of *(69)* to *(68)* is also observed.



Protonation of *(66)* with fluorosulfonic acid in $SO_2ClF$ at −78 °C gives the cation *(70)* which reacts with methanol to the tricarbonyliron complex *(71)* of cyclopentadienylacetic acid methyl ester. *(70)* looses a molecule of CO at −10 °C giving the cationic ketene complex *(72)*. Thus, *(1)* has been transformed into the cyclopentadienyl ligand while coordinated to the iron atom. *(72)* is hydrolyzed by acid to *(74)*, presumably *via* the ketene hydrate complex *(73)*. This complex is regenerated from *(74)* at −30 °C through the action of fluorosulfonic acid, and at −10 °C is further dehydrated to *(72)*. The thermolysis of *(66)* in methanol at 40 °C gives benzene and the methyl ester of *(74)*.



*(75)*



*(76)*, R = H; *(77)*, R = $CH_3$

In contrast to the photochemically induced reaction of *(1)* with $Fe(CO)_5$ no primary product can be obtained in the thermal reaction with $Fe_2(CO)_9$ at 20 °C[74,75]. The hexacarbonylfulvenediiron *(75)* is obtained together with the two-center cyclopentadienyl and methylcyclopentadienyl complexes *(76)* and *(77)*, presumably *via* the common precursor *(66)*.

### 3.3.6. Orientation of Electrophilic Attack

So far, in all the reactions described for *(1)*, the reaction partners have been electrophiles; even the thio radicals can be so described. Most electrophiles selectively attack the double bond in *(1)*: 4-phenyl-1,2,4-triazolinedione, chlorosulfonyl isocyanate, sulfenyl chlorides, thio radicals, and carbonyliron complexes. Halogens also transfer a cation to the double bond in most cases, although with bromine and chlorine an *endo* attack on C-1 with inversion appears to compete to a small extent.

Protons, mercuric acetate and probably also silver ions attack C-1, as is usual for bicyclo[1.1.0]butanes, from the *endo* side. Retention of configuration is, however, observed.

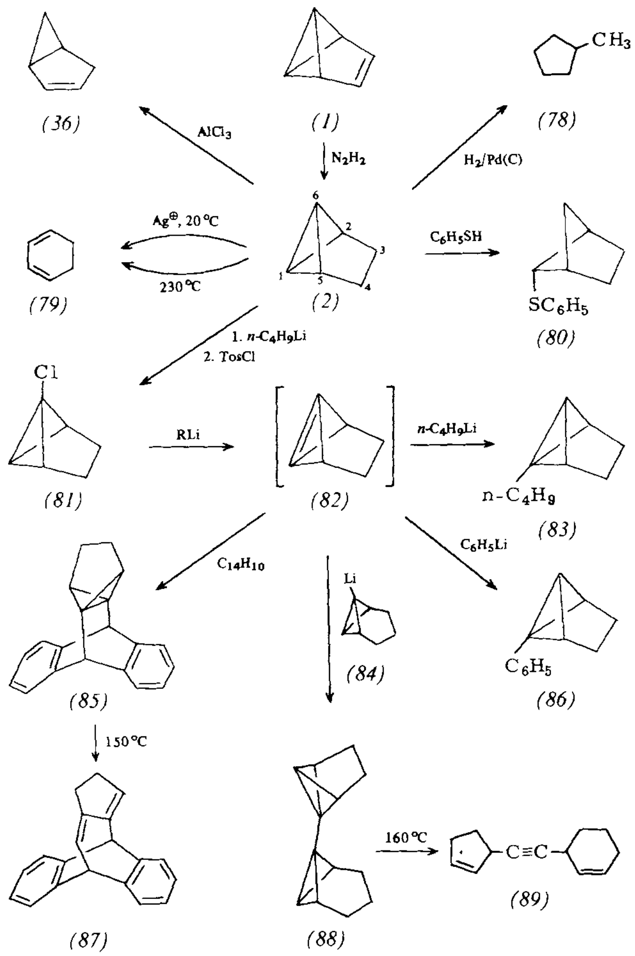
The reactions at the double bond of *(1)* are probably HOMO controlled, since the HOMO is represented by the π orbital (see Section 2). The *endo* addition to the σ system of *(1)* might be favored by the partial negative charge on the *endo* side. These ideas are opposed by the fact that mercury and silver ions are soft electrophiles.

## 3.4. Concerted Additions to the Benzvalene Double Bond

Electrophiles adding to *(1)* in multistep reactions can do so by attack at either the σ or π system. In contrast, the σ system is not capable of undergoing concerted additions. Consequently, all products arising from a concerted reaction retain the tricyclo[3.1.0.0$^{2,6}$]hexane framework *(2)*.

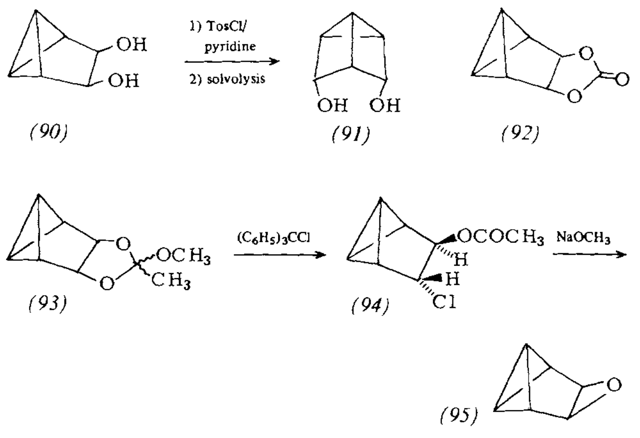
### 3.4.1. Hydrogenation with Diimine and *cis*-Hydroxylation

The double bond in *(1)* cannot be selectively saturated by catalytically activated hydrogen, since under these conditions dihydrobenzvalene *(2)* is transformed into methylcyclopentane *(78)*[76]. Furthermore, *(1)* should rearrange to fulvene in the presence of the usual hydrogenation catalysts (see Section 3.2.1) more rapidly than hydrogen is added. In contrast, diimine smoothly transfers two hydrogen atoms to the double bond of *(1)*[22]. Thus, *(2)*, which is also formed in low yield together with other $C_6H_8$ isomers on irradiation of 3-cyclopentenyldiazomethane[76], can be obtained in 10 g quantities for use in a variety of reactions (cf. Scheme 3).



Scheme 3. Products derived from tricyclo[3.1.0.0$^{2,6}$]hexane *(2)*.

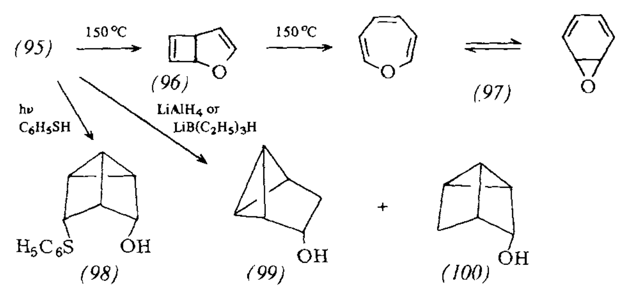
At 20 °C silver ions catalyze the isomerization of *(2)* to 1,3-cyclohexadiene *(79)*[22]. This reaction requires at least 230 °C in the absence of a catalyst. The kinetics of the latter reaction has been studied[46]. Aluminum chloride transforms *(2)* into bicyclo[3.1.0]hexene *(36)*. Thiophenol adds to *(2)* giving the bicyclo[2.1.1]hexane derivative *(80)*[71,72]. In analogy to *(1)*, *(2)* is also metalated with *n*-butyllithium. Treatment with $D_2O$ causes deuteration and a repetition of this procedure gives the 1,6-dideuterio derivative[22]. Using lithiated *(2)* and tosyl chloride *Szeimies et al.*[77] synthesized the 1-chloro derivative *(81)*; this in turn reacts with organolithium compounds, to the reactive intermediate *(82)* which is an isomer of *(1)*. As a highly strained bridgehead olefin, *(82)* readily adds *n*-butylltihium, phenyllithium, and tricyclo[4.1.0.0$^{2,7}$]hept-1-yllithium *(84)*, giving the hydrocarbons *(83)*, *(86)* and *(88)*, respectively. The latter compound isomerizes at 160 °C to give a quantitative yield of the substituted acetylene *(89)*. When *(82)* is generated in the presence of anthracene, a Diels-Alder addition occurs giving the propellane *(85)* which rearranges to the diene *(87)* at 150 °C.



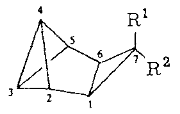
The *cis*-glycol *(90)* can be prepared from *(1)* and $KMnO_4$ using standard reaction conditions, or even better with *tert*-butyl hydroperoxide and $OsO_4$ as catalyst[78]. The ditosylate is formed when tosyl chloride in pyridine is employed. This in turn is solvolyzed in buffered aqueous acetone to the tricyclic diol *(91)* isomeric with *(90)*[70]. The cyclic carbonate *(92)* is formed from *(90)* and phosgene in pyridine. A mixture of two ortho esters *(93)* is formed from *(90)* and trimethyl orthoacetate when benzoic acid is used as a catalyst. The chlorohydrin acetate *(94)* can be prepared by reaction of *(93)* with trityl chloride and transformed into benzvalene oxide *(95)*[78].

### 3.4.2. [2 + 1]-Cycloaddition Reactions: Epoxidation and Halocarbene Additions

Attempts at the direct epoxidation of *(1)* using the usual peracids have so far met without success. Benzoylperoxycarbamic acid is the only reagent which affords *(95)* in good yield[78] together with benzamide und carbon dioxide. Preliminary thermolyses in solution at 150 °C indicate a rearrangement to the oxepin-benzene oxide system *(97)* *via* the 2-oxabicyclo[3.2.0]hexa-3,6-diene intermediate *(96)*[70]. On irradiation, thiophenol adds to *(95)* to give the rearranged tricyclic compound *(98)*; *(95)* is reduced by complex hydrides to give a 1 : 1 ratio of the isomeric alcohols *(99)* and *(100)*.



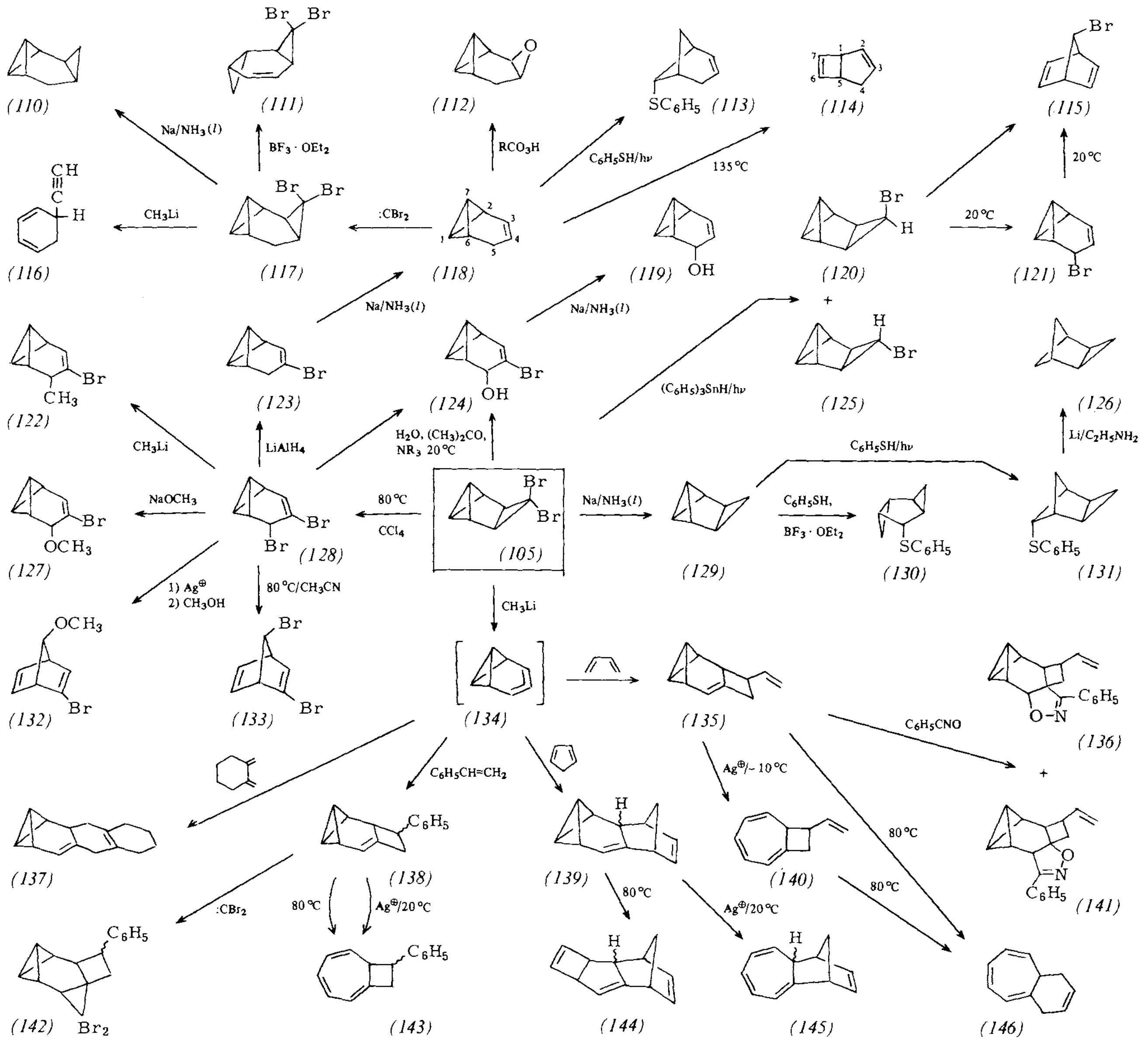
The synthesis of a large variety of new small-ring polycycles is made possible by the addition of halocarbenes to *(1)*. Difluoro-, chlorofluoro-, dichloro-, dibromo-, chloro-, chlorophenyl-, and bromophenylcarbene all react with *(1)* to give the tetracyclo[4.1.0.0$^{2,4}$.0$^{3,5}$]heptane derivatives *(101)*–*(107)*[79] as well as *(108)* and *(109)*[80].



| | (101) | (102) | (103) | (104) | (105) | (106) | (107) | (108) | (109) |
|---|---|---|---|---|---|---|---|---|---|
| $R^1$ | F | F | Cl | Cl | Br | Cl | H | $C_6H_5$ | $C_6H_5$ |
| $R^2$ | F | Cl | F | Cl | Br | H | Cl | Cl | Br |

The known reactions of *(105)* and products derived from it are summarized in Scheme 4. As in the case of *(104)*, reduction with sodium in liquid ammonia furnishes the parent hydrocarbon *(129)*[79]. The $^{13}$C-NMR spectra of this compound, as well as those of the heterocyclic analogs *(60)*, *(95)* and *(207)*, are remarkable because of the large difference in the chemical shifts of C-3 and C-4[24]. The thermal isomerization of *(129) via* tricyclo[3.2.0]hepta-2,6-diene *(114)* to cycloheptatriene only occurs at temperatures above 180 °C. The mechanism has been the subject of kinetic and deuterium labeling studies[46]. Cycloheptatriene is formed by the rapid isomerization of *(129)* caused by an $Ag^{\oplus}$-catalyst already at 0 °C. A simple synthesis of 3,4-dideuteriocycloheptatriene is available by using [3,4-$D_2$]-*(129)* as the starting material[79]. Thiophenol can add to *(129)* in two different ways: in the presence of boron trifluoride etherate it adds to one of the lateral bonds of the bicyclo[1.1.0]butane molecule to give *(130)*. Irradiation causes addition to occur at the central bond with formation of *(131)*, which can be desulfurized to the unsubstituted tricyclo[3.1.1.0$^{2,4}$]heptane *(126)*[72].

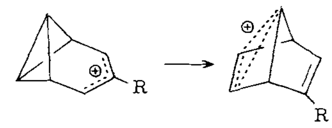
Partial dehalogenation of *(104)* and *(105)* using triphenyltin hydride with irradiation leads to the formation of



Scheme 4. Products derived from 7,7-Dibromotetracyclo[4.1.0.0$^{2,4}$.0$^{3,5}$]heptane *(105)*.

the monochloro compounds *(106)* and *(107)* and the monobromo derivatives *(120)* and *(125)*, respectively. Similarly, *(102)* and *(103)* are reduced with sodium in liquid ammonia, giving the monofluorine analogs. The *endo*-bromo derivative *(120)* is, like the corresponding chloride *(106)*, thermally labile. Already at 20 °C, it is transformed into the 7-bromonorbornadiene *(115)*. The probable intermediates in this reaction are the tricyclo[4.1.0.$0^{2,7}$]heptenyl cation *(147)* and the 7-norbornadienyl cation *(148)*. NMR spectroscopy shows evidence of a dead end equilibrium with *(121)*[81].

*(147)*, R = H
*(149)*, R = Br



*(148)*, R = H
*(150)*, R = Br

The transformation of *(105)* into *(128)*[81] and *(124)*[82], as well as that of *(128)* into *(124)*, proceed *via* the intermediate cation *(149)*, which is trapped by either bromide ions or water before rearranging to give *(150)*. Starting from *(128)* this rearrangement can be initiated either by heating to 80 °C in acetonitrile[81], giving norbornadiene *(133)*, or Ag$^{\oplus}$-catalyzed[82], whereby on work-up with methanol *(132)* is the product. With sodium in liquid ammonia, *(124)* gives the debrominated alcohol *(119)*[82] which can also be obtained by an alternative route[83]. The reaction of the alcohol *(119)* with fluorosulfonic acid at $-120$ °C[84], as well as the solvolysis of its 3,5-dinitrobenzoic acid ester[82] provide evidence for the rearrangement *(147)*→*(148)*.

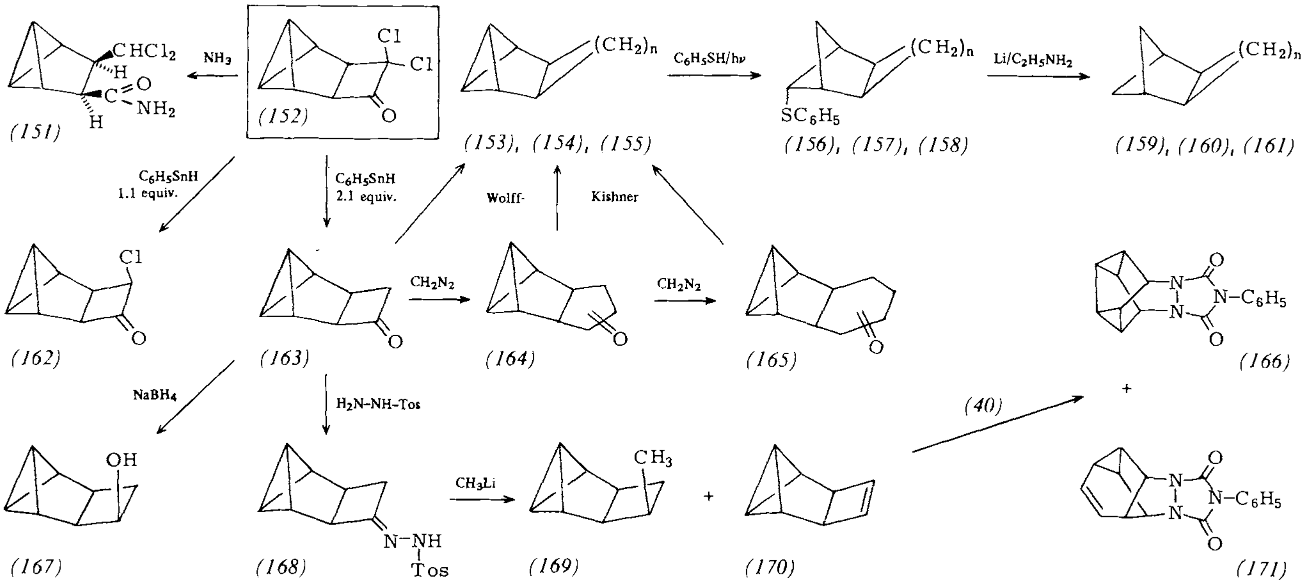
There are no skeletal changes involved when *(128)* reacts with methyllithium, sodium methylate, or LiAlH$_4$, giving *(122)*[57], *(127)*[82], and *(123)*[81], respectively. *(103)* and *(104)* rearrange in a series of reactions analogous to that of *(105)*→*(128)*→*(123)*. The unsubstituted tricyclo[4.1.0.$0^{2,7}$]hept-3-ene *(118)* is obtained in good yield by dehalogenation of *(123)* and the corresponding chloro compound with sodium in liquid ammonia[81], or else by reduction of the dichloro compound analogous to *(128)* with sodium and *tert*-butyl alcohol[57]. This synthesis from benzvalene is useful for preparing *(118)* in quantity; there are, however, two other albeit less productive routes[85,86].

When *(118)* is heated at 135 °C (half-life ≈ 1 h), it is transformed *ca*. 500 times quicker than the isomer *(129)*[46]; the only product formed is *(114)*. Use of 1,7-dideuteriated *(118)* leads selectively to *(114)* labeled in positions 6 and 7. On the other hand, the Ag$^{\oplus}$-catalyzed reaction already occurs at room temperature, giving 2,3-dideuteriocycloheptatriene[81]. In contrast to benzvalene (see Section 3.3.4), *(118)* adds thiophenol exclusively at the bicyclo[1.1.0]butane central bond to give the norpinene derivative *(113)*[56]. The reaction is accelerated by irradiation. The different nature of the HOMO's of *(1)* and *(118)* is regarded as responsible for the rather different reactions of these two substrates. The epoxidation of *(118)* with benzoylperoxycarbamic acid gives the epoxide *(112)*[87]; dibromocarbene addition gives the dibromocyclopropane *(117)*[88]. The latter is much more stable than *(105)* and when heated gives the dibromo-*trans*-bishomobenzene *(111)*[57,89]. This rearrangement is said to be concerted[89] although there is strong evidence that it is acid-catalyzed, *e.g.* by traces of HBr[57]. Indeed, *(117)* is transformed into *(111)* in the presence of boron trifluoride etherate[57]. The isomerization of *(110)* to the *trans*-bishomobenzene is also acid-catalyzed[90]. Compound *(110)* can be prepared by reaction of *(117)* with sodium in liquid ammonia[88] or *via* a shorter, more efficient route[90]. On the other hand, *(110)* rearranges thermally at 210 °C to give *trans*-tricyclo[4.2.0.$0^{2,4}$]oct-7-ene as the main product[88].

The homologous dibromocyclopropanes *(105)* and *(117)* behave very differently with methyllithium. It is probable that *(117)* first gives rise to a cyclopropylidene which stabilizes itself through skeletal rearrangement to the acetylenic compound *(116)*[88]. Both isotope labeling[88] and methyl substitution[91] enabled clarification of the mechanism of this reaction. The cyclopropylidene arising from *(105)* undergoes ring expansion to give the new reactive intermediate *(134)*, a strained allene, which can be trapped by activated alkenes in what are probably two-step [2+4]- and [2+2]-cycloaddition reactions. *(134)* reacts with 1,2-bismethylenecyclohexane to give the pentacyclic compound *(137)*[87], and with styrene to give two isomers of the tetracyclic molecule *(138)*[92]. The double bond in *(138)* is highly reactive; it can be epoxidized[87], smoothly hydrogenated by diimine[92], and adds dibromocarbene to give the spiro compound *(142)*. The cycloheptatriene *(143)* is obtained from *(138)* using Ag$^{\oplus}$ catalysis[87] and also by an alternative route[93]. Furthermore, *(143)* is formed by purely thermal means at 80 °C from *(138)*; in comparison to the rearrangement *(118)*→*(114)* this is very unusual. Presumably, this is due to the lability of the cyclobutane moiety[87]. The 1,1-diphenylethylene adduct[92] analogous to *(138)* exhibits the same behavior[87]. In contrast, the two isomers of the cyclopentadiene adduct *(139)* formed from *(134)*[92] rearrange thermally to *(144)*[87] in a manner analogous to *(118)*. Ag$^{\oplus}$ catalyzes the formation of the two cycloheptatrienes *(145)*. The products which are formed from *(134)* and furan, or 1,3-cyclohexadiene are analogous both in structure[92], and thermal decay[87] to *(139)*. The butadiene adduct *(135)* behaves abnormally but similarly to *(138)*[92]. Heating at 80 °C leads not only to the formation of the cycloheptatriene system but also to a vinylcyclobutane-cyclohexene rearrangement[87] which gives rise to *(146)*. When Ag$^{\oplus}$ is used, the bicyclo[1.1.0]butane skeleton isomerizes at $-10$ °C, and the resulting compound *(140)* rearranges also to *(146)* on heating at 80 °C. The reactivity of the methylenecyclobutane double bond manifests itself in the benzonitrile oxide addition of *(135)* to give *(136)* and *(141)*. In spite of its greater substitution it is more reactive than the vinyl group.

### 3.4.3. [2+2]-Cycloadditions: Dichloroketene and Singlet Oxygen

As yet, only the addition of one ketene to benzvalene *(1)* is known: dichloroketene gives 8,8-dichlorotetracyclo[4.2.0.$0^{2,4}$.$0^{3,5}$]octan-7-one *(152)* in high yield[94]. Monochloroketene does not react with *(1)*. Scheme 5 summarizes the reactions of *(152)* which have so far been carried out.

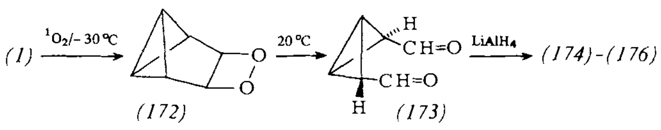


Scheme 5. Products derived from 8,8-Dichlorotetracyclo[4.2.0.$0^{2,4}$.$0^{3,5}$]octan-7-one *(152)*, *(153)*, *(156)* and *(159)*, $n=2$; *(154)*, *(157)* and *(160)*, $n=3$; *(155)*, *(158)* and *(161)*, $n=4$.

Ammonia opens the dichlorocyclobutanone ring to give the amide *(151)*; dimethylamine and hydrazine react analogously. The partial or complete dehalogenation of *(152)* can be carried out with triphenyltin hydride; this gives *(162)* or *(163)*. The ketone *(163)* is reduced with $NaBH_4$ to the *endo* alcohol *(167)*; the tosylate of the latter compound does not undergo a β-elimination to the olefin *(170)*. However, the ketone *(163)* permits access to the desired new $C_8H_8$ isomer *(170) via* the tosylhydrazone *(168)*. Here, the use of lithium 2,2,6,6-tetramethylpiperidide as a base afforded the best yield. The reaction of *(168)* with methyllithium gives a mixture of *(169)* and *(170)*, the ratio of which is solvent dependent. *(170)* isomerizes to cyclooctatetraene in $Ag^{\oplus}$-catalyzed, photochemical, or purely thermal ($>140°$) reactions. 4-Phenyl-1,2,4-triazoline-3,5-dione *(40)* adds to *(170)* in a stepwise manner. In an initially formed zwitterion, the cationic part rearranges and then reacts with the anionic nitrogen atom of the heterocycle giving the known *(166)* as the main product. One of the side products was identified as *(171)*. A Wolff-Kishner reduction of *(163)* leads smoothly to the saturated hydrocarbon *(153)*, which in the gas phase at 430 °C decomposes to a mixture of known $C_8H_{10}$ isomers and products derived therefrom.

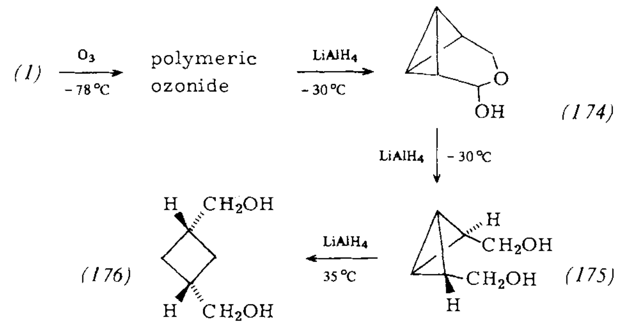
*(163)* undergoes two successive ring expansions with diazomethane, giving cyclopentanone *(164)* and cyclohexanone *(165)*. The positions of the carbonyl groups are uncertain[72]. Wolff-Kishner reduction of these ketones allows the preparation of the corresponding hydrocarbons *(154)* and *(155)*. Thiophenol adds photochemically to the central bond of the bicyclo[1.1.0]butane system in *(153)*—*(155)*; the resulting tricycloalkylphenyl thioethers *(156)*—*(158)* undergo reductive desulfurization with lithium in ethylamine to give the tricyclic hydrocarbons *(159)*—*(161)* possessing annelated four-, five- and six-membered rings. These compounds, together with *(126)*, and the corresponding tricyclo[3.1.0.$0^{2,6}$]hexane derivatives *(129)* and *(153)*—*(155)*, were the subject of a study of the effect of annelation on $^{13}C$-NMR chemical shifts of strained cyclopentanes[95].

The mechanism of the addition of singlet oxygen to olefins with dioxetane formation is still controversial[96]. Whereas norbornene reacts sluggishly with $^1O_2$[97], *(1)* reacts already at $-30$ °C in a [2+2]-cycloaddition giving the dioxetane *(172)*[78]; this is probably due to the higher energy HOMO (see Section 2). As is characteristic for compounds of this type, *(172)* decomposes to the dialdehyde *(173)* in a [2+2]-cycloreversion accompanied by chemiluminescence[70]. Proof of the structure of the dialdehyde *(173)* is provided by its reduction with $LiAlH_4$ to give, depending on reaction conditions, the products *(174)*—*(176)* (see Section 3.4.4).



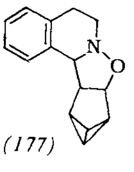
### 3.4.4. [2+3]-Cycloadditions: 1,3-Dipolar Cycloadditions

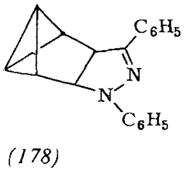
A polymeric ozonide is formed from *(1)* and $O_3$ at $-78$ °C[22]. Successive 1,3-dipolar cycloaddition to the



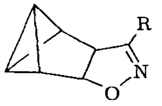
double bond, cycloreversion, and finally another cycloaddition reaction should leave the bicyclo[1.1.0]butane skeleton intact in accord with the findings after reductive workup with LiAlH$_4$[78].

When three equivalents of LiAlH$_4$ are employed in tetrahydrofuran at $-30\,^\circ$C, a 1:3 mixture of the hemiacetal *(174)* and the diol *(175)* is obtained. In the reaction using six equivalents of LiAlH$_4$, *(175)* is the only product. Surprisingly, when the reaction temperature is raised to 35 °C, the bicyclo[1.1.0]butane central bond in *(175)* is broken to give the known cyclobutane derivative *(176)*.


*(177)*

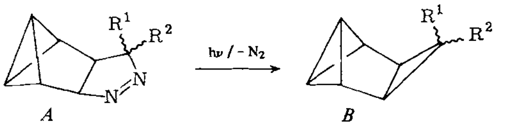


*(178)*



*(179)*, R = C$_6$H$_5$
*(180)*, R = 2,4,6-(CH$_3$)$_3$C$_6$H$_2$

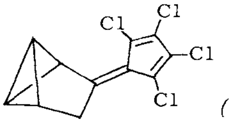
The nitrone 3,4-dihydroisoquinoline *N*-oxide reacts with *(1)* to give the hexacyclic adduct *(177)*; *(1)* and diphenylnitrile imine combine to give the 2-pyrazoline derivative *(178)*[98]. Benzonitrile oxide and its 2,4,5-trimethyl analog react with *(1)* giving the isoxazolines *(179)* and *(180)*, respectively.



| A | *(181)* | *(182)* | *(183)* | *(184)* | *(185)* | *(186)* | *(187)* |
|---|---|---|---|---|---|---|---|
| R$^1$ | H | CH$_3$ | C$_6$H$_5$ | biphenylylene | CH$_3$ | C$_6$H$_5$ | CH$_3$ |
| R$^2$ | H | CH$_3$ | C$_6$H$_5$ | | H | H | CO$_2$CH$_3$ |
| B | *(129)* | *(188)* | *(189)* | *(190)* | *(191)* | *(192)* | *(193)* |

The addition of diazoalkanes to *(1)* has been more thoroughly investigated. Symmetrical compounds such as diazomethane, 2-diazopropane, diphenyldiazomethane and diazofluorene all react with *(1)* to give the homogeneous 1-pyrazolines *(181)*[98]—*(184)*[99]. Unsymmetrical substrates such as diazoethane and phenyldiazomethane each give a mixture of the two possible isomers *(185)* and *(186)*. Ethyl diazoacetate is no longer reactive enough to compete with the isomerization of *(1)* to benzene[99]. On the other hand, methyl 2-diazopropionate does react with *(1)* to give the mixture *(187)*[100].

Tetrachlorodiazocyclopentadiene reacts only very slowly with *(1)* and the unobserved primary addition product eliminates nitrogen already at room temperature to give the fulvene *(193a)*[99].

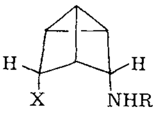


*(193a)*

Besides the additions of halocarbenes to *(1)* (see Section 3.4.2) a second synthesis of tetracyclo[4.1.0.0$^{2,4}$.0$^{3,5}$]heptanes is the result of the photochemical nitrogen extrusion from the 1-pyrazolines *(181)*—*(187)*. The parent substrate *(129)* is best obtained *via* the dichloro compound *(104)* where the yield is higher, but for the 7-alkyl [*(188)* and *(191)*][99] and the 7-aryl compounds [*(189)*, *(190)*, *(192)*][99], as well as the 7-carboxylic acid methyl esters *(193)*[100], the photolysis of the 1-pyrazolines is by far the method of choice.

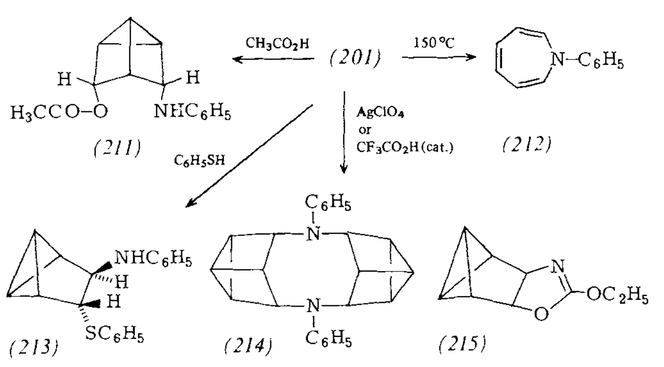
| | R | |
|---|---|---|
| *(194)* | C$_6$H$_5$ | *(201)* |
| *(195)* | 4-NO$_2$–C$_6$H$_4$ | – |
| *(196)* | 2,4,6-(CH$_3$)$_3$C$_6$H$_2$ | *(202)* |
| *(197)* | CH$_2$–C$_6$H$_5$ | *(203)* |
| *(198)* | CO$_2$C$_2$H$_5$ | *(204)* |
| *(199)* | CO$_2$C(CH$_3$)$_3$ | *(205)* |
| *(200)* | 4-CH$_3$–C$_6$H$_4$–SO$_2$ | *(206)* |
| – | H | *(207)* |

In view of the high reactivity of azides toward norbornene, their ready addition to *(1)* was not entirely unexpected. Phenyl, *p*-nitrophenyl, mesityl, and benzyl azides, as well as ethyl and *tert*-butyl azidoformate react with *(1)* to give the triazolines *(194)*—*(199)*[70,101] in acceptable yields. Tosyl azide reacts with *(1)* to give as the immediate product 7-*p*-toluenesulfonyl-7-azatetracyclo[4.1.0.0$^{2,4}$.0$^{3,5}$]heptane *(206)*, which is probably derived from the initially formed triazoline *(200)* by nitrogen elimination. *(201)*—*(203)* can be synthesized photochemically from *(194)*, *(196)*, and *(197)*, respectively; in the thermal reaction, the triazolines *(198)* and *(199)* give rise to *(204)* and *(205)*, respectively. The unsubstituted aziridine *(207)* is obtained by LiAlH$_4$ reduction of *(204)*, or from *(206)* with naphthalene- or, even better, biphenyl-sodium. It reacts *via* the *N*-metalated derivative to give the benzylated and sulfonated compounds *(203)* and *(206)*, respectively.



*(208)*, X = OH, R = CO$_2$C(CH$_3$)$_3$
*(209)*, X = O–COCH$_3$, R = 4-CH$_3$–C$_6$H$_4$–SO$_2$
*(210)*, X = S–C$_6$H$_5$, R = 4-CH$_3$–C$_6$H$_4$–SO$_2$

When *(199)* is treated with aluminum oxide of activity grade I, the aziridine *(205)* is obtained. When aluminum oxide of activity grade III is employed, nitrogen elimination also occurs. However, after rearrangement, probably *via* cationic intermediates, and addition of water, the *endo,endo*-disubstituted tricyclo[2.2.0.0$^{2,6}$]hexane *(208)* can be isolated[102]. *(206)* reacts with acetic acid and thiophenol to give also compounds of the type *(208)*[70]. Presumably, the nitrogen is protonated; this is followed by C—N bond cleavage and Wagner-Meerwein rearrangement to give a cation of the type *(41)*, which then adds a nucleophile to give *(209)* or *(210)*.

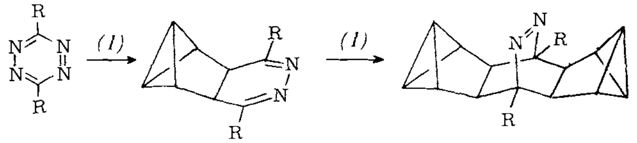


Whereas the *N*-phenyl compound *(201)* reacts with acetic acid to give the rearranged compound *(211)*, with thiophenol it gives the unrearranged molecule *(213)*. Apparently the aziridinium ion formed from *(201)* does not rearrange as easily as protonated *(206)* because $NHC_6H_5$ is a poorer leaving group than NHTos. Therefore, thiophenol directly opens the three-membered ring giving *(213)*. In contrast, in the presence of the less nucleophilic acetic acid, the rearrangement of protonated *(201)* occurs faster than the nucleophilic attack. With still weaker nucleophiles, the anilino group competes with the nucleophile, and dimerization to *(214)* results; this is the case, for example, on treatment of *(201)* with a catalytic amount of silver perchlorate or trifluoroacetic acid.

The thermolysis of *(201)* at 150 °C leads to cleavage of three σ bonds and the formation of three π bonds giving *N*-phenylazepine *(212)*[101] which can also be prepared *via* an alternative route. As is general for *N*-acylaziridines, *(204)* undergoes an expansion only of the aziridine ring on heating to 120 °C; this gives the oxazoline derivative *(215)* with retention of the tricyclo[3.1.0.$0^{2,6}$]hexane moiety.

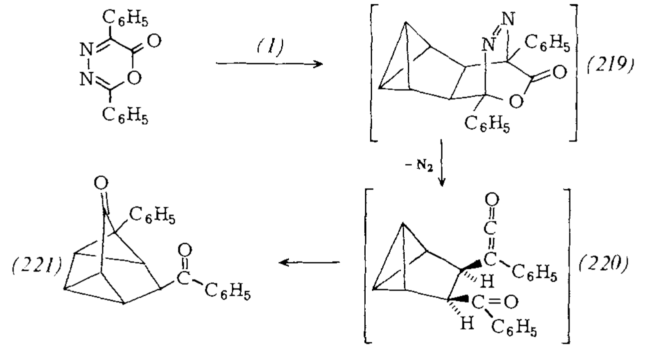
### 3.4.5. [2+4]-Cycloadditions: Diels-Alder Additions

Due to the high energy of the π orbital, benzvalene is predestined to be a good dienophile in Diels-Alder additions with inverse electron demand. 3,6-Bismethoxycarbonyl- and 3,6-diphenyl-1,2,4,5-tetrazine add to *(1)* in a manner typical of these dienes. A subsequent nitrogen elimination gives the dihydropyridazines *(216)* and *(217)*[103]. With excess *(1)*, *(216)* undergoes also a Diels-Alder addition leading to the octacyclic azo compound *(218)*[103], the configuration of which has been established by X-ray analysis[18].

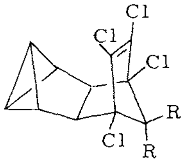


*(216)*, R = $CO_2CH_3$ *(218)*, R = $CO_2CH_3$
*(217)*, R = $C_6H_5$

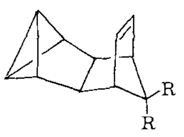
The newly reported 2,5-diphenyl-1,3,4-oxadiazin-6-one can be used as a diene[104]. Here, the reaction with *(1)* presumably gives *(219)* as the primary product, from which the ketene *(220)* is formed in a $[_{\sigma}2+_{\sigma}2+_{\sigma}2]$ cycloreversion, accompanied by nitrogen elimination; the ketene then further rearranges to the tetracyclic compound *(221)*[105]. This latter step involves a novel addition of a ketene function to the neighboring bicyclo[1.1.0]butane bond.



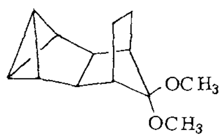
Although cyclopentadiene is unreactive toward *(1)*, hexachlorocyclopentadiene and tetrachlorocyclopentadienone dimethylketal react in accord with Alder's *endo* rule to give the pentacycles *(222)*[103] or *(223)*[106a] in good yields. On reaction with sodium in liquid ammonia or sodium and *tert*-butanol the chlorine atoms in these products are replaced by hydrogen with formation of *(224)* and *(225)*, respectively. The double bond in the ketal *(225)* is reduced with diimine to form *(226)*.



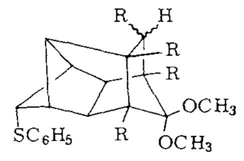
*(222)*, R = Cl
*(223)*, R = $OCH_3$



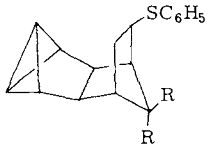
*(224)*, R = H
*(225)*, R = $OCH_3$



*(226)*

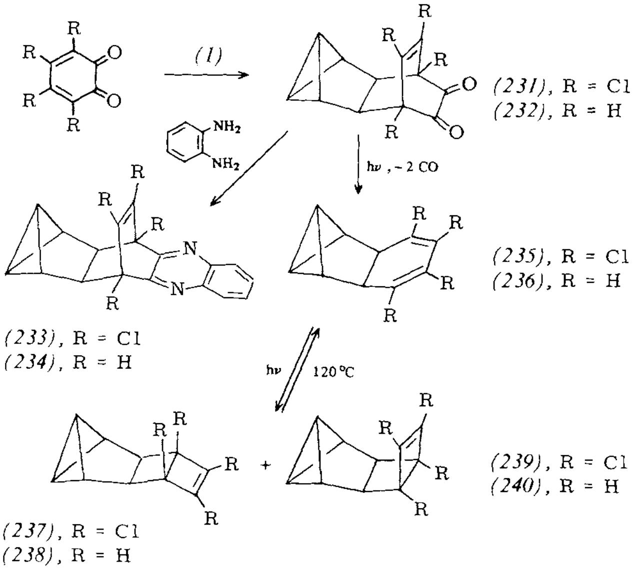


*(227)*, R = Cl
*(228)*, R = H

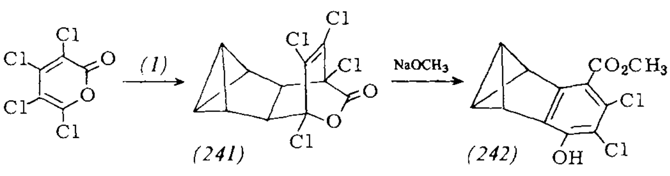


*(229)*, R = H
*(230)*, R = $OCH_3$

It is worth noting the thiophenol additions to *(223)*–*(225)* which probably involve radical chain process[106a]. Triggered by the phenylthiolyl radical the reaction of *(223)* begins at the bicyclo[1.1.0]butane ring, continues in a transannular ring closure with participation of the double bond, and finally gives the pentacyclic thioether *(227)*. When the starting compound is *(225)*, only about half the molecules follow this pathway giving *(228)*. The other half of the starting molecules add thiophenol to the double bond to give *(230)*. The analogous product *(229)* is formed as the sole product on reaction of *(224)* with thiophenol. Freed from steric hindrance due to the *syn*-methoxy group in *(223)* and *(225)*, and from the inductive effect of the chlorine atoms in *(223)*, the double bond in *(224)* is far more reactive toward thiophenol than is the case for the central bond in the bicyclo[1.1.0]butane system. This can be understood when one considers the energies of the highest occupied orbitals in tricyclo[3.1.0.$0^{2,6}$]hexane *(2)*[10] and norbornene[13b], which serve as models for the different functionalities of *(224)*.

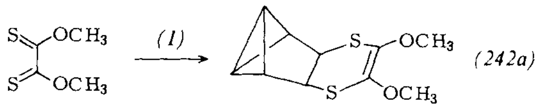


Tetrachloro-*o*-benzoquinone reacts instantaneously with *(1)*, whereas the addition of *o*-benzoquinone itself needs 15 h at 20 °C[103]. The configuration of the pentacyclic α-diketones *(231)* and *(232)* was established from the NMR spectra of the quinoxalines *(233)* and *(234)* which are easily obtained on treatment with *o*-phenylenediamine. Photochemical elimination of two CO molecules from the α-diketones *(232)* and *(231)* gives the new $C_{10}H_{10}$ hydrocarbon *(236)* and its tetrachloro derivative *(235)*, respectively. Further irradiation now at shorter wavelengths leads to an electrocyclization forming the isomeric cyclobutene derivatives *(238)* and *(240)*, or *(237)* and *(239)*, respectively. At 120 °C they isomerize back to *(236)* and *(235)*, respectively[57]. The double bonds in *(236)* each accept two hydrogen atoms from diimine, thus providing a second synthetic pathway to *(155)*[72] (see Section 3.4.3).



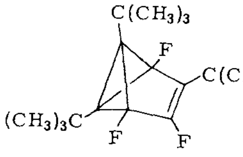
α-Pyrone does not react with *(1)*; tetrachloro-α-pyrone, on the other hand, gives a high yield of a lactone, for which configuration *(241)* is proposed[106a]. At 150 °C in solution, it looses $CO_2$, and *(235)* is formed. With sodium methylate in methanol *(241)* undergoes opening of the lactone ring and elimination of HCl, to give the first substituted naphthvalene *(242)*.

Dimethyl dithionooxalate—a 1,4-dithia-1,3-butadiene—reacts with *(1)* to give the Diels-Alder adduct *(242a)*[106b].

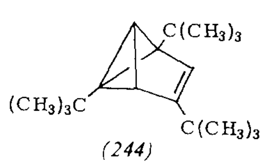


## 4. Substituted Benzvalenes

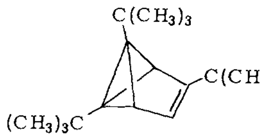
Despite the fact that substituted benzvalenes are not as easily accessible as *(1)*, they are of great importance because of their sometimes extremely varied properties. The first benzvalene derivative, tri-*tert*-butyltrifluorobenzvalene *(243)*, was found, by *Viehe et al.*[1], along with other products in the spontaneous trimerization of *tert*-butylfluoroacetylene. 1,2,4-Tri-*tert*-butylbenzvalene *(244)* is formed when 1,3,5-tri-*tert*-butylbenzene is photolyzed[107]; on further irradiation it partially rearranges to the 1,3,6-isomer *(245)*, which is also formed in the photolysis of 1,2,4-tri-*tert*-butylbenzene[2].



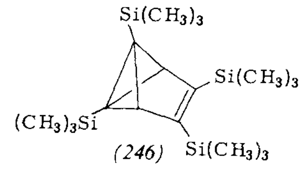
*(243)*



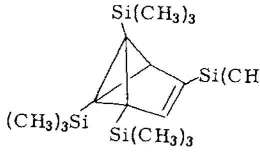
*(244)*



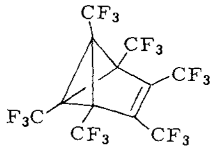
*(245)*



*(246)*



*(247)*

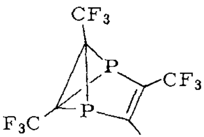


*(248)*

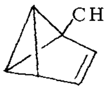
When 1,2,4,5-tetrakis(trimethylsilyl)benzene is irradiated, the substituted benzvalenes *(246)* and *(247)* as well as other isomers, are obtained[108]. Irradiation of hexakis(trifluoromethyl)benzene causes isomerization to the benzvalene *(248)*[109, 110], in quantitative yield. This product has been the subject of extensive studies.

Thermolysis of *(248)* causes reverse rearrangement to hexakis(trifluoromethyl)benzene[109]. This process has a considerably higher activation enthalpy (38.0 kcal/mol)[111], than the isomerization of *(1)* (see Section 3.2.3). *(248)* reacts analogously to *(1)* with phenyl azide to give the corresponding triazoline[112]. Because of the change in electronic properties due to the trifluoromethyl groups, *(248)* reacts with other dienes than does *(1)*: cyclopentadiene[112], pyrrole[112], butadiene[113] and its methyl substituted derivatives[114], furan and methylfuran[114] as well as cyclobutadiene[115, 116]. 1,3-Cyclohexadiene does not add to *(248)*; instead the double bond is hydrogenated[114].

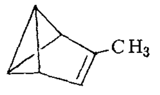
Also in contrast to *(1)*, *(248)* forms the monomeric ozonide[117] with which a variety of interesting reactions are made possible[118]. Acetone-sensitized irradiation of *(248)* in the presence of dialkylacetylenes leads to [2+2]-cycloaddition[119].



*(249)*

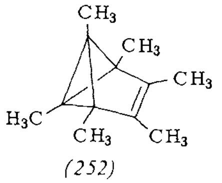


*(250)*

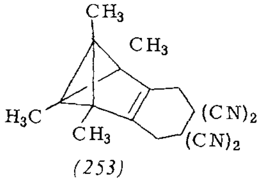


*(251)*

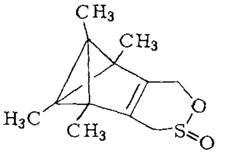
The $CF_3$-substituted 2,5-diphosphabenzvalene *(249)* is formed when tetrakis(trifluoromethyl)-1,4-diphosphabenzene is irradiated[120]. The 2- and 3-methylbenzvalenes *(250)* and *(251)*, as well as some toluene, are the products formed when methylcyclopentadienyllithium reacts with dichloromethane and methyllithium[28]. Although 1-methylbenzvalene *(4)* is not formed in this reaction, it can be synthesized by other methods (see Sections 3.1 and 3.2.2).



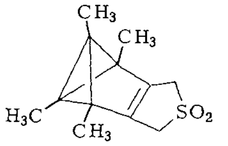
*(252)*



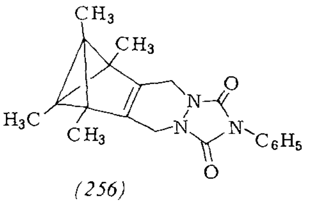
*(253)*



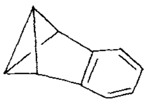
*(254)*



*(255)*



*(256)*

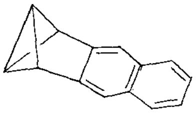


*(257)*

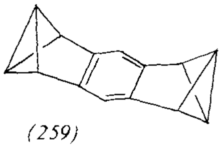
Hexamethylbenzvalene *(252)* is the proposed intermediate in the thermal isomerization of hexamethylprismane to hexamethylbenzene[121]. Its derivatives *(253)*[122], *(254)*[123], *(255)*[123], and *(256)*[124], were synthesized by *Hogeveen et al.* by reaction of 1,2,5,6-tetramethyl-3,4-bismethylenetricyclo[3.1.0.0$^{2,6}$]hexane with tetracyanoethylene, sulfur dioxide, and the triazolinedione *(40)*, respectively.

Analogously to *(1)*, benzobenzvalene (naphthvalene) *(257)* is synthesized from the indenyl anion and chlorocarbene[4]. The mechanism of its formation[29], as well as the $Ag^{\oplus}$- or Cu-catalyzed rearrangement[34] to naphthalene and benzofulvene have been investigated. *(257)* is thermally more stable than *(1)*; in $CCl_4$ at 80 °C it rearranges to benzofulvene with a half-life of *ca.* 30 h[4]. Acids add to one of the lateral bonds of the bicyclo[1.1.0]butane system[4]. Under radical reaction conditions, thiophenol does not react with *(257)*[57,71].

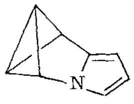
The anthracene isomers *(258)* and *(259)* are formed from the *s*-indacene dianion and chlorocarbene in a manner analogous to *(257)*[125]. The heterocyclic compound *(260)* can also be prepared by this method using 4-azapentalenyl anion[126]. On thermolysis, *(258)* rearranges to fulveno[*b*]naphthalene. *(259)* reacts *via* benzvalenobenzofulvene to give a mixture of 1,5- and 1,7-bismethylenedihydro-*s*-indacene[125]. Other substituted benzvalenes can be synthesized from *(1)*: the benzvalene sulfones *(55)* and *(57)* (see Section 3.3.4) and the naphthvalene *(242)* (see Section 3.4.5).



*(258)*



*(259)*



*(260)*

## 5. Conclusion and Outlook

The findings presented in this paper should give ample evidence that although benzvalene was first discovered only about a decade ago, it is more than a curiosity among the hydrocarbons. Its ready availability and high reactivity allows the synthesis of a multitude of new small-ring polycyclic compounds. Furthermore, the rearrangements and intermediates encountered are of mechanistic interest. Spectroscopic measurements on benzvalene and products derived therefrom provide information on σ-π and σ-σ interactions. A deeper understanding of these effects may contribute to the overall knowledge of the chemical bond.

This work is not a final review, however. The synthetic utilization of the new compounds has certainly not been exhausted, and so far benzvalene has mainly been treated with classical double bond reagents only. It is possible that new substrates will be found which are inert to normal olefins but reactive toward the benzvalene double bond.

Only a small number of reagents attack the bicyclo[1.1.0]butane moiety in benzvalene and related molecules. This is probably due to the fact that the chemistry of the bicyclo[1.1.0]butane system as such is little explored, the required starting materials, apart from a few exceptions, being difficultly accessible. *Via* benzvalene a variety of bicyclo[1.1.0]butane derivatives is available, therefore this area has been opened for more active study.

The chemistry of benzvalene demonstrates that the study of small-ring hydrocarbons is more than a playground for old-fashioned esoterics. Advances in the understanding of chemical properties have often been made by means of small and simple molecules.

*I wish to acknowledge the enthusiastic collaboration of H. Leininger, R. Lang, E. Brunn, S. Brengel, R. Herbert, G. Brüntrup, M. Lechner, G. Freitag, and P. Kemmer. Generous financial support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged, also on behalf of my co-workers. Thanks are also due to Union Rheinische Braunkohlen Kraftstoff AG for gifts of dimethyl ether used in the preparation of (1).*

Received: October 20, 1980 [A 367 IE]
German version: Angew. Chem. *93*, 515 (1981)

Translated by Edeline Wentrup-Byrne, Marburg

[1] *H. G. Viehe, R. Merényi, J. F. M. Oth, J. R. Senders, P. Valange,* Angew. Chem. *76*, 922 (1964); Angew. Chem. Int. Ed. Engl. *3*, 755 (1964).

[2] *K. E. Wilzbach, L. Kaplan,* J. Am. Chem. Soc. *87*, 4004 (1965).

[3] *K. E. Wilzbach, J. S. Ritscher, L. Kaplan,* J. Am. Chem. Soc. *89*, 1031 (1967).

[4] *T. J. Katz, E. J. Wang, N. Acton,* J. Am. Chem. Soc. *93*, 3782 (1971).

[5] *T. J. Katz, R. J. Roth, N. Acton, E. Carnahan,* Org. Synth. *53*, 157 (1973).

[6] *M. D. Newton, J. M. Schulman, M. M. Manus,* J. Am. Chem. Soc. *96*, 17 (1974), and references cited therein.

[7] *W. L. Jorgensen, W. T. Borden,* Tetrahedron Lett. *1975*, 223; *W. L. Jorgensen,* J. Am. Chem. Soc. *97*, 3082 (1975).

[8] *D. W. T. Griffith, J. E. Kent, M. F. O'Dwyer,* J. Mol. Spectrosc. *58*, 427 (1975).

[9] *K. B. Wiberg,* Adv. Alicyclic Chem. *2*, 185 (1968).

[10] *P. Bischof, R. Gleiter, E. Müller,* Tetrahedron *32*, 2769 (1976).

[11] *P. J. Harman, J. E. Kent, T. H. Gan, J. B. Peel, G. D. Willet,* J. Am. Chem. Soc. *99*, 943 (1977).

[12] *R. Gleiter,* Top. in Curr. Chem. *86*, 197 (1979).

[13] a) *P. Bischof, E. Heilbronner,* Helv. Chim. Acta *53*, 1677 (1970); b) *P. Bischof, J. A. Hashmall, E. Heilbronner, V. Hornung, ibid. 52*, 1745 (1969).

[14] *P. Bischof, R. Gleiter, R. T. Taylor, A. R. Browne, L. A. Paquette,* J. Org. Chem. *43*, 2391 (1978).

[15] *R. D. Suenram, M. D. Harmony,* J. Am. Chem. Soc. *95*, 4506 (1973).

[16] *R. R. Karl, Jr., S. H. Bauer,* J. Mol. Struct. *25*, 1 (1975).

[17] *K. W. Cox, M. D. Harmony, G. Nelson, K. B. Wiberg,* J. Chem. Phys. *50*, 1976 (1969).

[18] *H. Irngartinger, K. L. Lukas,* Angew. Chem. *91*, 750 (1979); Angew. Chem. Int. Ed. Engl. *18*, 694 (1979).

[19] *R. D. Suenram, M. D. Harmony,* J. Am. Chem. Soc. *94*, 5915 (1972).

[20] *D. W. T. Griffith, J. E. Kent, M. F. O'Dwyer,* Aust. J. Chem. *28*, 1397 (1975).

[21] *H. F. Shurvell, D. W. T. Griffith, J. E. Kent,* J. Raman Spectrosc. *2*, 147 (1974).

[22] *M. Christl, G. Brüntrup,* Chem. Ber. *107*, 3908 (1974).

[23] *M. Christl,* Chem. Ber. *108*, 2781 (1975).

[24] *M. Christl, R. Herbert,* Org. Magn. Reson. *12*, 150 (1979).

[25] Review: *U. Burger,* Chimia *33*, 147 (1979).

[26] *G. L. Closs, R. B. Larrabee,* Tetrahedron Lett. *1965*, 287.

[27] *R. J. Roth, T. J. Katz,* J. Am. Chem. Soc. *94*, 4770 (1972).

[28] a) *U. Burger, G. Gandillon,* Tetrahedron Lett. *1979*, 4281; b) *U. Burger, G. Gandillon, J. Mareda,* Helv. Chim. Acta *64*, 844 (1981).

[29] *U. Burger, F. Mazenod,* Tetrahedron Lett. *1976*, 2881.

[30] *E. Hückel,* Z. Elektrochem. *43*, 752 (1937).

[31] *H. G. Viehe,* Angew. Chem. *77*, 768 (1965); Angew. Chem. Int. Ed. Engl. *4*, 746 (1965).

[32] *R. B. Woodward, R. Hoffmann,* Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).

[33] *U. Burger, F. Mazenod,* Tetrahedron Lett. *1977*, 1757.

[34] *U. Burger, F. Mazenod,* Tetrahedron Lett. *1976*, 2885.

[35] *T. J. Katz, C. A. Renner,* unpublished results, quoted in *M. G. Hutchings, J. B. Johnson, W. G. Klemperer, R. R. Knight III,* J. Am. Chem. Soc. *99*, 7126 (1977).

[36] *L. A. Paquette, G. Zon,* J. Am. Chem. Soc. *96*, 203, 215, 224 (1974).

[37] a) *R. D. Suenram, M. D. Harmony,* J. Chem. Phys. *58*, 5842 (1973); b) *R. D. Suenram,* J. Am. Chem. Soc. *97*, 4869 (1975).

[38] *N. J. Turro, C. A. Renner, T. J. Katz, K. B. Wiberg, H. A. Connon,* Tetrahedron Lett. *1976*, 4133.

[39] *S. W. Benson:* Thermochemical Kinetics, 2nd Ed., Wiley, New York 1976.

[40] *R. C. Bingham, M. J. S. Dewar, D. H. Lo,* J. Am. Chem. Soc. *97*, 1294 (1975).

[41] *G. Favini, C. Rubino, R. Todeschini,* J. Mol. Struct. *53*, 267 (1979).

[42] *M. J. S. Dewar, S. Kirschner,* J. Am. Chem. Soc. *97*, 2932 (1975).

[43] *J. J. C. Mulder,* J. Am. Chem. Soc. *99*, 5177 (1977).

[44] *J. Aihara,* Bull. Chem. Soc. Jpn. *51*, 1788 (1978).

[45] Review: *D. Bryce-Smith, A. Gilbert,* Tetrahedron *32*, 1309 (1976).

[46] *M. Christl, U. Heinemann, W. Kristof,* J. Am. Chem. Soc. *97*, 2299 (1975).

[47] *P. Lechtken, R. Breslow, A. H. Schmidt, N. J. Turro,* J. Am. Chem. Soc. *95*, 3025 (1973).

[48] *C. A. Renner, T. J. Katz, J. Pouliquen, N. J. Turro, W. H. Waddell,* J. Am. Chem. Soc. *97*, 2568 (1975).

[49] *J. M. Blair, D. Bryce-Smith,* Proc. Chem. Soc. London *1957*, 287.

[50] *D. Bryce-Smith, H. C. Longuet-Higgins,* Chem. Commun. *1966*, 593.

[51] *L. Kaplan, K. E. Wilzbach,* J. Am. Chem. Soc. *90*, 3291 (1968).

[52] *H. R. Ward, J. S. Wishnok,* J. Am. Chem. Soc. *90*, 1085, 5353 (1968).

[53] *E. Müller,* Chem. Ber. *108*, 1394 (1975).

[54] *L. Kaplan, D. J. Rausch, K. E. Wilzbach,* J. Am. Chem. Soc. *94*, 8638 (1972), and references cited therein.

[55] *K. B. Wiberg, G. Szeimies,* J. Am. Chem. Soc. *92*, 571 (1970).

[56] *M. Christl, R. Lang, R. Herbert, G. Freitag,* Angew. Chem. *92*, 465 (1980); Angew. Chem. Int. Ed. Engl. *19*, 457 (1980).

[57] *M. Christl, G. Freitag,* unpublished results.

[58] *R. J. Roth, A. B. Woodside,* Synth. Commun. *10*, 645 (1980).

[59] *R. J. Roth,* Synth. Commun. *9*, 751 (1979).

[60] *R. J. Roth, T. J. Katz,* J. Org. Chem. *45*, 961 (1980).

[61] *T. J. Katz, N. Acton,* J. Am. Chem. Soc. *95*, 2738 (1973).

[62] *B. M. Trost, R. M. Cory,* J. Am. Chem. Soc. *93*, 5572 (1971); *B. M. Trost, R. M. Cory, P. H. Scudder, H. B. Neubold,* J. Am. Chem. Soc. *95*, 7813 (1973).

[63] a) *N. J. Turro, C. A. Renner, W. H. Waddell, T. J. Katz,* J. Am. Chem. Soc. *98*, 4320 (1976); b) *N. J. Turro, V. Ramamurthy,* Recl. Trav. Chim. Pays-Bas *98*, 173 (1979).

[64] *B. M. Trost, R. M. Cory,* J. Am. Chem. Soc. *93*, 5573 (1971).

[65] *B. M. Trost, P. H. Scudder, R. M. Cory, N. J. Turro, V. Ramamurthy, T. J. Katz,* J. Org. Chem. *44*, 1264 (1979).

[66] *L. A. Paquette, G. R. Allen, Jr., M. J. Broadhurst,* J. Am. Chem. Soc. *93*, 4503 (1971).

[67] *T. J. Katz, K. C. Nicolaou,* J. Am. Chem. Soc. *96*, 1948 (1974).

[68] *W. A. Smit, N. S. Zefirov, I. V. Bodrikov, M. Z. Krimer,* Acc. Chem. Res. *12*, 282 (1979).

[69] *M. U. Bombala, S. V. Ley,* J. Chem. Soc. Perkin Trans. I *1979*, 3013.

[70] *H. Leininger,* Dissertation, Universität Würzburg 1981.

[71] *G. Szeimies, A. Schloßer, F. Philipp, P. Dietz, W. Mickler,* Chem. Ber. *111*, 1922 (1978).

[72] *R. Herbert, M. Christl,* Chem. Ber. *112*, 2012 (1979).

[73] Review: *K. Griesbaum,* Angew. Chem. *82*, 276 (1970); Angew. Chem. Int. Ed. Engl. *9*, 273 (1970).

[74] *R. Aumann, H. Wörmann,* Chem. Ber. *112*, 1233 (1979).

[75] *R. M. Moriarty, K.-N. Chen, J. L. Flippen,* J. Am. Chem. Soc. *95*, 6489 (1973).

[76] *D. M. Lemal, K. S. Shim,* Tetrahedron Lett. *1964*, 3231.

[77] *U. Szeimies-Seebach, J. Harnisch, G. Szeimies, M. Van Meerssche, G. Germain, J.-P. Declerq,* Angew. Chem. *90*, 904 (1978); Angew. Chem. Int. Ed. Engl. *17*, 848 (1978).

[78] *H. Leininger, M. Christl,* Angew. Chem. *92*, 466 (1980); Angew. Chem. Int. Ed. Engl. *19*, 458 (1980).

[79] *M. Christl, G. Freitag, G. Brüntrup,* Chem. Ber. *111*, 2307 (1978).

[80] *E. Brunn,* Diplomarbeit, Universität Würzburg 1980.

[81] *M. Christl, G. Freitag, G. Brüntrup,* Chem. Ber. *111*, 2320 (1978).

[82] *M. Christl, G. Freitag,* Angew. Chem. *88*, 508 (1976); Angew. Chem. Int. Ed. Engl. *15*, 493 (1976).

[83] *H. Prinzbach, H. Babsch, H. Fritz,* Tetrahedron Lett. *1976*, 2129.

[84] *H. Volz, J.-H. Shin, H. Prinzbach, H. Babsch, M. Christl,* Tetrahedron Lett. *1978*, 1247.

[85] *G. W. Klumpp, J. J. Vrielink,* Tetrahedron Lett. *1972*, 539.

[86] *R. T. Taylor, L. A. Paquette,* Tetrahedron Lett. *1976*, 2741.

[87] *R. Lang,* Diplomarbeit, Universität Würzburg 1979 and Dissertation, in preparation.

[88] *M. Christl, M. Lechner,* Angew. Chem. *87*, 815 (1975); Angew. Chem. Int. Ed. Engl. *14*, 765 (1975).

[89] *R. T. Taylor, L. A. Paquette,* J. Am. Chem. Soc. *99*, 5824 (1977).

[90] *R. T. Taylor, L. A. Paquette,* Angew. Chem. *87*, 488 (1975); Angew. Chem. Int. Ed. Engl. *14*, 496 (1975).

[91] *L. A. Paquette, R. T. Taylor,* Tetrahedron Lett. *1976*, 2745.

[92] *M. Christl, R. Lang, M. Lechner,* Liebigs Ann. Chem. *1980*, 980.

[93] *E. E. Waali, W. M. Jones,* J. Am. Chem. Soc. *95*, 8114 (1973).

[94] *G. E. Gream, L. R. Smith, J. Meinwald,* J. Org. Chem. *39*, 3461 (1974); *L. R. Smith, G. E. Gream, J. Meinwald, ibid. 42*, 927 (1977).

[95] *M. Christl, R. Herbert,* Chem. Ber. *112*, 2022 (1979).

[96] *K. A. Zaklika, B. Kaskar, A. P. Schaap,* J. Am. Chem. Soc. *102*, 386 (1980), and references cited therein.

[97] *C. W. Jefford, A. F. Boschung,* Helv. Chim. Acta *57*, 2257 (1974).

[98] *M. Christl,* Angew. Chem. *85*, 666 (1973); Angew. Chem. Int. Ed. Engl. *12*, 660 (1973).

[99] *M. Christl, E. Brunn,* Angew. Chem. *93*, 474 (1981); Angew. Chem. Int. Ed. Engl. *20*, 468 (1981).

[100] *F.-G. Klärner,* private communication; *B. Muskulus,* Diplomarbeit, Universität Bochum 1978.

[101] *M. Christl, H. Leininger,* Tetrahedron Lett. *1979*, 1553.

[102] The *exo,exo* stereochemistry of *(208)* given in ref. [101] required revision.

[103] *M. Christl, H.-J. Lüddeke, A. Nagyrevi-Neppel, G. Freitag,* Chem. Ber. *110*, 3745 (1977).

[104] *W. Steglich, E. Buschmann, G. Gansen, L. Wilschowitz,* Synthesis *1977*, 252.

[105] *U. Lanzendörfer, S. Freund, M. Christl,* Angew. Chem., in press.
[106] a) *S. Brengel,* Diplomarbeit, Universität Würzburg 1980; b) *K. Hartke, G. Henssen, T. Kissel,* Liebigs Ann. Chem. *1980,* 1665.
[107] *I. E. Den Besten, L. Kaplan, K. E. Wilzbach,* J. Am. Chem. Soc. *90,* 5868 (1968).
[108] *R. West, M. Furue, V. N. M. Rao,* Tetrahedron Lett. *1973,* 911.
[109] *M. G. Barlow, R. N. Haszeldine, R. Hubbard,* Chem. Commun. *1969,* 202; J. Chem. Soc. Part C *1970,* 1232.
[110] *D. M. Lemal, J. V. Staros, V. Austel,* J. Am. Chem. Soc. *91,* 3373 (1969).
[111] *D. M. Lemal, L. H. Dunlap, Jr.,* J. Am. Chem. Soc. *94,* 6562 (1972).
[112] *M. G. Barlow, G. M. Harrison, R. N. Haszeldine, R. Hubbard, M. J. Kershaw, D. R. Woodward,* J. Chem. Soc. Perkin Trans. I *1975,* 2010.
[113] *Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Hanzawa, M. Honda,* Tetrahedron Lett. *1975,* 3819.
[114] *Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Hanzawa, M. Honda, Y. Iitaka, T. Date,* Tetrahedron Lett. *1976,* 2545.
[115] *R. N. Warrener, E. E. Nunn, M. N. Paddon-Row,* Tetrahedron Lett. *1976,* 2639.
[116] *Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Hanzawa, M. Honda, W. Miyashita, Y. Iitaka,* Tetrahedron Lett. *1977,* 1795.
[117] *Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Hanzawa, M. Honda, Y. Iitaka,* Tetrahedron Lett. *1975,* 3001.
[118] *S. Masamune, T. Machiguchi, M. Aratani,* J. Am. Chem. Soc. *99,* 3524 (1977); *Y. Kobayashi, Y. Hanzawa, Y. Nakanishi,* Tetrahedron Lett. *1977,* 3371; *Y. Kobayashi, Y. Hanzawa, Y. Nakanishi, T. Kashiwagi, ibid. 1978,* 1019; *Y. Kobayashi, Y. Hanzawa, W. Miyashita, T. Kashiwagi, T. Nakano, I. Kumadaki,* J. Am. Chem. Soc. *101,* 6445 (1979).
[119] *Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Hanzawa, M. Honda,* Tetrahedron Lett. *1976,* 2703.
[120] *Y. Kobayashi, S. Fujino, H. Hamana, I. Kumadaki, Y. Hanzawa,* J. Am. Chem. Soc. *99,* 8511 (1977).
[121] *J. F. M. Oth,* Recl. Trav. Chim. Pays-Bas *87,* 1185 (1968).
[122] *H. Hogeveen, P. W. Kwant,* J. Org. Chem. *39,* 2624 (1974).
[123] *R. F. Heldeweg, H. Hogeveen,* J. Am. Chem. Soc. *98,* 2341 (1976).
[124] *H. Hogeveen, W. F. J. Huurdeman,* J. Am. Chem. Soc. *100,* 860 (1978).
[125] *G. Gandillon, B. Bianco, U. Burger,* Tetrahedron Lett. *22,* 51 (1981).
[126] *U. Burger, F. Dreier,* Helv. Chim. Acta *62,* 540 (1979).

---

# Intermolecular Forces—An Example of Fruitful Cooperation of Theory and Experiment

By Peter Schuster[*]

New experimental techniques and extensive *ab initio* calculations have rendered it possible to gain a detailed knowledge of aggregates of atoms, small ions and/or small molecules in the vapor phase which are held together by intermolecular forces. Theory and experiment are often complementary regarding reliable predictions. The results obtained for complexes of three or more constituents are still fragmentary; nevertheless, they can be used to explain some properties of the condensed phase.

## 1. Introduction

For more than two decades most theoretical chemists have been engaged in developing and testing various numerical methods in quantum chemistry. An enormous amount of effort has been expended, involving many millions of hours of electronic computing time. The primary goal in this field has been and still is the calculation of precise approximations of the Schrödinger equation for the stationary states of atoms, molecules and molecular complexes. The limitations of the numerical methods available are already apparent: the computational problems concerning ground states of molecules have more or less been solved[1]. This is true for most molecular properties. The major obstacle opposing general applicability of *ab initio* calculations is the size of the molecules and molecular associations. The computer time required increases enormously with the size of the molecular structures to be studied.

The central role of intermolecular forces in any theory of the three states—gaseous, liquid and solid—is readily understood: in a world free of attractive forces between molecules or atoms there exists only ideal gases. Consequently, the investigation of intermolecular forces represents an extremely important but difficult chapter of chemical physics. The theory of intermolecular forces fits very well into the requirements and possibilities of quantum chemistry. Experimental data which are easy to interpret can be expected for very small and structurally simple molecular associates only. These systems, however, are notoriously difficult to investigate by conventional experimental techniques. Enormous experimental efforts and developments of new spectroscopic methods, *e.g.* "molecular beam electric resonance" spectroscopy[2] or high-pressure mass spectrometry[3] were necessary in order to obtain reliable experimental data on simple aggregates of small molecules. These small systems, however, are amenable also to precise numerical computation. The progress recently achieved in this field was a direct result of theoretical "predictions" and "precalculations" eventually being accurate enough for use by the experimentalist.

The interactions most commonly studied at present are those between rare gas atoms or between unpolar mole-

---

[*] Prof. Dr. P. Schuster
Institut für Theoretische Chemie und Strahlenchemie der Universität
Währingerstrasse 17, A-1090 Wien (Austria)

0570-0833/81/0707-0546 $ 02.50/0

cules. Nevertheless, this review will concentrate on the forces acting between polar molecules and between polar molecules and ions because they commonly attract the interest of a broader audience and because they are closer to our own field of research. They are more difficult to study theoretically but they lead to a much richer variety of ag-

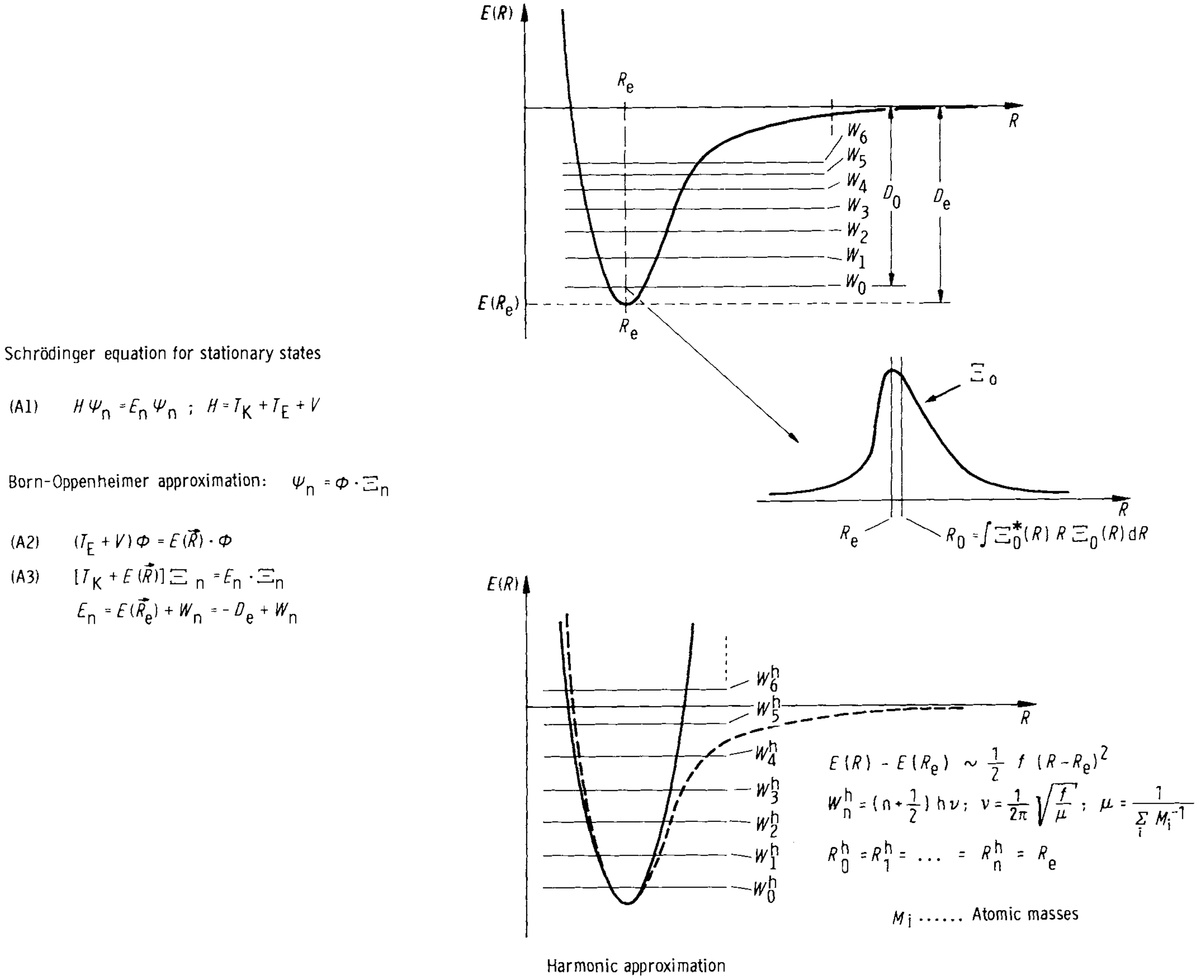


Fig. 1. Born Oppenheimer approximation and energy surface. The mathematical separation of the states of motion of a molecule or a molecular complex into fast motions of electrons and slow motions of the atomic nuclei is known as Born-Oppenheimer approximation. This approximation actually represents the basis of molecular spectroscopy. The nuclei are assumed to stay at fixed positions in comparison to the rapidly moving electrons. The wave function is approximated by a product, $\psi = \phi \cdot \Xi$ and the Schrödinger equation for stationary molecular states(A1) is separated into two equations, one for the electronic motion (A2) and one for the nuclear motion (A3). $H$ is the Hamilton operator or Hamiltonian of the molecule or the molecular complex. $T_E$ and $T_K$ are operators, which describe the kinetic energy of electrons and nuclei respectively. $V$ is the potential energy and it is calculated by Coulomb's law from the electric charges of nuclei and electrons as well as their mutual distances. Equation (A2) has to be solved point by point for different relative positions of the nuclei. Thereby we obtain the energy surface $E(\vec{R})$ of the molecule or the molecular complex. $\vec{R}$ represents the set of all internal degrees of freedom. The states of nuclear motion are described by equation (A3). The eigenvalues $W_k$ correspond to the stationary states of the molecules or molecular complexes. Their differences $(W_j - W_k)$ are measured in the vibrational spectra—apart from modifications due to rotational states. For the purpose of illustration we consider a system with a single degree of freedom only, *e. g.* a diatomic molecule, AB. The energy curve $E(R)$ shown is characteristic of a bound state. In general there will be many bound states of a molecule. In this overview we restrict ourselves to the energetically lowest electronic state or the electronic ground state of the molecule or the molecular complex. Therefore we omit any index referring to the electronic state and write simply $\phi$ and $E(R)$ respectively. The position of the energy minimum of the curve $E(R)$ corresponds to the "equilibrium geometry" $\vec{R}_e$—in our one-dimensional example this is simply the "equilibrium distance" $R_e$. The depth of the trough of the curve $E(R)$ represents the "equilibrium dissociation energy",

$$D_e = -\Delta E_{AB}(R_e) = -\{E_{AB}(R_e) - (E_A + E_B)\}$$

For each vibrational state $n$ we have a pair of values $R_n$ and $D_n = D_e - W_n$. In general, $R_n$ is only slightly longer than $R_e$ for small values of $n$. The vibrational ground state, $n=0$, is of particular importance since it represents the lowest experimentally accessible state. Accordingly, $R_0$ is the interatomic distance of the molecule which is measured at absolute zero (0 K). $D_0$ is the corresponding experimentally accessible energy of dissociation. In most cases higher vibrational levels are scarcely populated only at room temperature ($T \approx 300$ K). The avarage atomic distance, $\bar{R}$, therefore, is close to $R_0$ at these temperatures and the enthalpy of dissociation of the process $AB \rightarrow A + B$, $\Delta H_{300}^0$, is only slightly different from $D_0$.
In the case of molecules the harmonic approximation plays an important role. The potential curve is approximated by a parabola. Then, the Schrödinger equation (A3) can be solved easily. For the atomic distance and the dissociation energy in the vibrational ground state we obtain: $R_0^h = R_e$ and $D_0^h = D_e - W_0^h = D_e - 1/2\,h\nu$. The harmonic approximation is indicated by the superscript "h". In the case of some intermolecular complexes the potential curve $E(R)$ is so flat that there are only very few stationary vibrational states. In these cases, as we shall see later, the harmonic approximation does not provide a sufficient description of the molecular vibrations.

gregates in appearance and properties. Examples of aggregates of non-polar constituents will be mentioned only insofar as is inevitably unavoidable. Some new and comprehensive reviews on intermolecular forces are collected in Ref. [4].

## 2. Numerical Computation of the Structures and Properties of Molecules and Molecular Aggregates

Apart from some rare exceptions molecular systems have been studied within the framework of the Born-Oppenheimer approximation (Fig. 1). This approximation makes use of the difference in mass between electrons and nuclei, which amounts to more than three orders of magnitude, and assumes that the electrons move "infinitely fast" in the field of the slowly moving nuclei. This simplifying assumption is not only the starting point of quantum mechanical calculations but also represents the basis of practically all theories on intermolecular forces, chemical reactions and of molecular spectroscopy in general. The cardinal concept of all these theories is the energy surface. Because of its high dimensionality—the energy surface of a general aggregate of $N$ atoms has $3N-6$ degrees of freedom—it is often called the "energy hypersurface". It represents the energy of a molecule or a molecular association as a function of the positions of the nuclei. The minima of the energy surface, as far as they are deep enough (Fig. 1), correspond to stable stationary states with defined nuclear geometries. The curvatures or second derivatives of the energy surface at the minimum are the harmonic force constants of the molecule or the molecular aggregate in a given state. They contain the basic information of the vibrational spectrum.

Small molecules can be calculated theoretically as well as studied spectroscopically with incredible accuracy (Table 1). At present there are two generally accepted levels of

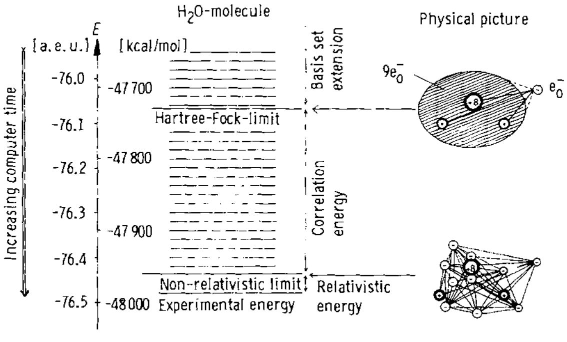


Fig. 2. The steps of the approximate solution of the electronic Schrödinger equation of the water molecule. Within the framework of the Hartree-Fock approximation the equation of motion of the individual electron is solved in the average potential of all other electrons. Explicit consideration of the motions of the individual electrons leads to the "non-relativistic" approximation. A computation of the relativistic energy leads beyond the frame of conventional quantum mechanics and is accompanied by enormous methodical difficulties. Experience, however, has shown that almost all important properties of molecules and molecular complexes containing light atoms ($Z < 36$) are described accurately within the non-relativistic approximation. For systems of atoms with heavy nuclei the calculations become extremely time consuming in any case and hence relevant predictions on the importance of relativistic corrections are not possible at present. Some molecular properties—equilibrium geometries, electron density distributions *etc.*—are reproduced very well already at the Hartree-Fock limit. For other quantities like force constants, vibrational spectra or bond energies the corrections due to electron correlation are substantial.

Table 1. Some properties of small polar molecules [a].

| HF | Geometry | | Force constant(s) | Dipole moment | | Quadrupole moment [b] unit: $10^{-26}$ esu cm$^2$ | | Electric polarizability unit: $10^{-25}$ cm$^3$ | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $R_e$ [Å] | $R_0$ [Å] | $f_{RR}$ [mdyn/Å] | $\mu_e$ [D] | $\mu_0$ [D] | $(\Theta_{\parallel})_e$ | $(\Theta_{\perp})_e$ | $\bar{\alpha}_e$ | $\bar{\alpha}_0$ | $(\alpha_{\parallel}-\alpha_{\perp})_e$ | $(\alpha_{\parallel}-\alpha_{\perp})_0$ |
| Hartree-Fock calculation [c] | 0.900 | | 11.17 | 1.92 | 1.96 | 2.35 | $(-1.17)$ | 7.26 | 7.38 | 1.90 | 2.15 |
| Electron-correlation [c] | 0.917 | | 9.92 | 1.79 | 1.82 | | | 8.28 | 8.40 | 1.88 | 2.13 |
| Exp. [c] | 0.917 | 0.932 | 9.66 | | 1.83 | 2.36 $(=(\Theta_{\parallel})_0)$ | | | 8.29 | | 2.21 |

| $H_2O$ | Geometry | | | | Force constants [mdyn/Å] | | | | Dipole moment | | Quadrupole moment [b] unit: $10^{-26}$ esu cm$^2$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $R_e$ [Å] | $R_0$ [Å] | $\gamma_e$ | $\gamma_0$ | $f_{RR}$ | $f_{\gamma\gamma}$ | $f_{RR'}$ | $f_{R\gamma}$ | $\mu_e$ [D] | $\mu_0$ [D] | $(\Theta_{xx})_e$ | $(\Theta_{yy})_e$ | $(\Theta_{zz})_e$ |
| Hartree-Fock calculation [c] | 0.940 | | 106.1 | | 9.79 | 0.875 | $-0.066$ | 0.258 | 1.99 | 1.99 | 2.65 | $-2.47$ | $-0.19$ |
| Electron correlation [c] | 0.957 | | 104.6 | | 8.51 | 0.799 | $-0.097$ | 0.273 | 1.84 | 1.85 | 2.62 | $-2.50$ | $-0.12$ |
| Exp. [c] | 0.958 | 0.972 | 104.5 | 104.6 | 8.45 | 0.761 | $-0.101$ | 0.228 | | 1.85 | 2.63 | $-2.50$ | $-0.13$ |
| | | | | | | | | | | | $(=(\Theta_{xx})_0, (\Theta_{yy})_0, (\Theta_{zz})_0)$ | | |

| $H_2O$ | Electric polarizability unit: $10^{-25}$ cm$^3$ | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | $(\alpha_{xx})_e$ | $(\alpha_{xx})_0$ | $(\alpha_{yy})_e$ | $(\alpha_{yy})_0$ | $(\alpha_{zz})_e$ | $(\alpha_{zz})_0$ | $\bar{\alpha}_e$ | $\bar{\alpha}_0$ |
| | 13.40 | 13.88 | 11.84 | 11.94 | 11.55 | 12.77 | 12.59 | 12.86 |
| | 14.54 | 15.03 | 14.21 | 14.31 | 14.28 | 14.67 | 14.34 | 14.61 |
| | | | | | | | | 14.55 |

[a] References are given in [55]. The original literature contains further hints on the accuracy of calculated and experimental data. In general, the error limits hardly exceed 2 or 3 units of the last digit shown. The coordinate system of $H_2O$ has been chosen such that the z-axis coincides with the $C_2$-axis of the molecule. The H-atoms lie in the xz-plane. In HF $\parallel$ denotes the direction of the $C_\infty$-axis. The index "e" refers to the equilibrium geometry, the index "0" to the vibrational ground state. [b] The quadrupole tensor was calculated relative to the center of gravity of HF and $H_2{}^{16}O$. [c] We give the available results of the SCF-calculation with the most extended basis set as the best approximation to the Hartree-Fock limit. Electron correlation was taken into account either by CEPA (coupled electron pair approximation) or by MBPT (many-body perturbation theory) techniques. For technical details see *W. Kutzelnigg, I. Shavitt* in [1]. The experimental results were taken from the references given in [55].

approximate solutions to the electronic Schrödinger equation:

1) the so-called Hartree-Fock limit, which represents the "best" approximation within the model of independently moving electrons (Fig. 2) and

2) the non-relativistic limit.

With the exception of some molecular systems with extremely flat energy troughs like the cation $H_5O_2^+$[4a,b] molecular geometries are computed fairly accurately in calculations close to the Hartree-Fock limit. This is not true for many other molecular properties. Force constants, in particular those of bond stretching vibrations, contain systematic errors: the calculated values are too high, the calculated energy surface is curved too much around the minimum. The origins of this deficiency is well understood (Fig. 3). Explicit consideration of the correlation of electron motion satisfactorily eliminates this failure. Within the framework of the non-relativistic approximation energy surfaces can be predicted with high accuracy. The non-relativistic approximation presumably fails only in the case of molecular systems with atoms of the fourth, fifth and sixth row of the periodic table—Rb, Sr and heavier atoms—where we can easily recognize the substantial relativistic contributions already in the atomic spectra. It must be admitted, however, that there are, as yet, no accurate numerical results available on the influence of relativistic corrections on computed properties of chemical bonds and intermolecular forces.

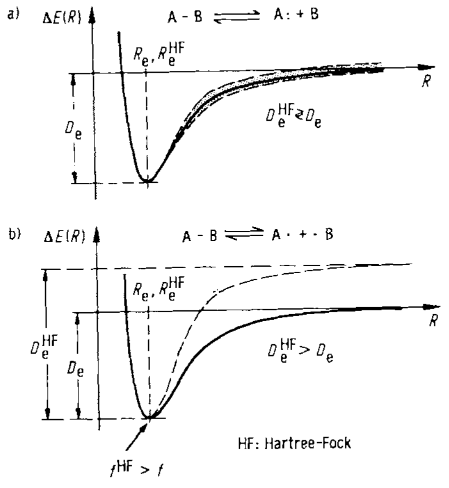


Fig. 3. Dissociation of a molecule or a molecular complex into a) two "closed shell" subsystems or b) into two "open shell" subsystems. In the first case the Hartree-Fock method is able to reproduce the dissociated state very well. In the latter example, however, this is not the case: the Hartree-Fock approximation fails to describe the homolytic dissociation of a chemical bond. This is also the cause, why bond energies and force constants can be predicted accurately only when electron correlation is considered explicitly. The scales for $E(R)$ and $R$ were chosen such that the correlation energy vanishes at the energy minimum. Hence, the minima of the curves $E(R)$ and $E^{SCF}(R)$ coincide at the energy minima. —— $\Delta E(R)$: non-relativistic limit; $\Delta E^{HF}(R)$: Hartree-Fock limit.

The wave functions of molecules and molecular associations are obtained together with the energy surfaces by *ab initio* calculations. They are also functions of the nuclear coordinates. The spatial electron density distribution (1)

$$\int \ldots \int \Psi^*(1,2,\ldots,n)\,\Psi(1,2,\ldots,n)\,ds_1\,d\tau_2 \ldots d\tau_n = \rho(x,y,z)^{[5]} \qquad (1)$$

is computed from the wave function by integration. In principle, the electron density distribution can be determined experimentally, *e.g.* by electron diffraction studies in the gaseous state. The electron density distribution is a function in three-dimensional space. For the purpose of illustration one commonly uses two-dimensional sections, *e.g.*$\rho(x, y = y_0, z)$ as shown in Figure 4. The choice of a flexible enough basis set and the explicit consideration of electron correlation often have a pronounced effect on the quality of the wave function, as we shall see in detail when we compare calculated and measured electric properties of molecules.

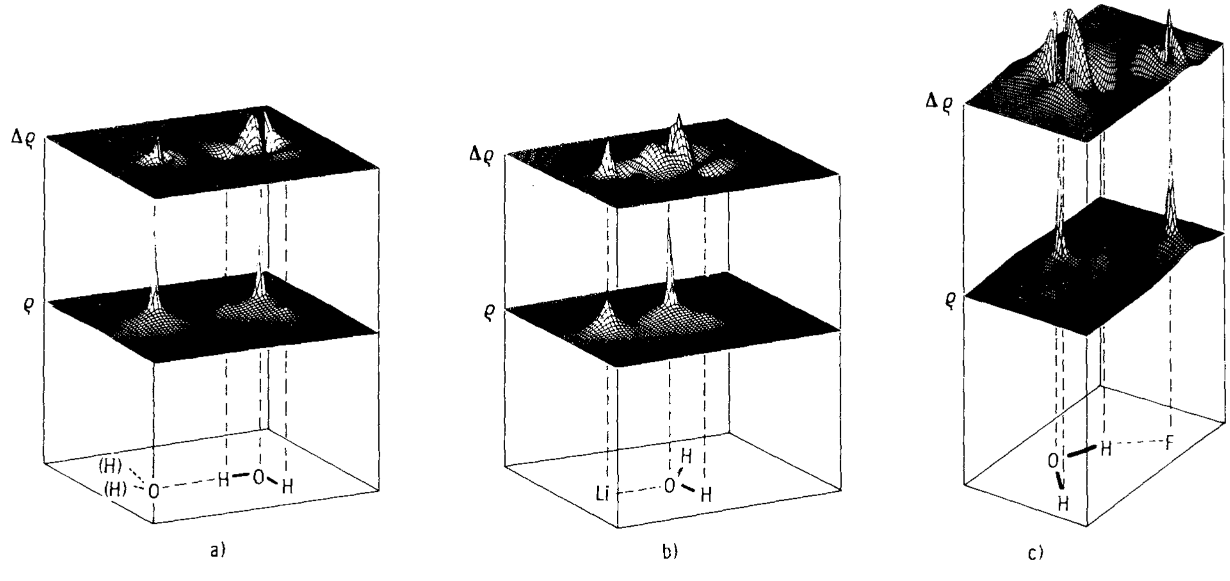


Fig. 4. Electron density- ($\rho$) and electron density difference functions ($\Delta\rho$) [see eq. (4)] of three examples of intermolecular complexes: a) $(H_2O)_2$, b) $Li^+ \cdot OH_2$ and c) $F^- \cdot HOH$. We show cuts through the three-dimensional functions in the xz-planes ($y = 0$). The maxima of the electron density functions coincide with the positions of the atomic nuclei. In case of the water dimer the two protons of the water molecule on the left-hand side cannot be recognized since they lie above the xy-plane. The density difference function $\Delta\rho$ shows the polarization of the electron densities as a consequence of intermolecular interactions. The decrease in electron density at the central proton of the two hydrogen bonds (a and c) can be recognized particularly well. The same decrease through polarization can be observed with protons in the complex $Li^+ \cdot OH_2$ (b).

Electron density distributions are troublesome in comparisons of different systems and do not contribute very much to an intuitive understanding of intermolecular forces. Therefore, it is very popular to use multipole expansions of electron density distributions. The coefficients of these expansions are the electric multipole moments of molecules. In most cases electric multipole moments are reproduced satisfactorily by accurate *ab initio* calculations. Sometimes electron correlation effects are important (cf. Table 1). The changes of electron density distributions in the electric field are known as polarization or induction effects. A homogeneous electric field ($\vec{\mathfrak{E}}$) induces a dipole moment ($\vec{\mu}_{\text{ind}}$), which can be described by the electric polarizability $\boldsymbol{\alpha}$ as long as the linear approximation is valid, *i.e.* at low field strengths:

$$\vec{\mu}_{\text{ind}} = \boldsymbol{\alpha} \cdot \vec{\mathfrak{E}} \tag{2}$$

Table 1 lists some results of *ab initio* calculations. It is worth mentioning that the anisotropy of the polarizability tensor, which is very difficult to measure in non-linear molecules, can be obtained easily and with high reliability by numerical computation.

Interactions between molecules cause changes in electron density distributions as well. These changes can be understood as relaxations in the fields of the molecular partners. The accuracy, with which the electric moments and polarizabilities of isolated molecules are predicted by calculations, can be considered as a proper criterion for the suitability of the method of calculation for describing intermolecular forces.

*Ab initio* calculations of magnetic properties of molecules, in particular those of magnetic susceptibilities and chemical shifts, cause more difficulties than the calculations of all other properties discussed so far[6]. The change in chemical shift will not be discussed in detail here.

So far we have not differentiated between molecules and molecular associations. There was no need for such a differentiation, since molecules and molecular complexes are treated in precisely the same way by *ab initio* methods (see Fig. 1). The results of these calculations are the energy surface and the wave function of the complex as an entity, and quantities are derived from them like the vibrational spectra and the electric and magnetic properties of the complex, respectively. For heuristic reasons we are much more interested in differences in the case of molecular associations than in the case of isolated molecules. We are not interested so much in the complete high-dimensional energy surface but in that part which is characteristic for the formation of the complex from its constituents. We do not intend to analyze the total electron density but rather its changes as a result of complex formation. In the case of weak interactions between the partners in the complex an approximation called the "frozen geometry" approach turned out to be very useful for approximative studies: we assume that the nuclear coordinates of the subsystems do not change on complex formation. The mutual approach of the molecules thus leads only to changes in electron density distributions. In this case the "intermolecular" energy surface of a binary complex

$$\Delta E(\vec{R}) = E_{\text{AB}}(R) - (E_{\text{A}}^{0} + E_{\text{B}}^{0}) \tag{3}$$

depends on a few coordinates only. Depending on the symmetries of the subsystem we have from one to six degrees of freedom (Fig. 5). Within the framework of the "frozen geometry" approach electron density difference functions (see Fig. 4) can be defined without any difficulty, since the nuclear geometries of the subsystems in the complex and in the isolated molecules are congruent.

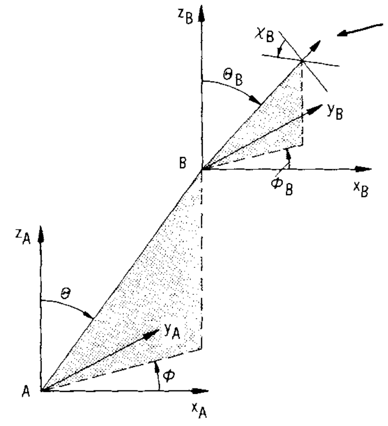


Fig. 5. Degrees of freedom of intermolecular energy surfaces within the "frozen geometry" approximation. The centers of gravity of both molecules A and B are chosen as the origins of Cartesian coordinate systems: $A = (x_A^0, y_A^0, z_A^0)$ and $B = (x_B^0, y_B^0, z_B^0)$. Depending on the nature of the two subsystems we need a different number of geometrical quantities in order to fix the relative position and orientation of A and B:

| Nature of A | Nature of B | Degrees of freedom |
|---|---|---|
| Atom | atom | 1: $R$ |
| Linear molecule (z-axis) | atom | 2: $R$, $\Theta$ |
| General molecule | atom | 3: $R$, $\Theta$, $\Phi$ |
| Linear molecule (z-axis) | linear molecule | 4: $R$, $\Theta$, $\Theta_{\text{B}}$, $\Phi_{\text{B}}$ |
| General molecule | linear molecule | 5: $R$, $\Theta$, $\Phi$, $\Theta_{\text{B}}$, $\Phi_{\text{B}}$ |
| General molecule | general molecule | 6: $R$, $\Theta$, $\Phi$, $\Theta_{\text{B}}$, $\Phi_{\text{B}}$, $\chi_{\text{B}}$ |

$R = \sqrt{(x_A^0 - x_B^0)^2 + (y_A^0 - y_B^0)^2 + (z_A^0 + z_B^0)^2}$. The arrow (above, right) points to an axis in the molecule B ($\Theta_{\text{B}}$, $\Phi_{\text{B}}$); rotation about ($\Theta_{\text{B}}$, $\Phi_{\text{B}}$): $\chi_{\text{B}}$.

$$\Delta\rho(x,y,z) = \rho_{\text{AB}}(x,y,z) - (\rho_{\text{A}}^{0} + \rho_{\text{B}}^{0}) \tag{4}$$

This electron density difference function describes the change in electron density as a result of forces of interaction in the aggregate.

For a deeper understanding of intermolecular forces a partitioning of the energy of interaction into individual contributions was found to be very useful:

$$\Delta E = \Delta E_{\text{COU}} + \Delta E_{\text{POL}} + \Delta E_{\text{DIS}} + \Delta E_{\text{EX}} + \Delta E_{\text{RES}} \tag{5}$$

The individual contributions have the following meaning:
1) $\Delta E_{\text{COU}}$ represents the electrostatic energy of interaction between both subsystems caused by their charge density distributions in the isolated state,
2) $\Delta E_{\text{POL}}$, the polarization- or induction-energy describes the additional stabilization of the aggregate by relaxation of electron densities in the field of the partner,
3) $\Delta E_{\text{DIS}}$ is the dispersion energy, a universal attractive contribution, which is caused by correlation of electron motions in both subsystems,

4) $\Delta E_{EX}$, the exchange energy, represents an interaction which is caused by mutual overlap between both subsystems and is always repulsive between two "closed-shell" molecules, and

5) $\Delta E_{RES}$, the residual contribution, which is frequently subdivided further into the charge transfer energy $\Delta E_{CHT}$ and additional terms. We restrict ourselves here to those complexes in which this residual contribution is small. Molecular aggregates with a high percentage of charge transfer energy, like the anion $[FHF]^-$, are considered more appropriately as uniform molecular entities with chemical bonds[7] and not as intermolecular complexes.

The partitioning of energies of interaction results from calculations of intermolecular forces by means of perturbation theory[8]. Thereby, the energy of interaction between the two subsystems is obtained as a sum of individual contributions, which are closely related to those mentioned above. In the case of *ab initio* calculations based on the molecular orbital method, energy partitioning can be performed exclusively by means of certain model considerations[9]. Without going into details we might merely mention that the individual contributions to the energy of interaction are not free from arbitrariness when the wave functions of the two subsystems overlap significantly. The overlap increases considerably with decreasing intermolecular distance. The source of arbitrariness is actually the same, both in calculations by perturbation theory and by molecular orbital methods. The exchange energy, $\Delta E_{EX}$, and the charge transfer or residual energy, $\Delta E_{RES}$, become very small at large intermolecular distances. At the same time, the three residual contributions, $\Delta E_{COU}$, $\Delta E_{POL}$ and $\Delta E_{DIS}$ approach asymptotically the well known "semiclassical" expression of the series expansion in $R^{-n}$ (Table 2). The coefficients of this series expansion are determined by the multipole moments and polarizabilities of the interacting subsystems as well as by their mutual orientation. The multipole expansion of intermolecular energies is of great practical value for approximation calculations in the case of large intermolecular distances. Nevertheless, it is not free of problems for the theorist: the series expansion is semi-convergent, *i.e.* the series converges only until a certain minimum term; the higher terms become larger again and ultimately the series diverges. Convergence is achieved only in the limit $R \rightarrow \infty$[10].

Table 2. Expansion of the intermolecular energy as a power series of $R$ as used in the "semiclassical" theory: $\Delta E = \sum_{n=1}^{\infty} C_n R^{-n}$.

| n | Type of interaction | Nature of interaction | Effective components [a] A | B |
|---|---|---|---|---|
| 1 | ion - ion | electrostatic | $q_A$ | $q_B$ |
| 2 | ion - dipole | electrostatic | $q_A$ | $\vec{\mu}_B$ |
| 3 | ion - quadrupole | electrostatic | $q_A$ | $\Theta_B$ |
|  | dipole - dipole | electrostatic | $\vec{\mu}_A$ | $\vec{\mu}_B$ |
| 4 | dipole - quadrupole | electrostatic | $\vec{\mu}_A$ | $\Theta_B$ |
|  | ion - polarizability | polarization (induction) | $q_A$ | $\boldsymbol{\alpha}_B$ |
| 5 | quadrupole - quadrupole | electrostatic | $\Theta_A$ | $\Theta_B$ |
| 6 | dipole - polarization | polarization (induction) | $\vec{\mu}_A$ | $\boldsymbol{\alpha}_B$ |
|  | polarizability - polarizability | dispersion | $\boldsymbol{\alpha}_A$ | $\boldsymbol{\alpha}_B$ |

[a] The expansion coefficients $C_n$ are functions of the angles $\Theta$, $\Phi$, $\Theta_B$, $\Phi_B$, $\chi_A$, $\chi_B$ as well as of the components of multipole moments and polarizabilities. $q_A$, $q_B$: charges $\vec{\mu}_A$, $\vec{\mu}_B$: dipole moments: $\vec{\mu} = (\mu_x, \mu_y, \mu_z)$; $\Theta_A$, $\Theta_B$: quadrupole moments; these are tensors which have only the components $\Theta_{xx}$, $\Theta_{yy}$ and $\Theta_{zz}$ different from zero after transformation to principal axes, moreover the relation $\Theta_{xx} + \Theta_{yy} + \Theta_{zz} = 0$ is fulfilled; $\boldsymbol{\alpha}_A$, $\boldsymbol{\alpha}_B$: polarizabilities, these are tensors with the components $\alpha_{xx}$, $\alpha_{yy}$, $\alpha_{zz}$ after transformation to principal axes.

The partitioning of intermolecular energies for a number of stable binary associations at the energy minimum is presented in Table 3. As expected, the electrostatic contribution, $\Delta E_{COU}$, dominates the energy of interaction in polar systems, which represent the main subject of this review. At the other end of this series of interacting systems we find the dimers of rare gas atoms, which are held together exclusively by the dispersion energy ($\Delta E_{DIS}$).

The essential limitation of the applicability of *ab initio* calculations in the study of intermolecular forces is not a major issue: calculations cannot be performed with the accuracy required in the case of systems that are too large—that is aggregates involving too many electrons. High com-

Table 3. Energy partitioning in some intermolecular complexes, AB, around the energy minimum. All energies are given in kcal/mol. The SCF energy of interaction is the sum of four contributions, which were obtained by means of Hartree-Fock energy partitioning.

$$\Delta E_{SCF} = \Delta E_{COU} + \Delta E_{EX} + \Delta E_{POL} + \Delta E_{RES}$$

| Atom, molecule or ion A | B | Hartree-Fock method $\Delta E_{COU}$ | $\Delta E_{EX}$ | $\Delta E_{POL}$ | $\Delta E_{RES}$ | $\Delta E_{SCF}$ [a] | Electron correlation $\Delta E_{DIS}$ | $\Delta E$ [a] | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| He | He |  |  |  |  | 0.0168 | −0.0379 | −0.0211 | [24] |
| Ne | Ne |  |  |  |  | 0.1022 | −0.1841 | −0.0819 | [24] |
| Ar | Ar |  |  |  |  | 0.2682 | −0.5100 | −0.2418 | [24] |
| $H_2$ | $H_2$ |  |  |  |  | 0.0920 | −0.1651 | −0.0731 | [24] |
| He | HF |  |  |  |  | −0.015 | −0.136 | −0.151 | [25] |
| $H_2$ | HF |  |  |  |  | −0.667 | −0.867 | −1.534 | [25] |
| HF | HF | −4.77 | −1.89 | −0.59 | −0.33 | −3.80 |  |  | [44] |
| $H_2O$ | $H_2O$ | −7.3 | 4.5 | −0.7 | −1.2 | −4.7 | −1.5 | −6.2 | [4b] |
| $H_2O$ | $Li^+$ | −41.5 | 15.3 | −12.8 | 5.2 | −33.7 |  |  | [4b] |
| $H_2O$ | $Na^+$ | −30.3 | 7.0 | −5.1 | 1.1 | −27.4 |  |  | [4b] |
| $F^-$ | $H_2O$ | −34.7 | 26.0 | −7.2 | −7.2 | −23.1 |  |  | [4b] |
| $Cl^-$ | $H_2O$ | −14.6 | 7.0 | −1.6 | −5.7 | −14.9 |  |  | [4b] |

[a] We use the notation "SCF" = "self-consistent field" in order to indicate that the basis set used was not sufficient to approach the Hartree-Fock limit very closely (cf. Fig. 2) in all cases. The total energy of interaction $\Delta E$ is obtained as the sum of the dispersion energy and the SCF energy of interaction: $\Delta E = \Delta E_{SCF} + \Delta E_{DIS}$ [cf. eq. (5)].

putational accuracy, however, is inevitably necessary, since the energies of interaction are obtained as small differences between large quantities. Experience with actual calculations revealed two sources of errors in calculations of low accuracy:

1) Calculations with small basis sets are not able to reproduce the properties of the isolated subsystems, atoms or molecules correctly, and this leads to errors in the energies of interaction, as can be seen immediately from an estimate by means of the conventional approximation formulas (Table 2). The consequences of this deficiency are almost always errors in equilibrium geometries and force constants.

2) The superposition of the basis sets of the subsystems in the association is the second source of errors: the individual systems are described better by the larger basis set of the complex. Consequently, we have smaller, *i. e.* more negative energies for the parts in the complex than at infinite intermolecular separation. The calculation thus predicts too great a stability for the aggregates. This artificial binding disappears when the calculations are performed with large basis sets[11].

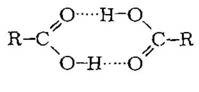
Electron correlation likewise provides essentially two contributions: the first contribution corresponds entirely to the effects described above under item (1). It accounts for the changes in calculated molecular properties as a consequence of electron correlation. In this class of erroneously calculated quantities we have, *inter alia,* the force constants of stretching vibrations, which are calculated too large at the Hartree-Fock limit and thereby lead to substantial differences between calculated and experimentally determined frequencies of the normal vibrations. The dispersion energy, $\Delta E_{DIS}$, is an electron correlation phenomenon and cannot be obtained by Hartree-Fock calculations. It represents the most important intermolecular contribution of electron correlation. In the case of polar systems the relative contribution of the dispersion energy to the total energy of interaction is fairly small. Therefore, most calculations on systems of this kind have been performed close to the Hartree-Fock limit.

If necessary, dispersion energies are added to the Hartree-Fock potentials by means of simple approximation formulas.

## 3. Binary Complexes in the Vapor Phase

*Ab initio* calculations on small aggregates of molecules yield a variety of results, which we will now correlate with the corresponding experimental data. The most interesting quantities which can be derived from intermolecular energy surfaces are the equilibrium geometries and dissociation energies of vapor phase aggregates. Both quantities can be easily calculated, but their experimental determination often leads to substantial difficulties.

Until a few years ago very little was known about the structures of stable intermolecular complexes in the vapor phase. Electron diffraction[12] is the conventional technique used in the study of molecular structures in the vapor phase. However, in only a few exceptional cases has this technique been applied to molecular associations. The best studied examples are the dimers of carboxylic acids[13].



R = H, $CH_3$, $C_2H_5$

No wonder, these systems, in particular the dimer of formic acid, were, now more than tens years ago, the first intermolecular complexes which were studied systematically. At that time semiempirical MO-methods were applied[14]. Later on, more accurate calculations were performed. One of the most recent, and at the same time, most extensive *ab initio* study of formic acid dimer[15] yielded essentially the same results as electron diffraction studies. Systems with as many electrons as formic acid dimer cannot, however, be calculated with a high degree of accuracy by *ab initio* techniques, at least with regard to presently available capacities for computation.

The experimental techniques which are used for the study of charged and of uncharged associations in the vapor phase are naturally very different. We shall therefore divide our survey of these into two sections.

### 3.1. Complexes of Atoms and Molecules

Such a variety of theoretical and experimental investigations have been performed on the vapor phase during the last two decades that we shall have to restrict ourselves to some characteristic examples. We have chosen the dimers formed from noble gas atoms and/or hydrogen halides and water, respectively, since these associations have been studied in great detail. Moreover, they are very well suited for demonstrating the universal manifestation of the underlying problems.

All noble gas dimers except $He_2$ are stable (Table 4). Only in this particular case is the trough of the potential curve $\Delta E(R)$ so shallow, and the vibrating mass so small,

Table 4. Experimental data and results of accurate calculations [a] of noble gas dimers in the electronic ground state.

| Dimer | Potential curve | | Vibrations | | Ref. |
|---|---|---|---|---|---|
| | $R_e$ [Å] | $-\Delta E(R_e) = D_e$ [cal/mol] | $D_0$ [cal/mol] | Number of states [b] | |
| HeHe | 2.97 (2.98) | 21.00 (21.1) | | 0 | [24] |
| HeNe | 3.01 (3.02) | 43.1 (40.7) | 5.3 | 1; $n=0$ | [24, 16, 56] |
| NeNe | 3.10 (3.08) | 83.5 (81.9) | 46.6 | 2 (3); $n=0$, 1 (2) | [24, 16, 56] |
| ArAr | 3.76 (3.83) | 284.6 (241.8) | 242 | | [24, 56] |
| | | | 220 | 6; $n=0,\ldots,5$ | [16] |

[a] We give the results of *ab initio* Hartree-Fock calculations combined with an empirical calculation of the dispersion energy [24] (calculated results are given in parantheses). [b] Vibrational states which have been found experimentally [16]. Isotopes: $^4$He, $^{20}$Ne and $^{40}$Ar.

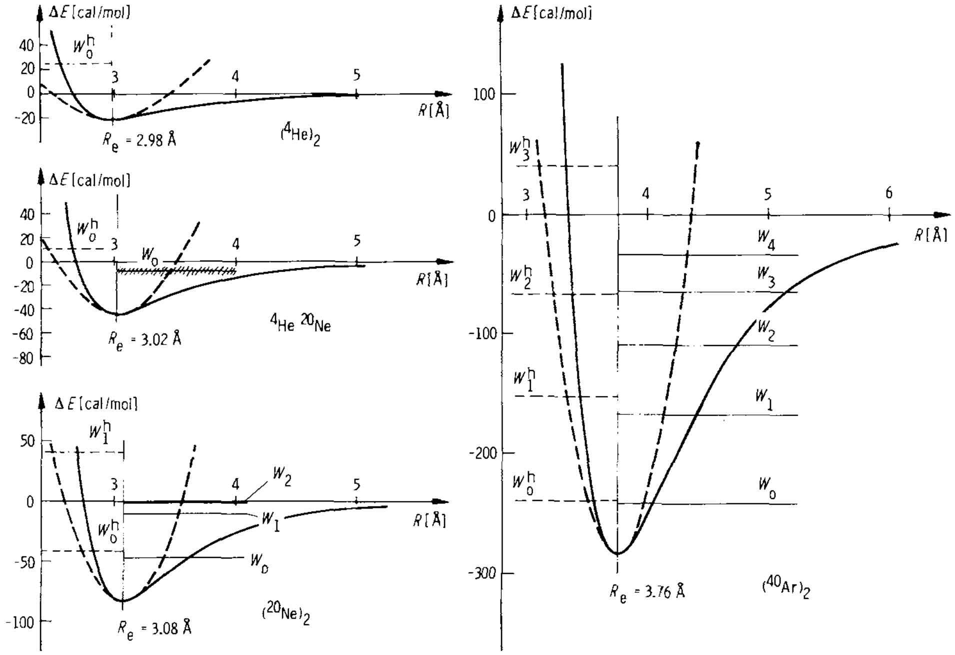


Fig. 6. Some potential curves and vibrational states of noble gas dimers. $(^4\mathrm{He})_2$ has no bound state. The potential curve of $^4\mathrm{He}^{20}\mathrm{Ne}$ supports just one stationary state. In the case of $(^{20}\mathrm{Ne})_2$ there are certainly two vibrational states, presumably there exists also a third one ($n=2$). $(^{40}\mathrm{Ar})_2$ has already a whole variety of stationary vibrational states. The best fits of harmonic potentials and the vibrational levels within the harmonic approximation are given as broken lines. The deeper the potential trough or, in other words, the more stationary states exist, the better the harmonic potential describes the actual vibrations of the dimer. In the whole series presented here the harmonic approximation predicts satisfactorily only the ground state of $(^{40}\mathrm{Ar})_2$.

that there is no stationary vibrational state of the dimer. The two next heavier "van der Waals-molecules" formed from noble gas atoms are stable: HeNe has one stable vibrational level, $\mathrm{Ne}_2$ at least two (Figure 6). The experimental information on noble gas dimers comes from different sources:

1) *Tanaka, Yoshino et al.*[16] succeeded in recording vacuum UV absorption spectra in pure noble gases and noble gas mixtures at 77 K and at pressures between 1 and 200 torr. The spectral lines were assigned to electron excitation processes in the dimers. The rotational and vibrational fine structures of these bands were used for determining the depths of the potential wells and the interatomic distance.

2) The most detailed results on noble gas dimers were obtained from molecular beam experiments mainly performed by *Lee* and his group[17]. So far, refinement of the measurements and further development of the techniques of evaluation have lost little of their primary importance[18]. In these experiments one measures the elastic, differential cross-sections (DCS) of the scattering process between crossed atomic beams which escape from supersonic nozzles into a high vacuum chamber ($p \approx 10^{-7}$ torr; see Fig. 7). The potential curve is calculated by inversion of the angular dependence of the DCS. Generally, certain analytical model potentials—the most simple functions are Lennard-Jones- and Morse-van-der-Waals potentials[19]—have to be applied.

3) Another technique, which has been used in the study of noble gas dimers, consists in the combination of the molecular beam method and a spectroscopic or structure determining method (Fig. 7). Under suitable conditions dimers and higher aggregates are formed by adiabatic cooling when the atomic beam escapes the nozzle and expands

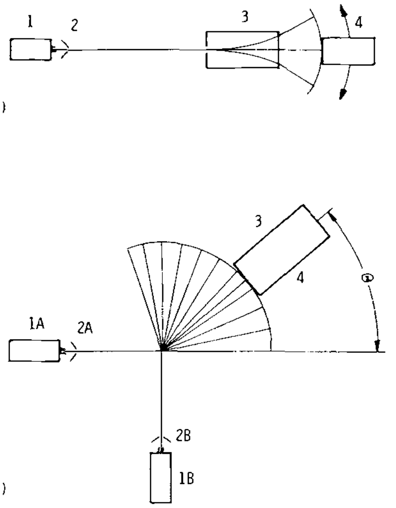


Fig. 7. Schematic setup of molecular beam experiments on intermolecular complexes. a) Single beam apparatus, b) crossed molecular beams technique. The molecular beam can be generated in both cases from a source (1, 1 A, 1 B) through expansion from a supersonic nozzle (2, 2 A, 2 B) [66]. The advantage of his technique consists essentially in a uniform translational energy of the atoms or molecules. The energy distribution function becomes narrower with increasing Mach number. During the expansion into high vacuum dimers and higher aggregates are formed which can be studied directly in the analyzer (3) (a) or which are scattered at a second molecular beam (from the source 1B) (b). In the latter case product analysis is performed as a function of the scattering angle $\Theta$. Thereby one obtains the "differential scattering cross section", $S(\Theta)$, from which conclusions on the potential surface can be drawn. A mass spectrometer generally serves as detector (4) for the species formed. Additional information may be obtained by other analytical techniques. Studies by means of "electric resonance-spectroscopy" [67] turned out to be particularly useful for intermolecular complexes. Examples are discussed in the text.

into the vacuum. *Audit*[20] determined the interatomic distances in $Ar_2$ and $Xe_2$ by means of electron diffraction in such an apparatus.

4) An important, but indirect source of information on intermolecular potentials in homodimers are the equations of state of gases in appropriate ranges of pressure and temperature[21]:

$$\frac{pV}{nRT} = 1 + \frac{B_2(T)}{V} + \frac{B_3(T)}{V^2} + \cdots \tag{6}$$

The second virial coefficient, $B_2(T)$, can be calculated from the potential curve $\Delta E(R)$ by integration. Again we need an assumption on the analytical shape of the potential curve in order to adjust energetic parameters and equilibrium distances to the $p, V, T$-data available.

In the case of noble gas dimers there is a great variety of experimental data available with which to determine a fairly simple one-dimensional energy curve. It is not surprising, therefore, that theory could not contribute much more than the shape of the potential curve and an independent verification of the experimental data. A very accurate potential curve of $He_2$ was obtained from extensive *ab initio* calculations with almost complete correlation of electron motion[22]. Because of the higher number of electrons a comparable calculation of $Ne_2$ is extremely time consuming and involved[23]. Hence, there is no completely *ab initio* calculated curve of $Ne_2$ available, which is of the same accuracy as that of $He_2$.

Another theoretical approach turned out to be extremely useful in calculations of potential curves for noble gas dimers. One calculates the energy of interaction within the framework of the Hartree-Fock approximation ($\Delta E^{HF}$). As we mentioned in the previous section $\Delta E^{HF}$ does not contain the dispersion energy and, consequently, is always repulsive. This dispersion energy, $\Delta E_{DIS}$, is calculated by means of the series expansion shown in Table 2. In order to improve the agreement with experimental data the computed dispersion energies are multiplied by an empirical factor at medium distances[24]:

$$\Delta E(R) = \Delta E^{HF}(R) - \left\{\frac{C_6}{R^6} + \frac{C_8}{R^8} + \frac{C_{10}}{R^{10}}\right\} f(R) \tag{7}$$

$$\begin{array}{lll} \text{where } f(R) = \exp\{-[1.28\,R_e/R - 1]^2\} & & \text{for } R < 1.28\,R_e \\ \text{and } f(R) = 1 & & \text{for } R \geq 1.28\,R_e \end{array}$$

$R_e$ denotes the equilibrium distance (Fig. 3). The HFD (Hartree-Fock-Dispersion) potential curves obtained thereby are considered to be the most reliable theoretical energy curves for all noble gas dimers.

The investigation of associations of noble gas atoms (E) and polar molecules is theoretically and experimentally substantially more difficult and involved than the investigation of noble gas dimers. This is also true for the most simple aggregates in which the polar molecule is diatomic. Extensive studies have been performed on complexes with hydrogen halides (HX). Some results are summarized in Table 5. Accurate *ab initio* calculations and experimental investigations are, to some extent, complementary: exact calculations are available for some representative parts of the energy surface of the He·HF[25], whereas extensive experimental data are available only for the complexes of Ne, Ar and Kr with HCl[26]. All these three systems are too large for extensive *ab initio* studies, at least at present.

Energy partitioning in case of He·HF (Table 5) demonstrates that we have stabilizing contributions to the Hartree-Fock energy of interaction in complexes of the type E·HX, in contrast to nobel gas dimers where $\Delta E^{HF}$ is repulsive. These complexes are already stable without the contribution of dispersion energy. This stabilization can be identified with a non-vanishing contribution of polarization energy, $\Delta E_{POL}$, in the semiclassical approach. An electrostatic contribution in the classical sense does not exist in the case of atom-molecule complexes.

At first we consider the complexes E·HX as general triatomic molecules. Consequently, the energy surface has three degrees of freedom. The "frozen geometry" approximation fixes the intramolecular distance $\overline{HX}$, and we are left with the problem of determining the two-dimensional energy surface $\Delta E(R, \Theta)$ (Fig. 5 and 8).

The justification of this approximation, which is essential for the interpretation of the experimental data, will be discussed later when we study the associations of polar molecules.

An elegant combination of molecular beam techniques and microwave spectroscopy corresponding schematically to the experimental setup in Figure 7a was used by *Klemperer et al.*[2,26] in their investigations on the energy surface $\Delta E(R, \Theta)$ of Ar·HCl. The complex is formed by adiabatic expansion of a mixture of Ar and HCl vapor from a supersonic nozzle. Excess of noble gas hinders the formation of

Table 5. Some complexes of noble gas atoms (E) and hydrogen halide molecules (HX) [a].

| Noble gas atom E | Hydrogen halide HX | Ground state geometry $R_0$ [Å] | $\Theta_0$ [b] | Equilibrium geometries $R_e$ [Å], $\Theta=0°$ | $R_e$ [Å], $\Theta=180°$ | Energies of interaction [cal/mol] $\Delta E\,(\Theta=0°)$ | $\Delta E\,(\Theta=180°)$ | $\Delta(\Delta E)$ | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| He | HF | | | (3.17) | (2.93) | (−151) | (−111) | (40) | [25] |
| Ne | HCl | (3.7–3.9) [c] | — | | | | | | [26] |
| Ar | HF | 3.55 | 41.0 | | | | | | [26] |
| | HCl | 4.01 | 41.6 | 3.97 | 3.78 | −524 | −367 | 157 | [26, 27] |
| | HBr | 4.14 | 42.2 | | | | | | [26] |
| Kr | HCl | 4.11 | 37.7 | | | | | | [26] |
| Xe | HCl | 4.26 | 34.8 | | | | | | [26] |

[a] Calculated or estimated values are given in parantheses. Isotopes: $^{1}H$, $^{40}Ar$, $^{82}Kr$, $^{132}Xe$, $^{19}F$, $^{35}Cl$, and $^{79}Br$. [b] The value of $\Theta_0$ corresponds to an average of $\cos^2\Theta$. [c] An estimate which is based on a comparison of interatomic distances in E·Ar and E·HCl für E = Ne, Ar, Kr und Xe.

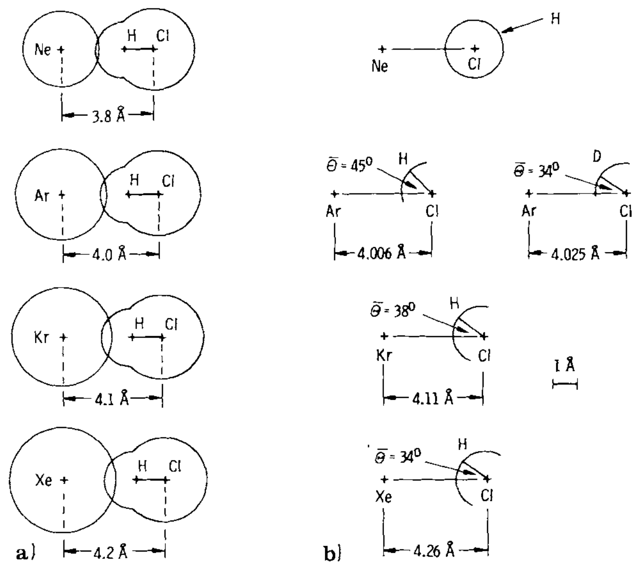


Fig. 8. a) Equilibrium- and b) ground-state geometries of some complexes of noble gas atoms and hydrogen halide molecules [26]. Note the extreme mobility of the hydrogen atom which leads to free rotational states of the HCl molecule in the complex Ne·HCl. The $\overline{\text{NeCl}}$ distance was estimated by an extrapolation from closely related systems (Table 5). In case of the best studied complex (Ar·HCl) we show the ground state geometries of two isotopic substitutions ($^{40}$ArH$^{35}$Cl and $^{40}$ArD$^{35}$Cl). Interestingly, the replacement of H by D leads to a substantial change in the geometry. In a) we have drawn spheres around the individual atomic nuclei which correspond to van der Waals radii ($R_H^w = 1.2$, $R_{Cl}^w = 1.8$, $R_{Ne}^w = 1.6$, $R_{Ar}^w = 1.9$, $R_{Kr}^w = 2.0$ Å and $R_{Xe}^w = 2.2$ Å). The values for H and Cl were taken from [68]. In the case of noble gas atoms we use one half of the atomic distance in the dimer (or in the crystal, see Table 10) as van der Waals-radius.

self-associations of hydrogen chloride, $(HCl)_n$. The constants of the rotational-vibrational spectrum of the four isotopic molecules Ar·H$^{35}$Cl, Ar·H$^{37}$Cl, Ar·D$^{35}$Cl and Ar·D$^{37}$Cl are determined. This information is sufficient to determine a substantial part of the energy surface, because the complex has a low frequency—large amplitude vibration. This normal mode corresponds to a deformation of the angle $\Theta$ at an almost constant interatomic distance $\overline{\text{ArCl}}(R)$. The large difference in the frequencies of the normal modes allows an approximation analogous to the Born-Oppenheimer approach, which separates the angular deformation—or hindered rotation of the HCl molecules within the complex—from the remaining vibrations[27].

The low frequency vibration with large amplitude mentioned above has an interesting consequence regarding the properties of the complex Ar·HCl: In contrast to most other molecules or molecular associations, equilibrium and zero-point geometries differ greatly. According to the energy surface the complex Ar·HCl has a linear equilibrium geometry ($\Theta = 0°$). The energy surface also shows a second local energy minimum at somewhat higher energy which corresponds to an arrangement Ar—Cl—H ($\Theta = 180°$). Qualitatively, these relative energies at $\Theta = 0°$ and $\Theta = 180°$ are in agreement with the data calculated on the system He·HF (Table 5). However, the second trough is extremely flat, and, accordingly, the evaluation of the experimental data is relatively uncertain. In both examples we find a somewhat larger distance between the two heavy atoms in the structure with the hydrogen atom between them. There is no doubt that the structure E·HX with $\Theta = 0°$ has the lower energy and, in other words, is more stable. We may interpret this result in terms of the stronger field effects at the H-end of the hydrogen halide compared to those at the X-end.

As a consequence of the zero-point contribution of this angular deformation vibration, the ground state of Ar·HCl appears to be bent when the geometry is determined by means of the nuclear quadrupole coupling constants of $^{35}$Cl or $^{37}$Cl. By this method the angle is obtained as an average of $\cos^2 \Theta$. The deviation from linearity ($\Theta = 41.5°$) demonstrates the mobility of the hydrogen atom in the vibrational ground state. Large vibrational amplitudes have the consequence that the mean geometries of the ground states depend strongly on the isotopic composition of the molecule (Fig. 8).

An analogous investigation was performed on the complex Kr·HCl[26]. The method used differs from that mentioned above, mainly by a pulse technique which is applied to the molecular beam ejected from the supersonic nozzle. This pulse technique is used to record the microwave spectrum by the Fourier method. The structure of Kr·HCl is closely related to that of Ar·HCl, only the amplitude of the angular deformation vibration is somewhat smaller (Fig. 8).

A molecular beam-microwave investigation of the complex Ne·HCl gave a remarkable result: The association is non-polar[26]. The lack of a permanent dipole moment in Ne·HCl has been interpreted in the following way: The HCl molecule bound to the Ne atom rotates essentially freely. In other words, the very flat potential curve observed for the angular deformation in the complexes Ar·HCl and Kr·HCl is still flatter in Ne·HCl. Consequently, there exists no vibrational state in the region around a certain value of $\Theta$, say $\Theta = 0°$. The hydrogen atom is delocalized on a sphere around the chlorine atom (Fig. 8).

The family of complexes, E·HCl, discussed above represents an illustrative example for demonstrating the usefulness of the partitioning of intermolecular energies according to eq. (5). We consider the angular dependence of the individual contributions at a constant or essentially constant intermolecular distance $R$ in order to provide an explanation for the different mobility of the HCl molecule in the three associations. $\Delta E_{\text{COU}}$ does not contribute at all, $\Delta E_{\text{RES}}$ is small, and $\Delta E_{\text{EX}}$ does not depend strongly on the angle $\Theta$. Accordingly, we restrict our estimation to the two contributions $\Delta E_{\text{POL}}$ and $\Delta E_{\text{DIS}}$. The semi-classical series expansion in $R^{-n}$ yields a first non-vanishing term with $n = 6$. We consider only this term which is assumed to be the largest:

$$\Delta E_{\text{POL}}(\text{E}\cdot\text{HX}) = -\frac{\alpha_E}{2R^6}\mu_{\text{HX}}^2(3\cos^2\Theta + 1) - \cdots \tag{8}$$

$$\Delta E_{\text{DIS}}(\text{E}\cdot\text{HX}) =$$

$$-\frac{\alpha_E}{4R^6}\cdot\frac{I_{\text{E}}\cdot I_{\text{HX}}}{I_{\text{E}}+I_{\text{HX}}}\{5\,\alpha_{\text{HX}}^{xx} + \alpha_{\text{HX}}^{zz} + 3\,(\alpha_{\text{HX}}^{zz} - \alpha_{\text{HX}}^{xx})\cos^2\Theta\} - \cdots \tag{9}$$

$I_{\text{E}}$ and $\alpha_{\text{E}}$ refer to the first ionization potential and the electric polarizability of the noble gas atom. $I_{\text{HX}}$, $\mu_{\text{HX}}$, $\alpha_{\text{HX}}^{zz}$ and $\alpha_{\text{HX}}^{xx}$ denote the first ionization potential, the electric dipole moment, and the electric polarizability parallel and perpendicular to the molecular axis of the HX molecule. Both contributions together yield the following angular dependence of the energy of interaction:

$$\Delta E_{\mathrm{POL}}+\Delta E_{\mathrm{DIS}} = -\frac{1}{R^6}\{A+B\cos^2\Theta\}-\cdots \qquad (10)$$

$$A=\frac{\alpha_{\mathrm{E}}}{2}\left\{\mu_{\mathrm{HX}}^2+\frac{1}{2}\cdot\frac{I_{\mathrm{E}}\cdot I_{\mathrm{HX}}}{I_{\mathrm{E}}+I_{\mathrm{HX}}}\left(5\,\alpha_{\mathrm{HX}}^{xx}+\alpha_{\mathrm{HX}}^{zz}\right)\right\}-\cdots$$

$$B=\frac{3}{2}\,\alpha_{\mathrm{E}}\left\{\mu_{\mathrm{HX}}^2+\frac{1}{2}\cdot\frac{I_{\mathrm{E}}\cdot I_{\mathrm{HX}}}{I_{\mathrm{E}}+I_{\mathrm{HX}}}\left(\alpha_{\mathrm{HX}}^{zz}-\alpha_{\mathrm{HX}}^{xx}\right)\right\}$$

A calculation of the numerical value of B for different noble gas atoms shows, that the first ionization potential $I_E$ has only little influence, and $B$ increases essentially with the polarizability $\alpha_E$ (Table 6). Consequently, $B$ makes an appreciable jump between Ne and Ar. This increase by a factor of four is not compensated by the somewhat larger intermolecular distance in Ar·HCl compared to in Ne·HCl and we expect a higher barrier for the rotation of the HCl molecule in the complex Ar·HCl, in qualitative agreement with the experimental results.

Table 6. A crude estimate of relative rotational barriers in complexes of noble gas atoms and hydrogen chloride according to eq. (10).

| E | Nobel gas atom | | Relative rotational barrier for E·HCl | |
|---|---|---|---|---|
| | $I_E$ [eV] | $\alpha_E$ [$10^{-25}$ cm$^3$] | $B_E/B_{Ar}$ | $\frac{B_E}{B_{Ar}}\left(\frac{R_{Ar}\cdot Cl}{R_E\cdot Cl}\right)^6$ |
| He | 24.6 | 2.2 | 0.14 | – |
| Ne | 21.6 | 4.0 | 0.25 | 0.3–0.4 [a] |
| Ar | 15.8 | 16.3 | 1 | 1 |
| Kr | 14.0 | 24.8 | 1.51 | 1.3 |
| Xe | 12.1 | 40.1 | 2.42 | 1.7 |

[a] Estimate based on the value of $R_{NeCl}$ taken from Table 5.

Investigation on complexes of two polar molecules turned out to be much more sophisticated than those discussed to far. This is true for theoretical studies because of the inevitably larger number of atoms in associations of polar molecules as well as for experimental investigations. We shall concentrate our interests on the complexes $(HF)_2$, $(H_2O)_2$ and $H_2O \cdot HF$ as well as on structures of the type $R_2O \cdot HF$. Apart from accurate *ab initio* calculations we have essentially four experimental techniques at our disposal for studies on polar aggregates:

1) Molecular beam electric resonance spectroscopy,
2) direct microwave spectroscopy,
3) IR-spectroscopy, and
4) $p, V, T$ measurements.

The combination of molecular beam techniques and microwave spectroscopy[28] led to the most reliable and most accurate results on the structure of the homodimers $(HF)_2$ and $(H_2O)_2$ (Fig. 9). Sufficiently large concentrations of dimers are again obtained by adiabatic expansion of HF or $H_2O$ molecular beams from supersonic nozzles. It has been shown by mass spectroscopic techniques that the dimer is the only polar oligomer in the case of hydrogen fluoride.

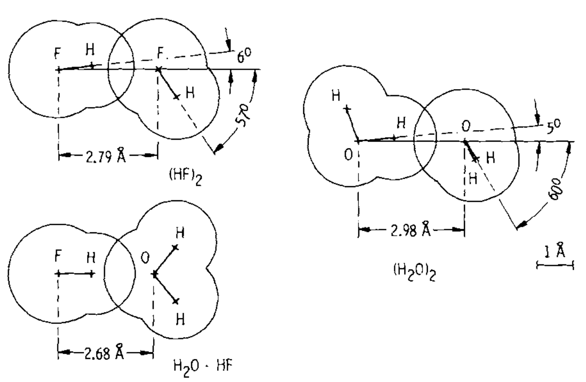


Fig. 9. Equilibrium geometries of the complexes $(HF)_2$, $H_2O \cdot HF$ and $(H_2O)_2$. The spheres around the atomic nuclei correspond to van der Waals-radii ($R_H^w = 1.2$, $R_O^w = 1.4$, and $R_F^w = 1.35$ Å). Because of the strong electrostatic dipole-dipole force the two molecules are pressed upon each other more strongly than in the case of pure dispersion forces. This shortening of the intermolecular distance is characteristic of complexes with hydrogen bonds.

All the other higher aggregates (see Section 4) apparently have cyclic structures and are non-polar. The same is true for higher aggregates of $H_2O$. The molecular beam is analyzed in an "electron resonance"-spectrometer[29] in the radio and microwave range of frequencies. Thereby one gains information on transitions between rotational levels and eventually between the energy levels of low frequency vibrations. The evaluation of the moments of inertia of as many isotopic complexes as possible provides information on the structures of the aggregates. The Stark effect in the rotational spectrum may be used to determine electric dipole moments of complexes. Despite this multitude of data the molecular structure of the simplest association of polar molecules, mainly that of $(HF)_2$, can be reconstructed only with simplifying assumptions. Generally, one uses the "frozen geometry" approximation.

Hydrogen fluoride dimer was found to be a very mobile aggregate: the complex is bent and the two protons switch

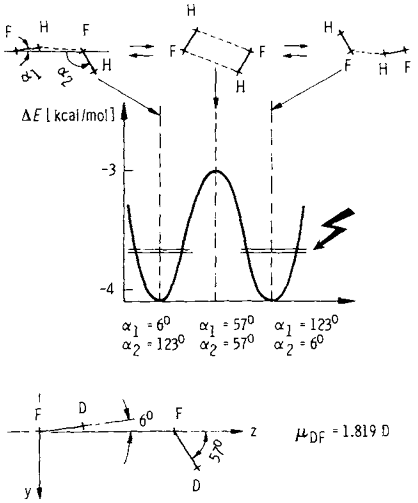


Fig. 10. Tunneling motion of the two protons in hydrogen fluoride dimer (arrow: cleavage by tunneling effect) and the superposition of the electric moments of the two monomers. Extensive calculations [29] have shown that the cyclic structure of the dimer corresponds to a saddle point of the energy surface.

Superposition: $\mu_z = 2.80$ D; $\mu_y = 1.34$ D
Experiment [28]: $\mu_z \sim \mu_a = 2.987$ D; $\mu_y \sim \mu_\perp = 1.6$ D

back and forth between two equivalent positions by a tunneling mechanism (Fig. 10). From the splitting of the rotational levels one calculates an energy barrier of 1.4 kcal/mol. The distance between the two heavy atoms ($R_{FF} = 2.79 \pm 0.05$ Å) can be determined with a high degree of accuracy. From the Stark coefficients of the rotational transitions we obtain the components of the dipole moment along the direction of the main axis of inertia (Fig. 10; note that it almost coincides with the $\overline{FF}$ bonding direction) and perpendicular to it. These two components confirm that the complex is, on average, bent. Moreover the dipole moment is larger than it would be in the case of a simple vectorial superposition of dipoles of two free HF molecules in the same geometry (Fig. 10).

Because of its relative smallness the system $(HF)_2$ has also been studied by theoretical methods for some time[30]. Long before the experimental determination of the equilibrium geometry, calculations predicted essentially the correct results. Later on, the theoretical studies were refined more and more and now complete the experimental data in some important details. The accuracy of the "frozen geometry" approximation, an indispensable constituent of the model for the evaluation of the experimental data, can be tested directly by means of accurately calculated equilibrium geometries (Fig. 9): Actually the bond distances in both HF molecules increase on complex formation. The changes, however, are very small and amount to a few thousandths of an Ångstrøm only. The hydrogen bond is not entirely linear: the central proton lies slightly displaced from the $\overline{FF}$ connecting line. The increase in dipole moment reflecting changes in electron density distributions on complex formation is a consequence of the mutual polarization of both molecules in the association.

In the case of the water dimer, $(H_2O)_2$, we encounter a completely analogous situation, although the theoretical calculations and the evaluation of the experimental data are much more difficult because of the greater number of atoms. Experiment and accurate *ab initio* calculations confirm and complement each other[28,31]. At the equilibrium geometry the dimer is not planar but has a plane of symmetry (Fig. 9). The hydrogen bond OH...O is not completely linear. The electric dipole moment increases substantially on complex formation. This increase in polarity in the two subsystems can be explained easily by means of the calculated differences in electron density distribution which are shown graphically in Figure 4.

Harmonic force constants were calculated for both dimers, and from these the vibrational spectra were predicted[30,31]. The calculations reproduce very well the shifts towards lower frequencies observed with the experimental HF and HO bond stretching vibrations[32]. Obviously, the *ab initio* calculations of vibrational spectra still suffer from some deficiencies. As we shall see in the next example, a profound interpretation of the experimental data requires also explicit consideration of the harmonic coupling force constant between HX bond stretching and intermolecular motion as well as the anharmonic correction to the HX stretching mode. Both constants were not taken into account in the calculations mentioned above.

Table 7. Energies and enthalpies of interaction in the dimers of hydrogen fluoride and water.

| Dimer | Energy of interaction [kcal/mol] | | $-D_0 = \Delta H_0^0$ [a] [kcal/mol] | $\Delta H_{298}^0$ [a] [kcal/mol] | Ref. |
|---|---|---|---|---|---|
| | $\Delta E_{SCF}$ | $\Delta E$ | | | |
| $(H_2O)_2$ | $-4.55$ | $-5.63$ | $-3.21$ | $-3.64$ | [31, 33] |
| | $-3.87$ | $-4.75$ | $-2.45$ | $-2.88$ | [b] |
| | | $-5.76$ | $-3.31$ | $-3.65$ | [c] |
| $(HF)_2$ | $-3.8$ | $-4.1$ | $-2.1$ | $-2.9$ | [29, 33] |

[a] $\Delta H_T^0$ is the enthalpy of dimerization at $T$ K under standard conditions. [b] Estimation based on the presently most accurate *ab initio* calculation. The Hartree-Fock energy was taken from [57], the value of the correlation energy from [31]. The total energy of interaction appears to be somewhat too small in absolute value. The same is true for the most accurate calculations on $(HF)_2$. Both calculations are of similar quality. [c] Empirical potential from [58] together with the vibrational corrections from [33].

The dissociation energy of vapor-phase dimers is of particular importance. Unfortunately, this quantity is neither easy to calculate[4d,33] nor accessible by direct experimental measurements. The difficulty with *ab initio* calculations lies in the sensitivity of the energy difference to the choice of the basis set and to electron correlation effects (Table 7). The binding energy of $(H_2O)_2$ has been evaluated from the second virial coefficient $B_2(T)$[34]. Theory and experiment converge at a value of $D_0[(H_2O)_2] = 3$–$4$ kcal/mol.

Heterodimers from polar molecules have been neglected for a long time since it was generally accepted that they are extremely difficult to study in the vapor phase. With the exception of some calculations, publications on such complexes hardly appeared in the literature until the mid-sixties. Searching for a simple hydrogen bonded system in the vapor phase *Millen et al.*[35] discovered, about 15 years ago, that the association constant in the system $(CH_3)_2O + HCl$ is large enough to allow direct recording of the infrared spectrum of the association $(CH_3)_2O \cdot HCl$ in the vapor phase. Meanwhile, these investigations have been extended to many other systems of the type $R^1R^2O \cdot HX$ and to other spectroscopic techniques — microwave and Raman spectroscopy as well as investigations in the far and near infrared[36]. For the sake of simplicity we shall consider here the systems $H_2O \cdot HF$ and $(CH_3)O \cdot HF$.

The complex $H_2O \cdot HF$ is best studied as far as theoretical calculations and experimental measurements are concerned. The microwave spectrum can be recorded directly in the vapor phase since the association constant is large enough. We therefore know the structure and the dipole moment of this complex very well (Fig. 9). The aggregate $H_2O \cdot HF$ is either planar ($C_{2v}$-symmetry) or it vibrates between two equivalent equilibrium geometries which are separated by an extremely small barrier only. In other words we have either a single minimum potential or a very flat double minimum potential for the corresponding bending vibration. The dipole moment of the complex ($\mu_a = 3.82 \pm 0.02$ D) is larger than the sum of the dipole moments of the two free molecules ($\mu_{HF} + \mu_{H_2O} = 3.68$ D). Thus, we find an increase in the dipole moment of $\Delta\mu_{H_2O \cdot HF} = 0.14$ D for the planar equilibrium geometry. In the case of a vibrating system with a planar average structure $\Delta\mu$ would be even larger. Because of the simple geometry of the association $H_2O \cdot HF$ we have here a direct experimental proof for the increase in polarity as a consequence of mutual polarization of the two subsystems in the complex.

The energy surface of $H_2O\cdot HF$ has also been the subject of extensive *ab initio* calculations[37]. An essentially correct equilibrium geometry was already predicted in the first theoretical investigation on this system. Recent, very extensive studies favor a double minimum potential with an extremely low barrier for the bending mode. There is no doubt that the complex is extremely flexible with respect to the out-of-plane bending vibration (Fig. 9).

Further details on the energy surfaces of $H_2O\cdot HF$ and $(CH_3)_2O\cdot HF$ can be derived from infrared spectra in the vapor phase. The associations with isotopes H and D have been studied in great detail. In the case of $(CH_3)_2O\cdot HF$ and $(CH_3)_2O\cdot DF$ the first overtones were recorded as well. An analysis of the observed frequencies and intensities clearly shows that a satisfactory description of the vibrational spectrum of the complex is possible only if the anharmonicity of the HF bond stretching vibration and the harmonic force constant for the coupling between HF and OF vibration are considered explicitly. Unfortunately, however, just these terms have so far been neglected in most *ab initio* calculations of vibrational spectra of associations with hydrogen bonds. An exception is a very recent study on $H_2O\cdot HF$ and $(CH_3)_2O\cdot HF$[37c] in which the force constants mentioned were calculated from the energy surface as well. This calculation still requires some refinement before definitive conclusion of the vibrational frequencies can be drawn. The authors of this latter mentioned publication, ***Bouteiller, Allavena*** and ***Leclercq,*** found that the higher force constants cannot be predicted with sufficient accuracy unless *all* degrees of freedom of the complex are subject to variation. Such a complete study of the energy surface, however, requires an enormous computational effort and has not yet been performed.

Accurate calculations and a careful analysis of the vibrational spectra agree very well with respect to equilibrium dissociation energies of the complex $H_2O\cdot HF$. *Thomas*[36] obtained a value of $D_e = 7.1$ kcal/mol. This corresponds to a zero-point dissociation energy of $D_0 = 6.2$ kcal/mol.

Considering the partitioning of intermolecular energies for some characteristic examples of associations of polar molecules (Table 3) we observe primarily a dominance of the electrostatic contribution. Indeed, the orientation of the molecules in the equilibrium geometries of the complexes is essentially determined by the angular dependence of the electrostatic energy. Electron density distributions in molecules in general have low symmetry and, hence, the angular dependence is a much more sophisticated function than the pure interaction of two point dipoles.

### 3.2. Ion-Molecule Complexes

*Ab initio* calculations do not fundamentally differentiate between molecule-molecule and ion-molecule associations, even though the dissociation energies of the complexes may differ by more than an order of magnitude. Equilibrium geometries and energy surfaces are obtained with about the same accuracy in both cases.

Naturally, the low volatility of ions makes the experimental investigation of ion-molecule associations an extraordinarily difficult problem. Since the sixties a new experimental technique, "high pressure-mass spectroscopy"[3], has become a generally accepted method. This technique provides direct access to the equilibrium constants of associations between ions and molecules. Reaction enthalpies and entropies are calculated in the conventional way from the temperature dependence of the equilibrium constants.

The ions, *e.g.* the cations $A^+$, react in the reaction chamber with molecules B and form ion-molecule aggregates $A^+B_n$. Collision partners M remove excess translational energy:

$$\begin{aligned}
&A^+ + B + M && \xrightleftharpoons{K_{0,1}} A^+B + M \\
&A^+B + B + M && \xrightleftharpoons{K_{1,2}} A^+B_2 + M \\
& && \quad\vdots \\
&A^+B_{n-1} + B + M && \xrightleftharpoons{K_{n-1,n}} A^+B_n + M
\end{aligned} \tag{11}$$

As a rule, equilibrium is already established after a fraction of a millisecond. The equilibrium constants are then calculated according to

$$K_{n-1,n} = \frac{[A^+B_n]}{[A^+B_{n-1}][B]} = \frac{I_n}{I_{n-1}[B]} \tag{12}$$

from the relative "peak intensities" of the ions $A^+B_n$ and $A^+B_{n-1}$, $I_n$ and $I_{n-1}$, as well as from the pressure of the monomer [B]. In the actual measurements, pressures up to

Table 8. Calculated and experimental (high pressure mass spectroscopy) enthalpies and entropies for the vapor phase hydration of some small ions [3, 38]. $\Delta H$ in kcal/mol, $\Delta S$ in cal $K^{-1}$ $mol^{-1}$.

| Ion | Number of water molecules $n-1$, $n$ | Calculated results | | | Exp. results | |
|---|---|---|---|---|---|---|
| | | $\Delta E$ | $-D_0 = \Delta H_0^0$ | $\Delta H_{298}^0$ | $\Delta H_{298}^0$ | $\Delta S_{298}^0$ |
| $Li^+$ | 0, 1 | −35.5 | −33.4 | −34.3 | −34 | −23 |
| | 1, 2 | | | | −25.8 | −21.1 |
| | 2, 3 | | | | −20.7 | −24.9 |
| | 3, 4 | | | | −16.4 | −29.9 |
| | 4, 5 | | | | −13.9 | −31.4 |
| | 5, 6 | | | | −12.1 | −32 |
| $Na^+$ | 0, 1 | −24.4 | −22.7 | −23.3 | −24 | −21.5 |
| | 1, 2 | | | | −19.8 | −22.2 |
| | 2, 3 | | | | −15.8 | −21.9 |
| | 3, 4 | | | | −13.8 | −25.0 |
| | 4, 5 | | | | −12.3 | −28.1 |
| | 5, 6 | | | | −10.7 | −26.0 |
| $K^+$ | 0, 1 | −17.0 | −15.7 | −16.2 | −17.9 | −21.6 |
| | 1, 2 | | | | −16.1 | −24.2 |
| | 2, 3 | | | | −13.2 | −23.0 |
| | 3, 4 | | | | −11.8 | −24.7 |
| | 4, 5 | | | | −10.7 | −25.2 |
| | 5, 6 | | | | −10.0 | −25.7 |
| $F^-$ | 0, 1 | −24.5 | −21.3 | −22.2 | −23.3 | −17.4 |
| | 1, 2 | | | | −16.6 | −18.7 |
| | 2, 3 | | | | −13.7 | −20.4 |
| | 3, 4 | | | | −13.5 | −36.9 |
| | 4, 5 | | | | −13.2 | −30.7 |
| $Cl^-$ | 0, 1 | −12.4 | −10.8 | −11.4 | −13.1 | −16.5 |
| | 1, 2 | | | | −12.7 | −20.8 |
| | 2, 3 | | | | −11.7 | −23.2 |
| | 3, 4 | | | | −11.1 | −25.8 |

a few mbar are commonly employed. The results for the "step by step" hydration of small ions are summarized in Table 8.

Accurate *ab initio* calculations on 1:1 complexes[38] reproduce the experimental enthalpies of the complex formation with remarkable precision (Table 8). For accurate comparisons the differences in zero-point energies and the temperature dependent contribution to $\Delta H$ have to be taken into account explicitly.

In contrast to the comprehensive thermodynamic data on ion-molecule complexes almost no experimental information on equilibrium geometries is available. Hence, in this context, we have to rely on *ab initio* calculations[38]. The results of the most accurate investigations performed so far on some simple hydrated ions are summarized in Figure 11. Associations of metal cations and water have planar equilibrium geometries with $C_{2v}$-symmetry. A deformation of the water molecule in the complex becomes recognizable only with cations which carry charges greater than +1. Associations between water molecules and halide ions are characterized by more complicated equilibrium geometries: $F^- \cdot H_2O$ has a hydrogen bond like structure with an almost linear arrangement of the atoms F, H and O. In the equilibrium geometry of $Cl^- \cdot H_2O$ the deviation from a linear arrangement of the three atoms Cl, H and O is much larger. More remarkable, however, is the fact that the potential curve for a partial rotation of the water molecule in the complex (Fig. 11) is surprisingly flat. We may conclude, therefore, that the water molecule in $Cl^- \cdot H_2O$ is highly mobile, like the hydrogen chloride molecule in the complex $Ar \cdot HCl$. The ions $H_5O_2^+$ and $H_3O_2^-$ are characterized by very flat potential curves for the motion of the central proton along the connection line $\overline{OO}$. This unusual mobility of the proton in these systems is responsible for a variety of properties in solution[39]. The two latter mentioned examples are cases in which the "frozen-geometry" approximation is no longer applicable. It would seem more appropriate therefore to consider the ions $H_5O_2^+$ and $H_3O_2^-$ as unique "chemical individuals" having a "four-electron three-center" bond which has close similarity to that in polyhalide ions like $I_3^-$.

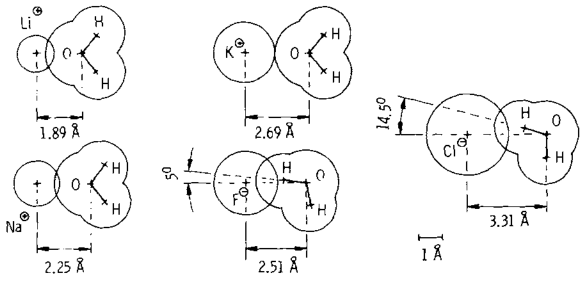


Fig. 11. Equilibrium geometries of the monohydrates of some monovalent ions [38]. The spheres around the atomic nuclei correspond to van der Waals-radii [68] ($R_H^w = 1.2$, $R_O^w = 1.4$ Å) as well as to ionic radii [69] ($R_{Li^+}^i = 0.78$, $R_{Na^+}^i = 0.95$, $R_{K^+}^i = 1.33$, $R_{F^-}^i = 1.36$ and $R_{Cl^-}^i = 1.81$ Å). In the case of anion-water complexes strong mutual penetration of the van der Waals spheres is observed as a consequence of hydrogen bond formation.

Energy partitioning in ion-molecule complexes (Table 3) shows the expected dominance of the electrostatic contribution. In comparison to the associations of polar molecules we find that $\Delta E_{COU}$ is roughly larger by one order of magnitude in the charged aggregates. The differences in intermolecular energies are essentially determined by this difference in the electrostatic contribution. The polarization of the electron density distribution in the molecules is much greater as a consequence of the strong field of the ions. Consequently, the polarization energy, $\Delta E_{POL}$, is larger in absolute value than in the case of molecule-molecule complexes. Electron density difference functions (Fig. 4) reveal the polarization of the water molecule in the field of the ions very well.

If we are able to define an appropriate surface boundary between the subsystems it is possible to calculate a charge transfer in the complex directly from the electron density distribution. For all systems discussed here except $H_5O_2^+$ and $H_3O_2^-$ this charge transfer is very small: The shifts are of the order of 0.001 $e_0$ to 0.01 $e_0$[4b].

## 4. Higher Aggregates in the Vapor Phase

A profound knowledge of the properties of higher aggregates—*i.e.* associations of more than two atoms, molecules or ions—is of particular importance for a better understanding of interactions in condensed phases. Recalling the problems we encountered in the preceding section we realize that investigations on higher aggregates are by no means easy to perform. Because of the large numbers of degrees of freedom and the inevitable size of the entire system, *ab initio* calculations are extremely time consuming. Accurate calculations can be performed only for small parts of the energy surface. Experimental investigations are in no way less involved: In general, it is very difficult to obtain defined higher aggregates in concentrations high enough for experimental studies. Should this however be the case it is nevertheless by no means granted that a few spectroscopic data are sufficient to provide conclusive information on the structure of something as complicated as an oligomer of molecules. Exceptions are provided only by molecular beam experiments and high pressure mass spectroscopic studies. Additional, although indirect, information on the energies of aggregate formation is available from an analysis of higher virial coefficients. At first we might mention some experimental results, primarily on polar systems, and consider the theoretical aspects later on.

Studies on clusters of noble gas atoms are comparatively simple because of the structural simplicity of these aggregates. We mention here two characteristic investigations[40] in which small and medium size clusters of Ar atoms were produced by escapement of a molecular beam from a supersonic nozzle. The structure of the cluster has been studied by electron diffraction. Despite these data, information on the structures of higher aggregates of noble gas atoms is rather fragmentary.

Aggregates of polar molecules have been studied experimentally by the "molecular beam electric resonance" technique[41]. The conditions were so chosen that higher aggregates were formed on expansion of the beam from the supersonic nozzle. The molecular weight of the clusters is determined in the mass spectrometer. The most important conclusion that can be drawn from these studies is of a negative nature: most higher aggregates cannot be focussed in the "electric-resonance" spectrometer and hence are nonpolar. In other words the clusters are characterized by a structure in which the electric moment vanishes because of symmetry reasons. Most probably the individual molecules are arranged cyclically in the aggregates (Fig. 12). Some years ago cyclic higher aggregates were postulated to explain the properties of hydrogen fluoride in the vapor phase: *Janzen* and *Bartell*[42b] proved the existence of cyclic hexamers $(HF)_6$ by means of an elegant combination of molecular beam electron diffraction techniques. These oligomers are very flexible, as can be seen from the large vibrational amplitudes. The thermodynamics of higher ion-molecule aggregates can be studied very well by high-pressure mass spectroscopy[3] (see Section 3.2).

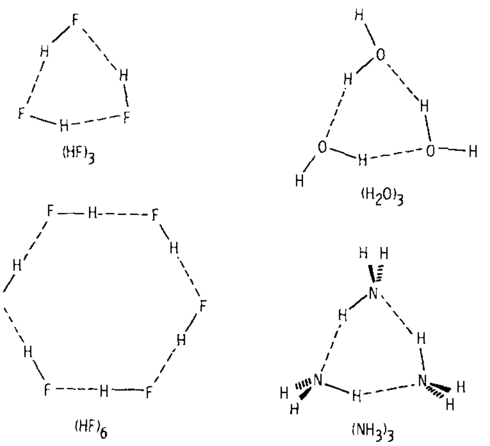


Fig. 12. Cyclic HF, $H_2O$ and $NH_3$ oligomers with hydrogen bonds.

*Ab initio* calculations have been performed on higher aggregates of polar molecules as well. In particular, the trimers of HF, $H_2O$ and $NH_3$ have been studied extensively[43]. Because of the size of these systems the accuracy of these calculations has to be evaluated critically. There is uncertainty concerning relative stabilities of open chain and cyclic oligomers. In contrast to some calculations on $(H_2O)_3$ with rather small basis sets extensive *ab initio* calculations led to the result that the sequential open chain trimer (Fig. 12) is more stable than the cyclic conformation of the complex. The most accurate studies performed so far, however, yield a lower energy for the cyclic trimer of water. There is no doubt, that theoretical investigations have not, as yet, reached the accuracy which would allow definite conclusions to be drawn regarding this question. It is hoped that future studies will clarify the influence of further basis set extension and electron correlation effects on the results of such calculations. Despite all uncertainties of the experimental data, it seems well established that trimeric water has no permanent electric dipole. This fact is most easily accounted for by a cyclic equilibrium geometry. In the case of $(NH_3)_3$ a cyclic equilibrium geometry was found in a calculation using a fairly large basis set.

*Ab initio* calculations on aggregates of $Li^+$, $Na^+$, $K^+$, $F^-$ and $Cl^-$ with water molecules[38] show good agreement with the corresponding hydration enthalpies determined by high-pressure mass spectroscopy (Table 8). In the case of the higher associations a systematic error is observed: with increasing number of water molecules, $n$, we find too large a stabilization energy. The origin of this error is to be seen in increasing contributions of the artificial basis set superposition stabilization of higher associations (see Section 2).

To obtain a better understanding of the forces acting in the molecular clusters we consider the partitioning of intermolecular energies. For the formation of an aggregate of the three subsystems A, B and C

$$A + B + C \rightleftharpoons ABC \qquad (13)$$

we find

$$\Delta E = E_{ABC} - (E_A^0 + E_B^0 + E_C^0) = \Delta E_{AB} + \Delta E_{BC} + \Delta E_{CA} + \Delta E_{ABC} \qquad (14)$$

Apart from binary interactions or pair potentials $\Delta E_{AB}$, $\Delta E_{BC}$ and $\Delta E_{CA}$ there is also the contribution of three-body forces, $\Delta E_{ABC}$. In higher clusters there are four-body, five-body and, in general, many-body interactions which are defined analogously.

Similarly, as in the case of interactions between two subsystems three-body forces can also be analyzed by means of energy partitioning[44].

$$\Delta E_{ABC} = \Delta E_{ABC}^{COU} + \Delta E_{ABC}^{POL} + \Delta E_{ABC}^{DIS} + \Delta E_{ABC}^{EX} + \Delta E_{ABC}^{RES} \qquad (15)$$

Using the definitions given in Section 2 we find that the electrostatic contributions of three- and many-body forces are zero:

$$\Delta E_{ABC}^{COU} = 0, \quad \Delta E_{ABCD}^{COU} = 0, \ldots \qquad (16)$$

In clusters of noble gas atoms there are two contributions to the "non-additivity" of intermolecular potentials, which originate from exchange and dispersion energy. By non-additivity we characterize that total contribution to the energy of interaction which comes from three-body and higher many-body forces. In the case of the trimers of the light noble gas atoms, $He_3$ and $Ne_3$, the exchange contribution $\Delta E_{ABC}^{EX}$ is obtained, as mentioned previously, within the Hartree-Fock approximation. It is of particular importance at small interatomic distances. The non-additivity of the long-range contribution, the dispersion energy, can be estimated by means of the approximation introduced by *Axilrod* and *Teller*[46]:

$$\Delta E_{ABC}^{DIS} \approx \frac{3}{2} \frac{(I_A + I_B + I_C)\, I_A\, I_B\, I_C}{(I_A + I_B)(I_B + I_C)(I_C + I_A)} \alpha_A \alpha_B \alpha_C \frac{3 \cos\alpha \cos\beta \cos\gamma + 1}{R_{AB}^3 R_{BC}^3 R_{CA}^3} \qquad (17)$$

$I_A$, $I_B$ and $I_C$ are the first ionization potentials, and $\alpha_A$, $\alpha_B$ $\alpha_C$ are the electric polarizabilities of the subsystems concerned. The definition of the angles $\alpha$, $\beta$ and $\gamma$ is shown in Figure 13. Both contributions, $\Delta E_{ABC}^{EX}$ and $\Delta E_{ABC}^{DIS}$, show a

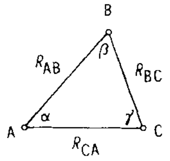


Fig. 13. Diagram for calculation of the non-additive contribution to the dispersion energy according to *Axilrod* and *Teller* [46].

pronounced dependence on the geometrical arrangement of the three atoms A, B and C: The long-range three-body dispersion forces are attractive in the linear arrangement ($\beta = 180°$, $\alpha = \gamma = 0°$) and repulsive in an equilateral triangle geometry ($\alpha = \beta = \gamma = 60°$). The three-body exchange forces which dominate at short distances have opposite sign: they lead to an attractive, *i. e.* negative contribution to the total energy in an equilateral triangle geometry and destabilize linear arrangements of the three atoms. In the neighborhood of the equilibrium geometries we find very small contributions of three-body forces to the energies of noble gas trimers.

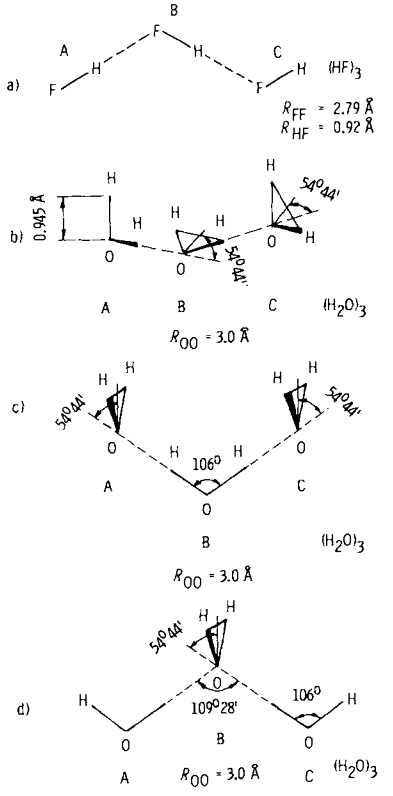


Fig. 14. Non-additivity of the energy of interaction in the trimers of hydrogen fluoride and water.

a) $(HF)_3$, sequential trimer:

$\Delta E^{EX}_{ABC} = -0.07$ kcal/mol
$\Delta E^{POL}_{ABC} = -0.42$ kcal/mol
$\Delta E^{RES}_{ABC} = -0.10$ kcal/mol

---

$\Delta E^{SCF}_{ABC} = -0.58$ kcal/mol
$\Delta E^{DIS}_{ABC} \approx 2 \times 10^{-3}$ kcal/mol
$\Delta E_{ABC} \approx \Delta E^{SCF}_{ABC} = -0.58$ kcal/mol

b) $(H_2O)_3$, sequential trimer

$\Delta E^{DIS}_{ABC} \approx 5 \times 10^{-3}$ kcal/mol
$\Delta E_{ABC} \approx \Delta E^{SCF}_{ABC} = -0.57$ kcal/mol

c) $(H_2O)_3$, double donor-trimer:

$\Delta E_{ABC} \approx \Delta E^{SCF}_{ABC} = 0.60$ kcal/mol

d) $(H_2O)_3$, double acceptor-trimer:

$\Delta E_{ABC} \approx \Delta E^{SCF}_{ABC} = 0.37$ kcal/mol

Energy partitioning in $(HF)_3$ shows that the non-additivity of the polarization energy is the largest contribution. The non-additive contributions of dispersion calculated by means of eq. (17) are very small compared to the non-additivity of polarization [43].

There are no electrostatic contributions to the three- and higher many-body forces. Hence we expect to find only one important contribution in addition to exchange and dispersion three-body energies in aggregates of polar molecules: This is the non-additivity of the polarization energy. The polarization term is already the largest contribution to the three-body energies in clusters of polar molecules like $(HF)_n$ or $(H_2O)_n$. In higher aggregates of ions and molecules the three-body polarization energy is the dominant contribution, compared to which the other terms are negligible. Several characteristic examples are summarized in Figure 14. The three-body dispersion energies were estimated by means of the Axilrod-Teller equation.

Qualitative hints on the nature of the non-additivity of polarization energies are easy to find. Let us consider the "sequential" trimer of hydrogen fluoride as a characteristic example (Fig. 15a). The electron density distribution in the central HF molecule is shifted in the direction C→A by the action of the electrostatic fields of its neighbors. As we already know from the shift in the electron density distribution in various dimeric aggregates, the hydrogen atom becomes more acidic and the basicity of the lone pair increases at the same time. Both interactions, AB and BC, are thus strengthened by the charge shift. We find a negative, *i. e.* a stabilizing contribution of the three-body polarization energy to the total energy of interaction. In general, sequential arrangements of polar molecules—*i. e.* those in which electric moments point approximately in the same direction—are favored (Fig. 14). In the case of the three possible open chain associations of three water molecules the "sequential" trimer is more stable than the "double do-

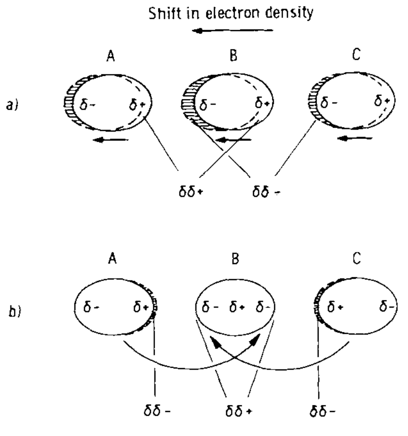


Fig. 15. Qualitative interpretation of the non-additivity of polarization energies in polar systems. The shift in electron densities in the potential field of the neighboring molecules leads a) to an increase or b) decrease of intermolecular forces. This qualitative picture largely corresponds to the concept of inductive forces used in physical organic chemistry which, *inter alia*, has been extended to general intermolecular interaction by *Gutmann* [70].

Table 9. Contributions to the non-additivity of energies of interaction in ion-molecule clusters [59]. Energies in kcal/mol [a].

| Cluster | $\Delta E$ | $\Delta E_{AB}+\Delta E_{BC}+\Delta E_{CA}$ | $\Delta E_{ABC}$ | $\Delta E^{EX}_{ABC}$ | $\Delta E^{POL}_{ABC}$ | $\Delta E^{RES}_{ABC}$ |
|---|---|---|---|---|---|---|
| $H_2O\cdot Li^+\cdot OH_2$ | −64.05 | −66.47 | 2.42 | −1.04 | 3.79 | −0.33 |
| $Li^+\cdot\overset{H_2}{O}\cdot OH_2$ | −46.40 | −43.84 | −2.55 | −0.28 | −2.61 | 0.33 |
| $Li^+\cdot\overset{H_2}{O}\cdot HOH$ | −24.08 | −25.61 | 1.54 | −0.23 | 2.33 | −0.56 |
| $HOH\cdot F^-\cdot HOH$ | −43.00 | −45.40 | 2.40 | −0.94 | 2.25 | 1.10 |
| $F^-\cdot\overset{H}{HO}\cdot\overset{H}{HO}$ | −32.94 | −30.39 | −2.54 | −0.04 | −2.24 | −0.27 |
| $F^-\cdot HOH\cdot OH_2$ | −20.91 | −23.03 | 2.12 | 0.13 | 1.62 | 0.38 |

[a] The numerical values are taken from Hartree-Fock calculations with large basis sets [59]. The non-additive contribution of the dispersion energy has been calculated by means of the formula by *Axilrod* and *Teller* [eq. (17)]. This contribution is negligibly small [43, 54].

nor" or the "double acceptor" arrangement. Cyclic oligomers are always of the sequential type. Moreover, they have one bond more than their open chain conformers. These various polarization effects can be evaluated quantitatively by means of the three-body forces discussed above.

Ion-molecule aggregates can be studied completely analogously (Table 9). Again the non-additivity of the polarization energy may be considered as the cause for weaker ion-ligand binding in the 1 : 2 complex. The ion-ligand bond energy per molecule is smaller in absolute value for the 1 : 2 aggregate compared to the energy for the 1 : 1 complex. Molecules in the second hydration shell are bound more strongly if the arrangement of the electrostatic field is sequential. This is clear to see in the two examples $Li^+\cdot(OH_2)_2$ and $F^-\cdot(H_2O)_2$. We do not intend to exaggregate here the importance of the polarization effect discussed. Other contributions play their role as well. Nevertheless, it should be pointed out that the sign and the geometrical dependence of non-additivities in complexes of the type discussed here can be predicted easily and correctly by the simple arguments presented above. Apart from a few exceptional cases three- and higher many-body forces contribute comparatively little to the total interaction. It would seem therefore that a quantitative correction to the sum of binary energies by means of semiclassical model calculations of the non-additivity of polarization is promising.

An important, though not completely solved problem concerns the role of higher contributions, namely those of four-body forces. In clusters of noble gas atoms, in characteristic intermolecular associations of polar molecules or simple ions and molecules the contributions of four-body energies are certainly very small. An entirely different situation is encountered in aggregates of atoms with partially filled electron shells ($1s^2\ldots ns^2$) like Be or Mg which form metals in the condensed phase. In these systems the three-body contributions are large and non-negligible four-body energies can be expected[47].

## 5. A World of Additive Binary Potentials and the Role of Three- and Many-body Forces

In the introduction to the preceding section we stressed the fact that a precise experimental analysis of three- and many-body forces in the vapor phase is very difficult if not impossible, as yet. Information on three-body energies obtained from higher virial coefficients is uncertain and very debatable. We shall now try to derive positive indications of the importance of these contributions from the molecular structures in condensed phases. Let us first imagine a world without three- and many-body forces, and begin with non-polar systems. The pair potential is of the Lennard-Jones type[19]:

$$\Delta E_{AB}=D_e\left\{\left(\frac{R_e}{R}\right)^{12}-2\left(\frac{R_e}{R}\right)^{6}\right\} \qquad (18)$$

$D_e$ is the depth of the trough in the potential curve and $R_e$ is the equilibrium distance. In the case of pairwise additivity of the potential the equilibrium distance is the same in the dimer, the trimer and the tetramer. The equilibrium geometry of the trimer is an equilateral triangle, that of the tetramer a tetrahedron. In the crystal we expect to find a hexagonal closed packed (hcp) arrangement of atoms. The equilibrium distance in the solid state will be shorter than that in the vapor phase dimer. The difference between both, however, should be negligibly small (Fig. 16).

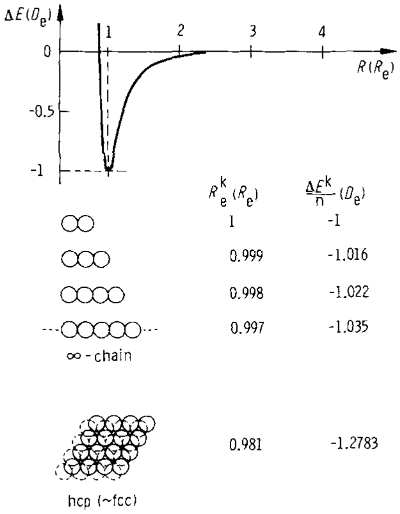


Fig. 16. Additivity of intermolecular energies in unpolar systems. The estimate presented is based on a pair potential of Lennard-Jones type: $\Delta E(R)=A\,R^{-12}-B\,R^{-6}$ [see eq. (18)]. Other potential functions for the interaction of unpolar systems lead to identical conclusions. As examples for the condensed phase we consider an infinite chain as well as a face centered cubic (fcc) or a hexagonal closed packed (hcp) lattice [71]. For the purpose of comparison we calculate the dimensionless quantities $R^k_e/R_e$ and $\Delta E^k/n\,D_e$. The superscript "k" denotes a certain cluster. $R_e$ and $D_e$ are the constants of the Lennard-Jones potential and correspond to the dimer in the vapor phase. The energy of cluster formation, $\Delta E^k$, is divided by the number of bonds to nearest neighbors ($n$). The atomic distance in the solid state appears to be only insignificantly smaller than in the vapor phase. The energy of interaction is increased by a few percent due to the presence of further atoms in the crystal.

In the case of polar systems we consider a linear chain in order to avoid sophisticated calculations caused by different orientations of the dipoles. The following simple expression is obtained for the electrostatic energy in a chain in which all dipoles point in the same direction:

$$\Delta E_{AB}^{COU} = -\mu_A \mu_B \frac{2}{R^3} \tag{19}$$

This contribution has to be added to the simple model potential given in equation (18). Summation of pair potentials yields a stronger contraction of the equilibrium distance than we find with non-polar systems when we compare the infinite linear chain with the isolated dimer in the vapor phase (Fig. 17). Nevertheless, this contraction is still small if we consider dipole moments in the range of those of ordinary polar molecules ($1\,D < \mu < 3\,D$). The stronger effect observed with polar systems has its origin in the longer effective range of dipole forces: the energy of interaction decreases with $R^{-3}$ instead of $R^{-6}$ in non-polar systems.

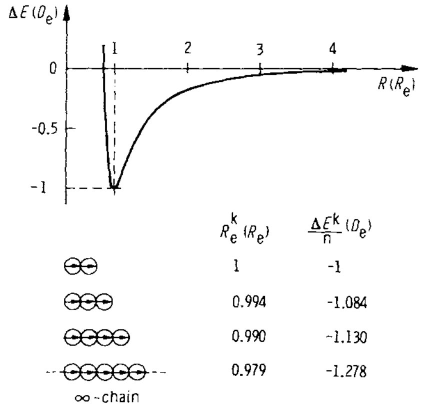


Fig. 17. Additivity of intermolecular energies in polar systems. In polar systems dipole-dipole forces (and further electrostatic and polarization forces of higher order) are superimposed upon the Lennard-Jones type interaction. In the limit of a very strong dipole-dipole force the potential approaches the function $\Delta E(R) = A \cdot R^{-12} - B \cdot R^{-3}$. For this limiting case we made similar considerations as those discussed in Figure 16. As a model for strong interaction in the solid state we consider a linear chain with parallel oriented dipoles. In this case the superimposed electrostatic fields are strongest. The effects observed strengthen the forces in condensed matter and are stronger than those found with non-polar systems: the intermolecular distance decreases by about 2%, the energy of interaction increases by 28% when the condensed phase is formed.

We shall now compare our ideas of a world of additive potentials with the actual experimental data on structures (Table 10). In the case of solids formed by noble gas atoms we find very small contractions indeed. The differences in equilibrium distances between vapor phase and crystal amount to only a few hundreths of an Ångstrøm or even less. A minute energetic effect which, nevertheless, has been debated extensively, is observed in crystal structures: Instead of the hexagonal closed packed (hcp) structure the face centered cubic lattice (fcc) is found to be the most stable arrangement[48]. The only exception is solid helium which prefers hcp structure.

Table 10. A comparison of interatomic or intermolecular distances in the vapor-phase dimers and crystals.

| Monomer | Dimer in the vapor-phase | | Crystal | | |
|---|---|---|---|---|---|
| X | $R_e^{xx}$ [Å] | Ref. | $R_e^{xx}$ [Å] | Structure [b] | Ref. |
| He | 2.97 | [56] | 3.0 | hcp | [60] |
| Ne | 3.15 | [56] | 3.156 | fcc | [61] |
| Ar | 3.758 | [56] | 3.755 | fcc | [61] |
| Kr | 4.03 | [56] | 3.992 | fcc | [61] |
| Xe | 4.36 | [56] | 4.335 | fcc | [61] |
| Li | 2.673 | [56] | 3.04 | bcc | [62] |
| | | | 3.09 | hbc | [62] |
| | | | 3.11 | fcc | [62] |
| Na | 3.079 | [56] | 3.72 | bcc | [62] |
| Be [a] | (4.3–4.5) | [63] | 2.29 | hcp | [62] |
| Mg | 3.891 | [56] | 3.21 | hcp | [62] |
| HF (X = F) | 2.79 | [28] | 2.49 | [c] | [64] |
| $H_2O$ (X = O) | 2.98 | [28] | 2.74 | ice I [c] hexagonal | [65] |

[a] The values in parantheses are results of *ab initio* calculations on $Be_2$. For this system there are no experimental data available. [b] Abbreviations hcp = hexagonal closed packed, bcc = body centered cubic and fcc = face centered cubic. [c] For the solid phase of HF and $H_2O$ see Figure 18.

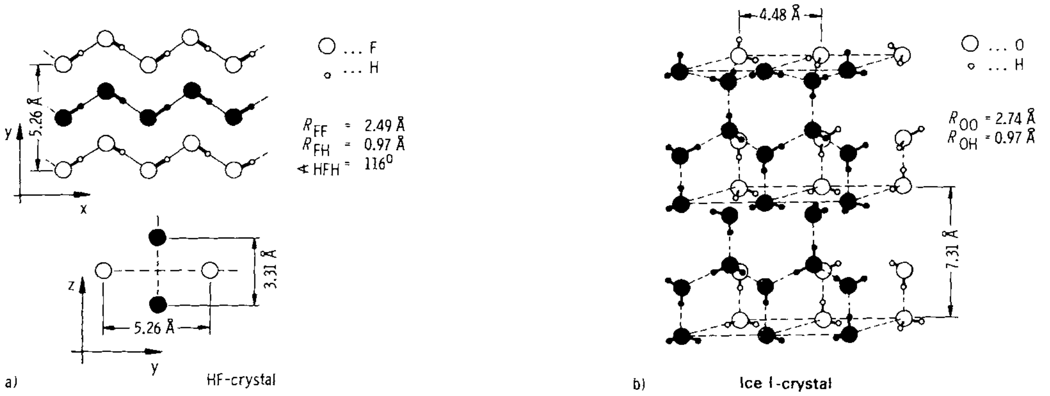


Fig. 18. The crystal structures of a) hydrogen fluoride and b) ice I (hexagonal). The HF crystal consists of loosely packed one-dimensional zig-zag chains of HF molecules. Apart from the tilt the electrostatic fields of the molecular dipoles are superimposed in optimal manner. All trimeric subsystems in the chain are of the sequential type. Therefore, all three-body forces are stabilizing and we expect a maximum effect with respect to contraction of the intermolecular distance relative to the vapor phase (Table 10). The water molecules in the ice I crystal are characterized by different orientations of their electric dipoles. In order to utilize all possibilities to form hydrogen bonds we have trimeric subunits of sequential, double-donor and double-acceptor type (see Figure 14). Consequently, there are three-body contributions of different sign. The contraction of the OO-distance relative to the vapor phase is smaller than in the HF crystal.

Simple metals, *i. e.* alkaline and alkaline-earth metals behave very differently in the solid state. The differences in equilibrium distances between vapor phase and crystal are large and very different. The dimers of alkaline metal atoms in the gas phase, $Li_2$ and $Na_2$, are characterized by a weak covalent bond. This bond is markedly stretched in the solid state. Accordingly, we find a repulsive contribution of three- and many-body forces. Alkaline earth metals behave completely differently: $Mg_2$ is a typical van der Waals molecule similar to the noble gas dimers $Ne_2$ and $Ar_2$. The data on $Be_2$ are uncertain. Attempts to prove the existence of a bonded ground state by spectroscopic techniques have so far failed. The most accurate calculations also favor a very flat potential curve with a shallow trough. Despite the smallness of the system—eight electrons only—the calculation of the electron correlation energy was found to be particularly problematical. Theoretical predictions should therefore be considered very carefully. It is, nevertheless, certain that in the case of Mg and Be the equilibrium distance in the crystal is much smaller than in the vapor phase. Both systems represent examples of stabilization through three-body forces. An extensive discussion of the role of three-body forces in various, covalently bound clusters of atoms including $Be_n$, has been presented by *Murrell*[49].

Let us now consider the systems formed by polar molecules which have been studied in most detail, namely hydrogen fluoride and water. The hydrogen fluoride crystal contains one-dimensional chains between which relatively weak mutual interactions take place (Fig. 18a). Despite the bent arrangement in the zig-zag chains the fields of the individual dipoles are strengthened by induction. All trimeric substructures are of the sequential type. Accordingly, a marked contraction in the equilibrium distance ($\Delta R_{FF} \approx 0.30$ Å) is observed on formation of the solid phase. Ice I has a fairly complicated three-dimensional structure (Fig. 18b). Apart from sequential trimer subunits we also observe "double donor" and "double acceptor" structures. The contraction of the equilibrium distance in the solid state is somewhat smaller ($\Delta R_{OO} \approx 0.24$ Å). In both cases the stabilizing contributions of the three-body forces originate essentially from the non-additivity of the polarization energy, as is known from an analysis of the vapor-phase trimers. The collection of data presented here enables us to conclude that an accurate description of condensed phases formed from polar molecules requires a proper consideration of the deviations from pairwise additive intermolecular potentials.

## 6. Polar Liquids

Needless to say, even a brief and superficial discussion of the various problems encountered with polar liquids would be beyond the scope of this review. What we intend to present, however, is an attempt to show how we can use our knowledge of intermolecular forces in the vapor phase in order to facilitate a description of polar liquids. The liquid state is notoriously difficult to characterize. It has so far been impossible to extend quantum mechanical calculations directly to the condensed liquid phase. Nevertheless, remarkable progress in the theory of liquids has been achieved during the last few years by proper application of the concepts of classical statistical mechanics. Calculations in "molecular dynamics" make an attempt at solving Newton's equations of motion for an ensemble of up to thousands of molecules. The dynamics of such a huge cluster is computed from a given potential function. In order to describe the situation in condensed matter properly the ensemble is embedded into a periodic lattice of equal ensembles (Fig. 19). The initial results of these calculations are

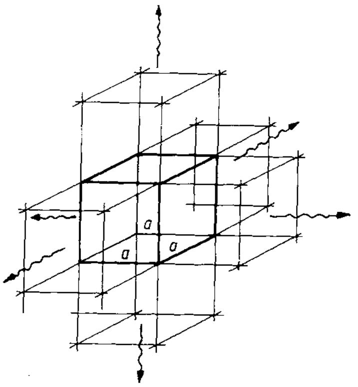


Fig. 19. Periodic boundary conditions applied with computer simulation experiments of liquids. In order to simplify the numerical calculations one assumes that a volume element of the liquid consisting of 200—1000 molecules is repeated periodically in the liquid phase. The most simple geometry of such an element is that of a cube. In each volume element ($a \cdot a \cdot a$) (arrow) "ghost particles" carry out the same motions as in the central box. This continues periodically *ad infinitum*.

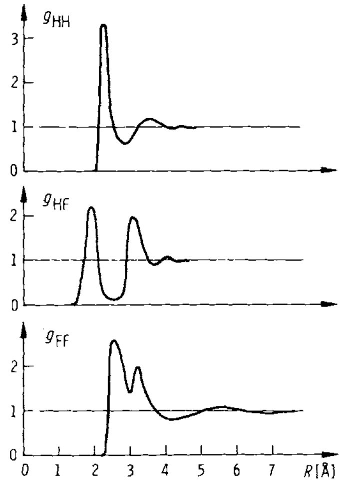


Fig. 20. The three atom-atom pair distribution functions, $g_{FF}$, $g_{FH}$ and $g_{HH}$ in liquid hydrogen fluoride under the conditions $\rho = 1$ g/cm³ and $T = 269$ K (curves taken from [50]). The pair distribution function $g_{AB}(R)$ counts the number of atoms B ($n_B$) which in the time average surround an atom A at a distance $R$.

$$\delta n_B = 4\pi R^2 \mathrm{d}R\, g_{AB}(R) \rho$$

Generally, the pair distribution function starts at $g_{AB}(0) = 0$ (at the position of one atom the probability of finding a second atom is zero), passes through several maxima and minima which are determined by the structure and local order in the liquid, and finally approaches a value of 1, which means that there is no far-reaching order in the liquid. A comparison of curves at different temperatures shows that the local order in the liquid disappears gradually with increasing temperature.

correlation functions which provide an abstract picture of the dynamic and static properties in a liquid. The static properties are obtained as time averages. A simple example of such a correlation function is the distance pair correlation (Fig. 20). It represents the average structure of the liquid, and its numerical value for a certain distance is the probability of encountering a particle of a certain class at this distance from the center.

"Monte Carlo" calculations are an alternative technique for simulating the liquid state. In this method one tries to calculate a representative set of most probable geometric arrangements of molecules. In principle, only static properties of liquids can be obtained by this approach. For example, one can calculate distance correlation functions, but not velocity correlation functions. As in molecular dynamics, Monte-Carlo calculations are based on our knowledge of the intermolecular potential.

All "computer simulation experiments" (*i.e.* Monte Carlo and molecular dynamics calculations) which have been carried out so far use intermolecular potentials which are either derived from the semiclassical theory and have model character or have been fitted to the results of *ab initio* calculations. The main interest, of course, centered on the associated liquids water, hydrogen fluoride and ammonia[50].

Two particular difficulties are encountered in simulation experiments on polar systems: For technical reasons it has not yet been possible to incorporate three-body potentials into actual calculations. As we have seen in the preceding sections, however, it is impossible to obtain correct average distances between neighboring molecules without considering three-body forces. One way of circumventing this problem is to use an effective pair potential which accounts globally for the stabilizing contribution of three- and many-body forces. The second problem, not yet solved satisfactorily, is concerned with the long effective range of potentials between dipole molecules. Correct summation of all contributions is extremely time consuming. Very popular, stringent simplifications like the "cut off" of potential curves at a certain distance introduce characteristic and crucial errors into the calculated dielectric properties[51].

The structures of liquids are amenable to experimental investigation by X-ray and neutron-scattering techniques. Combination of both methods provides the most detailed results obtained so far[52]. The quantities that can be compared best with the vapor phase are the HX stretching frequencies. With respect to these data the liquid state lies between the vapor phase and the crystal and resembles more closely the latter. Here, we may glean an indirect indication of the action of three-body forces (see Section 7).

At the moment there is very close collaboration between theorists and experimentalists regarding the physics of liquids. Experience in dynamics, gained by computer simulation experiments, helps the experimentalist in the evaluation of his data.

## 7. Crystals of Polar Molecules

In contrast to the liquid, the crystal is directly accessible to quantum mechanical investigations. In principle, *ab initio* calculations can be performed on molecular crystals if one makes use of the translational symmetry[53]. As we have already mentioned in the case of calculations on molecules, the number of electrons in the elementary cell must not be too large in order to ensure the computational accuracy required. A problem not yet solved is concerned with an economic and efficient consideration of electron correlation effects. The principles of the procedure are in complete analogy to calculations on molecules. An energy surface is calculated within the framework of the Born-Oppenheimer approximation, and from there one derives equilibrium geometries and force constants. Here, we consider exclusively the hydrogen fluoride crystal, since it is particularly well suited for *ab initio* calculations[54]. Solid hydrogen fluoride forms bent chains which are in relatively weak contact; in other words, the distance between these chains is large (Fig. 18). This quasi one-dimensional structure facilitates the theoretical investigation enormously. Large basis sets can be applied which guarantee highly accurate results. The computational efforts in real three-dimensional calculations are much larger, and so far only very small basis sets could be used in the elementary cells.

In the previous section we observed a basic feature of hydrogen bonded systems which consists in a contraction of the intermolecular distance on transition from the vapor phase dimer to the crystal. We shall now consider this difference in more detail (Table 11). The contraction of the intermolecular distance is accompanied by an increase in the HF bond length which is already present, albeit to a far less extent, in the dimer. Similarly, the shift in the HF stretching frequency between monomer and dimer in the vapor phase is very small compared to that between monomer and HF crystal. The substantial differences between the dimer and the infinite chain originate from two causes. At first we have the stabilizing effect of three-body forces

Table 11. A comparison of calculated and experimental data of hydrogen fluoride in the gaseous, liquid and solid state. References: Vapor phase: [28, 29]; liquid: [50]; crystal: [54, 64]; the calculations were performed on an ∞-chain of HF molecules as a model of the solid state.

| | Vapor phase | | Liquid | Crystal |
|---|---|---|---|---|
| | HF | $(HF)_2$ | | |
| *Calculation* | | | | |
| $R_{e(HF)}$ [Å] | 0.900 | 0.904<br>0.902 | | 0.917 |
| $R_{e(FF)}$ [Å] | | 2.84 | 2.6–2.7 | 2.59 |
| $\alpha(H\ldots FH)$ | | 130° | | 131° |
| $\Delta E$ [kcal/mol] | | −4.6 | −5.9 [a] | −6.3 [b] |
| $f_{HF}$ [mdyn/Å] [c] | 9.42 | 9.23 | | 6.85 |
| $f_{F..H}$ [mdyn/Å] [c] | | 0.23 | | 0.42 |
| *Experiment* | | | | |
| $R_{c(HF)}$ [Å] | 0.917 | | | 0.968 |
| $R_{e(FF)}$ [Å] | | 2.79 | | 2.50 |
| $\alpha(H\ldots FH)$ | | 120° | | 116° |
| $\Delta E$ [kcal/mol] | | $-6 \pm 1.6$ | −6.7 [a] | |
| $f_{HF}$ [mdyn/Å] | 9.66 | | | 6.52 [d]<br>5.24 |

[a] Negative heat of vaporization at $T = 293$ K [50]. [b] Energy of interaction per monomer in the HF chain. [c] Results of calculations using a smaller basis set and a linear chain [54]. [d] The numerical values correspond to the symmetric and asymmetric HF stretching vibration.

which strengthen the interaction between the subsystems. Secondly, we have a kind of symmetry in the infinite system which does not exist in the dimer. This symmetry has an additional influence on the properties of the chain. Let us go beyond the "frozen geometry" approximation and consider the energy curve for proton transfer (Fig. 21). The potential curve for simultaneous transfer of all protons along the infinite chain shows two equivalent minima, whereas the potential curve for proton transfer in the dimer has a single minimum only. Consequently there is an elongation of the HF bond length and a decrease in the curvature of the potential curve at the energy minimum which leads to a shift towards lower frequencies of the corresponding normal mode. *Ab initio* calculations and experiment agree completely within the expected error limits. The difference between the absolute values of calculated and experimentally measured HF stretching frequencies is explained by the lack of correlation effects in the calculation on the crystal.

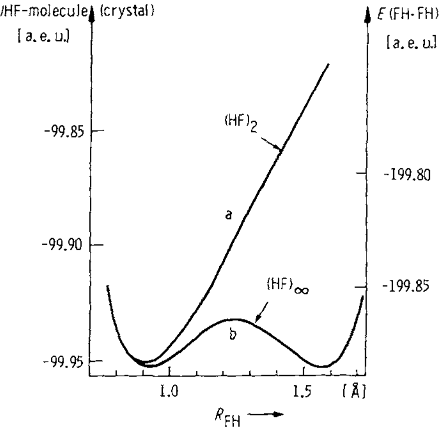


Fig. 21. The potential curve of proton displacement along the hydrogen bond in dimeric hydrogen fluoride (a) and of the synchronous, collective proton motion in the infinite hydrogen fluoride chain (b) [54]. Because of the symmetry in the solid state structure there exists a second minimum of the potential curve which has the same energy as the ordinary minimum and which corresponds to equivalent positions of all protons. Accordingly, the HF bond distance in the chain is longer than in the dimer. The curvature of the potential curve at the minimum and the harmonic force constant of the HF stretching vibration are smaller in the solid state than in the vapor phase dimer. 1 a.e.u. = 627.5 kcal/mol.

All three effects of the condensed phase, the contraction of the intermolecular distances, the elongation of the HX bonds, and the shift of the HX vibrational frequencies towards lower frequencies are observed with ice I, in exactly the same way as with solid hydrogen fluoride. Because of the essentially three-dimensional structure of ice the *ab initio* calculation is extremely complicated. No accurate data are available at present, so we shall dispense with enummerating the plethora of literature on this system.

In this brief section we were able to consider only those aspects of crystals of polar molecules which are directly related to the results obtained in the vapor phase.

## 8. Concluding Remarks

The data summarized in this review are the results of simultaneous efforts by theorists and experimental researchers. Thanks to their work our present knowledge of some intermolecular complexes is as complete as that of small molecules. The dimers of hydrogen fluoride and water count among the complexes which have been studied in more detail. This is of particular importance, because the forces acting in these dimers are essentially the same as those which determine the properties of these substances in the condensed state. Liquid water in particular has already attracted a great deal of interest for some time. This is fully justified in view of its primary importance. Unfortunately, associated liquids are the least understood systems at present. Simultaneous progress of theory and experiment obtained by computer simulation experiments and further combined X-ray and neutron scattering studies will inevitably provide further insights into the problem at hand.

The theorists found a powerful method for unifying a description of intermolecular associations and chemical bonds by means of numerical computations. The fundamental concept of (inter)molecular energy surface is the common basis also for a deeper understanding of the properties of all three states of aggregation. In retrospect one point appears to be worth mentioning: Concepts, based on unobservable indices and weakly defined quantities like bond orders, atomic charges, charge transfer *etc.* have contributed less to a better understanding of intermolecular forces than the consequent although tedious and sometimes boring calculation of quantities, which, in principle, are accessible to experimental observation.

No doubt, many systems will be studied by *ab initio* techniques during the next years. On the other hand, a clear limitation to the problems that can be treated in this way can be seen as well. The high degree of accuracy which is inevitably necessary in investigations of intermolecular forces requires enormous amounts of computer time and hence only small systems can be treated with the present day computational capacities. To go beyond this limitation would require a kind of revolution in electronic computers leading to an enormous increase in computational speed which is rather unlikely. Simulation experiments on liquids are similarly involved and they will face the same problem of technical limitation in the not too distant future. Nevertheless, in this field, the development of numerical techniques is in a state of rapid progress so that we may expect a variety of interesting results in the coming years.

*All my colleagues and coworkers have contributed a great deal to this review through their work, their advice, and their enthusiastic discussions. I should like to mention some by name: Prof. Dr. Werner Kutzelnigg, Prof. Dr. Volker Staemmler, Prof. Dr. Hans Lischka, Dr. Alfred Karpfen, Dr. Othmar Steinhauser and Dr. Anton Beyer. Dr. Bohumila Schreiber and Mrs. Judith Jakubetz worked hard with the typing of the manuscript. The Österreichische Fonds zur Förderung der wissenschaftlichen Forschung kindly provided financial support, and the Interuniversitäre Rechenzentrum Wien generously allotted computer time. I wish to take this opportunity of sincerely thanking all of them.*

Received: September 22, 1980 [A 368 IE]
German version: Angew. Chem. 93, 532 (1981)

[1] Reviews on the present status of computational methods: *H. F. Schaefer III:* Methods of Electronic Structure Theory, Plenum Press, New York 1977.

[2] Technique of "molecular-beam-electric-resonance"-spectroscopy: *J. S. Muenter, W. Klemperer,* J. Chem. Phys. *52,* 6033 (1970); *E. W. Kaiser, ibid. 53,* 1686 (1970). Overviews on the application of this technique to intermolecular forces: *W. Klemperer,* Faraday Discuss. Chem. Soc. *62,* 179 (1977); J. Mol. Struct. *59,* 161 (1980).

[3] Topical reviews on the technique and the molecular systems investigated: *P. Kebarle* in *J. L. Franklin:* Ion-Molecule Reactions, Vol. 1, Butterworths, London 1972, p. 315—362; *A. W. Castleman, Jr.,* Adv. Colloid Interface Sci. *10,* 73 (1979).

[4] Reviews: a) *P. Schuster* in *P. Schuster, G. Zundel, C. Sandorfy:* The Hydrogen Bond—Recent Developments in Theory and Experiments, Vol. 1, North Holland, Amsterdam 1976, p. 118ff.; b) *P. Schuster* in *B. Pullman:* Intermolecular Interactions from Diatomics to Biopolymers, Wiley, Chichester 1978, p. 383ff., p. 389; c) *A. van der Avoird, P. E. S. Wormer, F. Mulder, R. M. Berns,* Top. Curr. Chem. *93,* 1 (1980); d) *P. Hobza, R. Zahradnik, ibid. 93,* 53 (1980).

[5] The wave function of a system containing *n* electrons depends on 4*n* coordinates, $x_1 y_1 z_1 s_1 x_2 y_2 \ldots s_n$. Here $x_i, y_i$ and $z_i$ denote space coordinates of the "*i*"-th electron. The spin state is characterized by $s_i$. All four coordinates of an electron are summarized by the symbol $\tau$: $\tau_i = x_i y_i z_i s_i$. The spatial electron density distribution is derived from the square of the absolute value of the wave function by integration over all coordinates of $n-1$ electrons and over the spin-coordinate of the remaining *n*-th electron.

[6] *W. T. Raynes* in *R. J. Abraham:* Nuclear Magnetic Resonance, The Chemical Society, London 1977, Vol. 7, p. 1ff.

[7] See [4b], p. 418ff.

[8] Reviews: a) *B. Jeziorsky, W. Kołos,* Int. J. Quantum Chem. *S 12,* 91 (1977), and references cited therein; b) *D. M. Chipman, J. D. Bowman, J. O. Hirschfelder,* J. Chem. Phys. *59,* 2830 (1973), and references cited therein.

[9] *K. Kitaura, K. Morokuma,* Int. J. Quantum Chem. *10,* 325 (1976).

[10] *R. Ahlrichs,* Theor. Chem. Acta *41,* 7 (1976); *J. Morgan, B. Simon,* Int. J. Quantum Chem. *17,* 1143 (1980).

[11] *W. Kołos,* Theor. Chim. Acta *52,* 219 (1979), and references cited therein.

[12] Overview: *K. Kuchitsu* in *G. Allen:* Molecular Structures and Properties, Butterworth, London 1972, p. 203ff.

[13] $(HCOOH)_2$: *A. Almenningen, O. Bastiansen, T. Motzfeld,* Acta Chem. Scand. *23,* 2848 (1969); *24,* 747 (1970); $(CH_3COOH)_2$: *J. L. Derissen,* J. Mol. Struct. *7,* 67 (1971); $(C_2H_5COOH)_2$: *ibid. 7,* 81 (1971).

[14] *P. Schuster, T. Funck,* Chem. Phys. Lett. *2,* 587 (1968); *P. Schuster,* Int. J. Quantum Chem. *3,* 851 (1969).

[15] *P. Bosi, G. Zerbi, E. Clementi,* J. Chem. Phys. *66,* 3376 (1977).

[16] *Y. Tanaka, K. Yoshino,* J. Chem. Phys. *50,* 3087 (1969); *53,* 2012 (1970); *57,* 2964 (1972); *59,* 564 (1973); *D. E. Freeman, K. Yoshino, Y. Tanaka, ibid. 67,* 3462 (1977); *71,* 1780 (1979); *Y. Tanaka, W. C. Walker, K. Yoshino, ibid. 70,* 380 (1979).

[17] From the great variety of papers by *Y. T. Lee et al.* we choose some representative examples: J. Chem. Phys. *53,* 2123; 3755 (1970); *55,* 5762 (1971); *56,* 1511, 5801 (1972); *59,* 601 (1973).

[18] *K. M. Smith, A. M. Rulis, G. Scoles, R. A. Aziz, V. Nain,* J. Chem. Phys. *67,* 152 (1977); *M. Keil, A. Kuppermann, ibid. 69,* 3917 (1978); *M. Keil, J. T. Slankas, A. Kuppermann, ibid. 70,* 482 (1979).

[19] The functions $\Delta E(R) = D_e\{(R_e/R)^{12} - 2(R_e/R)^6\}$ (Lennard-Jones-Potential) and $\Delta E(R) = D_e\{e^{-\beta(R-R_e)^2} - 1\}$ (Morse-Potential) are the most commonly used basic expressions for fitting intermolecular energy surfaces to data measured on non-polar systems. The actually fitted functions are extensions of these expressions which contain many adjustable parameters, see *e.g. P. E. Siska, J. M. Parson, T. P. Schafer, Y. T. Lee,* J. Chem. Phys. *55,* 5766 (1971).

[20] *P. Audit,* J. Phys. (Paris) *30,* 192 (1969).

[21] Reviews: *J. O. Hirschfelder, C. F. Curtiss, R. B. Bird:* Molecular Theory of Gases and Liquids, Wiley, New York 1954, p. 131ff.; *T. Kihara:* Intermolecular Forces, Wiley, Chichester 1978, p. 39ff.

[22] The most accurate *ab initio* calculation of a potential curve for $He_2$ has been performed by means of a CEPA-PNO wave function: *P. G. Burton,* J. Chem. Phys. *70,* 3112 (1979), and references cited therein.

[23] *W. J. Stevens, A. C. Wahl, M. A. Gardiner, A. M. Karo,* J. Chem. Phys. *60,* 2195 (1974). An attempt to calculate the potential curve for $Ne_2$ by independent computations of Hartree-Fock and correlation energy has been reported by *J. Prisette, E. Kochanski,* Chem. Phys. Lett. *47,* 391 (1977). A potential curve which has been computed from experimental data is presented by *B. Brunetti, R. Cambi, F. Pirani, F. Vecchiocattivi, M. Tomassini,* Chem. Phys. *42,* 397 (1979), and references cited therein.

[24] *J. Hepburn, G. Scoles, R. Penco,* Chem. Phys. Lett. *36,* 451 (1975). The method has been improved and applied to all possible dimers of He, Ne and Ar: *R. Ahlrichs, P. Penco, G. Scoles,* Chem. Phys. *19,* 119 (1977).

[25] *H. Lischka,* Chem. Phys. Lett. *20,* 448 (1973); Chem. Phys. *2,* 191 (1973).

[26] Ne·HCl: *K. C. Janda, L. S. Bernstein, J. M. Steed, S. E. Novick, W. Klemperer,* J. Am. Chem. Soc. *100,* 8074 (1978); Ar·HCl: *S. E. Novick, P. Davies, S. J. Harris, W. Klemperer,* J. Chem. Phys. *59,* 2273 (1973); *S. E. Novick, K. C. Janda, S. L. Holmgren, M. Waldman, W. Klemperer, ibid. 65,* 1114 (1976); Kr·HCl: *T. J. Balle, E. J. Campbell, M. R. Keenan, W. H. Flygare, ibid. 72,* 922 (1980); Xe·HCl: *K. V. Chance, K. H. Bowen, J. S. Winn, W. Klemperer, ibid. 70,* 5157 (1979); Ar·HF: *S. J. Harris, S. E. Novick, W. Klemperer, ibid. 60,* 3208 (1974); Ar·HBr: *K. C. Jackson, P. R. R. Langridge-Smith, B. J. Howard,* Mol. Phys. *39,* 817 (1980).

[27] *S. L. Holmgren, M. Waldman, W. Klemperer,* J. Chem. Phys. *67,* 4414 (1977); *69,* 1661 (1978).

[28] $(HF)_2$: *T. R. Dyke, B. J. Howard, W. Klemperer,* J. Chem. Phys. *56,* 2442 (1972); $(H_2O)_2$: *T. R. Dyke, K. M. Mack, J. S. Muenter, ibid. 66,* 498 (1977); *J. A. Odutola, T. R. Dyke, ibid. 72,* 5062 (1980).

[29] Most accurate calculation of $(HF)_2$ around the equilibrium geometry: *H. Lischka,* Chem. Phys. Lett. *66,* 108 (1979); most extended study of a large region of the $(HF)_2$ energy surface: *D. R. Yarkony, S. V. O'Neil, H. F. Schaefer III, G. P. Baskin, C. F. Bender,* J. Chem. Phys. *60,* 855 (1974). Both investigations were preceded by numerous papers of several groups of authors. Calculation of an extensive force field based on ten harmonic force constants and the corresponding normal frequencies: *L. A. Curtiss, J. A. Pople,* J. Mol. Spectrosc. *61,* 1 (1976).

[30] Analysis of the wave function of $(HF)_2$ on the basis of a somewhat less accurate *ab initio* calculation: *P. A. Kollman, L. C. Allen,* J. Chem. Phys. *52,* 5085 (1970).

[31] Most extensive investigation of the energy surface of $(H_2O)_2$: *A. Matsuoka, E. Clementi, M. M. Yoshimine,* J. Chem. Phys. *64,* 1351 (1976); somewhat earlier paper with explicit consideration of electron correlation effects: *G. H. F. Diercksen, W. P. Kraemer, B. O. Roos,* Theor. Chim. Acta *36,* 249 (1975); calculation of an extensive force field of water dimer and the corresponding vibrational spectrum: *L. A. Curtiss, J. A. Pople,* J. Mol. Spectrosc. *55,* 1 (1975).

[32] The experimental data on the vibrational spectra of $(HF)_2$ and $(H_2O)_2$ are not very good. In the former case we have to rely on a somewhat older analysis of pressure and temperature dependence of the infrared spectrum of HF vapor which were interpreted by means of a monomer-dimer equilibrium: *D. F. Smith,* J. Mol. Spectrosc. *3,* 473 (1959). The infrared spectrum of water dimer was recorded only by matrix isolation technique: *A. J. Tursi, R. E. Nixon,* J. Chem. Phys. *52,* 1521 (1970). The influence of the matrix, commonly one uses Ar or $N_2$ crystals, on the spectra recorded is frequently debated.

[33] *B. Hobza, P. Carsky, R. Zahradnik,* Int. J. Quantum Chem. *16,* 257 (1979).

[34] The second virial coefficients and the transport coefficients at low pressures ($p \leq 8$ atm) and temperatures up to 500 °C were used to calculate an empirical potential surface of $(H_2O)_2$: *J. P. O'Connell, J. M. Prausnitz,* Ind. Eng. Chem. Fundam. *8,* 453 (1969); *9,* 579 (1970). An interesting more recent publication is that by: *C. Braun, H. Leidecker,* J. Chem. Phys. *61,* 3104 (1974), in which the authors calculated the complete rotational-vibrational spectrum in order to compare calculated and measured thermodynamic data.

[35] *J. E. Bertie, D. J. Millen,* J. Chem. Soc. *1965,* 497. For references to later works see: *D. J. Millen,* J. Mol. Struct. *45,* 1 (1978).

[36] a) $H_2O \cdot HF$: IR spectrum: *R. K. Thomas,* Proc. R. Soc. London *A 344,* 579 (1975); b) microwave spectrum: *J. W. Bewan, A. C. Legon, D. J. Millen, S. C. Rogers,* J. Chem. Soc. Chem. Commun. *1975,* 341; c) $(CH_3)_2O \cdot HF$: IR spectrum: *R. K. Thomas,* Proc. R. Soc. London *A 322,* 137 (1971); d) overtone spectrum in the near IR: *J. W. Bevan, B. Martineau, C. Sandorfy,* Can. J. Chem. *57,* 1341 (1979); e) $(CH_3)_2O \cdot HCl$: IR spectrum: *J. E. Bertie, D. J. Millen,* J. Chem. Soc. *1965,* 497, 514; f) Raman spectrum: *B. Desbat, J. C. Lassegues,* J. Chem. Phys. *70,* 1824 (1979).

[37] a) Equilibrium geometries and some properties of $H_2O \cdot HF$: *P. A. Kollman, L. C. Allen,* J. Chem. Phys. *52,* 5085 (1969); b) Calculation of the energy surface, harmonic force constants, anharmonicities, and vibrational frequencies: *D. G. Lister, P. Palmieri,* J. Mol. Struct. *39,* 295 (1977); c) *Y. Bouteiller, M. Allavena, J. M. Leclercq, ibid. 69,* 521 (1980); d) $(CH_3)_2O \cdot HF$: vibrational spectrum including the first overtone: *Y. Bouteiller, Y. Guissani, ibid. 69,* 280 (1980); e) $(CH_3)_2O \cdot HCl$: vibrational spectrum, IR and Raman intensities: *Y. Bouteiller, E. Marechal,* Mol. Phys. *32,* 277 (1976); *Y. Bouteiller, Y. Guissani, ibid. 38,* 617 (1979).

[38] Overview of the numerous calculations on ion-molecule complexes: *P. Schuster, W. Jakubetz, W. Marius,* Top. Curr. Chem. *60,* 1 (1975); complexes of some ions with higher positive charges ($Mg^{2+}$, $Al^{3+}$) and water: *H. Lischka,* Pure Appl. Chem. *51,* 1627 (1979). For a critical investigation of the accuracy of *ab initio* calculations see: *P. Schuster, H. Lischka, A. Beyer* in *I. G. Csizmadia:* Progress in Theoretical Chemistry, Vol. 2, Elsevier, Amsterdam 1976, p. 89ff. Electron correlation effects are described in: *G. H. F. Diercksen, W. P. Kraemer, B. O. Roos,* Theor. Chim. Acta *36,* 249 (1975). Zero point energy differences and the temperature

dependent contributions to $\Delta H$ were calculated in: *H. Kistenmacher, H. Popkie, E. Clementi*, J. Chem. Phys. *59*, 5842 (1973).

[39] *G. Zundel* in *P. Schuster, G. Zundel, C. Sandorfy:* The Hydrogen Bond, North Holland, Amsterdam 1976, Vol. 2, p. 681 ff.

[40] *A. van Deursen, A. van Lumig, J. Reuss*, Int. J. Mass Spectrom. Ion Phys. *18*, 129 (1975); *J. Farges, B. Raoult, G. Torchet*, J. Chem. Phys. *59*, 3454 (1973).

[41] $(H_2O)_n$: *T. R. Dyke, J. S. Muenter*, J. Chem. Phys. *57*, 5011 (1972); $(NH_3)_n$: *J. A. Odutola, T. R. Dyke, B. J. Howard, J. S. Muenter, ibid. 70*, 4884 (1979); numerous systems of the type $(ROH)_n$, $(RSH)_n$ and $(RR'NN)_n$: *J. Odutola, R. Viswanathan, T. R. Dyke*, J. Am. Chem. Soc. *101*, 4787 (1979).

[42] a) IR spectrum of HF in the vapor phase: *D. F. Smith*, J. Chem. Phys. *28*, 1040 (1958); b) electron diffraction on $(HF)_6$ in the vapor phase: *J. Janzen, L. S. Bartell, ibid. 50*, 3611 (1969).

[43] $(HF)_n$: *J. Del Bene, J. A. Pople*, J. Chem. Phys. *55*, 2296 (1971); *A. Beyer, A. Karpfen, P. Schuster*, Chem. Phys. Lett. *67*, 369 (1979); $(H_2O)_n$: *J. Del Bene, J. A. Pople*, J. Chem. Phys. *52*, 4858 (1970); *58*, 3605 (1973); *D. Hankins, J. W. Moskowitz, F. H. Stillinger, ibid. 53*, 4544 (1970); *B. R. Lentz, H. Scheraga, ibid. 58*, 5296 (1973); *H. Kistenmacher, G. C. Lie, H. Popkie, E. Clementi, ibid. 61*, 546 (1974); *E. Clementi, W. Kołos, G. C. Lie, G. Ranghino*, Int. J. Quantum Chem. *17*, 377 (1980); $(NH_3)_3$: *Y. Jean*, Chem. Phys. Lett. *69*, 216 (1980); dispersion energy: *D. J. Margoliash, T. R. Proctor, G. D. Zeiss, W. J. Meath*, Mol. Phys. *35*, 747 (1978).

[44] A recent review with numerous references: *P. Schuster, A. Karpfen, A. Beyer* in *W. J. Orville-Thomas, H. Ratajczak:* Molecular Interactions, Wiley, London 1980, p. 117 ff.

[45] $He_3$: *O. Novaro, V. Beltran-Lopez*, J. Chem. Phys. *56*, 815 (1972); $Ne_3$: *O. Novaro, F. Nieves, ibid. 65*, 1109 (1976).

[46] The first work: *B. M. Axilrod, E. Teller*, J. Chem. Phys. *11*, 299 (1943), has been supplemented: *B. M. Axilrod, ibid. 19*, 719 (1951).

[47] The most recent, extensive study on this subject: *J. P. Daudey, O. Novaro, W. Kołos, M. Berrondo*, J. Chem. Phys. *71*, 4297 (1979), gives a good selection of references to previous work apart from the presently most accurate analysis of non-additive contributions to the Hartree-Fock energy.

[48] *K. F. Niebel, J. A. Venables* in *M. L. Klein, J. A. Venables:* Rare Gas Solids, Academic Press, London 1976, p. 558 ff. A somewhat older review on this problem seems to have put too much emphasis on the influence of three-body forces on the equilibrium structure of rare gas crystals: *L. Jansen*, Adv. Quantum Chem. *2*, 119 (1965).

[49] *J. N. Murrell*, Chem. Phys. Lett. *55*, 1 (1978).

[50] Computer simulations of liquid water: Molecular dynamics: *F. H. Stillinger, A. Rahman*, J. Chem. Phys. *60*, 1545 (1974); *A. Rahman, F. H. Stillinger, H. L. Lemberg, ibid. 63*, 5223 (1975); Monte Carlo calculations: *A. J. C. Ladd*, Mol. Phys. *33*, 1039 (1977); Molecular dynamics calculation on liquid hydrogen fluoride: *M. L. Klein, I. R. McDonald*, J. Chem. Phys. *71*, 298 (1979); on liquid ammonia: *M. L. Klein, I. R. McDonald, R. Righini, ibid. 71*, 3673 (1979).

[51] *M. Neumann, O. Steinhauser*, Mol. Phys. *39*, 437 (1980).

[52] For a recent review on the application of diffraction techniques to liquids and of the interpretation of the results obtained see: *M. D. Zeidler*, Angew. Chem. *92*, 700 (1980); Angew. Chem. Int. Ed. Engl. *19*, 697 (1980); *L. Blum, A. H. Narten*, Adv. Chem. Phys. *34*, 203 (1976). Example for the combination of X-ray and neutron scattering data to determine pair correlation functions in acetonitrile: *H. Bertagnolli, M. Zeidler*, Mol. Phys. *35*, 177 (1978). A recent publication on liquid water: *E. Kalman, G. Palinkas, P. Kovacs, ibid. 34*, 502, 525 (1977).

[53] The best known method for the calculation of (periodic) solid state structures on the basis of the Hartree-Fock theory has been called the "crystal-orbital" method: *G. Del Re, J. Ladik, G. Biczo*, Phys. Rev. *155*, 997 (1967); *J. M. André, L. Gouverneur, G. Leroy*, Int. J. Quantum Chem. *1*, 451 (1967).

[54] *A. Karpfen, P. Schuster*, Chem. Phys. Lett. *44*, 459 (1976); *A. Karpfen*, Chem. Phys. *47*, 401 (1980); *A. Karpfen, P. Schuster, A. Beyer*, Int. J. Quantum Chem., in press.

[55] HF-molecule: *H. Lischka*, J. Am. Chem. Soc. *96*, 4761 (1974); Chem. Phys. Lett. *66*, 108 (1979); *P. Swanstrøm, W. P. Kraemer, G. H. F. Diercksen*, Theor. Chim. Acta *44*, 109 (1977); *R. J. Bartlett, G. D. Purvis III*, Phys. Rev. *A 20*, 1313 (1979); $H_2O$-molecule: *B. J. Rosenberg, I. Shavitt*, J. Chem. Phys. *63*, 2162 (1975); *B. J. Rosenberg, W. C. Ermler, I. Shavitt, ibid. 65*, 4072 (1976); *R. J. Bartlett, I. Shavitt, G. D. Purvis III, ibid. 71*, 281 (1979); polarizabilities: *H. J. Werner, W. Meyer*, Mol. Phys. *31*, 855 (1976).

[56] *K. P. Huber, G. Herzberg:* Molecular Spectra and Molecular Structure IV. Constants of Diatomic Molecules, Van Nostrand Reinhold Co., New York 1979.

[57] The most accurate calculation of the interaction between two water molecules by means of perturbation theory was performed by *B. Jeziorski, M. van Hemert*, Mol. Phys. *31*, 713 (1976). This publication reports a very accurate Hartree-Fock calculation on the water dimer as well. The contribution of dispersion energy was calculated with the aid of an expression derived from perturbation theory. Other contributions of electron correlation like the changes in the properties of the monomers were neglected. These contributions, however, have a non-negligible influence on the total energy of interaction.

[58] An empirical, six-dimensional potential function of the water dimer has been proposed by *L. L. Shipman, H. A. Scheraga*, J. Phys. Chem. *78*, 909 (1974). This function was subjected to extensive testing and is able to reproduce the well known results from *ab initio* calculations [31] as well as the data from microwave spectroscopy [28]: *L. L. Shipman, J. C. Owicki, H. A. Scheraga, ibid. 78*, 2055 (1974).

[59] Energy partitioning in the complex ions $H_2O \cdot Li^+ \cdot OH_2$ and $HOH \cdot F^- \cdot HOH$: *A. Karpfen, A. Beyer, P. Schuster*, unpublished results.

[60] *R. E. Dobbs, G. O. Jones*, Rep. Prog. Phys. *20*, 560 (1957).

[61] *G. K. Horton* in *M. L. Klein, J. A. Venables:* Rare Gas Solids, Academic Press, London 1976, p. 87.

[62] *J. C. Slater*, Quantum Theory of Molecules and Solids, McGraw-Hill, New York 1965, Vol. 2, p. 334 ff.

[63] From the numerous calculations on dimers and higher clusters of Be we might mention, apart from [47], *C. E. Dykstra, H. F. Schaefer III, W. Meyer*, J. Chem. Phys. *65*, 5141 (1976); *B. Liu, A. D. McLean, ibid. 72*, 3418 (1980); *R. A. Chiles, C. E. Dykstra, ibid. 74*, 4544 (1981).

[64] The structural data on solid hydrogen fluoride are taken from *M. Atoji, W. N. Lipscomb*, Acta Crystallogr. *7*, 173 (1954); *M. W. Johnson, E. Sandor, E. Arzi, ibid. B31*, 1998 (1975).

[65] *D. Eisenberg, W. Kauzmann:* The Structure and Properties of Water, Clarendon Press, Oxford 1969, p. 74.

[66] *J. B. Anderson, R. P. Anders, J. B. Fenn*, Adv. Chem. Phys. *10*, 275 (1966).

[67] *T. R. Dyke, G. R. Tomasevich, K. Klemperer, W. F. Falconer*, J. Chem. Phys. *57*, 2277 (1972).

[68] *J. A. A. Ketelaar:* Chemische Konstitution, Vieweg, Braunschweig 1964, p. 184 ff.

[69] *F. Barsolo, R. G. Pearson:* Mechanisms of Inorganic Reactions, 2nd edit., Wiley, New York 1967, p. 81 ff.

[70] *V. Gutmann:* The Donor-Acceptor Approach to Molecular Interactions, Plenum Press, New York 1978.

[71] The face centered cubic (fcc) and hexagonal closed packed (hcp) lattice structures have the same numbers of first and second neighbors. Further neighbor contributions lead to a slight energetic preference of the hcp-structure [48].

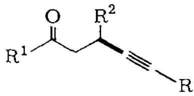
## Michael Addition of Lithium Acetylides to Propenyl Trityl Ketone

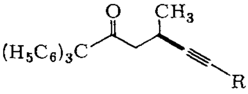
By *Rita Locher* and *Dieter Seebach*[*]

The synthetically valuable 4-alkyne-1-ones *(1)* can only be prepared indirectly from enones and terminal acetylenes, *i.e.* by formation of the prominant C—C bond in formula *(1)*[1]. To our knowledge, the direct 1,4-addition of alkali metal- or alkaline earth-acetylides[2] to simple enones has not been previously observed.

We have now found, that between −45 and +25 °C, lithium acetylides in tetrahydrofuran (THF) add to 1,1,1-triphenyl-3-penten-2-one to give good yields of the alkynones *(2)* (Table 1). This result and the Michael addition of other lithium compounds to trityl enones[3a] show that the a$^3$-reactivity of enones can be *purely sterically*[3b] controlled, independent of the mechanism (radical[4a], charge- or orbitalcontrol[4b]), the structure of the nucleophile[5a] or solvent[5b] and temperature effects[5c].

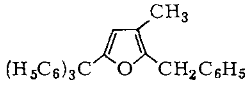
*(1)*



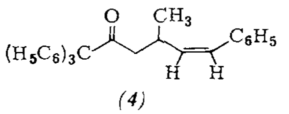


*(2)*

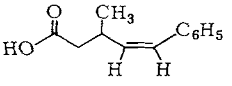
This C—C bond forming process is only synthetically useful when cleavage of the bond between the carbonyl carbon and the trityl carbon is possible under mild conditions. The Haller-Bauer-type cleavage with potassium *tert*-butoxide/H$_2$O in THF[6] used previously[3a], could not be successfully applied to *(2)*, R = C$_6$H$_5$, the furan *(3)* being formed[7]. However, hydrogenation of the triple- to a *cis* double-bond [*(2)*→*(4)*, Lindlar catalyst/H$_2$, quantitative], permits hydrolysis of the trityl ketone [*(4)*→*(5)*] in 76% yield. Moreover, we have now found that trityl ketones are smoothly cleaved by LiBHEt$_3$[8], in THF upon warming from −45 °C to room temperature, to triphenylmethane and primary alcohols. Thus, the alkynone *(2)*, R = C$_5$H$_{11}$, reacts in 77% yield to the alkynol *(6)* without interference from the triple bond. The IR- and mass-spectra, as well as the $^1$H- and $^{13}$C-NMR spectra are in accord with the given structures. Applications[9] for the described Michael additions are currently being investigated.



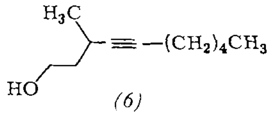
*(3)*



*(4)*



*(5)*



*(6)*

Table 1. Yields and melting points of the products *(2)* purified by chromatography on silica gel and/or by recrystallization.

| R | Yield [%] | M.p. [°C] |
|---|---|---|
| C$_6$H$_5$ | 89 | 109—110 |
| (CH$_2$)$_4$CH$_3$ | 86 | 59 |
| C(CH$_3$)$_2$OH | 32 | 128 |
| Si(CH$_3$)$_3$ | 66 | 102 |
| CH$_2$OCH$_3$ | 66 [a] | 86 |
| CH$_2$N(CH$_2$CH$_3$)$_2$ | 65 | oil [b] |

[a] In addition to 15% unreacted starting material. [b] After chromatography (SiO$_2$/EtOEt : MeOH 19 : 1).

### *Procedure*

A solution of the Li-acetylide at −50 °C in 15 cm$^3$ THF, prepared from heptyne (0.61 cm$^3$, 4.6 mmol) and butyllithium (4.7 mmol, ≈1.6 N in hexane) under argon (−45° to −10 °C), is added to a solution of 1,1,1-triphenyl-3-penten-2-one (1.32 g, 4.2 mmol) in 50 cm$^3$ THF stirred at −50 °C. After warming to room temperature overnight, the mixture is poured into water and extracted with ether. "Flash" chromatography[10] of the crude product over SiO$_2$ (5 cm diameter column, CH$_2$Cl$_2$/hexane 3 : 1) yielded 1.46 g (86%) *(2)*, R = C$_5$H$_{11}$ (4-methyl-1,1,1-triphenyl-5-undecyn-2-one).—A solution of this ketone (190 mg, 0.46 mmol) in 8 cm$^3$ THF at −45 °C is treated with 1.4 cm$^3$ of a 1 N solution of LiBHEt$_3$ in THF. After warming-up and stirring (40 h), the mixture is treated with 3 cm$^3$ 1 N hydrochloric acid and worked-up with ether. Triphenylmethane is removed on a short SiO$_2$ column and the 3-methyl-4-decyn-1-ol purified by Kugelrohr distillation [60 mg (77%); b.p. = 60 °C (oven)/10$^{-2}$ torr; $^{13}$C-NMR (75.5 MHz, CDCl$_3$): $\delta$ = 84.14 (s), 81.53 (s), 61.58 (t), 39.93 (t), 31.12 (t), 28.87 (t), 23.18 (d), 22.22 (t), 21.74 (q), 18.72 (t), 13.96 (q)].

Received: October 31, 1980 [Z 787 IE]
German version: Angew. Chem. *93*, 614 (1981)

---

[*] Prof. Dr. D. Seebach, Dipl.-Chem. R. Locher
Laboratorium für Organische Chemie
Eidgenössische Technische Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

[1] *G. Stork, R. Borch*, J. Am. Chem. Soc. *86*, 935 (1964); *R. T. Hansen, D. B. Carr, J. Schwartz, ibid. 100*, 2244 (1978), and literature cited therein.

[2] Cu-acetylides do not add to enones: *G. H. Posner*, Org. React. *19*, 1 (1972). *E. J. Corey, D. J. Beames*, J. Am. Chem. Soc. *94*, 7210 (1972).

[3] a) *D. Seebach, R. Locher,* Angew. Chem. *91,* 1024 (1979), and literature cited therein. b) For steric effects in Michael additions see also *J. Mulzer, G. Hartz, U. Kühl, G. Brüntrup,* Tetrahedron Lett. *1978,* 2949; *C. H. Heathcock, J. E. Ellis, J. S. Dutcher,* J. Org. Chem. *41,* 2670 (1976); *R. H. Schlessinger, J. L. Herrmann, J. E. Richman,* Tetrahedron Lett. *1973,* 3271.

[4] a) *H. O. House,* Acc. Chem. Res. *9,* 59 (1976); b) *I. Fleming:* Frontier orbitals and Organic Chemical Reactions. Wiley, New York 1976; see also the discussion in *S. Hünig, G. Wehner,* Chem. Ber. *113,* 302, 324 (1980).

[5] a) *A. Loupy, J.-M. Lefour, B. Deschamps, J. Seyden-Penne,* Nouv. J. Chim. *4,* 121 (1980); b) *J.-M. Lefour, A. Loupy,* Tetrahedron *34,* 2597 (1978); *C. A. Brown, A. Yamaichi,* J. Chem. Soc. Chem. Commun. *1979,* 100; c) *M. El-Bouz, L. Wartski,* Tetrahedron Lett. *1980,* 2897, and literature cited therein.

[6] *P. G. Gassman, P. K. G. Hodgson, R. J. Balchunis,* J. Am. Chem. Soc. *98,* 1275 (1976).

[7] Cf. *K. E. Schulte, J. Reisch, A. Mock,* Arch. Pharm. Weinheim *295,* 627 (1962).

[8] *H. C. Brown, S. C. Kim,* Synthesis *1977,* 635.

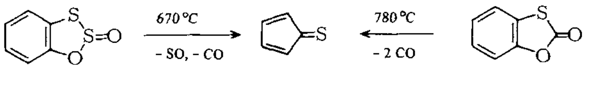
[9] See *e.g.* the review articles on acetylenes as intermediates in syntheses: *K. Sonogashira, S. Takahashi,* J. Synth. Org. Chem. Jpn. *38,* 648 (1980); *C. A. Henrick,* Tetrahedron *33,* 1845 (1977); *R. Rossi,* Synthesis *1977,* 817.

[10] *W. C. Still, M. Kahn, A. Mitra,* J. Org. Chem. *43,* 2923 (1978).

## Cyclopentadienethione[**]

By *Reinhard Schulz* and *Armin Schweig*[*]

We report here the first synthesis of cyclopentadienethione *(2)*[1]. It is formed by gas phase pyrolysis (VTPES method[2], reactor *ca.* 20 × 0.5 cm, 0.05 mbar pressure) of 1,2,3-benzoxadithiol 2-oxide *(1)* and 1,3-benzoxathiol-2-one[3] *(3)*.



*(1)* *(2)* *(3)*

*(2)* is unambiguously characterized from its photoelectron spectrum (Fig. 1b and d). Band ① (at 8.87 eV), due to its shape, position and energy-dependence of the intensity[4], is unequivocally the $^2B_2(n_S)$-band. Band ② (at 9.18 eV) is, because of its position (expected at 9.2 eV from the position of the corresponding band in cyclopentadienone[5] and from the *ca.* 0.2 eV smaller inductive effect of the thiocarbonyl group[6]), assigned as an $^2A_2(\pi)$-band. Band ③ (at 10.35 eV) is identified from a relationship[7] for the $^2B_1(\pi)$-ionization energy of fulvene-type molecules—again in excellent agreement with the measured value—expected at 10.4 eV, as a $^2B_1(\pi)$-band. These conclusions are corroborated by CNDO/S-[8a], MNDO-[8b] and PERTCI[8c]-calculations (Fig. 2).

Thermal fragmentation of *(1)* and *(3)* probably proceeds[9] *via* the monothiobenzoquinone *(4)*[10]. From MNDO-calculations, the valence isomeric benzoxathiete *(5)* is considerably more energy-rich than *(4)*; the thiocarbonyl compounds *(2)* and *(4)* have *ca.* 50 kcal/mol more energy than the carbonyl compounds cyclopentadienone and 1,2-benzoquinone. In fact, when *(1)* is pyrolyzed be-

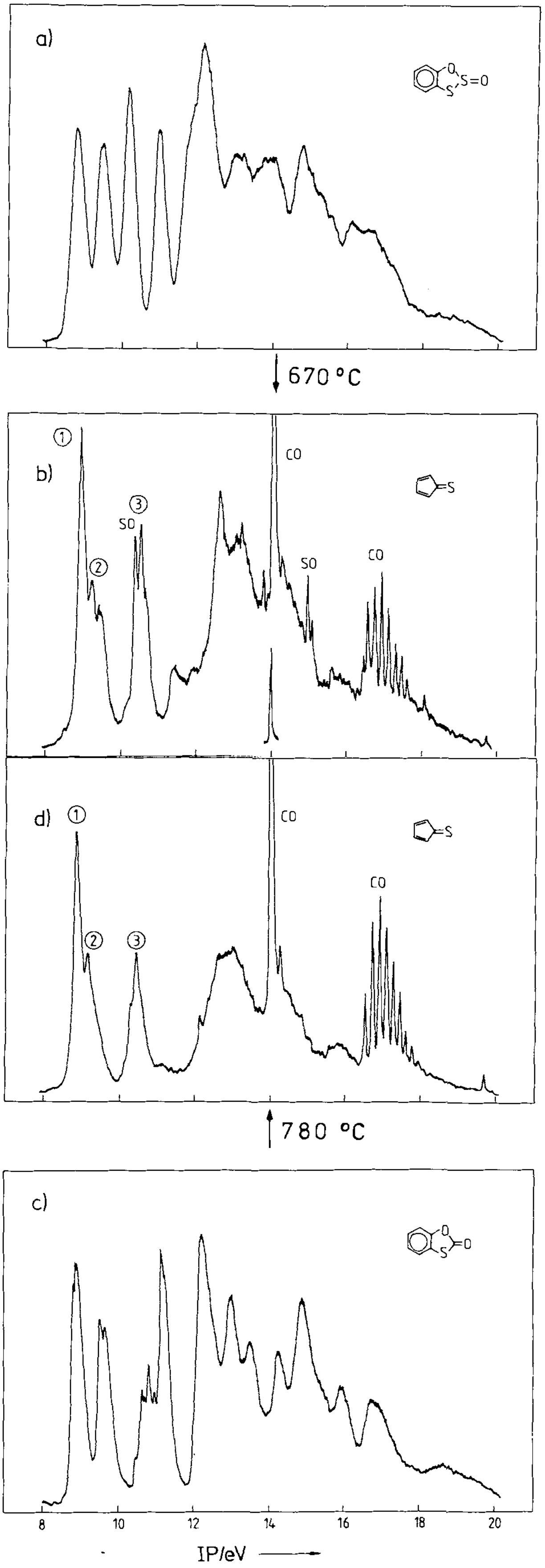


Fig. 1. He-I photoelectron spectra of a) the educt *(1)*, b) its pyrolysis products *(2)*, CO and SO, c) the educt *(3)* and d) its pyrolysis products *(2)* and CO.

---

[*] Prof. Dr. A. Schweig, Dipl.-Chem. R. Schulz
Fachbereich Physikalische Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)

[**] Theory and Application of Photoelectron Spectroscopy, Part 92. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 91: *A. Schweig, N. Thon, S. F. Nelsen, L. A. Grezzo,* J. Am. Chem. Soc., *102,* 7438 (1980).

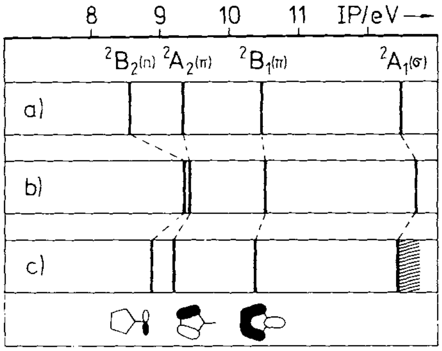
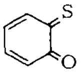
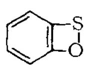


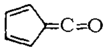
Fig. 2. Calculated a) MNDO-PERTCI, b) CNDO/S-PERTCI and c) measured vertical ionization energies (IP) of cyclopentadienethione *(2)*.

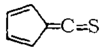
tween 550 °C and 600 °C, a compound is obtained as intermediate whose photoelectron spectrum indicates the monothiobenzoquinone *(4)* (bands at 8.85, 9.45 (high intensity) and 11.6 eV; from qualitative rules, MNDO- and CNDO/S-PERTCI-calculations, expected at $^2A'(n_S)$ 8.9, $^2A'(n_O)/^2A''(\pi)$ *ca.* 9.4 and $^2A''(\pi)$ *ca.* 11.5 eV). Because of the high temperature (>700 °C) required for the cleavage of *(3)*, this intermediate cannot be observed. Other possible products, fulven-6-one *(6)* and fulven-6-thione *(7)*, whose photoelectron spectra are known[11], do not appear.

The thermal behavior of *(1)* and *(3)* has parallels in the electron-impact induced fragmentation of the cations. $SO_2$-cleavage from $(1)^{\oplus}$ and $CO_2$-cleavage from $(3)^{\oplus}$ only takes place to a minor extent; the principle fragmentation route is the formation of the $C_5H_4S$ ion ($m/e=96$) [MS[12] (70 eV): *(1)*: $m/e=172$ $M^{\oplus}$ (100%), 124 (16), 108 (14), 96 (57); *(3)*: $m/e=152$ $M^{\oplus}$ (20%), 124 (4), 108 (12), 96 (100)].


*(4)*


*(5)*


*(6)*


*(7)*

From the results of preliminary theoretical investigations (π-conjugation energy, π-charge-transfer and bond length equalization) *(2)* can be assigned an electronic structure between that of cyclopentadienone and fulvene.

### *Procedure*

*(1)*: Solutions of 2-mercaptophenol (9 g) and $SOCl_2$ (8.5 g), each in 100 cm$^3$ $CS_2$, are simultaneously dropped into a stirred solution of pyridine (11.5 g) in 200 cm$^3$ $CS_2$ under $N_2$ at 0–5 °C. After heating under reflux (15 min), the mixture is filtered, the filtrate concentrated to *ca.* 5 cm$^3$ and taken up in 100 cm$^3$ $CCl_4$. After filtration, concentration and distillation *in vacuo* (bath 150 °C; 0.8 torr), *(1)* is isolated as a yellow oil, which crystallizes upon standing. Yield 1.4 g (9.8%); m.p. = 46.5 °C; IR: $\nu=3070$, 1450, 1180 cm$^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta=7.37$ (m); $^{13}$C-NMR[12] ($CDCl_3$): $\delta=114.9$, 121.5, 123.3, 125.4, 127.0, 153.9. *Photoelectron spectroscopic data for (1) and (3)*: *(1)*: 8.77 (π), 9.48 (π), 10.14, 10.97 eV; *(3)*: 8.84 (π), 9.55 (π), 10.80 ($n_O$), 11.12 (π) eV.

Received: December 1, 1980 [Z 780 IE]
German version: Angew. Chem. *93*, 603 (1981)

CAS Registry numbers:
*(1)*, 77825-98-0; *(2)*, 77825-99-1; *(3)*, 7735-53-7

---

[1] *P. de Mayo, A. C. Weedon, G. S. K. Wong,* J. Org. Chem. *44*, 1977 (1979). These authors have obtained results in low temperature photochemical experiments, which point to the existence of substituted cyclopentadienethiones.

[2] *A. Schweig, H. Vermeer, U. Weidner,* Chem. Phys. Lett. *26*, 299 (1974); *W. Schäfer, A. Schweig, Z.* Naturforsch. *A 30*, 1785 (1975); *R. Schulz, A. Schweig,* Angew. Chem. *92*, 752 (1980); Angew. Chem. Int. Ed. Engl. *19*, 740 (1980).

[3] *D. Greenwood, H. A. Stevenson,* J. Chem. Soc. (London) *1953*, 1514; *R. M. Dodson, J. B. Hanson,* J. Chem. Soc. Chem. Commun. *1975*, 926.

[4] *P. Dechant, A. Schweig, W. Thiel,* Angew. Chem. *85*, 358 (1973); Angew. Chem. Int. Ed. Engl. *12*, 308 (1973); *A. Schweig, W. Thiel,* J. Electron Spectrosc. Relat. Phenom. *3*, 27 (1974).

[5] *V. Eck, G. Lauer, A. Schweig, W. Thiel, H. Vermeer, Z.* Naturforsch. *A 33*, 383 (1978); *T. Koenig, M. Smith, W. Snell,* J. Am. Chem. Soc. *99*, 6663 (1977).

[6] *C. Müller, A. Schweig, H. Vermeer,* J. Am. Chem. Soc. *100*, 8056 (1978).

[7] *R. Schulz, A. Schweig,* Angew. Chem. *92*, 52 (1980); Angew. Chem. Int. Ed. Engl. *19*, 69 (1980).

[8] a) *K.-W. Schulte, A. Schweig,* Theor. Chim. Acta *33*, 19 (1974); calculations with MNDO-optimized molecular geometries; b) *M. J. S. Dewar, W. Thiel,* J. Am. Chem. Soc. *99*, 4899 (1977); *M. J. S. Dewar, M. L. McKee, J. S. Rzepa, ibid. 100*, 3607 (1978); all calculations with full geometrical optimization; c) *H.-L. Hase, G. Lauer, K.-W. Schulte, A. Schweig,* Theor. Chim. Acta *48*, 47 (1978).

[9] In the gas phase pyrolysis of 1,3,2-benzodioxathiol 2-oxide, intermediate 1,2-benzoquinone is observed between 450 °C and 500 °C: [5] and *O. L. Chapman, C. L. McIntosh,* J. Chem. Soc. Chem. Commun. *1971*, 770.

[10] Substituted monothiobenzoquinones have, until now, been mentioned twice: [1] and *O. L. Chapman, C. L. McIntosh,* J. Chem. Soc. Chem. Commun. *1971*, 383.

[11] *R. Schulz, A. Schweig,* Tetrahedron Lett. *1979*, 59.

[12] The mass spectra were recorded in the mass spectroscopy section of the Department of Chemistry, Universität Marburg. $^{13}$C-NMR spectra were recorded by Dr. *S. Berger* of the same section.

## 4,13-Diaza[$2_4$](1,2,4,5)cyclophane and 4,16-Diaza[$2_4$](1,2,4,5)-cyclophane[**]

By *Hee Chol Kang* and *Virgil Boekelheide*[*]

The pyrolysis of *o*-chloromethyltoluenes to give *o*-xylylenes and their thermal dimerization, either inter- or intramolecularly, has proved to be an extremely useful synthetic sequence for preparing [$2_n$]cyclophanes[1]. We have now investigated the extension of this method to heterocycles and find that it provides convenient, seven-step syntheses to the title compounds *(11)* and *(12)*.

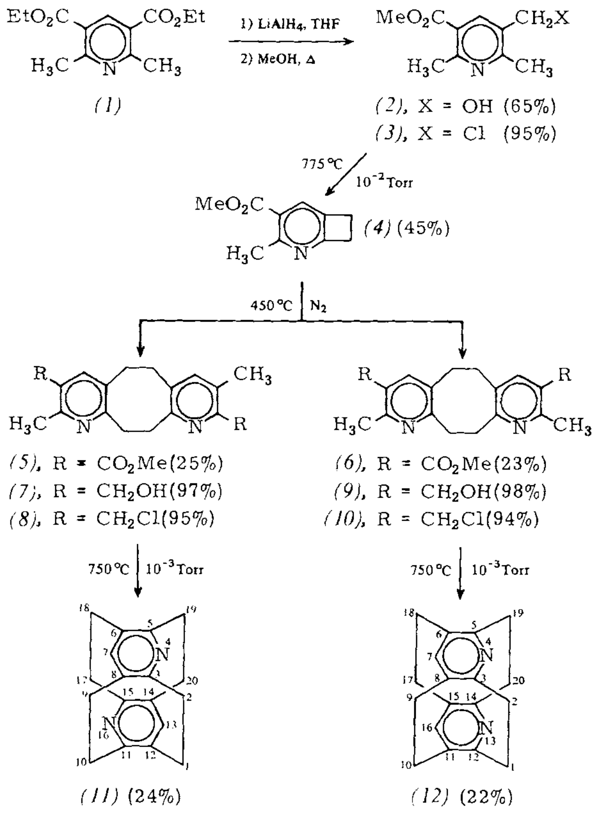
As outlined in the reaction scheme shown below, treatment of diethyl 2,6-dimethylpyridine-3,5-dicarboxylate *(1)* with 2 equiv. lithium aluminum hydride in tetrahydrofuran (THF), followed by heating the product with methanol to effect ester interchange, gave *(2)*[2]. Conversion of *(2)* to *(3)* was accomplished with $SOCl_2$; sublimation of *(3)* at $10^{-2}$ torr into the hot zone (775 °C) of an empty quartz tube gave a colorless oil whose spectroscopic properties [$^1$H-NMR ($CDCl_3$): $\delta=7.70$ (s, aryl-*H*), 3.83 (s, —$CO_2CH_3$), 3.27–3.41 (m, —$CH_2$—), 2.97–3.11 (m, —$CH_2$—), 2.73 (s, —$CH_3$); UV (EtOH), $\lambda=228$ ($\varepsilon=5271$), 283 nm (6410)] are in accord with structure *(4)*.

Although intermolecular dimerizations of *o*-xylylenes to [2.2]orthocyclophanes have previously been carried out in boiling diethyl phthalate[1,3], we have recently found that

---

[*] H. C. Kang, Prof. Dr. V. Boekelheide
Department of Chemistry, University of Oregon
Eugene, Oregon 97403 (USA)

[**] This work was supported by the National Science Foundation. We thank Dr. *A. W. Hanson* for the X-ray structure analysis.



they can be accomplished much more conveniently, and in higher yield, in the gas phase at 450 °C at atmospheric pressure using $N_2$ as carrier gas[4]. When *(4)* was subjected to these conditions, both possible dimers, *(5)* (m.p. = 220–221 °C) and *(6)* (m.p. = 191–192 °C), were formed in approximately equal amounts. Structures *(5)* and *(6)* could readily be distinguished by their $^1$H-NMR spectra, *i.e.* the bridging protons of *(6)* appear as two singlets of four protons each at $\delta = 3.13$ and 3.39, whereas the bridging protons of *(5)* appear as a symmetrical multiplet of eight protons at $\delta = 3.06-3.46$. Silica gel chromatography followed by fractional crystallization from ethyl acetate cleanly separates isomers *(5)* and *(6)*.

Conversion of *(5)* to the corresponding hydroxymethyl derivative *(7)* (m.p. = 290–291 °C) was readily accomplished using lithium aluminum hydride in ether. Similarly, treatment of *(7)* with $SOCl_2$ easily gave the chloride *(8)* (m.p. = 252 °C, decomp.). In a similar manner, *(6)* could be converted first to *(9)* (m.p. = 284–285 °C) and then to *(10)* (m.p. = 238 °C decomp.). Gas phase pyrolysis of *(8)* at 750 °C and $10^{-3}$ torr gave the desired cyclophane *(11)* [m.p. > 350 °C (decomp.); $^1$H-NMR ($CDCl_3$), $\delta = 6.63$ (s, aryl-*H*), 2.80–3.66 (m, —$CH_2$—); UV (EtOH), $\lambda = 298$ ($\varepsilon = 4369$), 307 nm (5243)]. Similarly, gas phase pyrolysis of *(10)* at 750 °C and $10^{-3}$ torr gave *(12)* [m.p. > 310 °C (decomp.); $^1$H-NMR ($CDCl_3$), $\delta = 6.24$ (s, aryl-*H*), 3.12–3.58 (m, —$CH_2$—), 2.68–2.87 (s, —$CH_2$—); UV (EtOH), $\lambda = 300$ ($\varepsilon = 6166$), 307 nm (6143)].

The geometries of *(11)* and *(12)* were determined by *Hanson* by single crystal X-ray analysis, and these are very similar to each other as well as to $[2_4](1,2,4,5)$cyclophane[5]. In each case, the aromatic rings have boat conformations in which the tips are inverted to the outside. For $[2_4](1,2,4,5)$cyclophane, the distance between "decks" is 2.688 Å, whereas for both *(11)* and *(12)* it is approximately 2.64 Å. In *(11)*, the N4 to C13 distance is 2.868 Å, whereas for *(12)* the N4 to N13 distance is only 2.84 Å.

The cyclophanes *(11)* and *(12)* are relatively strong bases and should serve as ligands in transition metal complexes. Since cyclophanes behave as a single π-electron system, *(11)* is the cyclophane analogue of pyrazine. In view of the classic work of *Creutz* and *Taube* on the mixed-valence, bis-ruthenium complex of pyrazine[6], it would be of interest to prepare a similar mixed-valence, bis-ruthenium complex of *(11)* and examine its properties.

Received: December 8, 1980 [Z 768 IE]
German version: Angew. Chem. 93, 587 (1981)

CAS Registry numbers:
*(1)*, 1149-24-2; *(2)*, 77825-09-3; *(3)*, 77825-10-6; *(4)*, 77825-11-7; *(5)*, 77825-12-8; *(6)*, 77825-13-9; *(7)*, 77825-14-0; *(8)*, 77825-15-1; *(9)*, 77825-16-2; *(10)*, 77825-17-3; *(11)*, 77225-38-8; *(12)*, 77825-18-4.

---

[1] *V. Boekelheide, G. Ewing*, Tetrahedron Lett. *1978*, 4245; *V. Boekelheide*, Acc. Chem. Res. *13*, 65 (1980).

[2] Satisfactory elemental analyses and high resolution mass spectra were obtained for all new compounds reported; their $^1$H-NMR, ultraviolet, and infrared spectra are all in accord with the structural assignments.

[3] *M. P. Cava, A. A. Deana*, J. Am. Chem. Soc. *81*, 4267 (1959).

[4] *V. Boekelheide et al.*, Proc. Natl. Acad. Sci. USA, in press.

[5] *A. W. Hanson*, Acta Crystallogr., Sect. *B 33*, 2003 (1977).

[6] *C. Creutz, H. Taube*, J. Am. Chem. Soc. *91*, 3988 (1969).

## Non-planar Double Bonds and Increased Reactivity in Olefins with Low Strain

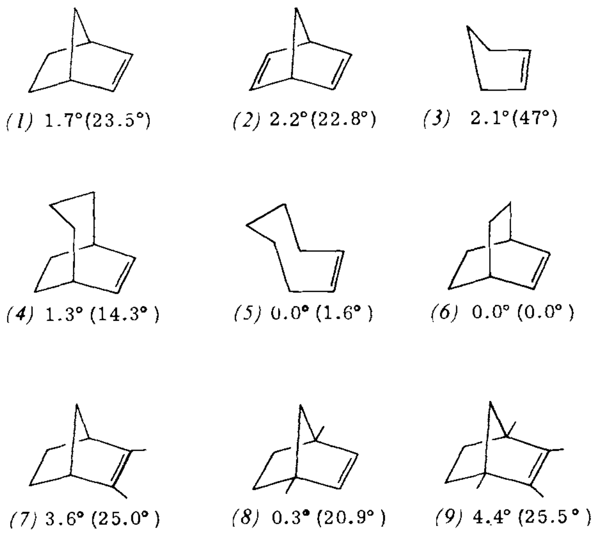
By *Ulrich Burkert*[*]

In highly strained olefins, nonplanar double bonds with an increased reactivity occur frequently[1]. In this connection deplanarization of double bonds as a consequence of torsion, such as in tetra-*tert*-butylethylene[2], and of *out-of-plane bending*, such as in 9,9′,10,10′-tetrahydrodianthracene[3], should be distinguished. On the other hand, the double bonds in slightly strained olefins are considered to be planar. We have now found from *molecular mechanics* calculations[4], however, that pure torsional strain in otherwise slightly strained olefins can cause deplanarization of the double bonds.

According to *ab initio* calculations by *Wipff* and *Morokuma* (geometry optimization with an STO-3G basis set), norbornene *(1)* and norbornadiene *(2)* have nonplanar double bonds with the olefinic hydrogen atoms on the *endo*-side of the molecule[5]. In the structure calculated for *(1)*, the angle that the plane C1—C7—C4 makes with the plane of the olefin bridge (C1—C2—C3—C4) is larger than the angle which it makes with the saturated bridge (C1—C6—C5—C4). These structural details were explained by a repulsion between the methylene bridge and the $\pi_{23}$-orbital[5]. Experimental investigations do not, as yet, permit definite statements to be made concerning the planarity of these double bonds[6]. Bearing in mind the tendency of STO-3G calculations to underestimate the magnitude of bond angles, and hence, to spuriously produce a nonplanar geometry at the trigonal atoms[7], the results of the *ab initio* calculation were tested with the molecular mechanics method, which permits a very precise calculation of hydrocarbon geometries.

---

[*] Dr. U. Burkert
Fakultät für Chemie der Universität
Postfach 5560, D-7750 Konstanz (Germany)


(1) 1.7°(23.5°)    (2) 2.2°(22.8°)    (3) 2.1°(47°)

(4) 1.3° (14.3°)    (5) 0.0° (1.6°)    (6) 0.0° (0.0°)

(7) 3.6° (25.0°)    (8) 0.3° (20.9°)    (9) 4.4° (25.5°)

Fig. 1. Nonplanar olefins: Deviation $\Delta\omega$ of the CCCH-torsion angle from 180°, and (in brackets) magnitude of $\omega^*$. (Cycloheptene ring of *(4)* in chair conformation. Boat conformation is 1.16 kcal/mol higher in energy [4b].)

The geometries of *(1)* and *(2)* obtained from the molecular mechanics[4b] and *ab initio* methods[5], as well as those from electron diffraction experiments[6a], are in excellent agreement with each other[8]. The molecular mechanics calculations indicate that the double bonds in *(1)* and *(2)* are nonplanar; the deviation of the olefinic hydrogen atoms to the *endo*-side, amounting to around 1.7° in *(1)* and 2.2° in *(2)*, is significant in view of the high precision of the method. In addition, both computational methods yielded the same angle between the three bridging planes. The argument that the deplanarization of the double bond stems primarily from orbital repulsion is therefore invalid, since this concept does not exist within the formalism of molecular mechanics calculations. An exhaustive analysis of the individual interaction terms shows that the torsion angle $\omega^*$ between the olefinic H-atoms and the bridgehead H-atoms (at C1 and C4), is increased by the bending and hence leads to reduction of unfavorable torsional strain with the bridgehead H-atoms (Fig. 2). Such torsional strain has previously been discussed in connection with the increased reactivity of *exo*- relative to *endo*-norbornyl derivatives[9] and the preferred *exo*-orientation of cycloadditions to *(1)* and *(2)*[10], but not its effect on the geometry of *(1)* and *(2)* (or of the norbornyl cation, which also evades torsional strain in this way).

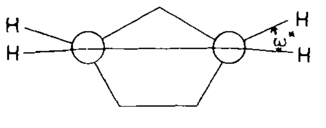


Fig. 2. Newman projection of *(1)* along the bonds C1—C2 and C3—C4 (C5 and C6 below, C7 above).

The explanation of the nonplanarity of *(1)* and *(2)* *via* torsional strain permits the prediction of the same effects in other cyclic olefins. Nonplanarity should occur in those olefins in which the methyl groups of *cis*-2-butene are bridged such that a conformation, where these groups are rotated away from the energy minimum of the *cis*-2-butene ($\omega^* = 60°$, Fig. 2) in a disrotatory manner, is fixed. This has been confirmed by molecular mechanics calculations on various species (Fig. 1). Thereby, a maximum value of the deplanarization occurs at intermediate values of $\omega^*$; if the torsion angle is small, the torsional potential is very flat, *i. e.* the deplanarization costs more energy than is gained in torsional energy. The double bonds in cycloheptene *(5)* and bicyclo[2.2.2]octene *(6)* are therefore planar. In contrast, the deplanarization increases in the case of alkylated double bonds, as in *(7)* and *(9)*.

A correlation appears to exist between the nonplanarity of double bonds and their reactivity. *Huisgen et al.* found that the rate of cycloaddition reactions in a series of planar olefins can be adequately explained by the reduction in strain caused by conversion of the olefin into a saturated product; in comparison, cycloadditions to *(1)* occur considerably more rapidly than is expected from the strain energy[10]. Effects such as the unequal extension of the π-orbitals above and below the double bond[5,10,11], which have been suggested as additional reaction-accelerating factors are, however, to be expected in all olefins having *out-of-plane* bent double bonds. In fact, the same increased reactivity as in *(1)* is found for cyclopentene *(3)*. In contrast to the olefins investigated by *Huisgen et al.*[10], the strain increases on hydrogenation of *(3)* (calculated strain energies[4b]: *(3)* 7.13 kcal/mol, cyclopentane 8.12 kcal/mol), and hence, using strain arguments, *(3)* must be less reactive than cyclohexene. In fact, it reacts approximately a hundred times faster[12] and when the various strain effects in *(1)*[10] and *(3)* are considered, the additional reaction acceleration factors in *(1)* and *(2)* are of the same order of magnitude.

Received: November 24, 1980 [Z 779 IE]
German version: Angew. Chem. *93*, 602 (1981)

CAS Registry numbers:
*(1)*, 498-66-8; *(2)*, 121-46-0; *(3)*, 142-29-0; *(4)*, 7124-86-9; *(5)*, 628-92-2; *(6)*, 931-64-6; *(7)*, 529-16-8; *(8)*, 77944-22-0; *(9)*, 77944-23-1.

---

[1] a) *T. T. Tidwell*, Tetrahedron *34*, 1855 (1978); b) *J. F. Liebman, A. Greenberg*, Chem. Rev. *76*, 311 (1976); *A. Greenberg, J. F. Liebman:* Strained Organic Molecules, Academic Press, New York 1978.

[2] a) *O. Ermer, S. Lifson*, Tetrahedron *30*, 2425 (1974); b) *U. Burkert, ibid. 37*, 333 (1981).

[3] *R. L. Viavettene, F. D. Greene, L. D. Cheung, R. Majeste, L. M. Trefonas*, J. Am. Chem. Soc. *96*, 4342 (1974).

[4] a) *N. L. Allinger*, Prog. Phys. Org. Chem. *13*, 1 (1976); *C. Altona, D. H. Faber*, Fortschr. Chem. Forsch. *45*, 1 (1974); *O. Ermer*, Struct. Bonding (Berlin) *27*, 161 (1976); b) All calculations reported were performed with the MM2-force field of *Allinger (N. L. Allinger*, J. Am. Chem. Soc. *99*, 8127 (1977), *N. L. Allinger, Y. Yuh*, QCPE *12*, 395 (1980)).

[5] *G. Wipff, K. Morokuma*, Tetrahedron Lett. *1980*, 4445. I thank *G. Wipff* for a preprint of this article.

[6] a) Planarity of the double bonds was assumed in the electron diffraction experiments on *(1)* and *(2)*. *(1): J. F. Chiang, R. Chiang, K. C. Lu, E.-M. Sung, M. D. Harmony*, J. Mol. Struct. *41*, 67 (1977); *(2): A. Tokozeki, K. Kuchitsu*, Bull. Chem. Soc. Jpn. *44*, 2356 (1971); b) X-ray structure analyses of norbornene derivatives frequently show the olefinic hydrogen atoms on the *endo*-side of the double bond: *R. Destro, G. Filippini, C. M. Gramaccioli, M. Simonetta*, Acta Crystallogr. *B 25*, 2465 (1969); *C. E. Pfluger, R. L. Harlow, S. H. Simonsen*, J. Cryst. Mol. Struct. *3*, 277 (1973).

[7] *N. R. Carlsen, L. Radom, N. V. Riggs, W. R. Rodwell*, J. Am. Chem. Soc. *101*, 2233 (1979).

[8] The only large deviation occurs in the angles C1—C7—H of *(1)* and *(2)* (molecular mechanics calculation [4b]: *(1)* 113.2°/113.6°, *(2)* 113.5°; electron diffraction [6a]: *(1)* 114.7°; *ab initio* calculation [5]: *(1)* 125.6°/124.5°, *(2)* 125.0°).

[9] *P. von R. Schleyer*, J. Am. Chem. Soc. *89*, 701 (1967).

[10] *R. Huisgen, P. H. J. Ooms, M. Mingin, N. L. Allinger*, J. Am. Chem. Soc. *102*, 3951 (1980).

[11] *S. Inagaki, H. Fujimoto, K. Fukui*, J. Am. Chem. Soc. *98*, 4054 (1976).

[12] a) *K. Bast, M. Christl, R. Huisgen, W. Mack*, Chem. Ber. *106*, 3312 (1973); b) *R. Huisgen, G. Szeimies, L. Möbius, ibid. 100*, 2494 (1967).

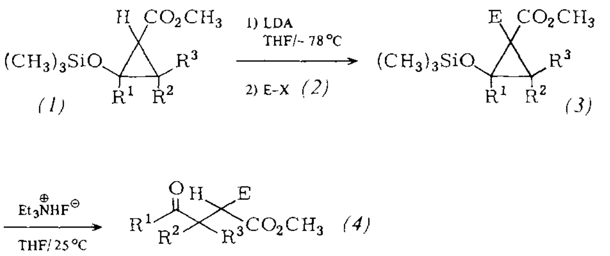
# Alkylation of Donor-Acceptor Substituted Cyclopropanes: A Flexible Route to 4-Oxocarboxylic Acid Esters[**]

By *Ingrid Böhm, Elisabeth Hirsch,* and
*Hans-Ulrich Reissig*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

We recently reported on the synthesis of the donor-acceptor substituted cyclopropanes *(1)* from silylenol ethers and methyl diazoacetate[1]. Their smooth ring-opening with fluoride ions leads to the methyl 4-oxocarboxylates *(4)* (E = H), which are useful precursors for cyclopentane, furan and lactone systems. The preparation of substituted derivatives of *(1)* and *(4)* with E = alkyl was therefore also of interest.

The use of higher diazoalkane carboxylic acid esters for the cyclopropanation of silylenol ethers is conceivable in principle, however the required diazoalkanes are generally not readily available[2]. Nonetheless, we anticipated that the subsequent alkylation of the cyclopropanecarboxylic acid ester *(1)* would lead to a better route to highly substituted derivatives of *(4)*.



In fact, solutions of the ester *(1)* in tetrahydrofuran (THF) can be smoothly deprotonated at –78 °C by lithium diisopropylamide (LDA). The ester enolate ions react with reactive alkyl halides *(2)*[3] to give the substituted cyclopropanecarboxylic acid esters *(3)* in excellent yields (Table 1)[4]. Whereas 1-iodobutane reacts without complications, 2-iodopropane cannot be used, even under different reaction conditions; presumably an elimination reaction occurs with secondary halides.

Table 1. Synthesized methyl siloxycyclopropanecarboxylates *(3)* and methyl 4-oxoalkanecarboxylates *(4)*.

| | R¹ | R² | R³ | E—X *(2)* | *(3)* [a] Yield [%] | *(4)* [a] Yield [%] [b] |
|---|---|---|---|---|---|---|
| *a* | $t$-$C_4H_9$ | H | H | $CH_3$—I | 92 | 82 |
| *b* | $t$-$C_4H_9$ | H | H | $n$-$C_4H_9$—I | 91 | 90 |
| *c* | $t$-$C_4H_9$ | H | H | $CH_2$=CH—$CH_2$—Br | 98 | 95 |
| *d* | $t$-$C_4H_9$ | H | H | $C_6H_5$—$CH_2$—Br | 91 | 86 |
| *e* | $CH_3$ | H | H | $CH_3$—I | 85 | 81 |
| *f* | $CH_3$ | H | H | $n$-$C_4H_9$—I | 71 | 98 |
| *g* | $C_6H_5$ | H | H | $CH_3$—I | 84 | 99 |
| *h* | —$(CH_2)_4$— | | H | $CH_3$—I | 75 | 84 |
| *i* | —$(CH_2)_4$— | | H | $C_6H_5$—$CH_2$—Br | 81 | 71 |
| *j* | H | $CH_3$ | $CH_3$ | $CH_3$—I | 87 | 79 |
| *k* | H | $CH_3$ | $CH_3$ | $CH_2$=CH—$CH_2$—Br | 81 | 85 |

[a] Non-optimized yields of isolated products after Kugelrohr distillation; all novel compounds gave appropriate spectra and satisfactory combustion analyses. [b] Degree of alkylation after GC analysis > 95%.

To our knowledge, the reaction *(1)*→*(3)* represents the first alkylation of a cyclopropanecarboxylic acid ester[5]. The ester enolate ions of *(1)* can also be considered as homoenolates; after hydrolysis, compounds are obtained in which an electrophile has been introduced in the β-position to the keto- or aldehyde functionality, respectively, which was originally masked in our version of the "cyclopropane trick"[6].

Using the readily available triethylammonium fluoride[7], ring opening of *(3)* proceeds under mild, almost neutral conditions to give the 2-substituted methyl 4-oxoalkanecarboxylates *(4)* in good yield. Even the methyl 3-formylpropionates *(4j)* and *(4k)* can be synthesized without difficulty.

Since the starting silylenol ethers are readily accessible and can be manifoldly varied[8], the reaction sequence described is one of the most flexible routes to highly substituted 4-oxo-carboxylic acid esters as far as both R¹- to R³-moieties and the group E are concerned[9]. Ring opening reactions with strong electrophiles (*e.g.* halogens or carbonyl compounds/$TiCl_4$) indicate that siloxy-substituted cyclopropanecarboxylic acid esters are valuable building blocks for use in other syntheses[10].

## *Procedure*

A solution of *(1a)* (1.00 g, 4.10 mol) in 1 cm³ THF is dropped into a solution of LDA (4.9 mmol) in 10 cm³ THF at –78 °C and the mixture stirred for 1 h at this temperature. The clear, pale yellow solution is treated with 1-iodobutane (1.51 g, 8.2 mmol), left first for 5 h at –78 °C and then slowly warmed up to room temperature within 15 h. The usual work-up conditions ($NH_4Cl$, diethyl ether) gave, after Kugelrohr distillation at 80 °C/0.01 torr, 1.12 g (91%) analytically pure *(3b)*.

Received: December 19, 1980 [Z 771 IE]
German version: Angew. Chem. *93*, 593 (1981)

CAS Registry numbers:
*(1a)*, 77903-42-5; *(1e)*, 77903-43-6; *(1g)*, 77903-44-7; *(1h)*, 77982-78-6; *(1j)*, 77903-45-8; *(2)* (E = $CH_3$, X = I), 74-88-4; *(2)* (E = $n$-$C_4H_9$), X = I), 542-69-8; *(2)* (E = $CH_2$=CH—$CH_2$, X = Br), 106-95-6; *(2)* (E = $C_6H_5$—$CH_2$, X = Br), 100-39-0; *(3a)*, 77903-46-9; *(3b)*, 77903-47-0; *(3c)*, 77903-48-1; *(3d)*, 77903-49-2; *(3e)*, 77903-50-5; *(3f)*, 77903-51-6; *(3g)*, 77903-52-7; *(3h)*, 77903-53-8; *(3i)*, 77903-54-9; *(3j)*, 77903-55-0; *(3k)*, 77903-56-1; *(4a)*, 77903-57-2; *(4b)*, 77903-58-3; *(4c)*, 77903-59-4; *(4d)*, 77903-60-7; *(4e)*, 32811-25-9; *(4f)*, 77903-61-8; *(4g)*, 36057-38-2; *(4h)*, 5697-75-6; *(4i)*, 77924-75-5; *(4j)*, 77903-62-9; *(4k)*, 77903-63-0.

---

[*] Dr. H.-U. Reissig, I. Böhm, E. Hirsch
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *H.-U. Reissig, E. Hirsch,* Angew. Chem. *92*, 839 (1980); Angew. Chem. Int. Ed. Engl. *19*, 813 (1980).

[2] *M. Regitz:* Diazoalkane, Eigenschaften und Synthesen, Thieme, Stuttgart 1977.

[3] Other electrophiles such as alkylsulfonates, $D_2O$, carbonyl compounds and trialkylchlorosilanes can also be used; *H.-U. Reissig,* unpublished results.

[4] A feasible model system for the stereochemistry of the alkylation is currently being investigated and may provide insight into the structure of the ester enolate anion.

[5] For the deprotonation of cyclopropanecarboxylic esters see: *H. W. Pinnick, Y.-H. Chang, S. C. Foster, M. Govindan,* J. Org. Chem. *45*, 4505 (1980) and literature cited therein.

[6] *D. Seebach,* Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979), and literature cited therein.

[7] *S. Hünig, G. Wehner,* Synthesis *1975*, 180.

[8] *J. K. Rasmussen,* Synthesis *1977*, 91.

[9] *M. Miyashitu, T. Kumazawa, A. Yoshikoshi,* Chem. Lett. *1980*, 1043, and literature cited therein.

[10] *H.-U. Reissig,* unpublished results.

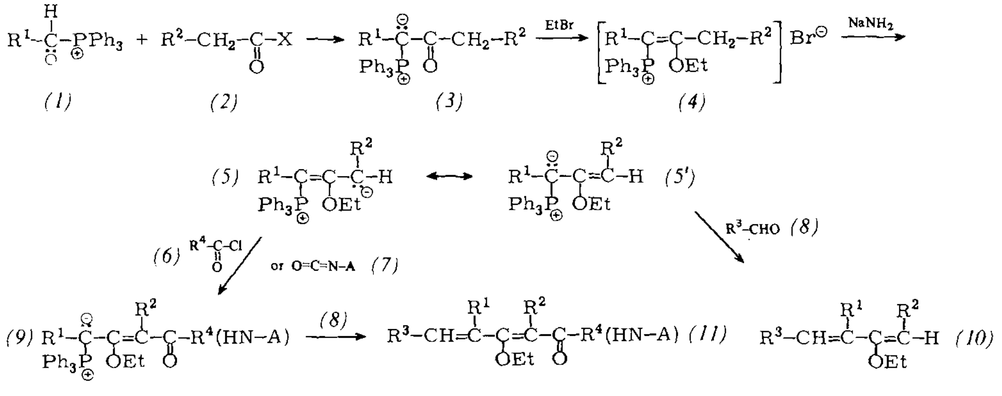
# A Novel Route to 2-Ethoxybutadienes; Diels-Alder Reaction of 1,2-$\lambda^5$-Oxaphosphorines

By *Hans-Jürgen Bestmann* and *Kurt Roth*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

2-Ethoxybutadienes are, as enol ethers of α,β-unsaturated carbonyl compounds, versatile and useful synthons. We describe here, a variable synthetic method for this class of compounds starting from primary alkyl halides, carboxylic acids and aldehydes.

Alkylidenetriphenylphosphoranes *(1)*, whose ylide substructure is formed from a primary alkyl halide or alcohol, can be transformed by treatment with the carboxylic acid derivatives *(2)* to acyl ylides *(3)*[1]. The ambidentate[2] phosphoranes *(3)* are *O*-alkylated[3], by treatment with ethyl bromide, to the phosphonium salts *(4)*, from which a γ-proton can be abstracted by sodium amide[4]. The 2-ethoxyallylidenetriphenylphosphoranes, which are described in the mesomeric limiting structures *(5)* and *(5′)* are thus formed, and formally react as *(5′)* with aldehydes *(8)* in a Wittig reaction to the 2-ethoxybutadienes *(10)* (Table 1); as enol ethers they are readily converted into α,β-unsaturated ketones by known methods.



On the other hand, the ylides *(5)* react with acid chlorides *(6)* at the γ-position to the P atom[5]. Thus, apart from 1 mole of the phosphonium salt ($Cl^{\ominus}$ instead of $Br^{\ominus}$), the acylphosphoranes *(9)* are formed from *(5)* and *(6)* (2 : 1 molar ratio). Isocyanates *(7)* also attack the allyl ylides *(5)* at the γ-position to form, after proton rearrangement, the carbamoyl-substituted compounds *(9)*[6]. Wittig reaction of *(9)* with *(8)* produces the 1-acyl-2-ethoxybutadienes *(11)* (Table 1), from which, *inter alia*, γ,δ-unsaturated 1,3-dicarbonyl compounds and derivatives of the 2,3-dihydro-4-pyrones can be obtained[7].

*(9)*, which is describable *via* mesomeric limiting structures, should exist in several different conformations. It therefore follows, in particular when $R^2 \neq H$, that reaction of *(8)* with *(9)* should lead to formation of compound *(11)* having a mixture of *Z*,*E*-isomers at the 1-position. In contrast, carbonyl olefination forms a new double bond having *E*-geometry which is in accord with our concepts of the mechanism of the Wittig reaction[8a].

It should be possible to cyclize *(9′)* to the 1,2-$\lambda^5$-oxaphosphorines *(12)*, in which the oxygen atom primarily occupies the apical position[8]. In the $^{31}$P-NMR spectra, particularly that of *(9)* ($R^2 \neq H$), two broad signals appear at $\delta = +10$ to $+16$ and $-20$ to $-50$ ($H_3PO_4$ as external standard); these indicate an equilibrium between *(9)* and *(12)*. In polar solvents such as $CDCl_3$, this lies more on the side of *(9)*, while in nonpolar solvents, such as benzene and toluene, *(12)* is more predominant. If solutions of *(9)*/*(12)* $R^1 = H$ in toluene are treated with *N*-methylmaleimide *(13)*, the substituted *N*-methylphthalimides *(17)*[9] and triphenylphosphane oxide *(15)* can be isolated whose formation we account for by the following mechanism: *(12)*, in a Diels-Alder reaction with *(13)*, yields the bicycle *(14)*. After ligand rearrangement to *(14′)*, the bridgehead C-atom bonded to the phosphorus occupies an apical position in the trigonal bipyramid, permitting cleavage of the C—P bond[8], which is cleaved in a cycloreversion to *(15)*. The dihydrophthalimide derivative *(16)* is formed, which is dehydrated in the work-up to *(17)*. In principle, a cycloaddi-

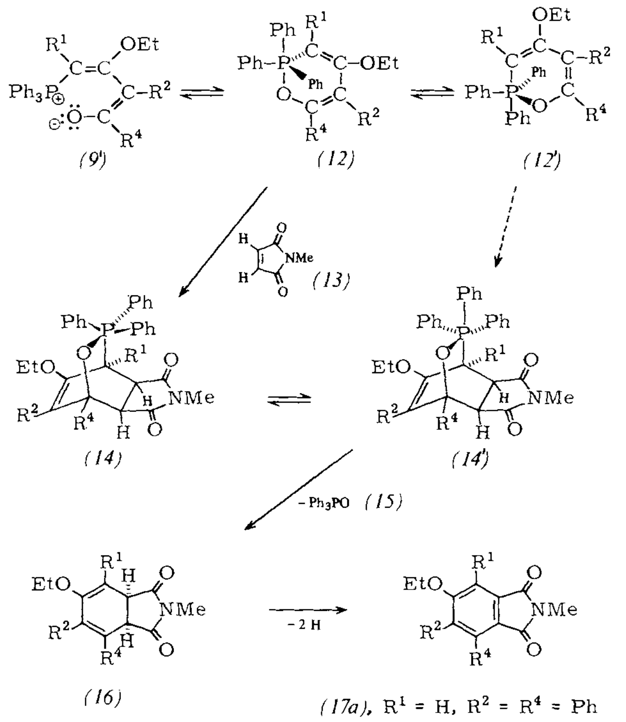
Table 1. Yields and melting points of the compounds *(4)*, *(5)*, *(9)*, *(10)* and *(11)*; for *(9)*, *(10)* and *(11)* only a selection of the derivatives prepared is shown.

| Cpd. | $R^1$ | $R^2$ | $R^3$ | $R^4$ | M.p. [°C]<br>B.p. [°C/torr] | Yield [%] |
|---|---|---|---|---|---|---|
| *(4a)* | H | H | — | — | 173 (dec.) | 95 |
| *(4b)* | H | Ph | — | — | 164 (dec.) | 84 |
| *(4c)* | H | Me | — | — | 205 (dec.) | 88 |
| *(4d)* | Me | H | — | — | 190 (dec.) | 85 |
| *(5a)* | H | H | — | — | >60 (dec.) | 87 |
| *(5b)* | H | Ph | — | — | >85 (dec.) | 72 |
| *(5c)* | H | Me | — | — | >60 (dec.) | 88 |
| *(5d)* | Me | H | — | — | >40 (dec.) | 73 |
| *(9a)* | H | H | — | Ph | 174 | 81 [a] |
| *(9b)* | H | H | — | *i*Pr | 148 | 53 [a] |
| *(9c)* | H | H | — | OEt | 166 | 67 [a] |
| *(9d)* | H | H | — | *p*-Ph—$NO_2$ | 151 | 92 [a] |
| *(9e)* | H | H | — | NHMe | 163 | 92 [b] |
| *(9f)* | H | H | — | NHPh | 175 | 84 [b] |
| *(9g)* | H | Ph | — | Ph | 193 | 71 [a] |
| *(9h)* | H | Ph | — | OEt | 172 | 76 [a] |
| *(9i)* | H | Me | — | Ph | 174 | 79 [a] |
| *(9j)* | Me | H | — | Et | 175 | 88 [a] |
| *(10a)* | H | H | Ph | — | 105/1.5 | 63 |
| *(10b)* | H | H | *i*Pr | — | 76/33 | 60 |
| *(10c)* | H | H | *t*Bu | — | 92/47 | 37 |
| *(10d)* | H | Me | *i*Pr | — | 80/17 | 69 |
| *(10e)* | Me | H | *t*Bu | — | 86/24 | 81 |
| *(11a)* | H | H | Ph | Ph | 87 | 62 |
| *(11b)* | H | H | Ph | *i*Pr | 43 | 76 |
| *(11c)* | H | H | Ph | OEt | 55 | 66 |
| *(11d)* | H | H | *p*-Ph—$NO_2$ | NHMe | 194 | 86 |
| *(11e)* | H | H | Ph | NHPh | 198 | 61 |
| *(11f)* | H | Ph | Ph | OEt | — [c] | 82 |
| *(11g)* | H | Me | Ph | Ph | — [c] | 30 |
| *(11h)* | Me | H | Ph | Et | — [d] | 30 |

[a] Relative to *(6)*. [b] Relative to *(7)*. [c] Oil, two isomers, [d] Oil, one isomer.

---

[*] Prof. Dr. H. J. Bestmann, Dipl.-Chem. K. Roth
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)



*(17a)*, $R^1$ = H, $R^2$ = $R^4$ = Ph
*(17b)*, $R^1$ = H, $R^2$ = Me, $R^4$ = Ph
*(17c)*, $R^1$ = H, $R^2$ = Ph, $R^4$ = Me

tion between the pseudorotamers *(12)* and *(13)* of the 1,2-oxaphosphorine to *(14')* is possible, which then immediately decomposes[10].

Received: June 13, 1980 [Z 769 IE]
German version: Angew. Chem. *93*, 587 (1981)

CAS Registry numbers:
*(4a)*, 77882-26-9; *(4b)*, 77882-27-0; *(4c)*, 77882-28-1; *(4d)*, 77882-29-2; *(5a)*, 62639-98-9; *(5b)*, 77882-30-5; *(5c)*, 77882-31-6; *(5d)*, 77882-32-7; *(6a)*, 98-88-4; *(6b)*, 79-30-1; *(6c)*, 541-41-3; *(6d)*, 122-04-3; *(6e)*, 6452-47-7; *(6f)*, 2040-76-8; *(8a)*, 100-52-7; *(8b)*, 78-84-2; *(8c)*, 630-19-3; *(8d)*, 555-16-8; *(9a)*, 27271-21-2; *(9b)*, 64483-30-3; *(9c)*, 27271-28-9; *(9d)*, 77882-33-8; *(9e)*, 77882-34-9; *(9f)*, 77882-35-0; *(9g)*, 77882-36-1; *(9h)*, 77882-37-2; *(9i)*, 77882-38-3; *(9j)*, 77924-83-5; *(10a)*, 77882-39-4; *(10b)*, 77902-55-7; *(10c)*, 77882-40-7; *(10d)*, 77882-41-8; *(10e)*, 77882-42-9; *(11a)* isomer 1, 77882-43-0; *(11a)* isomer 2, 77882-44-1; *(11b)* isomer 1, 77882-45-2; *(11b)* isomer 2, 77882-46-3; *(11c)* isomer 1, 77882-47-4; *(11c)* isomer 2, 77882-48-5; *(11d)* isomer 1, 77882-49-6; *(11d)* isomer 2, 77882-50-9; *(11e)* isomer 1, 77882-51-0; *(11e)* isomer 2, 77882-52-1; *(11f)* isomer 1, 77882-53-2; *(11f)* isomer 2, 77882-54-3; *(11g)* isomer 1, 77882-55-4; *(11g)* isomer 2, 77882-56-5; *(11h)* isomer 1, 77882-57-6; *(11h)* isomer 2, 77882-58-7; *(12a)*, 77882-59-8; *(12b)*, 77882-60-1; *(12c)*, 77882-61-2; *(13)*, 930-88-1; *(14a)*, 77882-62-3; *(14b)*, 77882-63-4; *(14c)*, 77882-64-5; *(16a)*, 77902-56-8; *(16b)*, 77882-65-6; *(16c)*, 77882-66-7; *(17a)*, 77882-67-8; *(17b)*, 77882-68-9; *(17c)*, 77882-69-0.

---

[1] *H. J. Bestmann, B. Arnasòn*, Chem. Ber. *95*, 1513 (1962); Review: *H. J. Bestmann*, Angew. Chem. *77*, 651 (1965); Angew. Chem. Int. Ed. Engl. *4*, 645 (1965).

[2] *H. J. Bestmann, G. Graf, H. Hartung*, Justus Liebigs Ann. Chem. *706*, 68 (1967).

[3] *F. Ramirez, S. Dershowitz*, J. Org. Chem. *22*, 41 (1957); *A. A. Grigorenko, M. J. Shevchuk, A. V. Dombrovskii*, Zh. Obshch. Khim. *36*, 506 (1966); Chem. Abstr. *65*, 737g (1966).

[4] For the reaction of an analogue of *(4)* ($R^1 = R^2 = H$) with *n*-butyllithium and subsequent reaction with α,β-unsaturated carbonyl compounds to cyclohexenone derivatives, see: *S. F. Martin, S. R. Desai*, J. Org. Chem. *42*, 1664 (1977).

[5] For reactions at the γ-position to the P atom in allylidenetriphenylphosphoranes, see: *H. J. Bestmann, O. Kratzer, H. Simon*, Chem. Ber. *95*, 2750 (1962); *H. J. Bestmann, H. Schulz*, Justus Liebigs Ann. Chem. *674*, 11 (1964).

[6] For reactions of isocyanates with alkylidenetriphenylphosphoranes *cf. H. Staudinger, J. Meyer*, Ber. Dtsch. Chem. Ges. *53*, 72 (1920); *S. Trippett, D. M. Walker*, J. Chem. Soc. (London) *1959*, 3874.

[7] *H. J. Bestmann, R. W. Saalfrank*, Chem. Ber. *109*, 403 (1976).

[8] a) *H. J. Bestmann, K. Roth, E. Wilhelm, R. Böhme, H. Burzlaff*, Angew. Chem. *91*, 945 (1979); Angew. Chem. Int. Ed. Engl. *18*, 887 (1979); b) *D. Marquarding, F. Ramirez, I. Ugi, P. Gillespie, ibid. 85*, 99 (1973), resp. *12*, 91 (1973).

[9] *(17a)*: m.p. = 210 °C; yield 31%; $^1$H-NMR (CDCl$_3$) $\delta$ = 1.31 (t, 3H), 3.12 (s, 3H), 4.19 (q, 2H), 6.90–7.45 (m, 10H), 7.48 (s, 1H).—*(17b)*: m.p. = 178 °C; yield 14%; $^1$H-NMR (CDCl$_3$) $\delta$ = 1.47 (t, 3H), 2.02 (s, 3H), 3.02 (s, 3H), 4.20 (q, 2H), 7.07–7.60 (m, 5H), 7.34 (s, 1H).—*(17c)*: m.p. = 125 °C; yield 10%; $^1$H-NMR (CDCl$_3$) $\delta$ = 1.23 (t, 3H), 2.35 (s, 3H), 3.12 (s, 3H), 4.06 (q, 2H), 7.00–7.55 (m, 5H), 7.32 (s, 1H).

[10] *Note added in proof:* In the meantime, reaction of a compound of type *(5)* ($R^1 = R^2 = H$, OMe instead of OEt) with acyl chlorides has been reported: *E. Öhler, E. Zbiral*, Chem. Ber. *113*, 2852 (1980).

---

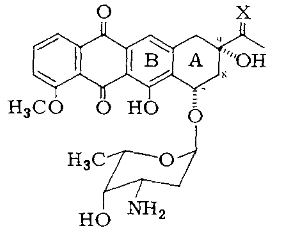
# Synthesis of (±)-13-Deoxo-11-deoxydaunorubicinone[**]

By *Karsten Krohn*[*]

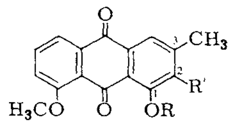
*Dedicated to Professor Albert Mondon on the occasion of his 70th birthday*

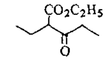
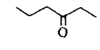
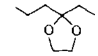
In the search for novel anthracycline antibiotics *Acramone et al.*[1] succeeded in isolating 13-deoxo-11-deoxydaunorubicin *(1)* and 11-deoxydaunorubicin *(2)*, which proved to have particularly useful antitumor effects in animals.

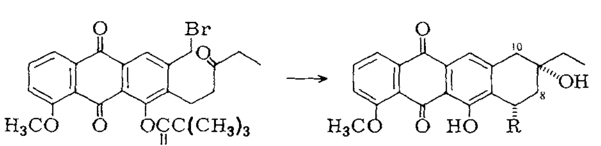
The synthesis of anthracyclinones, having only one hydroxy group at ring B, derived from the chromophore 1,8-dihydroxy-9,10-anthraquinone, has been reported to be difficult using existing methods[2]. We have, however, been able to prepare the naturally occurring 13-deoxo-11-deoxydaunorubicinone *(11)* for the first time, using a novel variation of the cyclization of doubly alkylated anthraquinones[3].



*(1)*, X = $H_2$
*(2)*, X = O



| | R | R' |
|---|---|---|
| *(3)* | H | H |
| *(4)* | H | $CH_2OH$ |
| *(5)* | H | $CH_2Cl$ |
| *(6)* | H |  |
| *(7)* | H |  |
| *(8)* | OCO–C$(CH_3)_3$ |  |



*(9)*

*(10)*, R = H
*(11)*, R = OH

The starting material was the readily accessible 8-*O*-methyl ether of chrysophanol *(3)*[4]. Hydroxymethylation of *(3)* in the *o*-position using formaldehyde, in a modification of the Marschalk reaction[5], gave the benzyl alcohol *(4)* in 82% yield (decomp. above 190 °C). Reaction of *(4)* with thionyl chloride led, quantitatively, to the chloromethyl

---

[*] Prof. Dr. K. Krohn
Institut für Organische Chemie und Biochemie,
Abt. Biochemie, der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)
New address:
Institut für Organische Chemie der Technischen Universität
Schleinitzstrasse, D-3300 Braunschweig (Germany)

[**] Synthetic Anthracyclinones, Part 17. Part 16: [4].

compound *(5)* (m.p. = 135 °C), which could be converted into the β-keto ester *(6)* (m.p. = 130 °C; 97%) by treatment with ethyl 2-oxovalerate (EtONa, 50 °C, 1 h). Saponification to the acid and decarboxylation (160 °C, 15 min) produced the ketone *(7)* (m.p. = 155–156 °C, 94%) as the main intermediate. To ensure that the planned reaction with *N*-bromosuccinimide selectively functionalized only the C-3 methyl group, the α-position to the keto group was protected by formation of the ethylene acetal (m.p. = 154—155 °C, 96%). The competing benzyl site on the side chain at C-2 was sterically shielded by formation of the pivolate *(8)* (m.p. = 143 °C, 94%). In the subsequent light-induced bromination of *(8)* with *N*-bromosuccinimide, the monobromo-product *(9)* (m.p. = 141–142 °C, 70%) was the major product formed. The ring-closure to the anthracyclinone *(10)* (m.p. = 185—186 °C) proceeded in 63% yield by treatment of *(9)* with magnesium, which had previously been activated with 1,2-dibromoethane. As in previous instances[5b], the cyclization of *(10)* could be easily recognized from the coupling constants of the C-8 protons in the $^1$H-NMR spectrum[6].

Introduction of a hydroxy group at the C-7 position of *(10)* was carried out *via* photolytic bromination; the labile products were dissolved in 0.5 N NaOH. Apart from aromatization products, only the racemic 7,9-*cis*-diol *(11)* (m.p. = 216 °C), formed in a stereoselective reaction, could be isolated in 62% yield. It's chromatographic and spectroscopic properties are in accord with the naturally occurring substance[7]. – Starting from *(9)*, it should also be possible to synthesize the pharmacologically important class of akalavinones[8].

Received: November 13, 1980 [Z 765 IE]
German version: Angew. Chem. *93*, 575 (1981)

CAS Registry numbers:
*(3)*, 3300-25-2; *(4)*, 77825-00-4; *(5)*, 77825-01-5; (±)-*(6)*, 77825-02-6; *(7)*, 77825-03-7; *(8)*, 77825-04-8; *(9)*, 77825-05-9; (±)-*(10)*, 77825-06-0; (±)-*(11)*, 77880-65-0; ethyl 3-oxovalerate, 4949-44-4.

---

[1] *F. Arcamone, G. Cassinelli, F. DiMatteo, S. Forenza, M. C. Ripamonti, G. Rivola, A. Vigevani, J. Clardy, T. McCabe*, J. Am. Chem. Soc. *102*, 1462 (1980).

[2] Review: *T. R. Kelly*, Annu. Rep. Med. Chem. *14*, 288 (1979).

[3] *K. Krohn, M. Radeloff*, Chem. Ber. *111*, 3823 (1978).

[4] *K. Krohn*, Tetrahedron Lett. *1980*, 3557.

[5] a) *C. Marschalk, F. Koenig, N. Ouroussof*, Bull. Soc. Chim. Fr. *3*, 1545 (1936); b) *K. Krohn, B. Behnke*, Chem. Ber. *113*, 2994 (1980).

[6] *(10)*, $^1$H-NMR (270 MHz, $CDCl_3$): $\delta = 1.75$ (dt, $J_{gem} = 13.3$, $J_{7,8} = 7.8$, $J_{7,8} = 8.0$ Hz; 1 H, 8a-H), 1.94 (dt, $J_{gem} = 13.3$, $J_{7,8} = 5.6$, $J_{7,8} = 5.5$, $J_{8e,10e} = 1.0$ Hz; 1 H, 8e-H).

[7] Prof. *F. Arcamone* (Farmitalia, Milan) is thanked for providing a sample of *(11)*.

[8] Review: *H. Brockmann*, Fortschr. Chem. Org. Naturst. *21*, 121 (1963); *T. Oki*, J. Antibiot. *30*, S-70 (1977).

---

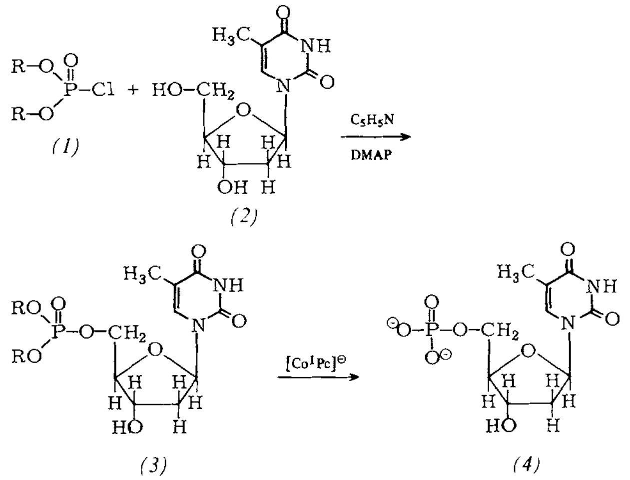
## Bis(2,2,2-trichloro-1,1-dimethylethyl) Monochlorophosphate, a Selective Reagent for the Phosphorylation and Protection of the 5′-OH Group of Nucleoside Derivatives[**]

By *Herbert A. Kellner, Ruth G. K. Schneiderwind, Heiner Eckert*, and *Ivar K. Ugi*[*]

*Dedicated to Professor Helmut Zahn on the occasion of his 65th birthday*

5′-Phosphorylated oligonucleotides, required for enzymatic nucleotide syntheses, are normally obtained by deblocking the 5′-trityl- or 5′-dimethoxytrityl-derivatives followed by enzymatic or conventional preparative 5′-phosphorylation[1].

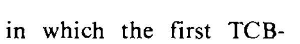
In a preliminary investigation, we found that of the many reagents studied, bis(2,2,2-trichloro-1,1-dimethylethyl) monochlorophosphate *(1)*[2] [bis(trichloro-*tert*-butyl) monochlorophosphate = bis-2-TCB monochlorophosphate] was the only one able to simultaneously selectively phosphorylate and protect the terminal 5′-OH group in the synthesis of 5′-phosphorylated oligonucleotides. This reagent attacks the 5′-OH group, in the presence of a free 3′-OH group, just as selectively as trityl chloride and its analogues. The TCB-phosphate group survives all the necessary steps in the oligonucleotide synthesis, but can readily be removed by the cobalt(I)-phthalocyanine anion $[Co^IPc]^{\ominus}$[3].



R = $Cl_3C{-}C(CH_3)_2{-}$

The synthetic principles are illustrated in the following example:

Thymidine *(2)* reacts with *(1)* in pyridine, in the presence of ≥ 10 mol% 4-dimethylaminopyridine (DMAP)[4], to give *(3)* in 72% yield. The latter product when treated with $[Co^IPc]^{\ominus}$ releases thymidine 5′-phosphate *(4)*. The DMAP-catalysis of the reaction *(1)* + *(2)* → *(3)* depends on the intermediate formation of *(5)* from *(1)* and DMAP[5].

*(5)*


Deblocking with $[Co^IPc]^{\ominus}$, in which the first TCB-moiety is cleaved considerably more rapidly that the second, proceeds almost quantitatively at sufficiently long reaction times. For example, from a molar solution, 84% *(4)* and 16% of the mono-TCB derivative were obtained after 2 d at 20 °C, while after 4 d the ratio was 90 : 10.

### *Procedure*

Improved synthesis of *(1)* (cf.[2a]): A solution of dry 2-trichloromethyl-2-propanol (177.5 g, 1 mol) and pyridine (80.5 cm$^3$, 1 mol) in 300 cm$^3$ pentane is treated with $PCl_3$ (43.5 cm$^3$, 0.5 mol) in 150 cm$^3$ pentane at 0 °C under an $N_2$-atmosphere; the mixture is stirred for 1 d at room temperature and finally stirred and refluxed for 2 h. The precipitate of pyridine hydrochloride is filtered off, the

---

[*] Prof. Dr. I. K. Ugi, Dr. H. A. Kellner,
Dipl.-Chem. R. G. K. Schneiderwind, Dr. H. Eckert
Institut für Organische Chemie der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

solvent removed and the residue fractionally distilled *in vacuo*. 150 g (71%) of bis(2,2,2-trichloro-1,1-dimethylethyl) monochlorophosphite (m.p. = 46 °C, b.p. = 134°/0.015 torr) is obtained. A cooled solution of the phosphite (109 g, 259 mmol) in 200 $cm^3$ chloroform is added in the dark under an $N_2$-atmosphere to a suspension of (diacetoxyiodo)benzene[6] (91 g, 294 mmol) in 500 $cm^3$ chloroform cooled to −15 °C. The mixture is allowed to warm up slowly to room temperature and is stirred for 2 d. After evaporation of the solution and covering the residue with pentane, 74 g (65%, relative to the phosphite) of crystalline *(1)* is obtained (m.p. = 81 °C).

*(3):* A mixture of *(2)*[7] (0.24 g, 1 mmol), *(1)* (0.87 g, 2 mmol) and DMAP (0.02 g, 0.2 mmol) is stirred for 24 h at 50 °C. The solvent is then removed, the residue taken up in a little chloroform and precipated with 100 $cm^3$ pentane. The precipate is dissolved in 50 $cm^3$ chloroform, filtered, washed twice with citrate buffer (pH 6) and twice with water, and then dried over $Na_2SO_4$. Chromatography on silica gel (Merck $60\,F_{254}$) using chloroform/methanol (9 : 1) as eluent gives *(3)* (0.46 g, 72%) (m.p. = 186 °C).

*(4):* A solution of $Li^I[Co^IPc]\cdot 4.5$ tetrahydrofuran (2.51 g, 2.8 mmol) and *(3)* (0.39 g, 0.6 mmol) in 20 $cm^3$ acetonitrile is stirred in the absence of oxygen at room temperature for 48 h. The green mixture is treated, at 0 °C, with 40 $cm^3$ $H_2O$ and $CO_2$ and air immediately passed in for 5 min. The violet precipate is centrifuged off (5 min, 3000 r.p.m.) and washed three times with water. The combined centrifugates are treated with 1 N hydrochloric acid until decomposition of the $LiHCO_3$ at pH 6.5 occurs, concentrated and the product converted to the Na salt on a Lewatit S100 G1 ion exchanger: 300 mg *(4)*, which contains 16% of the mono-TCB-derivative as impurity, is obtained.

Received: October 17, 1980 [Z 770 IE]
German version: Angew. Chem. *93*, 581 (1981)

CAS Registry numbers:
*(1)*, 17677-92-8; *(2)*, 50-89-5; *(3)*, 77825-23-1; *(4)*, disodium salt, 33430-62-5.

---

[1] *A. Kössel, H. Seliger,* Fortschr. Chem. Org. Naturst. *32*, 297 (1975); *H. Köster, H. Blöcker, R. Frank, S. Geussenhainer, W. Kaiser,* Hoppe Seyler's Z. Physiol. Chem. *356*, 1585 (1975); *P. I. Zdhanov, S. M. Zhenodarova,* Synthesis *1975*, 222; *L. A. Slotin,* Synthesis *1977*, 737; *F. Eckstein,* Kontakte *3*, 3 (1978); *H. Köster, H. Blöcker, R. Frank, S. Geussenhainer, W. Kaiser,* Justus Liebigs Ann. Chem. *1978*, 839; *H. Köster,* Nachr. Chem. Tech. Lab. *27*, 694 (1979).

[2] a) *H. A. Kellner, I. Ugi,* Z. Naturforsch. *B 34*, 1159 (1979); b) *W. Gerrard,* J. Chem. Soc. *1944*, 85; *W. Gerrard, P. L. Wyvill,* Research (London) *2*, 536 (1949); *W. Gerrard, M. J. D. Isaacs, G. Machell, K. B. Smith, P. L. Wyvill,* J. Chem. Soc. *1953*, 1920; *J. B. Honeycutt,* C. A. *49*, 157 (1955); *V. S. Abramov, V. K. Khairullin,* J. Gen. Chem. USSR **27**, 501 (1957); *K. Sasse* in *E. Müller:* Methoden der organischen Chemie (Houben-Weyl), Vol. XII/2, p. 45f., Thieme, Stuttgart 1964.

[3] *H. Eckert, I. Ugi,* Angew. Chem. *87*, 847 (1975); Angew. Chem. Int. Ed. Engl. *14*, 825 (1975); see also *R. Taube, M. Zach, K. A. Stanske, S. Heidrich,* Z. Chem. *3*, 392 (1963); *H. Eckert,* Dissertation, Technische Universität München 1976; *H. Eckert, I. Ugi, W. Breuer, J. Geller, I. Lagerlund, M. Listl, D. Marquarding, S. Stüber, S. Zahr, H. v. Zychlinski,* Pure Appl. Chem. *51*, 1219 (1979); *H. Eckert, I. Ugi,* Liebigs Ann. Chem. *1979*, 278.

[4] *G. Höfle, W. Steglich, H. Vorbrüggen,* Angew. Chem. *90*, 602 (1978); Angew. Chem. Int. Ed. Engl. *17*, 569 (1978).

[5] *H. A. Kellner,* Dissertation, Technische Universität München 1980.

[6] *K. H. Pausacker,* J. Chem. Soc. *1953*, 107.

[7] Before the reaction, thymidine (Fa. Merck) was treated several times with pyridine (10 $cm^3$/mmol), which was then removed (azeotropic drying) [5].

## Redox Reltionship between Carbeneiron and σ-Alkyliron Porphyrins[**]

By *Doris Lexa, Jean-Michel Savéant, Jean-Paul Battioni, Marc Lange,* and *Daniel Mansuy*[*]

Porphyrin complexes with Fe—C bonds are likely to be involved in the enzymatic reactions of cytochrome P450 hemoproteins of the monooxygenase systems responsible for the detoxification of exogenous compounds by living organisms. In this connection, evidence has been given for the formation of iron-carbene bonds during the oxidation of 1,3-benzodioxole derivatives by the active oxygen cytochrome P450 complex[1]. Involvement of σ-alkyliron complexes as intermediates in this reaction has also been proposed[1c]. On the other hand, carbeneiron complexes are formed upon reduction of various polyhalogenated compounds by cytochrome P450-$Fe^{II}$[2] or by reacting the polyhalogenated substrates with iron(II)-porphyrins under reducing conditions[3]. These reactions may involve the intermediacy of σ-halogenated alkyliron porphyrins of the same type as those recently observed in a pulse radiolysis study of the reaction of halogenated alkyl radicals with $Fe^{II}$-porphyrins[4]. It is noteworthy that only one σ-alkyl[5a] and very few σ-aryliron porphyrins[5] have been reported so far: they have all been obtained as $Fe^{III}$ σ-derivatives, prepared by reaction of a Grignard reagent with $Fe^{III}$-porphyrins.

We report here the preliminary results of a study based on an electrochemical investigation of the reduction of carbeneiron(II)-porphyrin complexes in aprotic media[6], which establishes a redox relationship between carbeneiron and σ-alkyliron porphyrins and opens a new route to σ-alkyliron porphyrins both at the $Fe^{II}$ and $Fe^{III}$ oxidation levels.

The three *meso*-tetraphenylporphyrin complexes (TPP[7])

$(TPP)FeC{=}X$ *(1a):* $X = C(p\text{-}C_6H_4Cl)_2$
*(2a):* $X = C(C_6H_5)_2$
*(3a):* $X = S$

were prepared according to previously described procedures[8]; the reaction medium was a 0.1 M solution of $Bu_4NBF_4$ in DMF[9]. Typical cyclic voltammograms obtained under these conditions are shown in Figure 1.

The $Fe^{II}$-carbene complex is reduced in two successive one-electron steps. While the first one-electron reduction gives rise to products [*(1b)*, *(2b)* or *(3b)*] which are stable for *ca.* 1 s, the second reduction product undergoes irreversible decomposition leading to new types of complexes [*(1d)*, *(2d)* or *(3d)*] which can be electrochemically reoxidized between −0.4 and −0.6 V. This process is reversible for complexes *(1d)* and *(2d)* and irreversible for *(3d)* at low sweep rates. In the latter case, reversibility can, however, be restored by raising the sweep rate. The standard potentials for this new redox couple are: *(1c/d)* −0.62 V, *(2c/d)* −0.64 V and *(3c/d)* −0.44 V (*vs.* SCE). The second wave can also be rendered reversible by drastically raising the sweep rate to *ca.* 100—1000 $vs^{-1}$. Addition of water de-

---

[*] Prof. J.-M. Savéant [+], Dr. D. Lexa
Laboratoire d'Electrochimie de l'Université Paris 7
2, place Jussieu, F-75221 Paris Cedex 05 (France)
Dr. D. Mansuy [+], Dr. J.-P. Battioni, Dr. M. Lange
Laboratoire de Chimie de l'Ecole Normale Supérieure
24, rue Lhomond, F-75005 Paris (France)

[+] Author to whom correspondence should be addressed.

[**] This work was supported in part by the CNRS (ATP "Composés de coordination, Catalyse homogène").

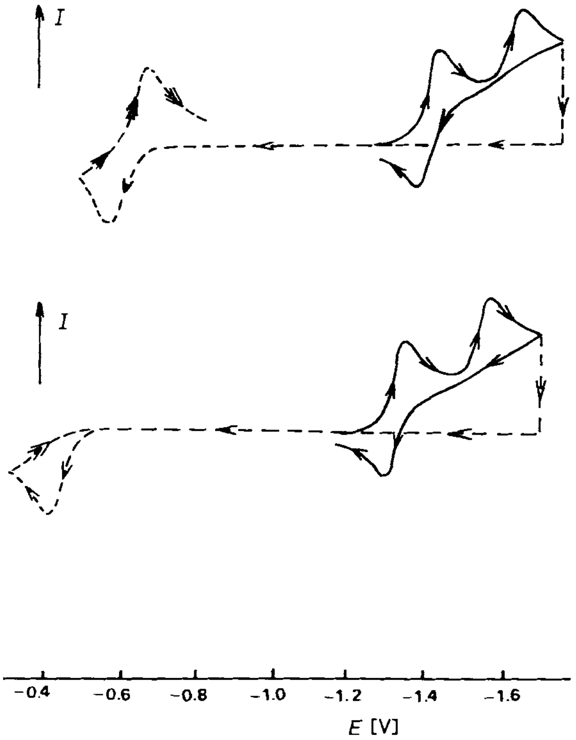
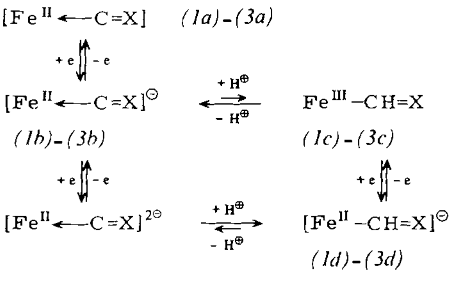


Fig. 1. Cyclic voltammograms of the carbeneiron(II) porphyrins *(1a)* and *(2a)* (top) as well as *(3a)* (bottom) at low sweep rate (0.2 V s$^{-1}$). (——): reduction of complexes; (-----): reoxidation of complexes obtained by 2e-reduction of *(1a)*—*(3a)*.

creases the reversibility of the wave. Coulometric investigations of the second wave, under standard electrolysis conditions, shows the exchange of two Faradays per mole.

These results suggest the redox mechanism shown in Scheme 1 for the observed reactions, which involves formation of the σ-alkyl Fe(II) complexes *(1d)*—*(3d)* by (2e + H$^{\oplus}$)-reduction of *(1a)*—*(3a)*.



Scheme 1. *(1)*, X = C($p$-$C_6H_4Cl)_2$; *(2)*, X = C($C_6H_5)_2$; *(3)*, X = S.

That a σ-alkyliron(II) complex is actually formed was demonstrated for *(2d)* by independent synthesis. The σ-vinyl Fe(III) complex *(2c)* was prepared as a purple crystalline air-sensitive solid by reaction of BrMgC=CPh$_2$ with (TPP)FeClO$_4$ in THF[10]. Its elemental analysis and mass spectrum are in accord with the suggested structure. Furthermore, the UV-spectrum [λ = 529 (ε = 9100), 426 nm (11 500)] is very similar to that of (TPP)Fe$^{III}C_6H_5$[5c]. The nature of the axial ligand of iron was further confirmed by reaction of *(2c)* with HCl which leads quantitatively to (TPP)Fe$^{III}$Cl and 1,1-diphenylethene. *(2c)* gives rise to a cyclic voltammetric one-electron reversible wave at exactly the same potential as the reoxidation wave from the (2e + H$^{\oplus}$)-reduction of the carbeneiron(II) complex *(2a)*. Moreover, the UV/VIS spectrum obtained upon one electron reduction of *(2c)* is the same as that of the product obtained by (2e + H$^{\oplus}$)-reduction of *(2a)* [λ = 795 (ε = 4700), 511 (12 600), 428 (75 000), 356 nm (31 500)]. The complex resulting from this reduction decomposes upon addition of 1 M HCl with quantitative formation of diphenylethene. Very similar reduction patterns were obtained with the carbene complexes of octaethylporphyriniron(II), the characteristic potentials being more negative by *ca.* 100 mV.

In conclusion, the results show that σ-alkyliron(II) porphyrins are formed upon (2e + H$^{\oplus}$)-reduction of the corresponding carbeneiron(II) complex. The σ-alkyliron(III) complexes can then be obtained by a 1e-reoxidation reaction. In the case of *(3a)* this redox relationship can be reversed. This is shown by the chemical irreversibility of the reoxidation wave of the σ-alkyliron(II) complex [Fig. 1, *(3a)*] and by the fact that upon slow reoxidation it forms the carbene complex *(3a)* again. This type of reversibility could not be observed in *(1a)* and *(2a)* where the σ-alkyliron(III) derivative slowly cleaves off the carbon ligand rather than deprotonate and reoxidize to the carbeneiron(II) complex.

Received: September 11, 1980 [Z 767 IE]
German version: Angew. Chem. *93*, 585 (1981)

CAS Registry numbers:
*(1a)*, 72042-21-8; *(2a)*, 77745-20-1; *(3a)*, 67583-11-3.

---

[1] a) *V. Ullrich* in *D. J. Jollow, J. J. Kocsis, R. Saryder, H. Vainio:* Biological Reactive Intermediates, Plenum Press, New York 1977, p. 65ff.; b) *D. Mansuy, J. P. Battioni, J. C. Chottard, V. Ullrich,* J. Am. Chem. Soc. *101*, 3973 (1979); c) *D. Mansuy, J. C. Chottard, M. Lange, J. P. Battioni,* J. Mol. Catal. *7*, 215 (1980).

[2] a) *D. Mansuy, W. Nastainczyk, V. Ullrich,* Naunyn-Schmiedeberg's Arch. Pharmacol. *285*, 315 (1974); b) *C. R. Wolf, D. Mansuy, W. Nastainczyk, G. Deutschmann, V. Ullrich,* Mol. Pharmacol. *13*, 698 (1977).

[3] *D. Mansuy,* Pure Appl. Chem. *52*, 681 (1980), and literature cited therein.

[4] *D. Brault, C. Bizet, P. Morliere, M. Rougée, C. J. Land, R. Santus, A. J. Swallow,* J. Am. Chem. Soc. *102*, 1015 (1980).

[5] a) *D. A. Clarke, D. Dolphin, A. W. Johnson, H. A. Pinnock,* J. Chem. Soc. C *1968*, 881; b) *D. A. Clarke, R. Grigg, A. W. Johnson,* Chem. Commun. *1966*, 208; c) *C. A. Reed, T. Mashiko, S. P. Bentley, M. E. Kastner, W. R. Scheidt, K. Spartalian, G. Lang,* J. Am. Chem. Soc. *101*, 2948 (1979); d) *H. Ogoshi, H. Sugimoto, Z. Yoshida,* IX. International Conference on Organometallic Chemistry, Dijon 1979, Frankreich.

[6] The apparatus and procedures for the cyclic voltametric and spectrochemical investigations were described by: *D. Lexa, J. M. Savéant, J. Zickler, ibid. 99*, 2786 (1977).

[7] Abbreviations used: TPP = dianion of *meso*-tetraphenylporphyrin; OEP = dianion of octaethylporphyrin; DMF = dimethylformamide; THF = tetrahydrofuran.

[8] *D. Mansuy, M. Lange, J. C. Chottard,* J. Am. Chem. Soc. *100*, 3213 (1978); *D. Mansuy, J. P. Battioni, J. C. Chottard, ibid. 100*, 4311 (1978).

[9] No special precautions were taken to remove traces of water, which was present in concentrations of 0.1-0.5%.

[10] Standard procedure: A solution of 0.5 mmol (TPP)FeCl in THF was successively treated with one equivalent of AgClO$_4$ and three equivalents ($C_6H_5)_2$C=CHMgBr (0.5 M in THF). The reaction mixture was filtered, the THF removed, benzene added and washed with degassed water; the benzene was partially removed. Upon addition of pentane, the complex *(2c)* was obtained as a fine, purple powder. The crystals retain 1 mol water, as shown by the elemental analysis.

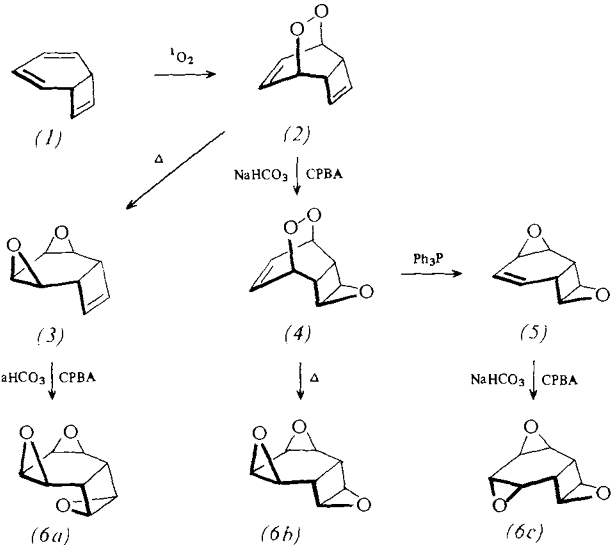
# Triepoxides of Bicyclo[4.2.0]octa-2,4,7-triene[**]

By *Waldemar Adam, Omar Cueto, Ottorino De Lucchi,*
*Karl Peters, Eva-Maria Peters*
and *Hans Georg von Schnering*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

A total of six diastereomeric triepoxides, *(6a)—(6f)* of the bicyclo[4.2.0]octa-2,4,7-triene *(1)*, a valence isomer of cyclooctatetraene, are possible. Here, we report on the diastereoselective synthesis of the triepoxides *(6a)—(6c)*. The starting material, the endoperoxide *(2)*, was prepared[2] by [4+2]-cycloaddition of singlet oxygen to the thermally labile triene *(1)*[1].

On heating a benzene solution of the endoperoxide *(2)* at 100 °C for 1 h, the diepoxide *(3)* was isolated in 80% yield[3]. Treatment of *(3)* with *m*-chloroperbenzoic acid (CPBA) in dichloromethane (25 °C, 48 h) in the presence of solid $NaHCO_3$ as buffer, afforded the triepoxide *(6a)* in 70% yield[4]. The NMR spectra did not permit an unequivocal assignment of the stereochemistry of the cyclobutane epoxide ring. X-ray structure analysis revealed, however, that the epoxidation had led to the *(6a)* isomer (Fig. 1). Dreiding models show that an *exo*-attack by CPBA should be preferred. Presumably stereoelectronic reasons must come into play to rationalize the unexpected *endo*-attack.



Epoxidation of the endoperoxide *(2)* with CPBA (25 °C, 36 h) gave the expected epoxy-endoperoxide *(4)* in 70% yield[5]. Steric reasons preclude *endo*-attack on the double bond of the four-membered ring. On heating a benzene solution of *(4)* (80 °C, 12 h) the triepoxide *(6b)* was obtained in 60% yield[6]. An X-ray structure analysis confirms the given configuration (Fig. 1).

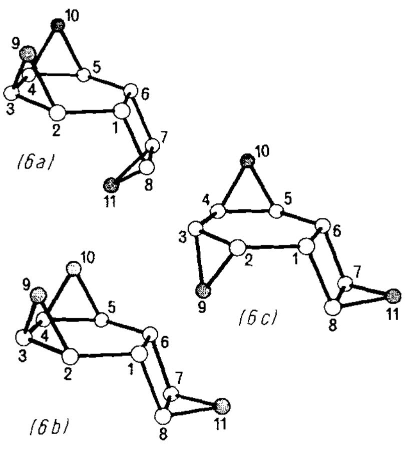
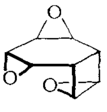
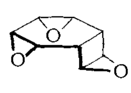


Fig. 1. Structures of *(6a)*, *(6b)* and *(6c)* in the crystal.

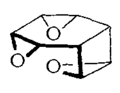
*(4)* also served as precursor in the stereoselective synthesis of the triepoxide *(6c)*; a chloroform solution of *(4)* reacts with triphenylphosphane (0 °C, 0.5 h and 25 °C, 1 h) to give the diepoxide *(5)* in 42% yield[7]. Epoxidation with CPBA (25 °C, 40 h) afforded the triepoxide *(6c)* in 60% yield[8]. An X-ray structure analysis of *(6c)* corroborated the proposed structural assignment (Fig. 1).



*(6d)*



*(6e)*



*(6f)*

By means of these diastereoselective syntheses the novel triepoxides *(6a)—(6c)* could be conveniently prepared from the endoperoxide *(2)*. For the remaining diastereomers *(6a)—(6f)* other strategies must be developed[9].

Received: January 8, 1981;
supplemented: February 11, 1981 [Z 788 IE]
German version: Angew. Chem. *93*, 618 (1981)

---

[*] Prof. Dr. W. Adam, Dr. O. Cueto, Dr. O. De Lucchi
Department of Chemistry, University of Puerto Rico
Rio Piedras, Puerto Rico 00931 (USA)

Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)
(address to which correspondence should be sent)

Prof. Dr. H. G. von Schnering, Dr. K. Peters, Dr. E.-M. Peters
Max-Planck-Institut für Festkörperforschung, Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the National Institutes of Health, the National Science Foundation and the Petroleum Research Fund.

[1] *E. Vogel, H. Kiefer, W. R. Roth*, Angew. Chem. *76*, 432 (1964); Angew. Chem. Int. Ed. Engl. *3*, 443 (1964).

[2] a) *W. Adam, O. Cueto, O. De Lucchi*, J. Org. Chem. *45*, 5220 (1980); b) all new compounds gave satisfactory elemental analyses. The reported yields are after silica gel chromatography with dichloromethane (in the case of *(4)* and *(5)* run at −10 °C) and recrystallization from a dichloromethane/*n*-alkane mixture.

[3] *(3)*: m.p. = 109–110 °C ($CH_2Cl_2$/*n*-hexane); $^1H$-NMR ($CDCl_3$, TMS): $\delta = 3.10$ (d, 2H, $J = 3$ Hz), 3.30 (s, 2H), 3.45 (d, 2H, 3 Hz), 6.20 (s, 2H); $^{13}C$-NMR ($CDCl_3$, TMS): $\delta = 39.4$ (d), 48.2 (d), 49.9 (d), 137.3 (d); IR (KBr): $\nu = 3130$, 3000, 2915, 1580, 1420, 1060, 950, 860 $cm^{-1}$.

[4] *(6a)*: m.p. = 209–210 °C ($CH_2Cl_2$/*n*-pentane); $^1H$-NMR ($CDCl_3$, TMS): $\delta = 2.81$ (s, 2H), 3.13 (m, 2H), 3.45 (m, 2H), 4.10 (s, 2H); $^{13}C$-NMR ($CDCl_3$, TMS): $\delta = 35.7$ (d), 47.9 (d), 48.4 (d), 52.1 (d); IR (KBr): $\nu = 3000$, 2980, 2940, 980, 940, 860 $cm^{-1}$.

[5] *(4)*: m.p. = 85–86 °C ($CH_2Cl_2$/*n*-hexane); $^1H$-NMR ($CDCl_3$, TMS): $\delta = 2.89$ (m, 2H), 3.58 (m, 2H), 4.77 (m, 2H), 6.73 (m, 2H); $^{13}C$-NMR ($CDCl_3$, TMS): $\delta = 39.8$ (d), 55.5 (d), 70.7 (d), 130.8 (d); IR (KBr): $\nu = 3020$, 2940, 1610, 1410, 1360, 1250, 1170, 970, 930, 890, 700 $cm^{-1}$.

[6] *(6b)*: m.p. = 160–161 °C ($CH_2Cl_2$/*n*-hexane); $^1H$-NMR ($CDCl_3$, TMS): $\delta = 2.60$ (m, 2H), 3.00 (m, 2H), 3.58 (m, 2H), 3.87 (m, 2H); $^{13}C$-NMR ($CDCl_3$, TMS): $\delta = 38.0$ (d), 47.4 (d), 48.1 (d), 54.5 (d); IR (KBr): $\nu = 2980$, 2940, 1430, 1330, 1270, 1200, 1065, 950, 940, 860, 820 $cm^{-1}$.

[7] *(5)*: liquid; $^1H$-NMR ($CDCl_3$, TMS): $\delta = 2.52$ (m, 1H), 2.83 (d, 1H, 5.7 Hz), 3.22 (m, 2H), 3.70 (t, 1H, 2.3 Hz), 3.92 (t, 1H, 2.3 Hz), 5.70 (A part of AB-system, 1H), 6.12 (B part of AB-system, 1H); IR ($CCl_4$): $\nu = 3040$, 3010, 2970, 2940, 1440, 1330, 1200, 1015, 940, 840, 825 $cm^{-1}$.

[8] *(6c)*: m.p. 83–84 °C ($CH_2Cl_2$/*n*-hexane); $^1H$-NMR ($CDCl_3$, TMS): $\delta=2.51$ (m, 2H), 3.04–3.65 (m, 4H), 3.78 (t, 1H), 4.00 (t, 1H); IR ($CDCl_3$): $\nu=3000$, 2940, 1450, 1330, 1240, 1200, 1020, 950, 860, 825 $cm^{-1}$.

[9] *W. Adam, M. Balci*, Tetrahedron *36*, 833 (1980); b) *H. Prinzbach, M. Maas, H. Fritz, G. McMullen*, Tetrahedron Lett. *21*, 4897 (1980).

---

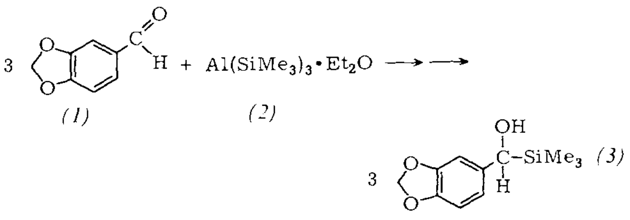
# Facile Nucleophilic Silylation Reactions at Carbonyl Functionalities Using Trimethylsilylaluminum Compounds[**]

By *Lutz Rösch, Gerald Altnau* and *Wolfgang Helmut Otto*

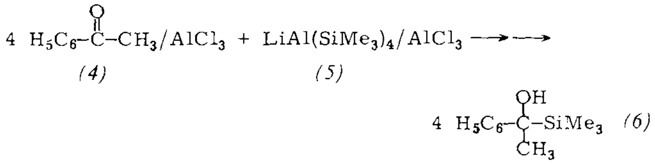
Silylated organic compounds are valuable starting materials in numerous syntheses. Hereby, the organosilyl group can assume both the function of a protecting group and in addition steer the course of the reaction. The trimethylsilyl group is most frequently used for this purpose[1]. While many effective methods for the electrophilic transfer of this group exist[2], directed nucleophilic silylation is generally only feasible with difficulty. Until now, the reagents available for this purpose—solutions of trimethylsilyl(alkali metal)[3] or bis(trimethylsilyl)mercury[4]—have been difficultly accessible and/or are only stable for short times; sometimes, the reactions are accompanied by side-reactions[5]. In contrast, trimethylsilylaluminum compounds are conveniently prepared, even in large amounts, and can be stored for long periods at room temperature under an inert gas.

It has already been shown that the reaction of such Si—Al compounds with inorganic substrates can be used to transfer trimethylsilyl groups[6]. In order to test to what extent they are also suitable for nucleophilic silylation in organic chemistry, the reaction of ether-coordinated tris(trimethylsilyl)aluminum *(2)*[7] and of lithium tetrakis(trimethylsilyl)aluminate *(5)*[8] with an aldehyde (piperonal) *(1)*, a ketone (acetophenone) *(4)*, and an ester (methyl benzoate) *(8)* was investigated. The reactions were performed in an analogous way to $LiAlH_4$ reductions, since silylation reactions of this type are readily comparable to these.

Reduction of aldehydes with $LiAlH_4$ produces primary alcohols. Reaction of piperonal *(1)* with *(5)* in diethyl ether firstly results in formation of a yellow solution; after decomposition with methanol/hydrochloric acid, removal of acid by washing and extraction, a green oil is obtained. Examination of this by thin layer chromatography reveals four products. The expected product, 3,4-methylenedioxy-α-(trimethylsilyl)benzyl alcohol *(3)*, can be isolated in 48% yield, in addition to 6.7% *(1)*, 5.8% 3,4-methylenedioxyphenyl trimethylsilyl ketone and 1.9% 3,4-methylenedioxybenzyl alcohol, by column chromatography. If the reaction is carried out with ether-coordinated tris(trimethylsilyl)aluminum *(2)*, the thin layer chromatogram reveals only one product, the desired α-silylalcohol *(3)*, which can be isolated in practically quantitative yield without recourse to separation procedures. All three trimethylsilyl groups *(2)* are transferred.



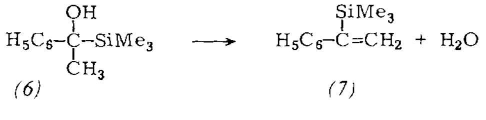
Ketones are converted to secondary alcohols by treatment with $LiAlH_4$. Acetophenone *(4)* does not react with *(5)*. This is, however, not astonishing, since *(4)* is a member of a group of ketones which are difficult to reduce and which cannot be simply reduced by $LiAlH_4$[9]. In these situations "mixed hydrides", for example the mixture $LiAlH_4$/$AlCl_3$, have been successfully used[10]. By analogy, *(4)* was coordinated with aluminum chloride and dropped into a "mixed silyl", in an ethereal solution of *(5)* and $AlCl_3$ (1:1).



$$4\ H_5C_6-\overset{O}{\overset{\|}{C}}-CH_3/AlCl_3\ +\ LiAl(SiMe_3)_4/AlCl_3 \longrightarrow 4\ H_5C_6-\underset{CH_3}{\underset{|}{\overset{OH}{\overset{|}{C}}}}-SiMe_3$$

*(4)* *(5)* *(6)*

Under these conditions the desired final product, 1-phenyl-1-(trimethylsilyl)ethanol *(6)* is formed. However, this compound is not particularly stable and decomposes quantitatively with loss of water to give α-(trimethylsilyl)styrene *(7)*.

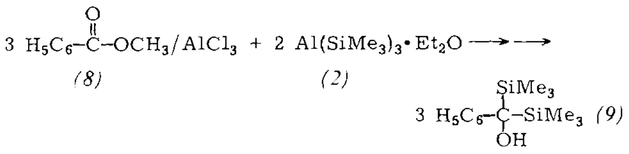


$$H_5C_6-\underset{CH_3}{\underset{|}{\overset{OH}{\overset{|}{C}}}}-SiMe_3 \longrightarrow H_5C_6-\overset{SiMe_3}{\overset{|}{C}}=CH_2\ +\ H_2O$$

*(6)* *(7)*

After drying with magnesium sulfate, the vinylsilane *(7)* can be isolated practically quantitatively. This is a particularly facile route to *(7)*. The analogous reaction of *(4)*/$AlCl_3$ with *(2)* leads to the same result.

Carboxylic acid esters are reduced by $LiAlH_4$ to primary alcohols. However, methyl benzoate *(8)* does not react with *(2)* or *(5)* or with *(5)* and $AlCl_3$. In contrast, if $AlCl_3$-coordinated *(8)* is reacted with *(2)* in boiling diethyl ether, the desired α,α′-bis(trimethylsilyl)benzyl alcohol *(9)* is obtained as the only silylated product in 79% yield after work-up.



$$3\ H_5C_6-\overset{O}{\overset{\|}{C}}-OCH_3/AlCl_3\ +\ 2\ Al(SiMe_3)_3\cdot Et_2O \longrightarrow 3\ H_5C_6-\underset{OH}{\underset{|}{\overset{SiMe_3}{\overset{|}{C}}}}-SiMe_3$$

*(8)* *(2)* *(9)*

These model reactions show that trimethylsilylaluminum compounds can be used for the nucleophilic silylation of carbonyl functionalities.

## *Procedure*

All reactions with *(2)* and *(5)* must be carried out in the abscence of air and moisture (argon as inert atmosphere).

---

[*] Priv.-Doz. Dr. L. Rösch, Dr. G. Altnau
Institut für Organische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12
Dr. W. H. Otto, Institut für Organische Chemie der Technischen Universität Berlin (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

Products were characterized by IR-, $^1$H-NMR- and mass spectroscopy.

*(3), (6), (9): (2)* or *(5)* are added to 20—30 mL $Et_2O$ and the organic component, dissolved in approximately the same volume of $Et_2O$, dropped into the mixture. (When $AlCl_3$-coordinated substances are used, the calculated quantity of $AlCl_3$ is added to the cooled substance dissolved in $Et_2O$.) After addition, the mixture is heated for 3—4 h under reflux. The mixture is subsequently cooled to room temperature, treated with 2 mL methanol and finally *ca.* 2 mL dilute HCl added until the precipitate just starts to dissolve. The solution is extracted with $Et_2O$ washed with saturated $NaHCO_3$ solution until free of acid and with saturated NaCl solution until neutral. The solution is then dried with $MgSO_4$, filtered and the solvent removed on a rotary evaporator; the desired substance remains as residue (see Table 1).

Table 1. Synthesis of compounds *(3), (6)* and *(9)*; some $^1$H-NMR data of compounds *(3), (6), (7)* and *(9)* ($\delta$-values) [a].

| Educt (6 mmol) | Al—Si Cpd. (2 mmol) | $Et_2O$ [mL] | $t$ [h] | Reaction product | Yield [%] |
|---|---|---|---|---|---|
| *(1)* | *(5)* [b] | 50 | 4 | *(3)* | 48 |
| *(1)* | *(2)* | 50 | 4 | *(3)* | 88 |
| *(4)*/$AlCl_3$ [c] | *(5)*/$AlCl_3$ [b, d] | 70 | 3 | *(6)* | 87 |
| *(4)*/$AlCl_3$ [c] | *(2)* | 70 | 3 | *(6)* | 83 |
| *(8)*/$AlCl_3$ [c] | *(2)* | 70 | 3 | *(9)* [e] | 79 |

| Cpd. | Aryl | | $^1$H-NMR | | |
|---|---|---|---|---|---|
| | (m) | O—$CH_2$—O/ $CH_3$ (s) | OH (s, br.) | $SiMe_3$ (s) | $=CH_2$ (d) |
| *(3)* | 6.65 | 5.88 | 1.80 | 0.0 | |
| *(6)* | 7.59 | 1.57 | 1.43 | 0.05 | |
| *(7)* | 7.22 | | | 0.20 | 5.82 [f] |
| *(9)* | 7.18 | | 1.22 | 0.05 | 5.62 [f] |

[a] In $CCl_4$ with $CH_3NO_2$ as lock substance. The integrated signals correspond to the composition of the respective compound. [b] 1.5 instead of 2 mmol. [c] 0.8 g $AlCl_3$. [d] 0.2 g $AlCl_3$. [e] *(9)* is rapidly oxidized by oxygen in the air to benzoic acid, and hence the work-up must be performed under a protective gas. [f] $J=3$ Hz.

*(6)→(7)*: *(6)* is allowed to stand for 12 h in a solution of $Et_2O$ containing traces of HCl; at the end of this time the solution is dried with $MgSO_4$ and filtered. After removal of ether on the rotarary evaporator, *(7)* is obtained quantitatively (see Table 1).

Received: May 30, 1980 [Z 784a IE]
German version: Angew. Chem. *93*, 607 (1981)

CAS Registry numbers:
*(1)*, 120-57-0; *(2)*, 75441-10-0; *(3)*, 78109-47-4; *(4)*, 98-86-2; *(5)*, 62465-40-1; *(6)*, 53173-00-5; *(7)*, 1923-01-9; *(8)*, 93-58-3; *(9)*, 31129-63-2

---

[1] Review: *T. H. Chan, I. Fleming*, Synthesis *1979*, 761; *G. M. Rubottom*, J. Organomet. Chem. Libr. *8*, 263 (1979).

[2] Review: *J. Y. Corey*, J. Organomet. Chem. Libr. *8*, 1 (1979).

[3] *W. C. Still*, J. Org. Chem. *41*, 3063 (1976); *H. Sakurai, F. Kondo*, J. Organomet. Chem. *117*, 149 (1976); *P. B. Dervan, M. A. Shippey*, J. Am. Chem. Soc. *98*, 1265 (1976).

[4] Reviews: *W. P. Neumann, K. Reuter*, J. Organomet. Chem. Libr. *7*, 229 (1979).

[5] Nucleophilic silylation of carbonyl functionalities is also possible with the system Li or Mg/$Me_3SiCl$/tetrahydrofuran or hexamethylphosphorus triamide, however, hereby simultaneous electrophilic transfer of trimethylsilyl groups occurs. Review: *R. Calas, J. Dunoques*, J. Organomet. Chem. Libr. *2*, 277 (1976).

[6] *L. Rösch, G. Altnau*, Angew. Chem. *91*, 62 (1979); Angew. Chem. Int. Ed. Engl. *18*, 60 (1979); *L. Rösch, G. Altnau, W. Erb, J. Pickardt, N. Bruncks*, J. Organomet. Chem. *197*, 51 (1980).

[7] *L. Rösch*, Angew. Chem. *89*, 497 (1977); Angew. Chem. Int. Ed. Engl. *16*, 480 (1977); *L. Rösch, G. Altnau*, J. Organomet. Chem. *195*, 47 (1980).

[8] *L. Rösch, G. Altnau*, Chem. Ber. *112*, 3934 (1979).

[9] *J. Broome, B. R. Brown*, Chem. Ind. (London) *1956*, 1317.

[10] *R. F. Nystrom, C. R. A. Berger*, J. Am. Chem. Soc. *80*, 2896 (1958).

## Trimethylsilylaluminium Compounds as Catalyst Components in the Polymerization of Ethene[**]

By *Lutz Rösch* and *Gerald Altnau*[*]

From the broad definition of the patent specifications, the Ziegler-Natta polymerization catalyst consists of a mixture of an alkyl-main group metal compound and a transition metal salt[1]. The combination of alkylaluminum and titanium compounds has proved to be particularly effective. Depending on the composition, the catalyst is obtained in soluble, insoluble or colloidal forms. Having recently found simple preparative routes to a series of trimethylsilylaluminum compounds, we investigated whether they were suitable for use as co-catalysts, in place of the homologous alkylaluminum derivatives, for the polymerization of ethene.

A soluble system results when dicyclopentadienyltitanium(IV) compounds are used as the metal component. Reactions with this system, however, proceed unsatisfactorily (Table 1). Uptake of ethene, in the presence of tris(trimethylsilyl)aluminum[2] or bis(trimethylsilyl)aluminum chloride[3], could not be observed, either at 20 or −25 °C. The $Cp_2Ti(Cl)Et/Al(SiMe_3)_2Cl$ and $Cp_2Ti(Cl)SiMe_3/AlEt_2Cl$ systems show only a small degree of activity; this appears to confirm the general hypothesis that for polymerization it is necessary to have a transition metal-carbon bond as the active center[4]. In the last mentioned system, it is assumed that the trimethylsilyl- and ethyl-groups exchange between the titanium[5] and aluminum compounds. The results obtained with a heterogenic catalyst system[6] of the Solvay type are also indicative of this hypothesis (Table 2). Only the $MgOTi/EtAl(SiMe_3)_2$ system, which can form a titanium-carbon bond, shows polymerization activity.

Table 1. Investigation of the polymerization of ethene with soluble catalyst systems [a].

| System | $T$ [°C] | $t$ [min] | PE [g] |
|---|---|---|---|
| $Cp_2TiCl_2/Al(SiMe_3)_2Cl$ | 20 | 60 | — |
| $Cp_2TiCl_2/Al(SiMe_3)_2Cl$ | −25 | 60 | — |
| $Cp_2TiCl_2/Al(SiMe_3)_3$ | 20 | 60 | — |
| $Cp_2TiCl_2/Al(SiMe_3)_3$ | −25 | 60 | — |
| $Cp_2TiCl/EtAl(SiMe_3)_2$ | 20 | 60 | — |
| $Cp_2Ti(Cl)Et/Al(SiMe_3)_2Cl$ | 20 | 30 | 4 |
| $Cp_2Ti(Cl)SiMe_3/AlEt_2Cl$ | 20 | 150 | 6 |

[a] PE = isolated polyethylene. Cp = cyclopentadienyl. All experiments in toluene, titanium component $10^{-3}$ mol/L, aluminum component $2\times10^{-3}$ mol/L.

---

[*] Priv.-Doz. Dr. L. Rösch, Dr. G. Altnau
Institut für Anorganische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. We thank Priv.-Doz. Dr. *G. Fink*, Technische Universität München, for discussions.

Table 2. Investigation of the polymerization of ethene with heterogeneous catalyst systems [a].

| System [6] | $T$ [°C] | $t$ [min] | PE [g] |
|---|---|---|---|
| MgOTi/Al(SiMe$_3$)$_3$ | 80 | 120 | — |
| MgOTi/EtAl(SiMe$_3$)$_2$ | 40 | 120 | 52 |
| MgOTi/Al(SiMe$_3$)$_2$Cl | 40 | 120 | — |

[a] All experiments in toluene, titanium component $10^{-3}$ mol/L, aluminum component $10^{-2}$ mol/L.

In previous investigations, the aluminum component was always used in excess. *Razuvaev et al.* reported, that tetrakis(trimethylsilyl)titanium, which decomposes at 0 °C[7], is formed from titanium tetrachloride and trimethylsilyllithium. We obtained similar results with the $TiCl_4/Al(SiMe_3)_3 \cdot Et_2O$ system. However, on the basis of the steric shielding of the four trimethylsilyl groups, a tetrakis(trimethylsilyl)titanium species should not be suitable as a catalyst. An olefin species would be offered better attacking possibilities by a partially silylated titanium compound. For this reason, an excess of titanium tetrachloride was used and because of the anticipated thermolability of the trimethylsilyl-titanium-chlorine compounds, the reactions were carried out at −30 °C. In order to avoid persilylation, the titanium tetrachloride was first placed in the flask and the aluminum component added to this in a dropwise fashion. Under these conditions uptake of ethene is observed, even in the absence of an alkylating reagent (Table 3). The activity depends on the ratio $TiCl_4/Al(SiMe_3)_3 \cdot Et_2O$, the best result to date being reached with a ratio of 5 : 2. This is the first catalyst in which, at least in the first polymerization step, a transition metal-silicon bond, instead of a transition metal-carbon bond, is present. In contrast to the usual Ziegler-Natta systems, the aluminum component is used in excess. The low temperature of the polymerization is also of note.

Table 3. Investigation of polymerization of ethene with the $TiCl_4/Al(SiMe_3)_3 \cdot Et_2O$ system [a].

| $TiCl_4$ [mol] | $Al(SiMe_3)_3 \cdot Et_2O$ [mol] | $t$ [min] | PE [g] |
|---|---|---|---|
| $1.5 \times 10^{-3}$ | $10^{-3}$ | 90 | 0.05 |
| $10^{-2}$ | $3 \times 10^{-3}$ | 120 | 1.4 |
| $10^{-2}$ | $5 \times 10^{-3}$ | 60 | 13 |
| $5 \times 10^{-3}$ | $2 \times 10^{-3}$ | 60 | 7 |
| $10^{-2}$ | $4 \times 10^{-3}$ | 60 | 23 |

[a] All experiments in pentane at −30 °C.

### *Procedure*

a) Soluble catalyst system: A solution of the titanium component in toluene is placed in a 1 L polymerization flask, a solution of the aluminum component in toluene added and ethene, at a pressure of 150 mbar, passed in. The polymerization is stopped by addition of methanol. After filtration, the polymerizate is washed with methanol, containing a few mL conc. hydrochloric acid, and dried using an oil pump vacuum.

b) Heterogenic catalyst system: Both catalyst components are allowed to pre-react under a protective gas atmosphere in a 50 mL flask. After 30 min, the mixture is added to a 1 L polymerization flask and treated as described in a).

c) The $TiCl_4/Al(SiMe_3)_3 \cdot Et_2O$ system. A solution of $TiCl_4$ in pentane is placed in a 300 ml cold-jacketed flask, the mixture cooled to −30 °C and saturated with ethene. Finally, a solution of $Al(SiMe_3)_3 \cdot Et_2O$ in pentane is injected into the flask *via* a serum cap. The ethene pressure is 150 mbar. Termination and work-up follows, as described in a).

Received: July 17, 1980 [Z 784b IE]
German version: Angew. Chem. *93*, 608 (1981)

CAS Registry numbers:
ethene, 74-85-1; $Al(SiMe_3)_2Cl$, 77944-77-5; $Al(SiMe_3)_3$, 65343-66-0; $AlEt_2Cl$, 96-10-6; $EtAl(SiMe_3)_2$, 77944-78-6

---

[1] Beginning with DRP 487727 (1930), ending with Belg. Pat. 527736 (1954). From 1927—1954 *K. Ziegler et al.* published *ca.* 32 articles and patent specifications.

[2] *L. Rösch*, Angew. Chem. *89*, 497 (1977); Angew. Chem. Int. Ed. Engl. *16*, 480 (1977); *L. Rösch, G. Altnau*, J. Organomet. Chem. *195*, 47 (1980).

[3] Prepared by stoichiometric reaction of $Al(SiMe_3)_3 \cdot Et_2O$ with $AlCl_3$ in pentane.

[4] *J. Boor:* Ziegler-Natta Catalysts and Polymerizations. Academic Press, New York 1979.

[5] *L. Rösch, G. Altnau, W. Erb, J. Pickardt, N. Bruncks*, J. Organomet. Chem. *197*, 51 (1980).

[6] A magnesium-fixed catalyst, prepared by reaction of titanium tetrachloride with magnesium di(ethanolate) in hexane at 60 °C, was used. We thank Prof. Dr. *K.-H. Reichert*, Technische Universität Berlin, for a sample of this catalyst.

[7] *G. A. Razuvaev, V. N. Latyaeva, L. I. Vyshinskaya, A. V. Malysheva, G. A. Vasil'eva*, Dokl. Akad. Nauk SSSR *237*, 605 (1977).

---

## Novel Molecules of the Phane-type with *p*-Benzoquinone and Oxahomobenzene Moieties[**]

By *Ihsan Erden, Peter Gölitz, Reinhard Näder,*
and *Armin de Meijere*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

In the search for organic compounds with electrical conductivity[1], attention has recently been focussed on molecules having intramolecular charge-transfer interactions[2]. In the known syntheses of phane-type bridged donor-acceptor complexes, the functional groups have frequently been introduced at a precursor stage. We describe here a three-step synthesis of the [2.2]paracyclophanedienemonoquinone *(5)* *via* functionalization of the hydrocarbon *(1)*[3]. The key intermediate, the endoperoxide *(2)*, also serves as starting material for bridged oxahomobenzenes such as *(8)* and *(9)*, which are also suitable as model compounds for the study of intramolecular interactions.

In view of the fact that singlet oxygen[4a] or other dienophiles[4] add to cyclophanes with sufficiently deformed benzene rings, the conveniently accessible [2.2]paracyclophanediene *(1)*[3] was photooxygenated ($CHCl_3$ solution, tetraphenylporphyrin (TPP), Na-vapor lamp) at 30—40 °C. After 16 h, *(1)* had completely reacted[5]; pure *(2)* was isolated in 74% yield by chromatography on silica gel. Table 1 contains the $^1$H-NMR data of all new compounds.

---

[*] Prof. Dr. A. de Meijere, Dr. I. Erden, Dr. P. Gölitz, Dr. R. Näder
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

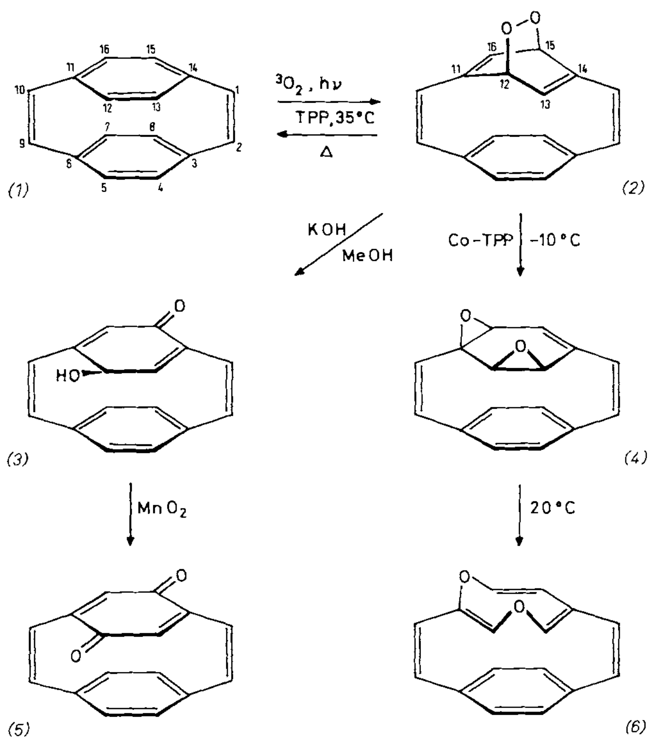


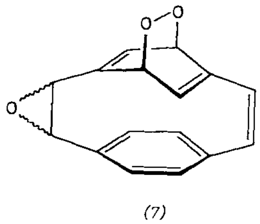
Table 1. 270 MHz $^{1}$H-NMR data of the novel compounds ($\delta_{TMS}$, coupling constants in Hz). With the exception of *(4)* and *(7)* all new compounds were also characterized by IR spectroscopy and elemental analysis.

| | |
|---|---|
| *(1)* | (CDCl$_3$): 6.50 (s, 4(5,7,8,12,13,15,16)-H); 7.19 (s, 1(2,9,10)-H) |
| *(2)* | (CDCl$_3$): 4.78 (dd, 12(15)-H, $^{3}J$=6.2, $^{4}J$=2.0); 5.93 (ddd, 13(16)-H, $^{3}J$=6.2, $^{4}J_1$=2.0, $^{4}J_2$=2.0); 6.28 (dd, 1(10)-H, $^{3}J$=10.3, $^{4}J$=2.0); 6.95 (2 d, 4(5,7,8)-H); 7.07 (d, 2(9)-H, $^{3}J$=10.3) |
| *(3)* | (CDCl$_3$): 4.01 (d, 12-H, $^{3}J$=5.8); 5.36 (br. s, 16-H); 5.99 (dd, 13-H, $^{3}J$=5.8); 6.48 (dd, 1-H, $^{3}J$=10.8); 6.75 (dd, 2-H, $^{3}J$=10.8); 6.78—7.30 (m, 4(5,7,8,9)-H); 7.16 (dd, 10-H, $^{3}J$=9.9) |
| *(4)* | (CD$_2$Cl$_2$): 2.83 (dd, 12-H, $^{3}J$=3.2, $^{4}J$=1.6); 3.01 (d, 16-H, $^{3}J$=5.0); 3.14 (dd, 13-H, $^{3}J$=3.2, $^{4}J$=0.9); 5.27 (d, 15-H, $^{3}J$=5.0); 6.19 (d, 10-H, $^{3}J$=10.1); 6.63 (dd, 1-H, $^{3}J$=10.1, $^{4}J$=1.6); 6.89—7.11 (m, 4(5,7,8)-H); 7.19, 7.26 (2 d, 2(9)-H, $^{3}J$=10.1) |
| *(5)* | (CDCl$_3$): 6.19 (d, 13(16)-H); 7.00 (dd, 1(10)-H, $^{3}J$=10.8); 7.24 (br. s, 4(5,7,8)-H); 7.65 (d, 2(9)-H, $^{3}J$=10.8) |
| *(6)* | (CDCl$_3$): 4.02 (d, 15-H, $^{3}J$=8.5); 5.70 (d, 12-H, $^{4}J$=1.5); 5.79 (d, 16-H, $^{3}J$=8.5); 5.90 (d, 13-H, $^{4}J$=1.5); 6.03 (dd, 10-H (or 1-H), $^{3}J$=9.8, $^{4}J$=1.6); 6.59 (dd, 1-H (or 10-H), $^{3}J$=9.8, $^{4}J$=1.0); 6.90—7.10 (m, 4(5,7,8)-H); 7.21 (d, 2-H (or 9-H), $^{3}J$=9.8); 7.32 (d, 9-H (or 2-H), $^{3}J$=9.8) |
| *(7)* | (CDCl$_3$): 3.67 (dd, 10-H, $^{3}J$=3.8, $^{4}J$=1.5); 4.46 (d, 9-H, $^{3}J$=3.8); 4.66 (ddd, 12(15)-H); 5.56 (ddd, 16-H); 6.13 (ddd, 13-H); 6.28 (dd, 1-H, $^{3}J$=10.0, $^{4}J$=2.0); 6.81—7.26 (m, 2(4,5,7,8)-H) |
| *(8)* | (CD$_2$Cl$_2$): 3.54 (d, 16-H, $^{3}J$=3.4); 4.18 (ddd, 12-H, $^{3}J$=7.0, $^{4}J_1$=1.2, $^{4}J_2$=1.2); 4.44 (m, 15-H); 5.58 (ddd, 13-H, $^{3}J$=7.0, $^{4}J_1$=1.9, $^{4}J_2$=1.9); 5.87 (d, 10-H, $^{3}J$=10.6); 6.16 (dd, 1-H, $^{3}J$=9.8, $^{4}J$=1.9); 6.90–7.37 (m, 2(4,5,7,8,9)-H) |
| *(9)* | (CD$_2$Cl$_2$): 2.79, 2.80 (2s, 12(13,15,16)-H); 6.11 (d, 1(10)-H, $^{3}J$=10.0); 7.07, 7.19 (2 d, 4(5,7,8)-H); 7.29 (d, 2(9)-H, $^{3}J$=10.0) |

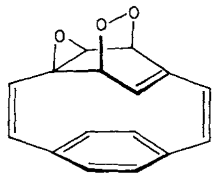
*(2)* is stable at room temperature; however, above 100 °C it cleaves to give the starting material *(1)*. Reaction of *(2)* with potassium hydroxide in methanol[4a] produced the ketol *(3)* in 65% isolated yield, which was oxidized by freshly prepared manganese dioxide in chloroform to the quinone *(5)* (yield 90%).

In the presence of catalytic amounts of cobalt-*meso*-tetraphenylporphyrin (Co-TPP), a solution of the endoperoxide *(2)* in dichloromethane, even at −10 °C, completely rearranges within a few minutes to the bisepoxide *(4)*[6]. *(4)* could be unequivocally characterized by $^{1}$H-NMR spectroscopy (see Table 1), however, it isomerizes rapidly at room temperature ($\tau_{1/2}$ (20 °C) ≈ 80 min) to the dioxocin *(6)*, in a process known for dioxa-bis-σ-homobenzene[7], so that only pure *(6)* could be obtained by column chromatography at room temperature.

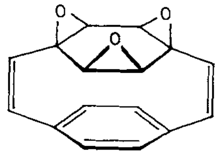
*(2)* can be smoothly epoxidized with *p*-nitroperoxybenzoic acid in dichloromethane, in the presence of sodium carbonate, to a mixture of *(7)* and *(8)* (ratio 1 : 9 from $^{1}$H-NMR). Treatment of the major product *(8)* with Co-TPP at room temperature leads, practically quantitatively, to the phane-type bridged *cis*-benzene trioxide, *cis*-trioxa-tris-σ-homobenzeno-[2,2]paracyclophane-1,9-diene *(9)*. The $^{1}$H-NMR spectrum (see Table 1) of the product *(9)*, which is either insoluble or only slightly soluble in all common organic solvents, shows only six signals, as expected. Like the unbridged *cis*-benzene trioxide[8], *(9)* is stable up to 150 °C; however, it does not melt without decomposition, and attempts to purify it by chromatography on silica gel also lead to its decomposition. In its general appearance, the UV spectrum of *(5)* with maxima at 275, 295 and 340 (sh) nm is similar to that of the already known quinone derived from [2.2]paracyclophane[9]. The UV spectrum of the bridged dioxocin *(6)* shows an absorption at 276 nm with a long wavelength branch out to ≈ 390 nm.



*(7)*



*(8)*



*(9)*

Received: November 28, 1980 [Z 781 IE]
German version: Angew. Chem. *93*, 605 (1981)

CAS Registry numbers:
*(1)*, 6572-60-7; *(2)*, 77944-50-4; *(3)*, 77944-51-5; *(4)*, 77944-52-6; *(5)*, 77944-53-7; *(6)*, 77944-54-8; *(7)*, 77944-55-9; *(8)*, 77944-56-0; *(9)*, 77944-57-1;

---

[1] *E. P. Goodings*, Chem. Rev. *5*, 95 (1976); *J. B. Torrance*, Acc. Chem. Res. *12*, 79 (1979); cf. *M. Hanack*, Nachr. Chem. Tech. Lab. *28*, 132 (1980).

[2] a) *H. A. Staab, J. Ippen, C. Tao-pen, C. Krieger, B. Starker*, Angew. Chem. *92*, 49 (1980); Angew. Chem. Int. Ed. Engl. *19*, 66 (1980); *J. Ippen, C. Tao-pen, B. Starker, D. Schweitzer, H. A. Staab, ibid. 92*, 51 (1980); *19*, 67 (1980); b) *K. Yamamura, T. Nakazawa, I. Murata, ibid. 92*, 565 (1980); *19*, 543 (1980); *T. Nakazawa, Y. Niimoto, K. Kubo, I. Murata, ibid. 92*, 566 (1980); *19*, 545 (1980); c) *H. Tatemitsu, B. Natsume, M. Yoshida, Y. Sakata, S. Misumi*, Tetrahedron Lett. *1978*, 3459, and literature cited therein; d) *H. A. Staab, G. H. Knaus, ibid. 1979*, 4261, and literature cited therein.

[3] a) *K. C. Dewhirst, D. J. Cram*, J. Am. Chem. Soc. *80*, 3115 (1958); b) *R. Näder*, Dissertation, Universität Göttingen 1978.

[4] a) *R. Gray, V. Boekelheide*, J. Am. Chem. Soc. *101*, 2128 (1979); b) *A. F. Murad, J. Kleinschroth, H. Hopf*, Angew. Chem. *92*, 388 (1980); Angew. Chem. Int. Ed. Engl. *19*, 389 (1980).

[5] [2.2]Paracyclophane does not react with singlet oxygen under the same reaction conditions.

[6] *J. D. Boyd, C. S. Forte, D. K. Imakawa*, J. Am. Chem. Soc. *102*, 3641 (1980).

[7] *H.-J. Altenbach, E. Vogel*, Angew. Chem. *84*, 985 (1972); Angew. Chem. Int. Ed. Engl. *11*, 937 (1972); *E. Vogel, J.-J. Altenbach, E. Schmidbauer, ibid. 85*, 862 (1973); *12*, 838 (1973).

[8] *R. Schwesinger, H. Prinzbach*, Angew. Chem. *84*, 990 (1972); Angew. Chem. Int. Ed. Engl. *11*, 942 (1972); *E. Vogel, H.-J. Altenbach, C.-D. Sommerfeld, ibid. 84*, 986 (1972); *11*, 939 (1972); *R. Schwesinger, H. Fritz, H. Prinzbach*, Chem. Ber. *112*, 3318 (1979).

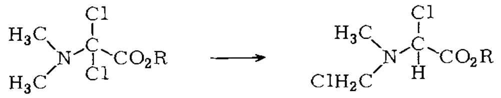
[9] *D. J. Cram, A. C. Day*, J. Org. Chem. *31*, 1227 (1966).

## A Novel Method of CC-Bond Formation: Thermolytic Elimination of Sulfur and Hydrogen Halides from α-Halosulfides[**]

By *Jean-Claude Pommelet, Claire Nyns, Francis Lahousse, Robert Merényi*, and *Heinz G. Viehe*[*]

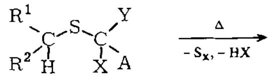
In a previous communication we reported an unusual 1,3-migration of chlorine atoms bonded to C atoms bearing *capto-dative (cd)* substituents[1]. The intramolecular Cl,H-disproportionation of *(1)* to *(2)*[2] may proceed in a similar manner to the reaction of oxamide chloride to the trichloroimidazolium salt[3]. We now describe attempts to extend this type of reaction to α-halosulfides *(3)*; hereby the acrylic acid derivatives *(4)* were unexpectedly obtained *via* HX- and $S_x$-elimination reactions.

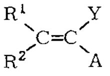
*(1)*



*(2)*

*(3)*





*(4)*

The educts *(3)* were obtained by reaction of the thiols (or thiolates) *(5)* with the halogen compounds *(6)* to give the sulfides *(7)*, and their subsequent halogenation with $SO_2Cl_2$ or $Br_2$ (Table 1).

$$\underset{(5)}{R^1R^2CH{-}SH} + \underset{(6)}{XCH_2{-}A} \longrightarrow \underset{(7)}{R^1R^2CH{-}S{-}CH_2{-}A} \xrightarrow[\text{or } Br_2(h\nu)]{SO_2Cl_2} (3)$$

Table 1. Yields and $^1$H-NMR data for the sulfides *(3)*.

| *(3)* | X | R$^1$ | R$^2$ | A | Y | Yield relative to *(6)* [%] | $^1$H-NMR (δ-values, $CDCl_3$) |
|---|---|---|---|---|---|---|---|
| *(a)* | Cl | $C_6H_5$ | H | $CO_2CH_3$ | Cl | 74 | 3.80 (s, 3 H), 4.21 (s, 2 H), 7.23 (s, 5 H) |
| *(b)* | Cl | H | H | $CO_2CH_3$ | Cl | 48 | 2.52 (s, 3 H), 3.94 (s, 3 H) |
| *(c)* | Cl | $CH_3$ | H | $CO_2C_2H_5$ | Cl | 65 | 1.35 (t, 3 H), 1.38 (t, 3 H), 3.0 (q, 2 H), 4.30 (q, 2 H) |
| *(d)* | Cl | $CH_3$ | $CH_3$ | $CO_2CH_3$ | Cl | 38 | 1.43 (d, 6 H), 3.58 (sept, 1 H, *J* = 7.0 Hz), 3.96 (s, 3 H) |
| *(e)* | Br | H | H | $CO_2CH_3$ | Br | 42 | 2.56 (s), 3.97 (s) |
| *(f)* | Br | $C_6H_5$ | H | $CO_2CH_3$ | H | 79 | 3.70 (s, 3 H), 3.95 (s, 2 H), 5.18 (s, 1 H), 7.23 (s, 5 H) |
| *(g)* | Br | $CH_3$ | H | $CO_2C_2H_5$ | H | 71 | 1.37 (2t, 6 H), 2.88 (q, 2 H), 4.3 (q, 2 H), 5.44 (s, 1 H) |
| *(h)* | Cl | $CH_3$ | H | CN | Cl | 47 | 1.43 (t, 3 H), 3.13 (q, 2 H) |
| *(i)* | Cl | H | H | $COC_6H_5$ | Cl | 90 | 2.55 (s, 3 H), 7.3–7.6 (m, 3 H), 8.25 (m, 2 H) |
| *(j)* | Br | H | H | $CO_2CH_3$ | H | 40 | 2.35 (s, 3 H), 3.83 (s, 3 H), 5.48 (s, 1 H) |

Table 2. Yields and pyrolysis temperatures for the synthesis of *(4)*, together with selected spectroscopic data of *(4)*.

| *(4)* | | *T* [°] | Yield [h] [%] | $^1$H-NMR (δ-values, $CCl_3$) R$^1$ | R$^2$ | A | $J_{R^1R^2}$ [Hz] | IR [cm$^{-1}$] |
|---|---|---|---|---|---|---|---|---|
| *(a)* | *Z*<br>*E* [a] | 490 | 53 | 7.3-7.5 (m, 3 H),<br>7.8 (m, 2 H)<br>7.86 (s) | 7.98 (s)<br>7.3–7.5 (m, 3 H),<br>7.8 (m, 2 H) | 3.93 (s)<br>3.88 (s) | — | 1715 (s), 1620 (w)<br>1715 (s), 1620 (w) |
| *(b)* [b] | | 490 | 62 | 5.96 (d) | 6.50 (d) | 3.83 (s) | 1.5 | 1730 (s), 1615 (w) |
| *(c)* [b] | *Z*<br>*E* [a] | 530 | 40 | 2.07 (d)<br>6.43 (q) | 7.06 (q)<br>1.95 (d) | 1.37 (t),<br>4.22 (q) | 6.9<br>7.3 | |
| *(d)* [b] | | 540 | 18 | 2.02 (s) | 2.27 (s) | 3.72 (s) | — | |
| *(e)* | | 420 | 49 [c] | 6.32 (d) | 7.02 (d) | 3.90 (s) | 1.7 | 1735 (s), 1620 (w) |
| *(f)* | *E* | 510 | 72 | 7.3–7.5 (m) | 7.62 (d) [d] | 3.79 (s) | — | 1710 (s), 1640 (m),<br>980 (m) |
| *(g)* | *E* | 480 | 43 [e] | 1.90 (d) | 7.02 (d, q) [f] | 1.30 (t),<br>4.21 (q) | 6.7 | |
| *(h)* | *Z*<br>*E* [a] | 550 | 24 | 1.97 (d)<br>6.54 (q) | 6.65 (q)<br>2.02 (d) | — | 6.7<br>7.0 | 2230 (m), 1620 (w) |
| *(i)* | | 510 | 27 [g] | 6.02 (d) | 6.22 (d) | 7.3–7.9 | 1.8 | |
| *(j)* | | 510 | 5 | — | — | — | — | |

[a] R$^1$ and R$^2$ are exchanged. [b] In $CCl_4$. [c] By-product: HBr adduct to *(4e)* [$^1$H-NMR: δ = 3.75, 3.92, and 4.53 (each 1 H)]. [d] Y = H, δ = 6.38 (d, *J* = 15.0 Hz). [e] By-product: HBr adduct to *(4g)* [$^1$H-NMR: δ = 1.75 (d, 3 H), 2.81 (m, 1 H), 2.89 (m, 1 H), 4.44 (m, 1 H)]. [f] Y = H, δ = 5.87 (d, q, *J* = 15 Hz and 1.3 Hz). [g] By-product: HCl adduct to *(4i)* [$^1$H-NMR: δ = 3.86, 4.21, 5.26 (each 1 H)]. [h] Including HX adducts.

The sulfides *(3)* are—in contrast to the chlorides *(1)*—stable at room temperature; however, in every case, acrylic esters or acrylic nitriles are formed upon gas phase thermolysis (Table 2).

The transformation of *(3)* into *(4)* is similar to the Ramberg-Bäcklund rearrangement[4], by means of which α-halosulfones (or -sulfoxides) react with bases to give alkenes; this process involves intermediate thiirane 1,1-dioxides (or

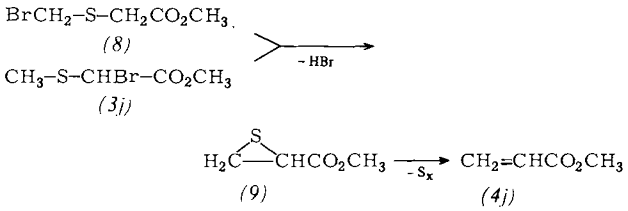
---

[*] Dr. J. C. Pommelet
Laboratoire de Chimie Organique Physique UER Sciences
BP 347, F-51062 Reims Cedex (France)
Prof. Dr. H. G. Viehe [*], Dipl.-Chem. C. Nyns, F. Lahousse, Dipl.-Ing. R. Merényi
Université de Louvain, Laboratoire de Chimie Organique
Place L. Pasteur 1, B-1348 Louvain-la-Neuve (Belgium)

[**] Prof. *C. Wentrup*, Marburg, is thanked for helpful discussions. This work was supported by the Fonds National de la Recherche Scientifique and by the Service de Programmation de la Politique Scientifique.

1-oxides). Furthermore, α-chlorodibenzyl- or α-chlorobis(benzoylmethyl)sulfides also yield the corresponding olefins upon treatment with bases[5].

The transformation of *(3)* into *(4)* may proceed *via* a thiirane such as *(9)*, which then loses a sulfur atom[6]. These thiiranes are either directly formed from *(3)* by elimination of HX or *via* a prior disproportionation step from compounds such as *(8)*: both *(8)* and *(3j)* react thermally to give the methyl acrylate *(4j)*.



It is interesting to note further the formation of 1,1-dichloroethene from trichloromethyl(methyl) sulfide (3k), $R^1 = R^2 = H$, $X = Y = A = Cl$.

*Procedure*

Solutions or pure samples of the sulfides *(3)* were vaporized at the top of an electrically heated quartz column filled with quartz beads. The temperature was held constant during the pyrolysis; the pressure at the foot of the column was maintained between $2 \times 10^{-2}$ and 16 torr. Products were condensed at −195 °C and analyzed both before and after distillation and separation.

Received: December 18, 1980 [Z 772 IE]
German version: Angew. Chem. 93, 594 (1981)

CAS Registry numbers:
*(3a)*, 53910-20-6; *(3b)*, 77825-46-8; *(3c)*, 77825-47-9; *(3d)*, 77825-48-0; *(3e)*, 77825-49-1; *(3f)*, 77825-50-4; *(3g)*, 73786-10-4; *(3h)*, 77825-51-5; *(3i)*, 18624-83-4; *(3j)*, 77825-52-6; *(E)-(4a)*, 14737-94-1; *(Z)-(4a)*, 14737-95-2; *(4b)*, 80-63-7; *(E)-(4c)*, 77825-53-7; *(Z)-(4c)*, 77825-54-8; *(4d)*, 77825-55-9; *(4e)*, 4519-46-4; *(E)-(4f)*, 1754-62-7; *(E)-(4g)*, 623-70-1; *(E)-(4g)* HBr, 77825-56-0; *(E)-(4h)*, 41866-37-9; *(Z)-(4b)*, 41866-36-8; *(4i)*, 19233-44-4; *(4i)* HCl, 77825-57-1; *(4j)*, 96-33-3

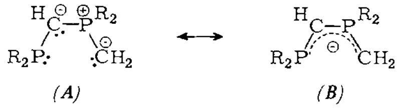
---

[1] a) *H. G. Viehe, R. Merényi, L. Stella, Z. Janousek*, Angew. Chem. *91*, 982 (1979); Angew. Chem. Int. Ed. Engl. *18*, 917 (1979); b) *L. Stella, Z. Janousek, R. Merényi, H. G. Viehe, ibid. 90*, 741 (1978) and *17*, 691 (1978).
[2] *F. Huys, R. Merényi, Z. Janousek, L. Stella, H. G. Viehe*, Angew. Chem. *91*, 650 (1979); Angew. Chem. Int. Ed. Engl. *18*, 615 (1979).
[3] *Z. Janousek, F. Huys, L. René, M. Masquelier, L. Stella, H. G. Viehe*, Angew. Chem. *91*, 651 (1979); Angew. Chem. Int. Ed. Engl. *18*, 616 (1979).
[4] *L. A. Paquette*, Org. Reac. *25*, 1 (1977).
[5] *R. H. Mitchell*, Tetrahedron Lett. *1973*, 4398; *K. Oka*, Heterocycles *12*, 461 (1979).
[6] *M. Sander*, Chem. Rev. *66*, 297 (1966).

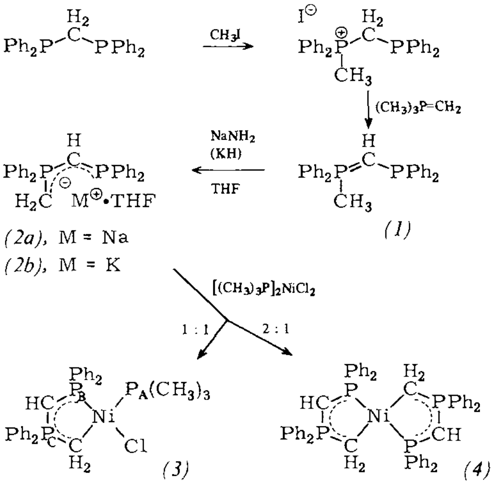
## A Novel Ylidic Organophosphorus Ligand[**]

By *Hubert Schmidbaur, Ulrich Deschler*, and
*Beatrix Milewski-Mahrla*[*]

Coordination chemistry, using organophosphorus ligands in their numerous variations, has retained its interest for over 40 years[1a,b]. We now wish to report on a chelate system in which the traditional donor function of a tertiary phosphane is intimately bound to the structural elements of a phosphorus ylide. As represented in a simplified way in formula *(A)*, a particularly robust ensemble is formed by the alternate attachment of two carbanions and a phosphonium center at the phosphane, which can be better described by the charge delocalization shown in *(B)*.


*(A)* *(B)*

In this arrangement the preferred donor properties of phosphanes[1] and ylides[1c] are particularly effectively combined, because the charge density on phosphorus is increased *via* the bridging carbanion without affecting the terminal carbanion function. Methyl(diphenyl)phosphonio(diphenylphosphino)methanide *(1)*, which is readily accessible by several different methods[2], can be converted into the alkali metal complexes *(2)* by treatment with $NaNH_2$ or KH in tetrahydrofuran (THF) with concomitant formation of $NH_3$ or $H_2$, respectively. These complexes crystallize as 1 : 1-adducts with the solvent and are characterized in solution by $^1$H-, $^{13}$C- and $^{31}$P-NMR spectroscopy[3]. Their structure in solution can be described as ion-pairs which show clear influence of the metal cation on the anion[4a]; in the solid state it should correspond to the principle recently determined by X-ray crystallography for benzylphosphonio-analogues[4].



*(2a)*, M = Na
*(2b)*, M = K
*(1)*
*(3)*
*(4)*

The alkali metal precursors *(2)* for the synthesis of the transition metal complexes do not have to be isolated, but can be reacted *in situ* with metal halides. Thus, the reaction with dry $[(CH_3)_3P]_2NiCl_2$ in the molar ratio 1 : 1 first gives, after separation of NaCl (KCl) and release of one of the two $(CH_3)_3P$-ligands, the orange brown complex *(3)*, m.p. = 192 °C, which is somewhat air and moisture sensitive. The broadening of the signals for $P_A$ and $P_B$, in the $^{31}$P-NMR spectrum of solutions of *(3)* in THF, indicates a $(CH_3)_3P$-exchange process ($\delta P_A = -13.5$, br; $\delta P_B = 28.7$, br. d, $^2J(P_BP_C) = 164.8$ Hz; $\delta P_C = 48.6$, d)[5].—Reaction of *(2)* with $[(CH_3)_3P]_2NiCl_2$ in the molar ratio 2 : 1 yields the complex *(4)* directly, which when formed from *(2a)* tenaciously retains NaCl; in contrast, it is readily obtained free

---

[*] Prof. Dr. H. Schmidbaur, Dipl.-Chem. U. Deschler, Dipl.-Chem. B. Milewski-Mahrla
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and by Hoechst AG.

of salt as lemon yellow crystals m.p. = 247 °C from *(2b)*. *(4)* is practically insensitive to air and moisture, but rapidly decomposes in methanol. The EI-mass spectrum shows the ion of highest mass at $m/z = 853$ ($M^+ - {}^{59}Ni$) which supports a monomeric formulation. The complex $^{31}P$-NMR spectrum, which can only be simulated with a set of data taking into account a strong *trans*= $P_AP_{A'}$ coupling through the nickel atom, indicates that *(4)* has a *trans*-structure (Fig. 1).

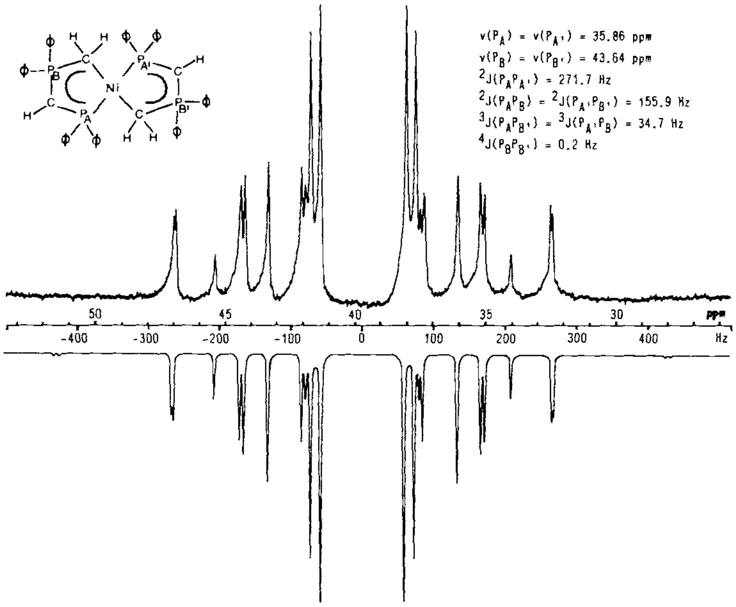


Fig. 1. Experimental and calculated $^{31}P\{^1H\}$-NMR spectra of *(4)* (in THF at 30 °C).

The X-ray structure analysis[6] confirms the square planar environment of the Ni atom in the diamagnetic complex *(4)* and provides important bond length criteria, which substantiate the concept of extensive charge equalization in the ligands. All three PC bond lengths in the ring (170—177 pm, standard deviation 0.6 pm) correspond to double bond character (standard values are 165 pm for P=C and 188 pm for P—C[7]). All PNiC-angles are approximately 90°. The unusually small PCP-angles of 108.1(3)° are caused by deformation of the five-membered rings in the centrosymmetric molecule, due to the square planar configuration of the metal center.

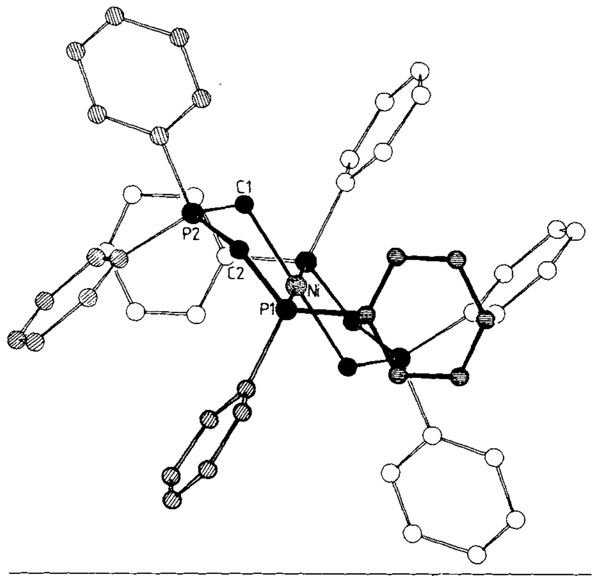
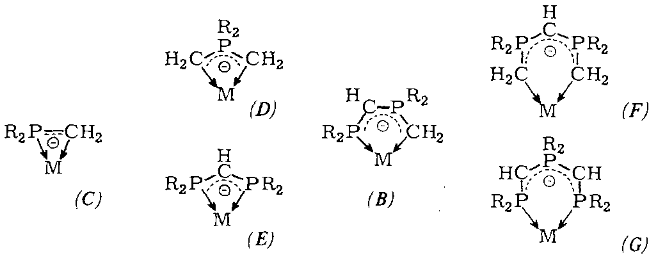


Fig. 2. Molecular structure [6] of the nickel complex *(4)*. Most important bond lengths [pm] and angles [°]: Ni—P1 221.0(2), P1—C2 174.1(6), C2—P2 170.3(6), P2—C1 177.2(7), C1—Ni 201.2(6); C1—Ni—P1 90.1(2), Ni—P1—C2 108.3(2), P1—C2—P2 108.1(3), C2—P2—C1 106.6(3), P2—C1—Ni 109.3(3).

Ni(II) complexes with two phosphanes and two alkyl or aryl ligands are considerably less stable than *(4)* and rapidly decompose both thermally and by the action of oxygen and water[8]. The chelate system *(B)* extends the known series of $P_mC_n$-ligands *(C)*—*(F)*[1c, 9].



### Procedure

$CH_3(C_6H_5)_2P{=}CHP(C_6H_5)_2$ (2 g, 5 mmol) is dissolved in 30 cm³ THF and heated under reflux with $NaNH_2$ (0.4 g, 10 mmol) for 3 d. After filtration, concentration of the filtrate to 10 cm³ and addition of pentane, 2.1 g *(2a)* (85%) precipitates. By analogy, 2.3 g *(2b)* (90%) is formed using KH.—The filtered reaction mixtures can be further reacted directly. Thus, 1.7g of complex *(3)* (60%) is formed from $[(CH_3)_3P]_2NiCl_2$ (1.41 g, 5 mmol) after heating for 5 h at 65 °C in 25 cm³ THF. *(4)* (1.9 g) (45%) is produced from 10 mmol *(2b)* and 1.41 g $[(CH_3)_3P]_2NiCl_2$. In contrast 10 mmol *(2a)* first gives 2.8 g yellow crystalline product (57% from THF/pentane), containing exactly 2 equivalents NaCl; repeated recrystallization from THF/toluene gives pure *(4)*.

Received: October 30, supplemented December 15, 1980 [Z 775 IE]
German version: Angew. Chem. *93*, 598 (1981)

CAS Registry numbers:
*(1)*, 28926-68-3; *(2a)*, 78004-86-1; *(2b)*, 78004-85-0; *(3)*, 78004-84-9; *(4)*, 78004-83-8; $[(CH_3)_3P]_2NiCl_2$, 19232-05-4

---

[1] a) *J. Chatt, F. G. Mann*, J. Chem. Soc. *1939*, 1622; b) *G. Booth*, Adv. Inorg. Chem. Radiochem. *6*, 1 (1964); *C. A. McAuliffe:* Transition Metal Complexes of Phosphorus, Arsenic and Antimony Ligands, Elsevier, New York 1979; c) *H. Schmidbaur*, Pure Appl. Chem. *52*, 1057 (1980); *50*, 19 (1978); Acc. Chem. Res. *8*, 62 (1975).

[2] a) *M. S. Hussain, H. Schmidbaur*, Z. Naturforsch. *B 31*, 721 (1976); *K. Issleib, H. P. Abicht*, J. Prakt. Chem. *312*, 456 (1970); *K. Issleib, R. Lindner*, Justus Liebigs Ann. Chem. *699*, 40 (1966); *707*, 120 (1967); b) *H. Schmidbaur, W. Tronich*, Chem. Ber. *101*, 3545 (1968); *H. Schmidbaur, A. Wohlleben-Hammer, ibid. 112*, 510 (1979); c) *R. Appel, G. Erbelding*, Tetrahedron Lett. *30*, 2689 (1978).

[3] $^{31}P$-NMR (THF/$C_6D_6$): $\delta P^V = 31.8$, d, $^2J(PP) = 128.2$ Hz; $\delta P^{III} = -16.3$, d. $^{13}C$-NMR: $\delta CH_2 = -2.44$, dd, $^1J(PC) = 65.4$, $^3J(PC) = 25.4$ Hz; $\delta CH = 14.69$, dd, $^1J(PC) = 134.8$ and 13.6 Hz. The values are considerably different for *(2b)*, which is indicative of the influence of coordination to the metal: $\delta P^V = 26.7$ (128.2); $\delta P^{III} = -16.6$; $\delta CH_2 = 2.57$ (76.2 and 16.6); $\delta CH = 15.24$ (126.9 and 4.9).

[4] a) *H. Schmidbaur, U. Deschler, B. Milewski-Mahrla, B. Zimmer-Gasser*, Chem. Ber. *114*, 608 (1981); b) *H. Schmidbaur, U. Deschler, B. Zimmer-Gasser, D. Neugebauer, U. Schubert, ibid. 113*, 902 (1980).

[5] $^1$H-NMR spectrum of *(3)* (in THF): $\delta CH_2 = 1.2$, d, $^2J(PH) = 9$ Hz; $\delta CH = 1.6$, d, $^2J(PH) = 6$ Hz; $\delta CH_3 = 1.55$, br.

[6] Triclinic crystals (from THF/pentane), space group $P\bar{1}$, $a = 988.7(3)$, $b = 1035.7(3)$, $c = 1218.9(3)$ pm, $\alpha = 106.09(2)$, $\beta = 83.93(2)$, $\gamma = 114.54(2)°$, $V = 1090.9(5) \cdot 10^6$ pm$^3$, $\rho_{calc} = 1.30$ g cm$^{-3}$; $C_{52}H_{46}P_4Ni$. Syntex P2$_1$/XTL, room temperature, $2° \leq 2\Theta \leq 48°$, $\lambda = 71.069$ pm (graphite monochromator), 2217 structure factors $F_0 \geq 3.9\sigma(F_0)$, Patterson method, $R_1 = 0.058$, $R_w = 0.050$.—We thank *J. Riede* for the measurements and Dr. *U. Schubert* for assistance.

[7] *H. Schmidbaur*, Adv. Organomet. Chem. *14*, 205 (1976).

[8] *H. F. Klein, H. H. Karsch*, Chem. Ber. *105*, 2628 (1972); *M. L. H. Green, M. J. Smith*, J. Chem. Soc. *A 1971*, 639; *G. Longa, P. Chini, F. Canziani, P. Fantucci*, Gazz. Chim. Ital. *104*, 249 (1974).

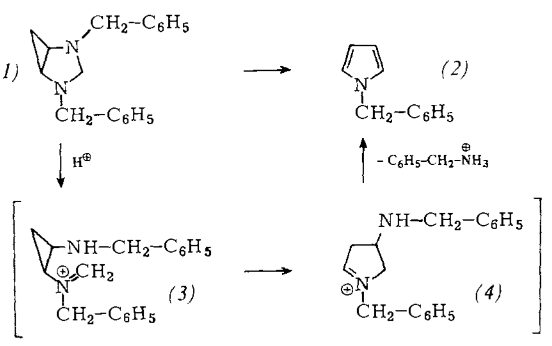
[9] *H. H. Karsch, H. F. Klein, H. Schmidbaur*, Angew. Chem. *87*, 630 (1975); Angew. Chem. Int. Ed. Engl. *14*, 637 (1975); *H. Schmidbaur, J. R. Mandl*, *ibid.* *89*, 679 (1977) and *16*, 640 (1977), respectively.

## A Simple Pyrrole Synthesis *via* an Unusually Facile 1,3 Shift in *N*-Benzyl-*N*-(2-benzylaminocyclopropyl)-*N*-benzylideneammonium Ions[**]

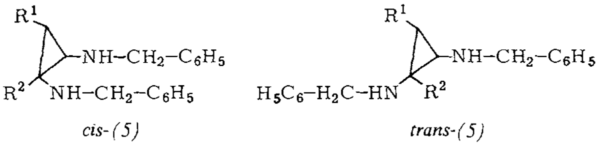
By *Helmut Quast, Wolfgang von der Saal*, and *Josef Stawitz*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

1,2-Cyclopropanediamines *(5)* retain their configuration in aqueous mineral acids even at elevated temperatures. In striking contrast, apart from slow ring-cleavage affording about 1 mole alkylamine, in aqueous neutral solution *(5)* undergoes rapid *cis-trans* equilibration, even at 25 °C[1]. We have now found that *(5)* and aromatic aldehydes *(6)* readily react to give pyrroles. The present experiments were stimulated by the very rapid, almost quantitative formation of 1-benzylpyrrole *(2)* and benzylamine upon hydrolysis of 2,4-diazabicyclo[3.1.0]hexane *(1)*[1] with dilute acetic acid or aqueous copper sulfate solution at 20 °C. Most probably, the pyrrolinium ion *(4)* was formed by opening of the imidazolidine ring of *(1)*, induced by protonation[2], and subsequent 1,3-shift in the methyleneammonium ion *(3)*. It, therefore, appeared reasonable to generate the analogous benzylideneammonium ions *(12)* by condensation of *(5)* with aldehydes *(6)* and to test their 1,3-shift propensity.

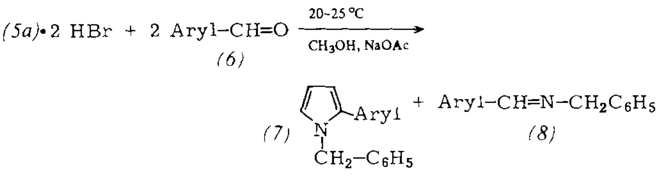


The ammonium bromides *(5)*·2HBr were obtained in good yields by Curtius degradation of diastereomerically pure dimethyl 1,2-cyclopropanedicarboxylates *via* the hydrazides[3]. The 1,2-bis(benzyloxycarbonylamino)cyclopropanes formed in benzyl alcohol were selectively alkylated at both N atoms by benzyl bromide in the presence of NaH and then cleaved with HBr in acetic acid. The configuration of all the cyclopropanediamines *(5)* and their precursors was established from LAOCOON III optimized $^1$H-NMR data.



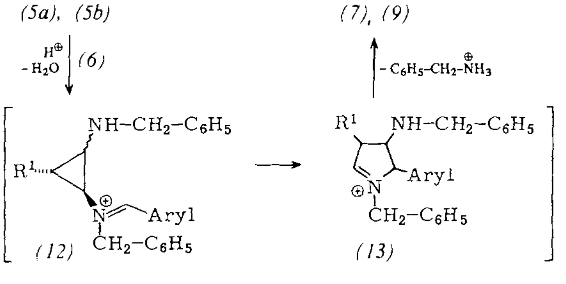
*(a)*, $R^1 = R^2 = H$; *(b)*, $R^1 = CH_3$, $R^2 = H$;
*(c)*, $R^1 = H$, $R^2 = CH_3$

When *(5a)*·2 HBr was reacted with 2 moles of aromatic aldehydes *(6)* in methanol or ethanol in the presence of 13 moles of sodium acetate, the 2-arylpyrroles *(7)* and the Schiff bases *(8)* were obtained after 15 h [3 d in the case of *(6d)*] at 20–25 °C. While *(7c)* crystallized directly from the reaction mixture, the other pyrroles *(7)* were isolated by preparative layer chromatography (alumina/petroleum ether (50–70 °C)) (Table 1). Irrespective of the configuration of the starting cyclopropane diamines *(5)* both *cis-(5a)* and *trans-(5a)* afforded the same pyrrole *(7c)* upon reaction with *(6c)*. This preparative advantage obviates the separation of the *cis-trans* diastereomeric cyclopropanedicarboxylates.



Aryl: *(a)* $C_6H_5$; *(b)* 4-$NO_2$–$C_6H_4$; *(c)* 4-$(CH_3)_2N$–$C_6H_4$;
*(d)* 2,4,6-$(CH_3)_3C_6H_2$; *(e)* 2-Pyridyl

The structures assigned to the pyrroles are based on elemental analyses, IR and mass spectra and, in particular, $^1$H-NMR spectra (Table 1). *(7a)* was identical with an authentic sample obtained by reaction of 3-chloropropene with benzoyl chloride in dichloromethane in the presence of aluminum chloride and heating the product under reflux for 4 h in benzyl amine (28% yield)[4].



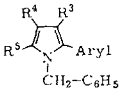
The substituted cyclopropanediamines *(5b)* and *(5c)* react analogously: from *trans-(5b)* and 4-nitrobenzaldehyde *(6b)*, only *(8b)* and *(9)* were formed, while *trans-(5c)* and *(6b)*, as well as *trans-(5c)* and *(6d)*, afforded a 6 : 4 ratio of the pyrroles *(10a)* and *(11a)* and a 7 : 3 ratio of the pyrroles *(10b)* and *(11b)*, respectively. Steric factors therefore lead to a low regioselectivity of the reaction.

---

[*] Prof. Dr. H. Quast, Dipl.-Chem. W. von der Saal, and Dr. J. Stawitz
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. The results are part of the dissertation of *J. S.*, Universität Würzburg 1978, and the prospective dissertation of *W. v. d. S.*

Even at 20 °C the benzylideneammonium ions *(12)* generated from *(5)* and aromatic aldehydes, ring-expand to the pyrrolinium ions *(13)*, which on loss of benzylamine, stabilize by formation of the pyrroles *(7)* [or *(9)*—*(11)*]. The ring-expansion of *(12)* probably proceeds equally rapidly and analogously to *N*-benzylidene(1,2,2-triphenylcyclopropyl)amines *via* trimethylene intermediates[5]. The present pyrrole synthesis provides an impressive example of the great acceleration of 1,3-shifts in vinylcyclopropanes by amino and alkoxide groups (LiO—, KO—)[6] attached to the migrating carbon atom. Despite the abundance of known pyrrole chemistry, novel and simple pyrrole syntheses are of timely interest[7].



*(9)*, Aryl = 4-$NO_2$–$C_6H_4$, $R^3 = R^5 = H$, $R^4 = CH_3$
*(10a)*, Aryl = 4-$NO_2$–$C_6H_4$, $R^3 = CH_3$, $R^4 = R^5 = H$
*(10b)*, Aryl = 2,4,6-$(CH_3)_3C_6H_2$, $R^3 = CH_3$, $R^4 = R^5 = H$
*(11a)*, Aryl = 4-$NO_2$–$C_6H_4$, $R^3 = R^4 = H$, $R^5 = CH_3$
*(11b)*, Aryl = 2,4,6-$(CH_3)_3C_6H_2$, $R^3 = R^4 = H$, $R^5 = CH_3$

Table 1. Yields of isolated products, physical constants, and $^1$H-NMR data in $CDCl_3$ of the 2-arylpyrroles *(7)*, *(9)*, *(10)*, *(11)* obtained from *trans*-*(5)*·2HBr. The data of the pyrrole protons and the methyl groups at the pyrrole ring were optimized using the LAOCOON III program.

| Cpd. m.p. [°C] (b.p. [°C/torr]) | Yield [%] | | | | | Pyrrole ring | | Me | $J_{H,Me}$ | N—$CH_2$ | Aryl-H | Aryl group substituents |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 3-H | 4-H | 5-H | $J_{3,4}$ | $J_{3,5}$ [Hz] | $J_{4,5}$ | | | | | |
| *(7a)* [a]<br>(103—105/$10^{-3}$) | 78 | 6.43 | 6.37 | 6.55 | 3.55 | 1.87 | 2.79 | — | | 4.78 | 6.7—7.4 | |
| *(7b)*<br>105 | 51 | 6.44 | 6.32 | 6.85 | 3.67 | 1.88 | 2.73 | — | | 5.22 | 6.9—8.3 | |
| *(7c)*<br>125 | 75, 70 [b] | 6.17 | 6.24 | 6.68 | 3.54 | 1.81 | 2.85 | — | | 5.09 | 6.6—8.5 | 2.45 (2 Me) |
| *(7d)*<br>67—68 | 95 | 6.10 | 6.39 | 6.66 | 3.49 | 1.69 | 2.81 | — | | 4.45 | 6.9—8.5 | 1.95 (2 Me),<br>2.15 (Me) |
| *(7e)*<br>(90 [c]/$10^{-2}$) | 55 | 6.60 | 6.22 | 6.78 | 3.73 | 1.83 | 2.74 | — | | 5.76 | 6.7—8.2 | |
| *(9)*<br>(110 [c]/$10^{-2}$) | 62 | 6.28 | — | 6.61 | — | 1.91 | — | 2.13 | $J_{3\text{-H},Me}$ 0.51<br>$J_{5\text{-H},Me}$ 0.94 | 5.12 | 7.0—8.5 | |
| *(10a)*<br>79—80 | 38 | — | 6.16 | 6.75 | — | — | 2.71 | 2.05 | $J_{4\text{-H},Me}$ 0.54 | 5.05 | 6.7—8.5 | |
| *(10b)*<br>(90 [c]/$10^{-2}$) | [d] | — | 6.10 | 6.69 | — | — | 2.68 | 1.95 | $J_{4\text{-H},Me}$ 0.48 | 4.65 | 6.8—7.5 | 1.86 (2 Me),<br>2.30 (Me) |
| *(11a)*<br>119—120 | 29 | 6.41 | 6.11 | — | 3.63 | — | — | 2.18 | $J_{4\text{-H},Me}$ 0.84 | 5.20 | 6.7—8.5 | |
| *(11b)*<br>(90 [c]/$10^{-2}$) | [d] | 5.91 | 6.04 | — | 3.36 | — | — | 2.21 | $J_{4\text{-H},Me}$ 0.91 | 4.80 | 6.8—7.5 | 1.82 (2 Me),<br>2.26 (Me) |

[a] $^1$H-NMR spectrum in $C_6D_6$. [b] From *cis*-*(5a)*. [c] Bath temperature during the distillation in a sublimation apparatus with cold finger at −195 °C. [d] 57% of a 7:3 mixture of *(10b)* and *(11b)*.

Received: January 15, 1981 [Z 789 IE]
German version: Angew. Chem. *93*, 619 (1981)

---

[1] *H. Quast, J. Stawitz*, Tetrahedron Lett. *1976*, 3803.

[2] *T. H. Fife, A. M. Pellino*, J. Am. Chem. Soc. *102*, 3062 (1980); *J. B. Lambert, M. W. Majchrzak, ibid. 101*, 1048 (1979).

[3] Unsubstituted 1,2-cyclopropanediamines have been synthesized by Curtius-degradation: *H. A. Staab, F. Vögtle*, Chem. Ber. *98*, 2691 (1965); *T. Shono, T. Morikawa, R.-I. Okayama, R. Oda*, Makromol. Chem. *81*, 142 (1965); *D. T. Witiak, H. J. Lee, H. D. Goldman, B. S. Zwilling*, J. Med. Chem. *21*, 1194 (1978).

[4] By analogy to *P. Rosenmund, K. Grübel*, Angew. Chem. *80*, 702 (1968); Angew. Chem. Int. Ed. Engl. *7*, 733 (1968).

[5] *P. Caramella, R. Huisgen, B. Schmolke*, J. Am. Chem. Soc. *96*, 2997, 2999 (1974); *K. H. Schröder*, Dissertation, Universität München 1975.

[6] *R. L. Danheiser, C. Martinez-Davila, J. M. Morin, Jr.*, J. Org. Chem. *45*, 1340 (1980) and literature cited therein.

[7] *N. Engel, W. Steglich*, Angew. Chem. *90*, 719 (1978); Angew. Chem. Int. Ed. Engl. *17*, 676 (1978); *B. M. Trost, E. Keinan*, J. Org. Chem. *45*, 2741 (1980); *B. Merah, F. Texier*, Bull. Soc. Chim. Fr. *1980*, 552; *T. L. Gilchrist, B. Parton, J. A. Stevens*, Tetrahedron Lett. *1981*, 1059; *J.-E. Bäckvall, J.-E. Nyström*, J. Chem. Soc. Chem. Commun. *1981*, 59.

---

## An Unusual Double Intramolecular Cyclization—Structural Analysis of 2,6-Dibromo-4,8-dimethyltetracyclo[3.3.0.0$^{2,8}$.0$^{4,6}$]octane-3,7-dione[**]

By *Krystina Kratzat, Franz W. Nader*, and *Thea Schwarz*[*]

*Dedicated to Professor Karl Freudenberg on the occasion of his 95th birthday*

In our investigations of the structural chemistry of cumulenes[1], we sought a route to bisallene-1,6-dicarboxylic acid derivatives. The most promising appeared to be the classic synthesis of allenes from 1,1-dihalocyclopropanes after *Doering*[2]. By means of this route, pentatetraenes[3b], in addition to numerous allene derivatives[3a], were first synthesized; furthermore, both acyclic-[4a] and cyclic-bisallenes[4b] have been prepared. A synthetic route to the bisallene-dicarboxylic acid diester *(5)* starting from the tetrabromobicyclopropyl dicarboxylic acid esters *(2)* and *(3)* should therefore also be feasible.

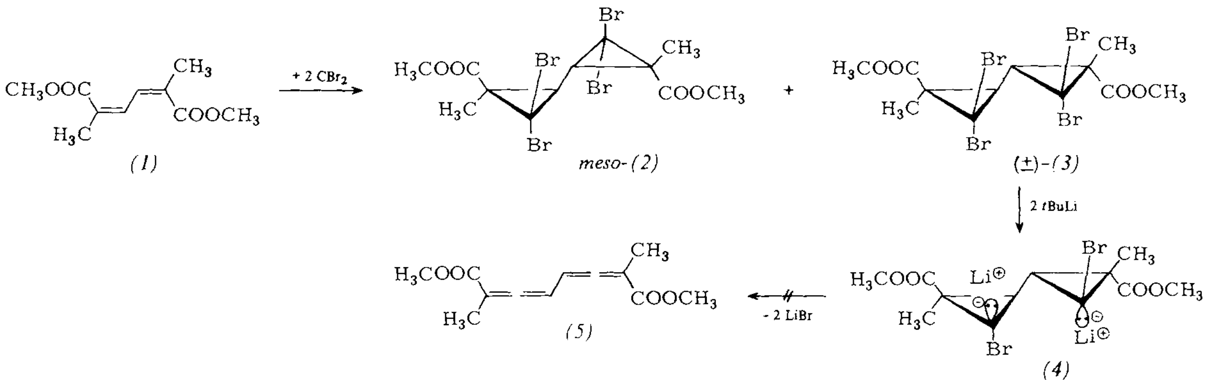
Double dibromocarbene addition to dimethyl (*Z,Z*)-2,5-dimethylmuconate[5] *(1)* occurred in approximately 20% total yield under phase-transfer catalysis at 50-70 °C. In addition to the expected stereoisomers *meso*-*(2)* and (±)-*(3)*, two further diastereomeric adducts, which were formed as a consequence of partial isomerization of (*Z,Z*)-*(1)* to (*E,E*)-*(1)*, could be obtained in pure form by column chromatographic separation. Configurational assignments were carried out by spectroscopic and chemical methods[6].

Reaction of *(3)* with *tert*-butyllithium (*t*BuLi) or lithium diisopropylamide at −60 °C in ether produced a crystalline compound, which after elemental analysis and mass spectroscopy, proved to have the empirical formula $C_{10}H_8Br_2O_2$. On the basis of the NMR spectroscopic data, this compound must have a symmetrical structure. The $^1$H-NMR spectrum contains only two singlets in the ratio 1:3,

---

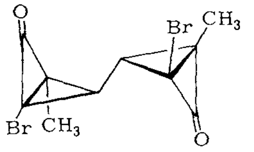
[*] Priv.-Doz. Dr. F. W. Nader, Dr. K. Kratzat, T. Schwarz
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

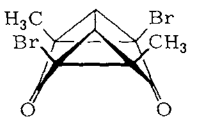
[**] This work was supported by the Deutsche Forschungsgemeinschaft.



which are indicative of aliphatic methine protons ($\delta = 3.15$) and methyl groups ($\delta = 1.48$); the signals are similar to those of the corresponding educt *(3)*. The $^{13}C$-NMR spectrum shows signals arising from five different C atoms. By virtue of their position and off-resonance decoupling, the following assignments could be made: $C{=}O$ ($\delta = 196.75$), methine $C{-}H$ (40.21), $CH_3$ (13.46), in addition to two aliphatic, quaternary C atoms (43.66 and 37.19). Metalation of *(3)* leading to formation of an allene system can therefore be excluded. On the contary, the product must result from an intramolecular condensation of the intermediate dicarbanions, formed by metalation of *(3)* with both ester functionalities. If this condensation occurs on the α-bromocarbanion intermediate *(4)*, the two structures *(6)* and *(7)* could result; if the carbanion attacks the ester group on the same respective cyclopropyl moiety the highly strained bisbicyclobutanone *(6)* is formed, while attack at the other ester group results in formation of the tetracycle *(7)*.

*(6)*





*(7)*

The structure *(6)* can most probably be excluded from its $C{=}O$ vibrational frequency of 1748 $cm^{-1}$ (*ca.* 1850 $cm^{-1}$ would be expected for a cyclopropanone) and from the investigation of analogous reactions on a model compound[7].

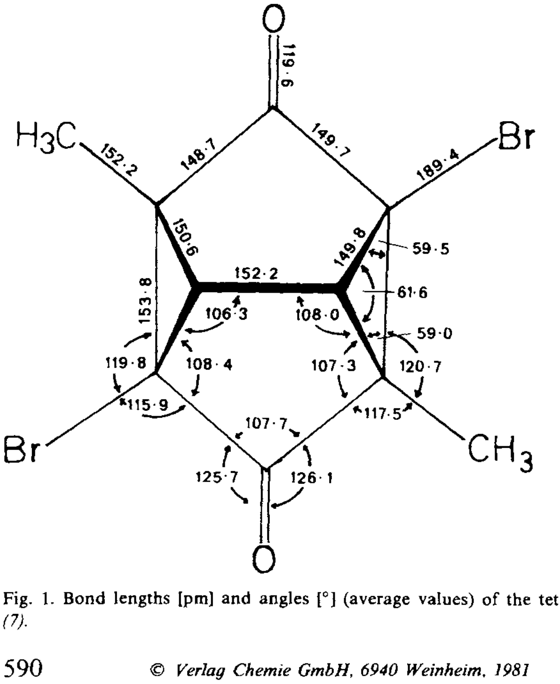
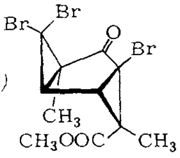


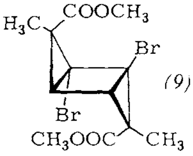
Fig. 1. Bond lengths [pm] and angles [°] (average values) of the tetracycle *(7)*.

An X-ray structure analysis[8] of the product confirmed the suggested structure *(7)*, which has approximate $C_2$ symmetry. Due to the influence of the β-ester function[7], the carbanionic intermediate *(4)* is so stable—even at high temperatures—that it does not spontaneously α-eliminate to the carbene; furthermore, although sterically hindered, it can react *via* double intramolecular cyclization to give *(7)*.

The structural analysis also proves that the stereochemical assignment of the starting material *(3)* was correct, since only in the (±)-diastereomer do the ester functions occupy positions from which double intramolecular cyclization is possible. In contrast, the *meso*-compound *(2)* can only cyclize to the tricyclic cyclopentanone *(8)*. In this latter compound both cyclopropane rings are *trans* to each other and hence the second coupling step is, for steric reasons, impossible. In fact, *(8)* can be obtained by metalation of *(2)*; an allene is not formed here either.

*(8)*





*(9)*

Metalation of *(3)* with *t*BuLi at 0°C in cyclohexane results, in addition to the tetracycle *(7)*, in isolation of a second crystalline compound, which on the basis of analytical and spectroscopic data[9], is assigned the structure of the tricyclo-[3.1.0.0$^{2,4}$]hexane derivative *(9)*; under these conditions a second coupling variation—coupling of both $CBr_2$ groups of *(3)*—is possible, which leads to the formation of cyclobutane and hence to the "chair-analogous" structure *(9)*.

Received: December 9, 1980 [Z 785 IE]
German version: Angew. Chem. 93, 611 (1981)

CAS Registry numbers:
*(Z,Z)-(1)*, 24407-02-1; *meso-(2)*, 77944-46-8; (+)-*(3)*, 77983-48-3; (+)-*(6)*, 77965-66-3; *(7)*, 77944-47-9; (+)-*(8)*, 77944-48-0; (+)-*(9)*, 77944-49-1

---

[1] *L. Leiserowitz, F. Nader*, Angew. Chem. *85*, 150 (1973); Angew. Chem. Int. Ed. Engl. *12*, 158 (1973); *Z. Berkovitch-Yellin, L. Leiserowitz, F. Nader*, Acta Crystallogr. *B 33*, 3670 (1977).

[2] *W. von E. Doering, A. K. Hoffmann*, J. Am. Chem. Soc. *76*, 6162 (1954).

[3] a) *L. Skattebøl*, Tetrahedron *23*, 1107 (1967); J. Org. Chem. *31*, 2789 (1966); *W. R. Moore, H. R. Ward, ibid. 27*, 4179 (1962); b) *J. C. Jochims, G. Karich*, Tetrahedron Lett. *1974*, 4215.

[4] a) *K. Kleveland, L. Skattebøl*, Acta Chem. Scand. *B 29*, 191 (1975); b) *E. V. Dehmlov, G. C. Ezimora*, Tetrahedron Lett. *1970*, 4047; *L. Skattebøl*,

Acta Chem. Scand. *17*, 1683 (1963); *R. Baker, P. J. Garratt, K. C. Nicolaon, F. Sondheimer*, Tetrahedron Lett. *1972*, 3425.

[5] *J. A. Elvidge, R. P. Linstead, B. A. Orkin, P. Sinis, H. Baer, D. B. Pattison*, J. Chem. Soc. *1950*, 2232.

[6] *K. Kratzat*, Dissertation, Universität Heidelberg 1979.

[7] As a model compound, 2,2-dibromo-1-methylcyclopropanecarboxylic acid was reacted with *t*BuLi under the same conditions. Only one stereospecific Br/H-exchange process, leading to ethyl *trans*-2-bromo-1-methylcyclopropanecarboxylate, occurred. This shows that an extraordinary stable carbanion is formed *syn* to the ester function, a fact which is in accord with the stereochemistry of both cyclization products *(7)* and *(9)*.

[8] Space group $P2_1/c$; $a=801.4$, $b=1073.7$, $c=1221.4$ pm, $\beta=97.55°$; $Z=4$, $\rho_{calc.}=2.04$ g·cm$^{-3}$. The structure was solved by direct methods with a multi-solution technique. [*G. Germain, M. M. Woolfson*, Acta Crystallogr. *B 24*, 91 (1968); see also *H. W. Kaufmann, L. Leiserowitz, ibid. B 26*, 442 (1970)]. The positions of the H atoms were obtained from the $|F_o - F_c|$ difference map. The refinement with 2531 reflections (of which 589 were unobserved) converged to an *R*-factor of 5.2%.

[9] Elemental Analysis and mass spectrum (molecular peak at $m/e=380$) gave the summation formula $C_{12}H_{12}Br_2O_4$. $^1$H-NMR: $\delta=1.35$ (s, 3H, CH$_3$), 2.69 (s, 1H), 3.81 (s, 3H, OCH$_3$); $^{13}$C-NMR: $\delta=169.40$ (C=O), 52.19 (OCH$_3$), 49.60 (quart. C), 45.71 (quart. C), 39.02 (CH), 19.01 (CH$_3$).

---

## A Diorganotin Oxide with a Planar Tin-Chalcogen Six-Membered Ring[**]

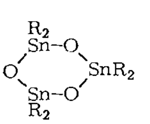
By *Heinrich Puff, Willi Schuh, Rolf Sievers,* and *René Zimmer*[*]

*Dedicated to Professor Rolf Appel on the occasion of his 60th birthday*

The properties of most diorganotin oxides would indicate polymeric structures[1]. Although molecular weight determinations indicated presence of trimers in solution in the case of di-*tert*-butyltin oxide[2] *Chu* and *Murray* assumed a polymeric structure in the solid state on account of the sparing solubility of the sample.

On reaction of $tBu_2SnCl_2$ with sodium hydroxide in boiling toluene we were able to obtain a form of the di-*tert*-butyltin oxide which is readily soluble in organic solvents in the cold and is therefore obviously of low molecular weight.

The compound crystallizes hexagonally in the space group $R\bar{3}c$-$D_{3d}^{6}$, $a=1035$, $c=5144$ pm[3]. The unit cell contains six molecules $(tBu_2SnO)_3$. As shown by the X-ray structure analysis[4] ($R=0.045$), tin and oxygen atoms are coupled to a planar six-membered ring.



R = C(CH$_3$)$_3$

| Bond length [pm] | | Angle [°] | |
|---|---|---|---|
| Sn—O | 196 | O—Sn—O | 106.9 |
| Sn—C | 219 | Sn—O—Sn | 133.1 |
| | | C—Sn—C | 119.9 |

Such a planar arrangement has so far not been detected in the case of diorganotin-chalcogen compounds; in the analogous sulfur, selenium, and tellurium compounds there are either puckered six-membered[5a] or four-membered[5b] rings, or open chains[5c]. The Sn—O bond lengths are of about the same order of magnitude as in comparable compounds with distinctly tetravalent tin, *e.g.* $Ph_3Sn{-}O{-}SnPh_3$ (195 to 196 pm)[6]. In contrast to other SnO-compounds[7], an association of the molecules with an increase in the bond numbers of tin and oxygen is not observed; the shortest intermolecular Sn—O distance is 644 pm.

Received: August 5, 1980 [Z 792 IE]
German version: Angew. Chem. *93*, 622 (1981)

---

[*] Prof. Dr. H. Puff, Dr. R. Sievers, Dr. R. Zimmer, W. Schuh
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Str. 1, D-5300 Bonn (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *W. P. Neumann:* Die Organische Chemie des Zinns, F. Enke Verlag, Stuttgart 1967, p. 133.

[2] *C. K. Chu, J. D. Murray,* J. Chem. Soc. *A 1971*, 360.

[3] The same compound was obtained by *A. Tzschach* and *M. Dräger* (private communication).

[4] Measurements at −85°C; four-circle diffractometer CAD 4, program system X-RAY 76, IBM/370-168 computer at the Regionales Hochschulrechenzentrum, Universität Bonn.

[5] Cf. a) *A. Blecher, M. Dräger,* Angew. Chem. *91*, 740 (1979); Angew. Chem. Int. Ed. Engl. *18*, 677 (1979); and references cited therein.—b) *H. Puff, R. Gattermayer, R. Hundt, R. Zimmer, ibid. 89*, 556 (1977) and *16*, 547 (1977);—c) *H. Puff, A. Bongartz, R. Sievers, R. Zimmer, ibid. 90*, 995 (1978) and *17*, 939 (1978).

[6] *C. Glidewell, D. Liles,* Acta Crystallogr. *B 34*, 1693 (1978).

[7] Compounds of type $[(RR'SnX)_2O]_2$: *P. G. Harrison, M. J. Begley, K. C. Molloy,* J. Organomet. Chem. *186*, 213 (1980): $R=R'=CH_3$, $X=Cl$; *H. Puff, E. Friedrichs, F. Visel,* Z. Anorg. Allg. Chem., in press: $R=R'=CH(CH_3)_2$, $X=Cl$ and $R=C(CH_3)_3$, $R'=CH_2Si(CH_3)_3$, $X=OH$.

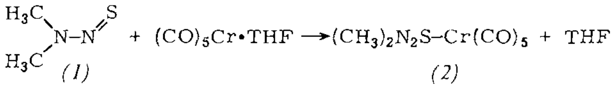
---

## Coordination of Dimethyl(thionitroso)amine to Pentacarbonylchromium *via* the Sulfur Atom[**]

By *Herbert W. Roesky, Ralf Emmert, William Clegg, Wilhelm Isenberg* and *George M. Sheldrick*[*]

*Dedicated to Professor Josef Goubeau on the occasion of his 80th birthday*

In all complexes of acyclic sulfur-nitrogen compounds known so far the N—S ligands are coordinated to the metal *via* nitrogen atoms[1]. Reaction of the unstable dimethyl(thionitroso)amine *(1)*[2]—prepared from dimethylhydrazine and sulfur—with $(CO)_5Cr\cdot THF$ in tetrahydrofuran (THF) affords the 1:1 complex *(2)*, which we isolated as ruby-red crystals, stable at room temperature. As shown by an X-ray structure analysis[3], the SN ligand in *(2)* is bound to chromium *via* the sulfur atom (Fig. 1).



$$(H_3C)_2N{-}N{=}S + (CO)_5Cr\cdot THF \longrightarrow (CH_3)_2N_2S{-}Cr(CO)_5 + THF$$

*(1)* *(2)*

---

[*] Prof. Dr. H. W. Roesky [+], R. Emmert
Anorganisch-chemisches Institut der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. G. M. Sheldrick, Dr. W. Clegg, Dipl.-Chem. W. Isenberg
Anorganisch-chemisches Institut der Universität
Tammannstr. 4, D-3400 Göttingen (Germany)

[+] Author to whom correspondence should be addressed. Present address: Anorganisch-chemisches Institut der Universität, Tammannstr. 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and Hoechst AG.

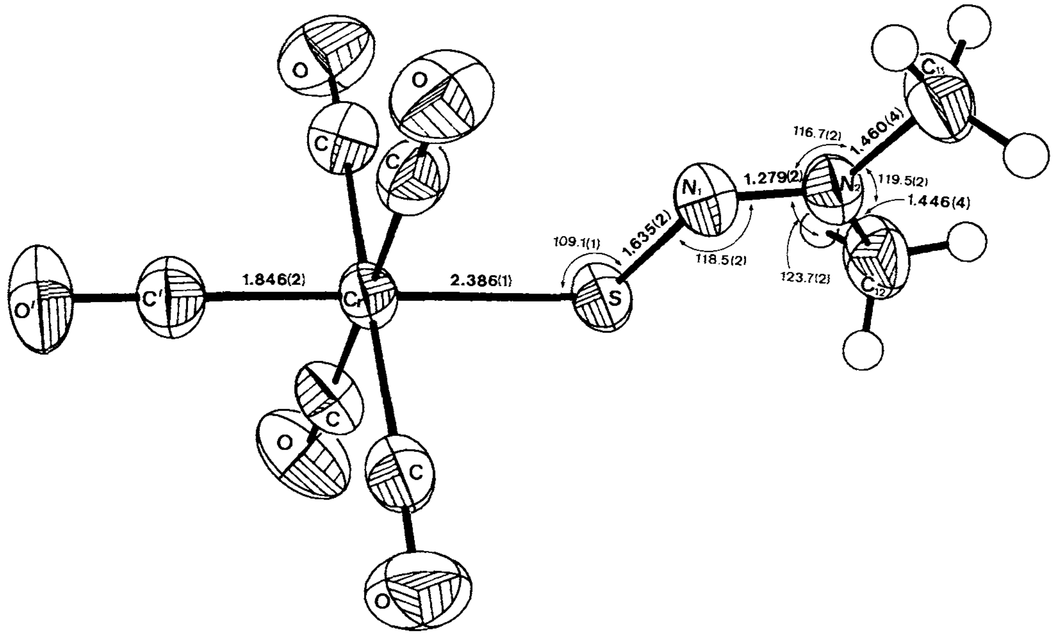
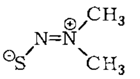


Fig. 1. Molecular structure of the complex *(2)*, showing the bond lengths [Å] and bond angles [°] (standard deviations in brackets). Mean values for 5 C—O 1.138(3), Cr—C(*cis*) 1.903(5) Å, S—Cr—C(*cis*) 89.8(4), S—Cr—C(*trans*) 178.2(1)°.

For the CO group in the *trans* position to the sulfur atom the Cr—C distance is shortened to 1.846(2) Å compared to the mean value of 1.903(5) Å for the remaining carbonyl ligands. The atoms Cr, S, N2 and C″ are coplanar within 0.012 Å, and the coordination octahedron about Cr is almost ideal. The S—N distance of 1.635(2) Å corresponds to a single bond, while the N—N bond (1.278(2) Å) is markedly shortened compared to that in hydrazine derivatives (1.45 Å). The bonding in the ligand can best be described in terms of the resonance structure *(1a)*.



In the mass spectrum of *(2)* the molecular ion appears at $m/z = 282$ with a relative intensity of 37%. The fragmentation follows a stepwise cleavage of the CO groups, so that $\mathrm{Cr[SNN(CH_3)_2]^+}$ appears at $m/z = 142$—and with a relative intensity of 100%.

### *Procedure*

*(1)* (0.57 g, 6.3 mmol) is treated at *ca.* $-15\,^\circ\mathrm{C}$ with a solution of $\mathrm{(CO)_5Cr \cdot THF}$ (7.5 mmol) in THF (100 ml). The mixture is allowed to warm to room temperature, then stirred for 1 hour, the solvent removed, and the residue taken up in 25 ml $CH_2Cl_2$. After filtration and cooling, $\mathrm{Cr(CO)_6}$ is removed from the resulting crystalline mixture by vacuum sublimation. Yield 0.4 g (24%) *(2)*, decomp. ≈ 100 °C.

Received: May 22, 1980 [Z 793a IE]
German version: Angew. Chem. *93*, 623 (1981)

---

[1] *B. Buss, p. G. Jones, R. Mews, M. Noltemeyer, G. M. Sheldrick,* Angew. Chem. *91*, 253 (1979); Angew. Chem. Int. Ed. Engl. *18*, 253 (1979); *M. W. Bishop, J. Chatt, J. R. Dilworth,* J. Chem. Soc. Dalton Trans. *1979*, 1; *R. Meij, T. A. M. Kaandorp, D. J. Stufkens, K. Vrieze,* J. Organomet. Chem. *128*, 203 (1977); *R. Meij, D. J. Stufkens, K. Vrieze, ibid. 144*, 239 (1978).

[2] *W. J. Middleton,* J. Am. Chem. Soc. *88*, 3842 (1966).

[3] Monoclinic, $P2_1/c$, $a = 1042.2(3)$, $b = 1250.7(4)$, $c = 954.6(3)$ pm, $\beta = 110.21(2)^\circ$, $Z = 4$; automatic diffractometer ($\mathrm{Mo_{K\alpha}}$, $\lambda = 71.069$ pm), 2387 independent reflections with $F > 3\sigma(F)$, heavy atom method; $R = 0.049$, $R_w = 0.044$.

# 1,5-Bis(dimethylamino)tetrasulfur Tetranitride—A Cage Molecule with a Non-Symmetric Nitrogen Bridge[**]

By *Herbert W. Roesky, M. N. S. Rao, Cornelia Graf, Alfred Gieren,* and *Erich Hädicke*[*]

*Dedicated to Professor Marianne Baudler on the occasion of her 60th birthday*

"Substitution products" of $S_4N_4$ with amino groups have so far not been reported in the literature. We have now found that $S_4N_4Cl_2$ *(1)* reacts with dimethyl(trimethylsilyl)amine *(2)* in the molar ratio 1 : 2 to give the dimethylamino derivative *(3)*.

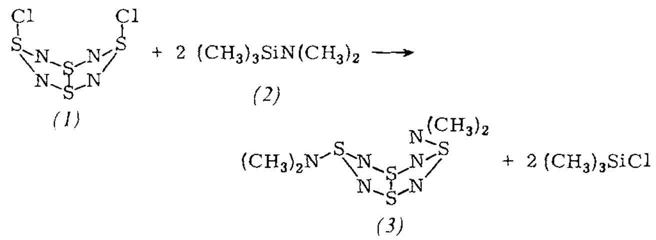
*(3)* could be isolated in good yields as pale yellow, transparent crystals. $S_4N_4$ is formed as by-product. Crystals of *(3)* and their solution in $CH_2Cl_2$ or $CHCl_3$ undergo decomposition and turn red at room temperature. However, the crystals can be stored for months at 0 °C without decomposition.

---

[*] Prof. Dr. H. W. Roesky [+], Dr. M. N. S. Rao, Dipl.-Chem. C. Graf
Anorganisch-chemisches Institut der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Dr. habil. A. Gieren
Max-Planck-Institut für Biochemie, Abteilung für Strukturforschung I
Am Klopferspitz, D-8033 Martinsried (Germany)
Dr. E. Hädicke
Ammoniaklaboratorium der BASF AG, D-6700 Ludwigshafen (Germany)

[+] Author to whom correspondence should be addressed. Present address: Anorganisch-chemisches Institut der Universität, Tammannstr. 4, D-3400 Göttingen (Germany)

[**] Studies on the structure of $S^{IV}N_3$ Groups, Part 5. This work was supported by the Deutsche Forschungsgemeinschaft. – Part 4: *A. Gieren, B. Dederer, I. Abelein,* J. Anorg. Allg. Chem. *465*, 191 (1980).



The molecule *(3)* (Fig. 1) exhibits only $C_s$ symmetry, and not the possible ($C2_v$ symmetry. The two $(CH_3)_2N$-groups are stereochemically non-equivalent. One (containing N6) occupies an *exo*-position on the $S_4N_4$ ring with trigonal-planar, the other (containing N5) an *endo*-position with pyramidal ligand arrangement. The bond lengths in the two $SN_3$ groups are markedly different. The group containing S3 contains one shorter exocyclic and two longer endocyclic S—N bonds, the group with S1 one longer exocyclic and two shorter endocyclic S—N bonds. The $C2_v$ symmetry is also destroyed with respect to the usual S—N bond lengths. The bonds from S2 (and S4) to N1 and N2 (and N4 and N3, respectively) are different in length. The average S—N bond length in the $S_4N_4$ ring (1.62 Å), however, has almost the same size as in the $S_4N_4$ eight-membered ring of $S_4N_4$[1a], $S_4N_5^-$[1b], $S_4N_5^+$[2a], $S_4N_5O^-$[2b], $S_4N_4\cdot 2C_7H_8$[3], $S_5N_6$[4], $S_5N_6(CH_2)_4$[5], $S_5N_6(CH_3)_2$[6a] and $S_5N_7Si(CH_3)_5$[6a], but distinctly greater than in the Lewis acid adducts of $S_4N_4$ with $BF_3$[6b], $SO_3$[7a], $FSO_2NCO$[7b] and $AsF_5$[8] (1.588–1.599 Å).

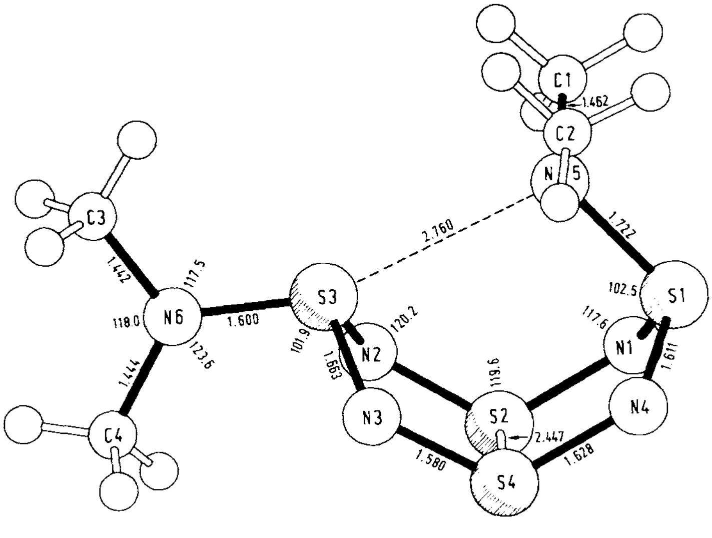


Fig. 1. Molecular structure of $S_4N_4[N(CH_3)_2]_2$ *(3)* with bond lengths [Å] and angles [°] determined *via* the molecular mirror symmetry. Further bond angles are: C1—N5—S1 111.8, C1—N5—C2 112.9, N1—S1—N4 106.5, N2—S3—N3 100.4, N1—S2—S4 92.4, N2—S2—S4 92.0°. Standard deviations of the determined values: bond lengths: S—S 0.002, S—N 0.005–0.008, C—N 0.007—0.013 Å; angles 0.2—0.7°.—*(3)* crystallizes in the triclinic space group $P\bar{1}$ with $a=7.559(5)$, $b=8.496(5)$, $c=9.480(6)$ Å, $\alpha=104.19(5)$, $\beta=93.4(5)$, $\gamma=103.13(5)°$, $Z=2$; diffractometer data: $Cu_{K\alpha}$ radiation, 1274 observed reflections ($I>2\sigma_I$), corrected for absorption, measured at −60 °C, $\Theta_{max}=57.5°$, $R=0.079$.

The conformation of the $S_4N_4$ ring in *(3)* corresponds to that of $S_4N_4$; however, one transannular S—S bond is opened, while the other is shortened by *ca.* 0.14 Å to 2.447 Å. The opened S—S bond becomes unsymmetrically bridged by a $(CH_3)_2N$-group: N5 in the substituent forms an S—N single bond to S1 and at the same time a strong transannular interaction with S3 (N5—S3: 2.760 Å); as a consequence the coordination number of S3 increases to four. N5 adds nucleophilically *via* the lone electron pair S3. The molecular geometry can be explained in terms of a frozen-in intramolecular rearrangement of an $(CH_3)_2N$-group from S1 to S3. Two sharp signals are observed in the $^1$H-NMR spectrum recorded at room temperature ($\delta=2.53$ for the *exo*- and $\delta=2.35$ for the *endo*-dimethylamino group). At −70 °C the exchange of the *exo*-methyl group is frozen-in, and two broad signals appear instead of the singlet. The signal of the *endo*-dimethylamino group remains sharp and in exactly the same position.

### *Procedure*

A suspension of *(1)*[9] (2.55 g, 10 mmol) in $CH_3CN$ (80 mL) is cooled, with stirring, to −35 to −40 °C and treated dropwise within 2.5 h with a solution of *(2)* (2.57 g, 22 mmol) in $CH_3CN$ (70 mL). The resulting solution is then warmed within 2 h to room temperature. A deep-red clear solution is obtained. After removal of solvent in a vacuum a red oil remains. This is extracted portionwise with 100 mL *n*-hexane, and the *n*-hexane solution is evaporated down to 60 mL. On cooling (in a deep-freeze) *(3)* (decomp. pt. 70–72 °C) is obtained as pale-yellow crystals in 40% yield. Further amounts of *(3)* can be obtained by concentration of the mother liquor. The residue insoluble in *n*-hexane contains $S_4N_4$ as identifiable product.

Received: July 7, 1980 [Z 793b IE]
German version: Angew. Chem. *93*, 624 (1981)

CAS Registry numbers:
*(1)*, 71699-97-3; *(2)*, 2083-91-2; *(3)*, 78167-47-2

[1] a) *B. D. Sharma, J. Donohue*, Acta Chryst. allogr. *16*, 891 (1963)); *M. L. De Lucia, P. Coppens*, Inorg. Chem. *17*, 2336 (1978); b) *W. Flues, O. J. Scherer, J. Weiss, G. Wolmershäuser*, Angew. Chem. *88*, 411 (1976); Angew. Chem. Int. Ed. Engl. *15*, 379 (1976).

[2] a) *T. Chivers, L. Fiedling, W. G. Laidlaw, M. Trsic*, Inorg. Chem. *18*, 3379); b) *P. Luger, H. Bradaczek, R. Steudel*, Chem. Ber. *109*, 3441 (1976).

[3] *A. Griffin, G. M. Sheldrick*, Acta Crystallorg. *B 31*, 895 (1975), *G. Ertl, J. Weiss*, Z. Anorg. Chem. *420*, 155 (1976).

[4] *T. Chivers, D. Proctor*, J. Chem. Soc. Chem. Commsn. *197*, 62; *H. W. Roesky, M. N. S. Rao, T. Nakajima, W. S. Sheldrick*, Chem. Ber. *112*, 3531 (1979).

[5] *H. W. Roesky, C. Graf, M. N. S. Rao, B. Krebs, G. Henkel*, Angew. Chem. *91*, 846 (1979); Angew. Chem. Int. Ed. Engl. *18*, 780 (1979).

[6] a) *W. S. Sheldrick, M. N. S. Rao, H. W. Roesky*, Inorg. Chem. *19*, 538 (1980); b) *M. G. B. Drew, D. H. Templeton, A. Zalkin, ibid. 6*, 1906 (1967).

[7] a) *A. Gieren, B. Dederer, H. W. Roesky, N. Amin, O. Petersen*, Z. Anorg. Allg. Chem. *440*, 119 (1978); b) *A. Gieren, Ch. Hahn, B. Dederer, H. W. Roesky, N. Amin, ibid. 447*, 179 (1978).

[8] *R. J. Gillespie, J. P. Kent, J. F. Sawyer*, Acta Crystallogr. *B 36*, 655 (1980).

[9] *L. Zborilova, P. Gebauer*, Z. Anorg. Allg. Chem. *448*, 5 (1979).

---

## Mononuclear Transition Metal Complexes with $CS_2$-Analogous Coordination of a Thioketene[1]

By *Helmut Werner, Oswald Kolb, Ulrich Schubert*, and *Klaus Ackermann*[*]

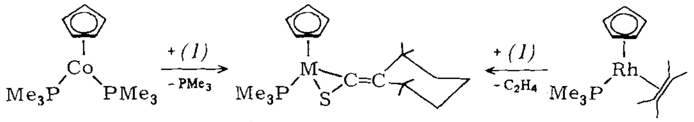
*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

Metal complexes of $CS_2$ and analogous ligands SCX (X = O, Se, NR *etc.*) are of interest as model substances for

---

[*] Prof. Dr. H. Werner, Dipl.-Chem. O. Kolb
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)
Priv.-Doz. Dr. U. Schubert, Dipl.-Chem. K. Ackermann
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

the complexation of $CO_2$[2]. We recently reported the synthesis of $C_5H_5(PMe_3)Co(\eta^2\text{-}CS_2)$[3] and $C_5H_5(PMe_3)Co(\eta^2\text{-}SCSe)$[4], which are formed by attack of the strong metal base $C_5H_5Co(PMe_3)_2$[5] at the electrophilic carbon atom of $CS_2$ and SCSe, respectively. 1,1,3,3-Tetramethyl-2-thiocarbonylcyclohexane *(1)*, which in contrast to other dialkylthioketenes is remarkably stable, also reacts with this metal base (in benzene, 25 °C), rapidly and quantitatively to give the cobalt complex *(2)*. The corresponding rhodium complex *(3)* is formed from $C_5H_5Rh(PMe_3)C_2H_4$[6] and *(1)* in benzene on warming to 60 °C for a day.



*(2)*, M = Co
*(3)*, M = Rh

The air-stable solids *(2)* and *(3)* are readily soluble in the usual organic solvents. The characteristic stretching frequency at 1750 cm$^{-1}$ for the S=C=C group in *(1)* is no longer observed in the IR spectra of the complexes. The *di-hapto*-($\eta^2$)coordination thus indicated for the thioketene is confirmed by the crystal structure analysis of *(2)*[7].

Table 1. Spectroscopic data of the new thioketene-metal complexes *(2)* and *(3)*.

*(2)*: $^1$H-NMR ([D$_6$]benzene): $\delta=4.70$ ($C_5H_5$; s), 1.96, 1.75, 1.65, 1.62 (4$CH_3$; s), 0.84 ($PMe_3$; d, $J_{PH}=9.8$ Hz), $CH_2$-signals of the six-membered ring masked by methyl resonances. MS (70 eV): $m/z$ ($I_r$) = 382 (13; $M^+$), 366 (2; $M^+-CH_4$), 334 (3; $M^+-3\,CH_4$), 306 (1; $M^+-PMe_3$), 200 (100; $C_5H_5CoPMe_3^+$), 189 (7; $Co(C_5H_5)_2^+$), 124 (15; $CoC_5H_5^+$).

*(3)*: $^1$H-NMR ([D$_6$]benzene): $\delta=5.16$ ($C_5H_5$; d×d, $J_{PH}=1.5$, $J_{RhH}=0.7$ Hz), 1.81, 1.66, 1.58, 1.57 (4$CH_3$; s), 1.05 ($PMe_3$; d×d, $J_{PH}=10.4$, $J_{RhH}=1.0$ Hz), $CH_2$-signals masked. MS (70 eV): $m/z$ ($I_r$) = 426 (35; $M^+$), 410 (3; $M^+-CH_4$), 244 (100; $C_5H_5RhPMe_3$), 168 (37; $RhC_5H_5^+$).

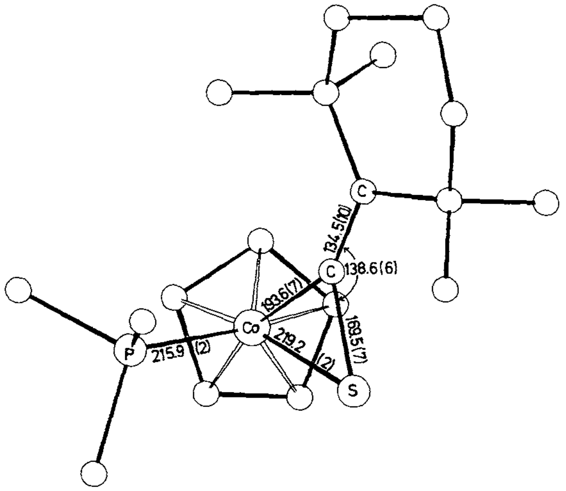


Fig. 1. Molecular structure of *(2)*, projected perpendicular to the plane of the $C_5H_5$-ring.

The bond lengths and angles between the Co atom and the S=C=C group of the thioketene ligand verify presence of a CoSC three-membered ring. Whereas the CoS bond length corresponds to that of a single bond, partial multiple bonding cannot be ruled out in the case of the Co—C bond[8]. Thus, similarly to $CS_2$, SCSe and other heteroallenes, *(1)* could also exhibit considerable π-acceptor character. The hypothesis of comparable ligand properties of $CS_2$ and dialkylthioketenes such as *(1)* is, moreover, supported by the very similar bond angles S—C—C = 138.6° in *(2)* and S—C—S = 141.2° in $C_5H_5(PMe_3)Co(\eta^2\text{-}CS_2)$[3].

Very few mononuclear thioketene-metal complexes have so far been mentioned in the literature. *Behrens et al.*[9a] describe a complex in which *(1)* is presumably bound only *via* the S atom to $Cr(CO)_5$. Iridium(I) and platinum(0) complexes with $\eta^2$-coordinated bis(trifluoromethyl)thioketene have been synthesized by *Stone et al.*[9b], not however from $(CF_3)_2C{=}C{=}S$ as starting material, but from heterocyclic, $CF_3$-substituted sulfur compounds.

Received: August 21, 1980 [Z 782 IE]
Revised: October 15, 1980
German version: Angew. Chem. *93*, 583 (1981)

---

[1] Complexes with Carbon Sulfides and Selenides as Ligands, Part 5. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and by gifts of chemicals from BASF AG, Ludwigshafen. We thank Dr. *U. Behrens* for supplying us with the the thioketene.—Part 4: *H. Werner, O. Kolb, R. Feser, U. Schubert*, J. Organomet. Chem. *191*, 283 (1980).

[2] *P. V. Yaneff*, Coord. Chem. Rev. *23*, 183 (1977); *I. S. Butler*, Acc. Chem. Res. *10*, 359 (1977).

[3] *H. Werner, K. Leonhard, C. Burschka*, J. Organomet. Chem. *160*, 291 (1978).

[4] *H. Werner, O. Kolb*, Angew. Chem. *91*, 930 (1979); Angew. Chem. Int. Ed. Engl. *18*, 865 (1979).

[5] *H. Werner, W. Hofmann*, Chem. Ber. *110*, 3481 (1977).

[6] *H. Werner, R. Feser*, Angew. Chem. *91*, 171 (1979); Angew. Chem. Int. Ed. Engl. *18*, 157 (1979).

[7] $C_{19}H_{32}CoPS$ ($M_r=382.5$), monoclinic, space group $P2_1/c$, $a=947.6(3)$, $b=1400(1)$, $c=1541.5(5)$ pm, $\beta=100.31(3)°$, $V=2012\times10^6$ pm$^3$, $\rho_{calc}=1.26$ g/cm$^3$, $Z=4$; 3126 reflections ($2°\leqslant2\Theta\leqslant48°$, $MoK_\alpha$, $\lambda=71.069$ pm, graphite monochromator, Syntex $P2_1$/XTL); heavy atom method, $R_1=0.073$, $R_2=0.071$ for 2214 structure factors, $F_0\geqslant4.2\,\sigma(F_0)$.

[8] *F. Carre, G. Cerveau, E. Colomer, R. J. P. Corriu, J. C. Young, L. Ricard, R. Weiss*, J. Organomet. Chem. *179*, 215 (1979).

[9] a) *U. Behrens, F. Edelmann*, J. Organomet. Chem. *118*, C41 (1976); b) *M. Green, R. B. L. Osborn, F. G. A. Stone*, J. Chem. Soc. *A 1970*, 944.

## Bis(tetraphenylphosphonium) Hexadecaphosphide, a Salt Containing the Novel Polycyclic Anion $P_{16}^{2-}$[1]

By *Hans Georg von Schnering, Victor Manriquez*, and *Wolfgang Hönle*[*]

We have recently shown[2] that the molecular compounds $P_7R_3$, $P_{11}R_3$ and $As_7R_3$ ($R=SiMe_3$) are formed in surprisingly high yields on reaction of the salts $Na_3P_7$, $Na_3P_{11}$ and $Rb_3As_7$ with chlorotrimethylsilane. In the mass spectra of $P_{11}R_3$ and $P_7R_3$, besides a series of fragments which differ by $P_2$- or $P_4$-units there also appear small amounts of $P_{16}R_2^+$. We have now been able to trap the $P_{16}^{2-}$ anion corresponding to this species by reaction with salts of large cations.

*$(Ph_4P)_2P_{16}$:* $Na_3P_7$[3] (3.16 g, ≈ 11 mmol) is suspended in 500 ml of tetrahydrofuran (THF) which has previously been freed of oxygen by treatment with K/benzophenone.

---

[*] Prof. Dr. H. G. von Schnering, Dipl.-Chem. V. Manriquez,
Dr. W. Hönle
Max-Planck-Institut für Festkörperforschung
Heisenbergstr. 1, D-7000 Stuttgart 80 (Germany)

A suspension of tetraphenylphosphonium chloride (12.43g, ≈33 mmol) in THF (100 ml) is added dropwise with stirring to the yellow suspension at 220 K. After warming to 298 K the suspension is stirred for *ca.* 20 h at 298 K. Red, rod-shaped crystals (length ≈0.4 mm) crystallize out from the filtrate within a week. Later, yellow amorphous "higher phosphanes" also separate out. However, the red crystals of $(Ph_4P)_2P_{16}$ can easily be separated mechanically from the by-products.

Compared to salts like $Na_3P_7$, $Na_3P_{11}$ and their derivatives, the hexadecaphosphide is remarkably stable. The crystals, which are practically insoluble in anhydrous solvents, hydrolyze and turn brown within two days on exposure to air. They decolorize within minutes in $H_2O$/ethanol mixtures, but their morphology is preserved. The phosphane odor typical for such reactions does not occur. Up to 570 K the mass spectrum (QMS) shows only the fragments of the cation and of $P_4$. In the presence of $Me_3SiCl$ the fragment $P_{16}R_2^+$ ($m/z=642$) is observed.

The X-ray structure analysis[4] gave a surprising result: The compound does not contain the anions $P_7^{3-}$, as would be expected in the synthesis, but the novel polycyclic hexadecaphosphorus dianion $P_{16}^{2-}$ (Fig. 1). Its skeletal structure, with mm2 symmetry, is made up of two $P_7$ units which are coupled *via* a common $P_2$ dumbbell; it can also be described in terms of the combination of a $P_7$-unit with a $P_9$-unit. The bond lengths show some peculiarities: The P—P distance *a* of 232 pm is very long. Here the strain caused by the 3m symmetry of the nortricyclic unit and the ψ-tetrahedral configuration of the bridgehead atoms linked directly to the $P_2$-dumbbell is effective. The shortest bond lengths (*h* and *i*) occur at the two divalent $P^{1-}$ atoms. The height 312 pm of the nortricyclene moieties lies directly between those in $P_7^{3-}$ and those in the neutral $P_7R_3$[5].

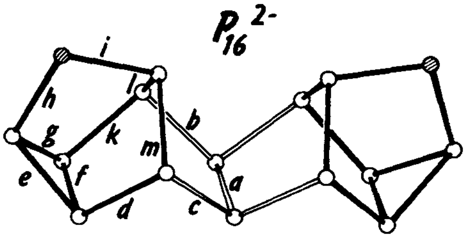


Fig. 1. The dianion in the $(Ph_4P)_2P_{16}$ structure. The bonds of the $P_7$-fragment are shown in bold lines. Bond lengths P—P in pm ($\sigma \leq 0.6$): $a=232.0$, $b=219.7$, $c=220.6$, $d=219.6$, $e=222.3$, $f=223.6$, $g=221.4$, $h=217.0$, $i=214.1$, $k=220.2$, $l=220.4$, $m=219.7$.

The slow crystallization of the sparingly soluble salt would indicate slow formation of the $P_{16}$-system. A number of disproportionation reactions are conceivable, which, *e.g.*, start with $P_7^{3-} \rightarrow P_3^{3-} + P_4$ and then lead from $2P_7^{3-}$ and $P_4$ directly or *via* $P_9^{3-}$ as intermediate to $P_{16}^{2-}$ and $P_2^{4-}$. The $P_9$-fragment of the dianion is isomeric with the framework of the prismane derivative $P_9R_3$ discussed earlier[2], into which it can be converted *via* a simple route by a double 1,2-bond shift.

Received: September 15, 1980 [Z 783 IE]
German version: Angew. Chem. *93*, 606 (1981)

---

[1] On the Chemistry of the Phosphides and Polyphosphides, Part 28.—Part 27: *H. G. von Schnering, G. Menge*, Z. Anorg. Allg. Chem., in press.

[2] *H. G. von Schnering, D. Fenske, W. Hönle, M. Binnewies, K. Peters*, Angew. Chem. *91*, 755 (1979); Angew. Chem. Int. Ed. Engl. *18*, 679 (1979).

[3] *H. G. von Schnering* "Catenation of Phosphorus Atoms" in *A. L. Rheingold* (Edit): Homoatomic Rings, Chains and Macromolecules of Main-Group Elements, Elsevier, Amsterdam 1977.

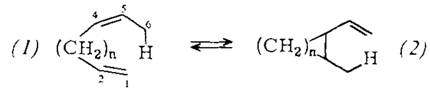
[4] $[(C_6H_5)_4P]_2P_{16}$, space group C2/c (No. 15), $a=2710.8(12)$, $b=1099.4(4)$, $c=2676.1(14)$ pm, $\beta=137.05(3)°$, $Z=4$, $\rho_{calc}=1.435$ g cm$^{-3}$; diffractometer data, 2443 reflections *hkl*, $Mo_{K\alpha}$ radiation $2\Theta \leq 40°$, large drop in intensity, $\bar{U}=0.06$ Å: $R=0.085$.

[5] *W. Hönle, H. G. von Schnering*, Z. Anorg. Allg. Chem. *440*, 171 (1978).

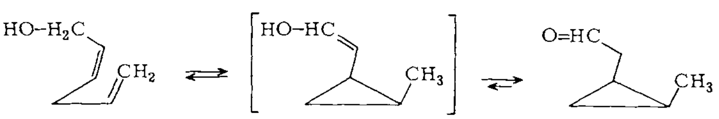
## Stereoselective Cyclopropane Syntheses by "Oxy-Homodienyl Hydrogen Shifts"[**]

By *Frank-Gerrit Klärner, Wolfgang Rüngeler*, and *Werner Maifeld*[*]

The thermally induced 1,5-homodienyl hydrogen shift *(1)*⇌*(2)* ($n=1$) belongs to the intramolecular ene reactions, which are of importance in the stereoselective synthesis of cyclic compounds[1]. With $n>2$, the equilibrium *(1)*⇌*(2)* lies on the side of the carbocycle, whereas with $n=1$ ring strain effects shift the equilibrium in favor of the acyclic diene[2].



Application of the reaction, despite its homogeneous course, has so far been limited to stereoselective olefin syntheses (*e.g.* 1,4,7-cyclononatriene[3a] or Cecropia juvenile hormone[3b]). The reaction should, in principle, be suitable in a reverse sense for stereoselective cyclopropane syntheses if it were possible to shift the equilibrium to the cyclic side, *e.g.* by an effect of substituents. A strong effect in this direction can be expected if during the reaction a CO-double bond can form at the expense of a less stable CC-double bond[4]. We have therefore studied the thermal behavior of the *cis*-2,5-hexadiene-1-ols *(1a)*—*(1e)*. The initial product of the hydrogen shift of *(1a)* should be the enol *(2a)*, which can be stabilized by enol-keto tautomerism to the aldehyde *(3a)*. According to an evaluation of the enthalpies of formation with the aid of Benson increments[5]



*(1a)* *(2a)* *(3a)*

the enol-keto tautomerism affords a gain in energy, hence the rearrangement *(1a)*→*(3a)* is *exo*-thermic ($\Delta\Delta H_f^0 = -8.8$ kcal/mol). The rearrangement *(1)*→*(2)* ($n=1$), on the other hand, is endothermic ($\Delta\Delta H_f^0 = +6.4$ kcal/mol).

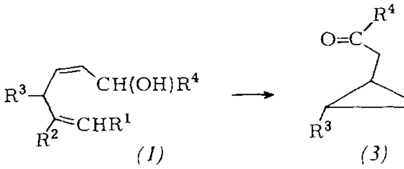
*(1b)*—*(1e)* can be prepared analogously to the synthesis of *(1a)*[6a] starting from propargyl alcohol and substituted alkyl halides in two steps by basic $Cu^{\oplus}$-catalyzed CC-coupling and subsequent selective catalytic *cis*-hydrogenation of the CC-triple bond. Thermolysis of *(1a)*—*(1e)* in the gas

---

[*] Prof. Dr. F.-G. Klärner, Dipl.-Chem. W. Rüngeler, W. Maifeld
Abteilung für Chemie der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

phase[7] at *ca.* 260 °C leads to the air-sensitive aldehydes *(3a)*—*(3d)*[8] and the ketone *(3e)* in yields between 75 and 90% (Table 1). Only small amounts of side products (< 3%; not isolated) are formed.



*(1)* *(3)*

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| *a* | H | H | H | H |
| *b* | H | H | $CH_3$ | H |
| *c* | $CH_3$ | H | $CH_3$ | H |
| *d* | H | $CH_3$ | H | H |
| *e* | H | H | H | $CH_3$ |

Table 1. Results of the thermolysis of *(1a)*—*(1e)* at 263.3° in the gas phase.

| Reaction | Half-life [min] | $\Delta G^{\neq}$ [kcal/mol] | Yield of *(3)* [%] [a] |
|---|---|---|---|
| *(1a)* → *(3a)* | 569 | 43.5 | 82 |
| *(1b)* → *(3b)* | 40 | 40.7 | 90 |
| *(1c)* → *(3c)* | 286 | 42.8 | 85 |
| *(1d)* → *(3d)* | 490 | 43.4 | 75 |
| *(1e)* → *(3e)* | 203 | 42.5 | 85 |

[a] The yields were determined gas-chromatographically (35 m glass capillary column "Marlophen", 1 mL He/min, flow division 1 : 60, 90 °C) against *p*-diethylbenzene as standard. The values refer to unreacted educt after two half-lives.

The structural and stereochemical assignment of the products follows mainly from the 250-MHz $^1$H-NMR spectra (Table 2). Especially characteristic are the coupling constants $^3J_c$ and $^3J_t$ of the vicinal, *cis* and *trans* cyclopropane hydrogen atoms, which were determined by double resonance experiments. As expected[9] one finds $^3J_c$ (8.2—8.7 Hz) > $^3J_t$ (4.4—4.8 Hz) in each case for *(3a)*—*(3e)*. The *cis*-position of the 1-$CH_2$-$COR^4$- and 2-$CH_3$-groups could also be demonstrated independently by conversion of *(3a)*[10] into the *cis*-1-methyl-2-vinylcyclopropane (*cis*-*(2)*[2]).

Table 2. $^1$H-NMR data of *(3a)*—*(3e)* (250 MHz, $C_6D_6$).

*(3a)*: $\delta = -0.44$ (q, 3-$H^s$ [a]$= {}^2J_{\text{gem.}} = -4.4$ Hz, $^3J_{t,1\text{-H},3\text{-H}^s} = J_{t,2\text{-H},3\text{-H}^s} = 4.4$ Hz), 0.56 (m, 3-$H^a$ [b], $^3J_{c,1\text{-H},3\text{-H}^a} = {}^3J_{c,1\text{-H},3\text{-H}^a} = 8.7$ Hz), 0.67 (m, 1,2-H), 0.80 (d, $CH_3$), 1.85 (m, $CH_2$—CHO), 9.38 (t, —$CH_2$—CHO).

*(3b)*: $\delta = -0.09$ (m, 3-$H^s$, $^3J_{t,1\text{-H},3\text{-H}^s} = {}^3J_{t,2\text{-H},3\text{-H}^s} = 4.4$ Hz, $^3J_{3\text{-H}^s,3\text{-CH}_3} = 6.0$ Hz), 0.44 (m, 1,2-H), 0.82 (d, 3-$CH_3$), 0.96 (d, 2-$CH_3$), 1.89 (m, $CH_2$—CHO), 9.40 (t, $CH_2$—CHO).

*(3c)*: $\delta = -0.05$ (m, 3-$H^s$, $^3J_{t,1\text{-H},3\text{-H}^s} = {}^3J_{t,2\text{-H},3\text{-H}^s} = 4.8$ Hz, $^3J_{3\text{-H}^s,\text{CH}_3} = 6.3$ Hz), 0.33 (m, 2-H, $J_{C,1\text{-H},2\text{-H}} = 8.2$ Hz), 0.52 (m, 1-H), 0.91 (t, $CH_2$—$CH_3$), 0.99 (d, 3-$CH_3$), 1.06 (m, $CH_2$—$CH_3$), 1.90 (m, CH—CHO), 9.40 (t, $CH_2$—CHO).

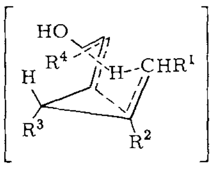
*(3d)*: $\delta = -0.20$ (t, 3-$H^s$, $^2J_{\text{gem.}} = -4.5$ Hz, $^3J_{t,1\text{-H},3\text{-H}^s} = 4.5$ Hz), 0.37 (dd, 3-$H^a$, $^3J_{c,1\text{-H},3\text{-H}^a} = 8.2$ Hz), 0.83 (s, 3-$CH_3^s$), 0.95 (s, 3-$CH_3^a$), 1.87 (m, $CH_2$—CHO), 9.46 (t, $CH_2$—CHO).

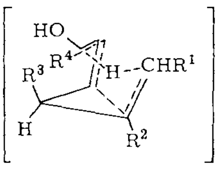
*(3e)*: $\delta = -0.35$ (q, 3-$H^s$, $^2J_{\text{gem.}} = -4.6$ Hz, $J_{t,1\text{-H},3\text{-H}^s} = J_{t,2\text{-H},3\text{-H}^s} = 4.6$ Hz), 0.65 (m, 3-$H^a$, $J_{c,1\text{-H},3\text{-H}^a} = J_{c,2\text{-H},3\text{-H}^a} = 8.5$ Hz), 0.76 (m, 1,2-H), 0.89 (d, 2-$CH_3$), 1.77 (s, $CH_2$—$COCH_3$), 2.0 (m, $CH_2$—$COCH_3$).

[a] s = *syn*. [b] a = *anti* (relative to the $CH_2COR^4$ group).

Owing to its high degree of stereoselectivity the hydrogen shift observed here provides a method for the synthesis of *cis*-1,2-disubstituted cyclopropanes. As the rearrangements *(1b)*→*(3b)* and *(1c)*→*(3c)* show, only the sterically less hindered transition states *(4b, c)* are utilized. The more unfavorable transition states *(5b, c)* would have led to *all-cis*-trisubstituted cyclopropanes. Thus, with this method variously substituted cyclopropane systems can also be prepared stereospecifically. Because of the analogy to the "oxy-Cope rearrangement"[11], we propose the designation "oxy-homodienyl hydrogen shift" for this reaction. As in the oxy-Cope rearrangement[12a], the 1,3-sigmatropic carbon shift[12b], or the [4+2]-cycloreversion[12c], a metalation of the hydroxy group could lead to the thermolysis already taking place at considerably lower temperatures.

*(4)*





*(5)*

Received: December 22, 1980 [Z 786 IE]
German version: Angew. Chem. *93*, 613 (1981)

CAS Registry numbers:
*(1a)*, 42185-95-5; *(1b)*, 78167-48-3; *(1c)*, 78167-49-4; *(1d)*, 78167-50-7; *(1e)*, 78167-51-8; *cis-(3a)*, 78167-52-9; *trans-(3a)*, 78167-53-0; *(3b)*, 78167-54-1; *(3c)*, 78167-55-2; *(3d)*, 78167-56-3; *cis-(3e)*, 78167-57-4; *trans-(3e)*, 54560-69-9

---

[1] Review: *W. Oppolzer, V. Snieckus*, Angew. Chem. *90*, 506 (1978); Angew. Chem. Int. Ed. Engl. *17*, 476 (1978).

[2] a) *R. J. Ellis, H. M. Frey*, J. Chem. Soc. Suppl. V *1964*, 5578; b) *W. R. Roth, J. König*, Justus Liebigs Ann. Chem. *688*, 28 (1965).

[3] a) *W. R. Roth*, Justus Liebigs Ann. Chem. *671*, 10 (1964); *D. S. Glass, R. S. Boikess, S. Winstein*, Tetrahedron Lett. *1966*, 999; b) *E. J. Corey, H. Yamamoto, D. K. Herron, K. Achiwa*, J. Am. Chem. Soc. *92*, 6635 (1970); *E. J. Corey, H. Yamamoto, ibid. 92*, 6636 (1970).

[4] Owing to this effect the equilibrium *cis*-2-vinylcyclopropanecarbaldehyde $\rightleftarrows$ 2,5-dihydrooxepin lies on the side of the cyclopropane: *S. J. Rhoads, R. D. Cockroft*, J. Am. Chem. Soc. *91*, 2815 (1969); see also *M. Rey, A. S. Dreiding*, Helv. Chim. Acta *48*, 1985 (1965).

[5] *S. W. Benson:* Thermochemical Kinetics, 2nd Edition. Wiley, New York 1976, p. 271 ff.

[6] *P. Kurtz*, Justus Liebigs Ann. Chem. *658*, 6 (1972); *J. M. Osbond, J. C. Wickens*, DOS 1961776 (1970). For the CC-coupling in the preparation of *(1c)*, tetrahydropyranyl-protected propargyl alcohol was allowed to react with 4-bromo-2-pentene analogously to an alternative procedure for *(1a)* by *F. Bohlmann* and *W. Karl* (Chem. Ber. *105*, 355 (1972).

[7] The thermolyses were carried out in evacuated 250-ml ampoules (0.5 g substance, 0.01 mbar) in a hot-air thermostat. *(1a)*—*(1e)* as allyl alcohols are extremely sensitive to acids at elevated temperatures, even towards catalytic amounts on the surface of the glass vessel. To avoid acid-catalysis, a 0.1 molar equivalent or triethylamine is added in each case in the thermolyses of *(1a)*—*(1e)*. All glass apparatus were rinsed with triethylamine before use.

[8] On exposure to air (also in solution) the aldehydes *(3a)*—*(3d)* readily form hydroperoxides. Solvents must therefore be degassed. *(3a)* can be oxidized with $Ag_2O$ in 96% yield to the air-stable *cis*-(2-methylcyclopropyl)acetic acid.

[9] *H. Günther:* NMR-Spektroskopie, Thieme, Stuttgart 1973, p. 106 ff.

[10] $LiAlH_4$-reduction, bromination with $PBr_3$, and dehydrobromination with *tert*-$C_4H_9OK$ in dimethyl sulfoxide.

[11] Review: *S. J. Rhoads, N. R. Raulins*, Org. React. *22*, 1 (1975).

[12] a) *D. A. Evans, A. M. Golob*, J. Am. Chem. Soc. *97*, 4765 (1975); *D. A. Evans, J. V. Nelson, ibid. 102*, 774 (1980); b) *B. Franzus, M. L. Scheinbaum, D. L. Waters, H. B. Bowlin, ibid. 98*, 1241 (1976); c) *O. Papies, W. Grimme*, Tetrahedron Lett. *1980*, 2799.

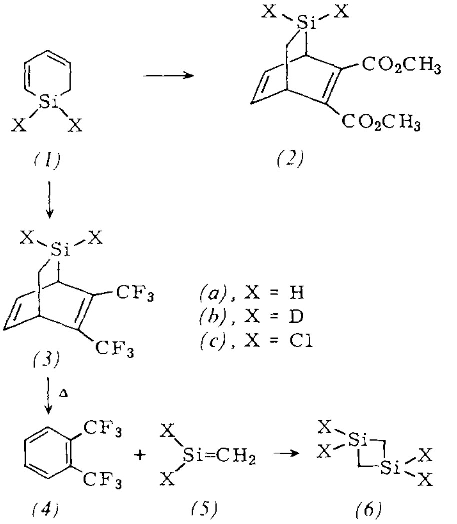
## Silaethene[**]

By *Günther Maier, Gerhard Mihm,* and
*Hans Peter Reisenauer*[*]

Encouraged by the successful matrix isolation of silabenzene[1], we ventured to approach unsubstituted silaethene[2]. While derivatives[3] are known, unequivocal evidence[4] for the parent compound, which is especially important in order to experimentally test theoretical predictions[5], was still awaited. We report the preparation of silaethene *(5a)* by retrodiene cleavage and its detection by IR and UV spectroscopy.

1,1-Dichloro-1-sila-2,4-cyclohexadiene *(1c)*[1a] and dimethyl acetylenedicarboxylate react to produce the adduct *(2c)* (Table 1), whose flash pyrolysis at 400 °C in the presence of benzene with nitrogen as the carrier gas, led to dimethyl phthalate and phthalic anhydride.

Attempts to trap the presumed intermediate product, 1,1-dichloro-1-silaethene *(5c)*, by carefully freezing the fragments formed by vacuum flash pyrolysis (650 °C, $10^{-4}$ torr)[6] in argon at 10 K, resulted in the detection of IR absorption bands at $\tilde{\nu} = 1008$, 732 and 593 $cm^{-1}$, in addition to those of the previously mentioned arenes. The same bands are also recognizable when the bicyclooctadiene *(3c)*[7] (Table 1), readily accessible from *(1c)* and perfluoro-2-butyne, is similarly cleaved. This observation and the fact that the normal flash pyrolysis (650 °C, 0.2 torr, product trapped at 77 K) of *(3c)* only yields *o*-bis(trifluoromethyl)benzene *(4)* and tetrachlorodisilacyclobutane *(6c)*[8], suggest that the absorptions measured in the matrix are assignable to *(5c)*.



The thermal behavior of the unchlorinated silaethene precursors *(3a)* and *(3b)*, which are readily obtained from *(1a)*[1a] and the silacyclohexadiene *(1b)*—prepared from *(1c)* and $LiAlD_4$—is even more assertive.

When *(3a)* or *(3b)* are heated to 420 °C with $N_2$ as the flow gas, in the presence of cyclohexane[7], *(4)* is smoothly formed together with the hydrogenated or deuterated 1,3-disilacyclobutanes *(6a)* or *(6b)*, respectively[8].

Table 1. Synthetic conditions together with physical and spectroscopic properties of compounds *(2c)*, *(3a)*, *(3b)* and *(3c)*. IR (film) [$cm^{-1}$]; NMR: $\delta$-values relative to TMS (in $CDCl_3$, unless otherwise specified).

*(2c)*: 6 h reflux in toluene; 57%; B.p. = 130 °C/$10^{-2}$ torr.—IR: 1740, 1730, 1718 (C=O), 1635, 1600 (C=C), 562 (Si—Cl).—$^1$H-NMR ($CCl_4$): 1.00 (2 H, d), 3.40—4.30 (2 H, m, +2 $CH_3$), 6.13—6.54 (2 H, m).—$^{13}$C-NMR: 15.00, 37.12, 38.31, 51.81, 51.93, 128.72, 131.78, 136.46, 139.32, 164.31, 165.26.—Correct elemental analysis.

*(3a)*: autoclave; 5 h, 90 °C; 52%; B.p. = 90 °C/100 torr.—IR: 2160 (Si—H), 1655, 1605 (C=C).—$^1$H-NMR: 0.82 (2 H, q), 3.53 (2 H, d), 3.94 (1 H, d), 4.20 (1 H, m), 5.90—6.33 (2 H, m).—$^{13}$C-NMR [a]: 6.94, 29.23, 35.19, 116.37, 127.28, 129.85, 130.38.—MS: *m/e* = 258.0299 (calc.), 258.0291 (found).

*(3b)*: as *(3a)*, 50%; B.p. = 90 °C/100 torr.—IR: 1655, 1605 (C=C), 1585, 1565 (Si—D).—$^1$H-NMR: 0.82 (2 H, d), 3.92 (1 H, d), 4.20 (1 H, m), 5.88—6.28 (2 H, m).—$^{13}$C-NMR [a]: 6.85, 29.26, 35.18, 116.46, 127.33, 129.85, 130.42.—MS: *m/e* = 260.0425 (calc.), 260.0425 (found).

*(3c)*: as *(3a)*, 71%; B.p. = 75 °C/5 torr.—IR: 1660, 1610 (C=C), 570 (Si—Cl).—$^1$H-NMR: 1.01 (2 H, q), 3.94 (1 H, d), 4.14 (1 H, d), 6.01—6.56 (2 H, m).—$^{13}$C-NMR [a]: 14.26, 36.03, 37.56, 114.78, 128.98 [b], 132.04.—MS: *m/e* = 325.9520 (calc.), 325.9515 (found).

[a] The C-atoms of the $CF_3$ groups are not observable under the recording conditions. [b] Two olefinic C-atoms coincidently show the same chemical shift.

By means of a combination of vacuum flash pyrolysis (650 °C, $10^{-4}$ torr) and matrix isolation techniques, apart from the bands originating from *(4)*, the IR absorptions shown in Table 2 can also be measured. The latter disappear upon irradiation ($\lambda = 254$ nm) of the condensate[9]. This also occurs upon thawing of the argon matrix at 35 K. Hereby, the corresponding 1,3-disilacyclobutanes *(6a)* and *(6b)* are formed.

Table 2. IR and UV absorption bands of the silaethenes *(5a)*, *(5b)* and *(5c)*, together with those of the dimerization products *(6a)*, *(6b)* and *(6c)*.

| | Silaethenes *(5)* | | | 1,3-Disilacyclobutanes *(6)* |
|---|---|---|---|---|
| | IR [$cm^{-1}$] | UV [nm] | | IR [$cm^{-1}$] |
| *(5a)* | 2239 (m), 2219 (m), 985 (w), 927 (w), 817 (s), 741 (s) | 258 [a] | *(6a)* | 2160—2140 (m), 961 (s), 899 (s) |
| *(5b)* | 1635 (m), 1600 (m), 952 (w), 759 (s), 719 (s), 396 (w) | 259 [a] | *(6b)* | 1677 (m), 1654 (m), 786 (s), 689 (s) |
| *(5c)* | 1008 (m), 732 (s), 593 (m) | 246 [a] | *(6c)* | [b] |

[a] The extinction is considerably greater than that of the $\alpha$-band of *(4)*. [b] The low intensity of the bands from *(6c)* do not permit unambiguous identification.

Of the bands observed, the antisymmetric and symmetric Si—H and Si—D vibrational frequencies are of considerable diagnostic use. These frequencies are found above 2200 $cm^{-1}$ in silabenzene (2217 $cm^{-1}$)[1a]. The still higher wavenumbers (2239 and 2219 $cm^{-1}$) suggest that the product obtained from *(3a)* is in fact a compound with a hydrogen atom on an $sp^2$-hybridized silicon atom[3f]. These experimentally determined frequencies lie between the values obtained by calculation (2480[5c] and 2160[4] $cm^{-1}$). The correctness of the assignment follows from the shift of the bands mentioned above to much lower wavenumbers (1635 $cm^{-1}$ and 1600 $cm^{-1}$) in the product prepared from the deuterated precursor *(3b)*.

Comparison of the matrix UV spectrum of separately matrix isolated arene *(4)* with the matrix spectra obtained by pyrolysis of *(3a)*, *(3b)* and *(3c)*, indicates that the silaethenes *(5a)*, *(5b)* and *(5c)* are characterized by distinct UV

---

[*] Prof. Dr. G. Maier, Dipl.-Chem. G. Mihm, Dr. H. P. Reisenauer
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

maxima (Table 2)[10]. These disappear, as do the corresponding IR bands, upon irradiation or thawing of the matrices.

It should be noted that the most commonly used route to silaethenes, *i.e.* the pyrolysis of the corresponding silacyclobutanes[2,4], cannot be transferred to the parent compound. Instead of *(5a)* only propene, ethene and acetylene can be detected as cleavage products after vacuum flash pyrolysis[11].

The following conclusions can be drawn: 1) Unsubstituted silaethene *(5a)* and its derivatives *(5b)* and *(5c)* are species capable of existence and can be identified by IR and UV spectroscopy. 2) They are only stable under conditions of matrix isolation at 10 K. 3) On thawing of the matrix they dimerize to 1,3-disilacyclobutanes.

Received: January 14, 1981 [Z 790a IE]
German version: Angew. Chem. *93*, 615 (1981)

---

[1] a) *G. Maier, G. Mihm, H. P. Reisenauer*, Angew. Chem. *92*, 58 (1980); Angew. Chem. Int. Ed. Engl. *19*, 52 (1980); b) PE spectroscopic studies: *B. Solouki, P. Rosmus, H. Bock, G. Maier, ibid. 92*, 56 (1980) and *19*, 51 (1980).

[2] For a summary of the silaethene problem see: a) *P. Jutzi*, Angew. Chem. *87*, 269 (1975); Angew. Chem. Int. Ed. Engl. *14*, 232 (1975); b) *L. E. Gusel'nikov, N. S. Nametkin, V. M. Vdovin*, Acc. Chem. Res. *8*, 18 (1975); c) *L. E. Gusel'nikov, N. S. Nametkin*, Chem. Rev. *79*, 529 (1979).

[3] For the latest results on the characterization of 1,1-dimethyl-1-silaethene see: a) *O. M. Nefedov, A. K. Mal'tsev, V. N. Khabashesku, V. A. Korolev*, J. Organomet. Chem. *201*, 123 (1980); b) *L. E. Gusel'nikov, V. V. Volkova, V. G. Avakyan, N. S. Nametkin, ibid. 201*, 137 (1980); c) *P. G. Mahaffy, R. Gutowsky, L. K. Montgomery*, J. Am. Chem. Soc. *102*, 2854 (1980); d) 1,1,2-Trimethyl-1-silaethene: *O. L. Chapman, C.-C. Chang, J. Kolc, M. E. Jung, J. A. Lowe, T. J. Barton, M. L. Tumey, ibid. 98*, 7844 (1976); e) *M. R. Chedekel, M. Skoglund, R. L. Kreeger, H. Shechter, ibid. 98*, 7846 (1976); f) 1-Methyl-1-silaethene: *T. J. Drahnak, J. Michl, R. West, ibid. 101*, 5427 (1979); *103*, 1845 (1981); g) for silaethenes kinetically stabilized by steric hindrance see: *A. G. Brook, J. W. Harris, J. Lennon, M. El Sheikh, ibid. 101*, 83 (1979); *A. G. Brook, F. Abdesaken, B. Gutekunst, G. Gutekunst, R. K. Kallury*, J. Chem. Soc. Chem. Commun. *1981*, 191.

[4] Our results contradict a recent publication indicating that silaethene should be stable in the condensed phase at 77 K: *N. Auner, J. Grobe*, Z. Anorg. Allg. Chem. *459*, 15 (1979).

[5] Theory: a) Complete literature survey in [2c]; b) most recent theoretical work: *J. D. Goddard, Y. Yoshioka, H. F. Schaefer III*, J. Am. Chem. Soc. *102*, 7644 (1980); see also *M. Hanamura, S. Nagase, K. Morokuma*, Tetrahedron Lett. *1981*, 1813; c) calculated IR spectrum of silaethene: *H. B. Schlegel, S. Wolfe, K. Mislow*, Chem. Commun. *1975*, 246; a recent calculation gives the values 2346 and 2338 cm$^{-1}$ for the asymm. and symm. Si—H vibrational frequencies respectively. (*H. B. Schlegel*, personal communication.)

[6] Pyrolysis oven with directly coupled low temperature cell (Displex Closed Refrigeration System CSA 202, Air Products), quartz pyrolysis tube (8 x 50 mm). Oven outlet—window distance 50 mm.

[7] Diels-Alder adducts of this type have previously been suggested as potential sources of silaethene: *T. J. Barton, E. Kline*, J. Organomet. Chem. *42*, C 21 (1972); see also *T. J. Barton*, Pure Appl. Chem. *52*, 615 (1980).

[8] Identified by comparison with the published spectral data of compounds *(6)*: a) *G. Fritz, E. Matern*, Z. Anorg. Allg. Chem. *426*, 28 (1976); b) *R. M. Irwin, J. M. Cooke, J. Laane*, J. Am. Chem. Soc. *99*, 3273 (1977); c) *N. Auner, J. Grobe*, J. Organomet. Chem. *188*, 151 (1980).

[9] Thereby, new IR absorptions [stemming from *(5a)* at 2004 and 1935 cm$^{-1}$, from *(5b)* at 1454 and 1405 cm$^{-1}$] are observed, which could originate from silylenes (silanediylenes) or silyl radicals: *D. E. Milligan, M. E. Jacox*, J. Chem. Phys. *52*, 2594 (1970).

[10] 1,1-Dimethyl-1-silaethene, prepared by pyrolysis of 1,1-dimethyl-1-silacyclobutane, shows an absorption maximum at 244 nm in argon at 10 K.

[11] a) Own attempts; b) *A. K. Mal'tsev, V. N. Khabashesku, O. M. Nefedov*, Dokl. Akad. Nauk SSSR *247*, 383 (1979).

---

# Silaethene: Highly Correlated Wave Functions and Photoelectron Spectroscopic Evidence[**]

By *Pavel Rosmus, Hans Bock, Bahman Solouki, Günther Maier*, and *Gerhard Mihm*[*]

*Dedicated to Professor Edgar Heilbronner on the occasion of his 60th birthday*

*Ab initio* quantum mechanical calculations, which account for large portions of the electron correlation[1,2], yield reliable theoretical predictions of experimentally unknown molecular properties[3]. Thus, ionization energies can be calculated to an accuracy of *ca.* 0.1 to 0.3 eV, *i.e.* to a degree of accuracy sufficient to identify unknown molecules by photoelectron spectroscopy. We have used such a combination of theory and experiment in the search for thermal dissociation reactions through which silaethene could be formed[4,5].

The quality of the wave function plays an important role in calculations of energy differences: the total energies for silaethene calculated by us, are, to date, the most accurate for this molecule[6]. For all electronic states treated, we have obtained 70 to 80% of the valence electron correlation energies. The vertical energy differences are shown in Table 1.

Table 1. Vertical energy differences between the ground state of the neutral molecule $H_2Si{=}CH_2$ and the doublet state of the radical cation $H_2Si{=}CH_2^{\cdot\oplus}$.

| Method of calculation | | $\tilde{X}(^2B_1)$ | $\tilde{A}(^2B_2)$ | $\tilde{B}(^2A_1)$ | $\tilde{C}(^2B_2)$ | $\tilde{D}(^2A_1)$ | $\tilde{E}(^2A_1)$ |
|---|---|---|---|---|---|---|---|
| $\Delta E^{SCF}$ | [eV] | 7.40 | 12.6 | 12.3 | 14.7 | 18.0 | 23.0 |
| $\Delta E^{PNO-CEPA}$ | [eV] | 8.59 | 12.5 | 12.7 | 14.2 | 16.9 | 21.1 |
| "$IE_n$" | [eV] | 8.95±.1 | 12.5±.1 | 12.9±.1 | 14.1±.1 | 16.5±.2 | 20.4±.3 |

The ionization energies "$IE_n$" are estimated from the energy differences $\Delta E^{SCF}$ and $\Delta E^{PNO-CEPA}$, using the assumption that approximately 75% of the correlation contributions are covered.

It should be possible to detect silaethene by photoelectron spectroscopy, in particular from the predicted first ionization energy at 8.95±0.1 eV. However, in numerous pyrolysis experiments on promising precursors, such as 1,3-disilacyclobutane, no reproducible bands in the expected region were observed[4,5]. Finally, in the thermal retrodiene cleavage of the bis(trifluoromethyl)-substituted bicycle[5], a novel band with vibrational fine structure (Fig. 1) appears, whose intensity increases upon addition of argon to the flowing gas. Higher ionization bands are masked by the superimposed PE spectrum of the cleaved off component 1,2-bis(trifluoromethyl)benzene (Fig. 1).

The following additional arguments corroborate the assignment of silaethene as a retrodiene dissociation product[5]: The first ionization energy is observed in the pre-cal-

---

[*] Prof. Dr. H. Bock, Dr. P. Rosmus, Dr. B. Solouki
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. G. Maier, Dipl.-Chem. G. Mihm
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)

[**] For previous work on highly correlated wave functions see: *H. J. Werner, P. Rosmus*, J. Chem. Phys. *73*, 2319 (1980). Also Part 25 on Analysis and Optimization of Gas Phase Reactions.—Part 24: *H. Bock, T. Hirabayashi, S. Mohmand*, Chem. Ber., in press.

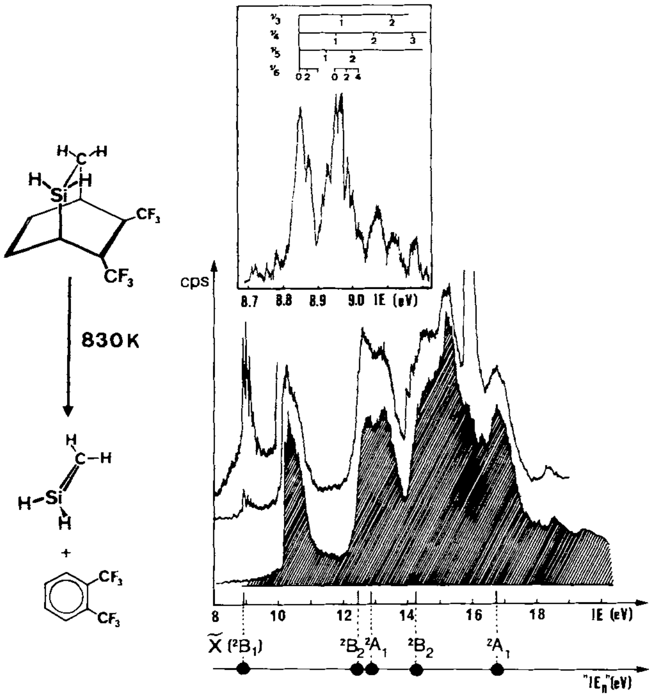


Fig. 1. He(I)-PE spectrum of the thermal retrodiene dissociation products of 5,6-bis(trifluoromethyl)-2-silabicyclo[2.2.2]octa-5,7-diene at 850 K (hatched: 1,2-bis(trifluoromethyl)benzene) as well as the expanded vibrational fine structure of the ground state of the silaethene radical cation with the following suggested assignments (from top to bottom: $\tilde{\nu}_3(a_1, \delta_{CH_2}) = 1010 \pm 40\ cm^{-1}$, $\tilde{\nu}(a_1; \nu_{Si=C} + \delta_{SiH_2}) = 840\ cm^{-1}$; $\tilde{\nu}_5(a_1; \nu_{Si=C} + \delta_{SiH_2}) = 620\ cm^{-1}$ and $\tilde{\nu}_6(a_2; \tau) \approx 200\ cm^{-1}$).

culated energy region; mixing with the inert gas argon apparently inhibits secondary reactions and the pronounced vibrational fine structure of the first PE band (Fig. 1) resembles that of the iso(valence)electronic ethene[7]. In particular, the vibrational progressions assigned (cf. Fig. 1: $\nu_4$ and $\nu_5$ $(\delta_{SiH_2} + \nu_{Si=C})$) preclude, with a high degree of probability, the presence of isomers[4] such as $CH_3$—Si—H or $H_3Si$—C—H. The PES-values of the analogously generated $D_2Si{=}CH_2^{\cdot\oplus}$ amount to 770 and 550 $cm^{-1}$.

The resolved fine structure of the first PES band indicates a twisted equilibrium structure in the ground state for the radical cation $H_2Si{=}CH_2^{\cdot\oplus}$: both the lowest doublet states (cf. Table 1, $\tilde{X}(^2B_1)$ and $\tilde{A}(^2B_2)$) are coupled *via* the torsional vibration $\nu_6(a_2)$. In addition to the totally symmetric vibrations, it becomes excited and is assigned to the frequencies observed at $\approx 200\ cm^{-1}$ (Fig. 1: $2n \cdot \nu_6$; for $D_2Si{=}CH_2^{\cdot\oplus} \approx 120\ cm^{-1}$). Furthermore, such an interpretation supports the twisted equilibrium structure deduced for the iso(valence)electronic radical cation $H_2C{=}CH_2^{\cdot\oplus}$, which has a similar PES-vibrational fine structure[7]—a classic example of structure alteration upon oxidation or reduction of molecules[8].

Received: April 2, 1981 [Z 790b IE]
German version: Angew. Chem. 93, 616 (1981)

CAS Registry numbers:
5,6-Bis(trifluormethyl)-2-silabicyclo[2.2.2]octa-5,7-diene, 78167-41-6; 1,2-bis(trifluoromethyl)benzene, 433-95-4; $H_2Si{=}CH_2$, 51067-84-6; $H_2Si{=}CH_2^{\cdot\oplus}$, 78167-42-7.

---

[1] For correlation of electrons cf. *e.g.* *W. Kutzelnigg:* Einführung in die Theoretische Chemie, Bd. 1, Verlag Chemie, Weinheim 1975, p. 201ff. The correlation contribution to the ionization energy is defined as $IE^{exp} - IE^{\Delta SCF}$.

[2] For the *P*seudo *N*atural *O*rbitals *C*oupled *E*lectron *P*air *A*pproach cf. *W. Meyer,* Int. J. Quantum Chem. Symp. *5,* 341 (1971); J. Chem. Phys. *58,* 1017 (1973); Modern Theoretical Chemistry, Vol. 2, Plenum Press, New York 1977. Professor *Meyer* is also thanked for the MOLPRO program.

[3] Cf. *e.g.* *W. Meyer, P. Botschwina, P. Rosmus, H. J. Werner* in *J. Bargon:* Computational Methods in Chemistry, The IBM Research Symposium Series, Plenum Press, New York 1980.

[4] Since 1973, in collaboration with *T. Barton* (silatoluene, J. Am. Chem. Soc. *102,* 420 (1980)), *G. Maier* (silabenzene, Angew. Chem. *92,* 56 (1980); Angew. Chem. Int. Ed. Engl. *19,* 51 (1980)), *E. Block* (St. Louis/Missouri) and in particular with *J. Grobe* and *N. Auner* (Technische Hochschule Darmstadt), we have studied the gas phase thermal decomposition of numerous silicon compounds and analyzed the reaction products by PE spectroscopy: Pyrolysis of sila- and disilacyclobutanes also produces unstable silicon compounds, which due to the many pyrolytic by-products, cannot be unambiguously characterized but are nonidentical with the compounds discussed here. For possible isomers cf. *J. D. Goddard, Y. Yoshioka, H. F. Schaefer III,* J. Am. Chem. Soc. *102,* 7644 (1980) or *R. T. Conlin, D. L. Wood, ibid. 103,* 1843 (1981).

[5] The generation of silaethene by retrodiene cleavage was first successfully achieved by *G. Maier, G. Mihm, H. P. Reisenauer,* Angew. Chem. *93,* 615 (1981); Angew. Chem. Int. Ed. Engl. *20,* 597 (1981). Cf. also the literature cited therein, particularly that on the structure determination of $(H_3C)_2Si{=}CH_2$ by *P. G. Mahaffy, R. Gutowsky, L. K. Montgomery,* J. Am. Chem. Soc. *102,* 2854 (1980). Evidence for $(H_3C)_2SiCH_2$ in the gas phase has been reported by *T. Koenig et al.,* J. Am. Chem. Soc. *103,* 1212 (1981). A sterically shielded stable silaethene has been isolated by *A. Brook et al.,* Chem. Eng. News *59,* March 30, p. 78 (1981).

[6] Starting from the quantum chemically optimized structure of silaethene (*R. Ahlrichs, R. Heinzmann,* J. Am. Chem. Soc. *99,* 7452 (1977): $d_{CSi} = 169$, $d_{SiH} = 148$, $d_{CH} = 108$ pm, ∢ HSiH = 115°, HCH = 112°) our calculations gave the following total energies of the neutral molecule: $E^{SCF} = -329.048316$, $E^{PNO-CI} = -329.285603$, $E^{PNO-CEPA} = -329.314987$ a.u. using a Gaussian basis set of the following size Si(11s, 7p, 2d), C(9s, 5p, 2d) and H(5s, 1p). For similar calculations with inclusion of electron correlation cf. *D. M. Hood, H. F. Schaefer III,* J. Chem. Phys. *68,* 2985 (1978).

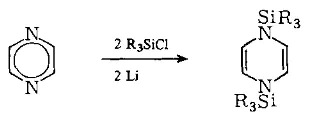
[7] Cf. also *R. Stockbauer, M. G. Inghram,* J. Electron Spectrosc. Rel. Phenom. *7,* 492 (1975); *H. Köppel, W. Domcke, L. S. Cederbaum, W. v. Niessen,* J. Chem. Phys. *69,* 4252 (1978), and literature cited therein.

[8] Cf. *e.g.* *H. Bock,* Angew. Chem. *89,* 631 (1977); Angew. Chem. Int. Ed. Engl. *16,* 613 (1977), and literature cited therein.

## The "Antiaromaticity" of 1,4-Dihydropyrazines[**]

By *Wolfgang Kaim*[*]

1,4-Dihydropyrazines, as cyclic 8π-electron systems, are potential antiaromatic compounds[1,2a]. Until now, the only known organic derivatives have been highly substituted[2]; however, the reductive silylation of pyrazine offers a straightforward route to the very reactive compound *(1)*[3].



*(1)*, R = $CH_3$

From the X-ray structure analysis of a 1,2,4,6-tetraaryl-1,4-dihydropyrazine, the central six-membered ring exists in a flat boat conformation; the cyclic conjugation appears to be markedly impaired by the bending of the aryl substituent on N-1[4]. Since silyl substituents are able to flatten the pyramidal configuration at the amine nitrogen atom[5], sufficient conjugation of *all* eight π-electrons should occur in a molecule such as *(1)*. As a criterion of "antiaromatic" behavior, the paramagnetic ring current concept is used[6], which—*cum grano salis*[7]—is specifically suitable for

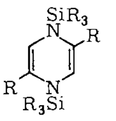
---

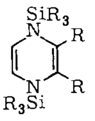
[*] Dr. W. Kaim
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

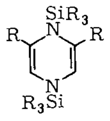
[**] The author acknowledges the award of a Liebig-Stipendium from the Fonds der Chemischen Industrie.

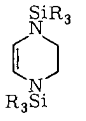
monocyclic compounds[6], and has been of particular heuristic value for comparative studies[8].

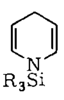
For this reason, in addition to the model compound *(1)*, the three isomeric dimethyl derivatives *(2)*—*(4)* were prepared[9a]; the 1,2,3,4-tetrahydropyrazine *(5)*[9b] and the 1,4-dihydropyridine *(6)*[9c] are given for comparison with non-conjugated systems. The $^1$H-NMR data of these compounds are collected in Table 1.


*(2)*


*(3)*


*(4)*


*(5)*


*(6)*

R = $CH_3$

Table 1. $^1$H-NMR chemical shifts of 1,4-bis(trimethylsilyl)-1,4-dihydropyrazine derivatives and pertinent compounds (60 MHz, $CDCl_3$, $TMS_{int}$, δ-values).

| Cpd. | CH | $CH_n$ | $SiCH_3$ | CH |
|---|---|---|---|---|
| *(1)* | 4.64 | — | 0.03 | 8.64 [b] |
| *(2)* | 5.00 | 1.57 | 0.16 | 8.31 [c] |
| *(3)* | 5.37 | 1.67 | 0.16 | 8.23 [d] |
| *(4)* | 5.46 | 1.64 | 0.09 (4)<br>0.17 (1) | 8.27 [e] |
| *(5)* | 5.38 | 3.14 | 0.08 | — |
| *(6)* [a] | 5.97 (2, 6)<br>4.62 (3, 5) | 3.17 | | — |

[a] In $C_6D_6$, $\delta_{SiCH_3}$ is not reported [9c]. [b] Pyrazine. [c] 2,5-Dimethylpyrazine. [d] 2,3-Dimethylpyrazine. [e] 2,6-Dimethylpyrazine.

Comparison of the data of *(5)* and *(6)* with that of *(1)* clearly shows the effect of the 8π-electron conjugation, which, on the basis of the paramagnetic ring current, leads to a high-field shift of the olefinic protons of *ca.* 0.75 ppm (Fig. 1). Similar high-field shifts have been observed in other "antiaromatic" molecules[8], however *aromatic* compounds have often been used for purposes of comparison[8c-e].

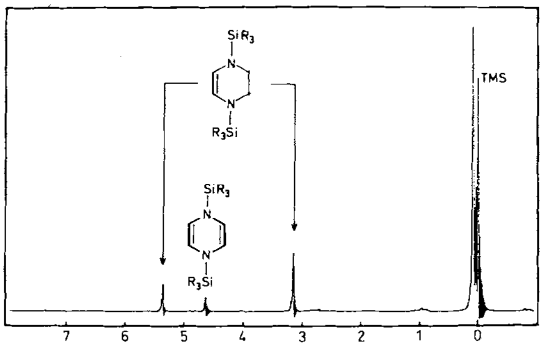


Fig. 1. $^1$H-NMR spectrum (60 MHz, $CDCl_3$) of the mixture of *(5)* and *(1)* obtained by partial hydrogenation of *(1)*. Signal at δ=2.8: *N,N'*-bis(trimethylsilyl)piperazine.

Investigation of the dimethyl derivatives *(2)*—*(4)* yields a remarkable result: In all of these compounds, both the olefinic and methylsilyl protons are shifted to *low field*, relative to the unsubstituted molecule *(1)*, although the methyl group normally exerts the opposite effect (cf. Table 1, pyrazines). The chemical shifts of the CH-protons follow a characteristic series: While a small paramagnetic ring current can still be determined upon 2,5-substitution, the 2,3- and 2,6-dimethyl derivatives exhibit no significant difference from the non-conjugated compound *(5)*.

These substitution effects are probably caused by steric interactions; as shown by the X-ray structure analysis[4], 2,6-substitution deforms the 1,4-dihydropyrazine framework so effectively, that the π-electron conjugation is interrupted. Similarly, the steric interaction of neighboring 2,3-substituents is expected to reduce the conjugation because of a more pronounced boat structure. Only 2,5-substitution still allows sufficient π-electron conjugation.

It is therefore comprehensible why all known organic 1,4-dihydropyrazine derivatives bear aryl substituents in the 2,3-[2a] or 2,6-[2b-d] positions; according to the NMR data[2] ($\delta_{CH} > 5.32$), these compounds have, in fact, no paratropic[6c] character.

Received: August 27, 1980 [Z 791a IE]
German version: Angew. Chem. *93*, 620 (1981)

CAS Registry numbers:
*(1)*, 31639-80-2; *(2)*, 78167-43-8; *(3)*, 78167-44-9; *(4)*, 78167-45-0; *(5)*, 78167-46-1; *(6)*, 3337-18-6; pyrazine, 290-37-9

---

[1] *R. R. Schmidt*, Angew. Chem. *87*, 603 (1975); Angew. Chem. Int. Ed. Engl. *14*, 581 (1975). See also *A. Streitwieser, Jr.:* Molecular Orbital Theory, Wiley, New York 1961, pp. 275.

[2] a) *S. J. Chen, F. W. Fowler*, J. Org. Chem. *36*, 4025 (1971); b) *J. W. Lown, M. H. Akhtar*, J. Chem. Soc. Perkin Trans. I *1973*, 683; c) *J. W. Lown, M. H. Akhtar, R. S. McDaniel*, J. Org. Chem. *39*, 1998 (1974); d) *R. R. Schmidt, M. Dimmler, P. Hemmerich*, Chem. Ber. *109*, 2395 (1976).

[3] *R. A. Sulzbach, A. F. M. Iqbal*, Angew. Chem. *83*, 145 (1971); Angew. Chem. Int. Ed. Engl. *10*, 127 (1971) and US-Pat. 3781291; Chem. Abstr. *80*, 60030w (1974). Cf. also *H. P. Becker, W. P. Neumann*, J. Organomet. Chem. *37*, 57 (1972).

[4] *J. Stezowski*, Cryst. Struct. Commun. *4*, 21 (1975); see also [1] and [2d].

[5] Cf. *W. Airey, C. Glidewell, A. G. Robiette, G. M. Sheldrick, J. M. Freeman*, J. Mol. Struct. *8*, 423 (1971); *4*, 215 (1969), and literature cited therein.

[6] a) *J. A. Pople, K. G. Untch*, J. Am. Chem. Soc. *88*, 4811 (1966); b) *R. C. Haddon, V. R. Haddon, L. M. Jackman*, Fortschr. Chem. Forsch. *16*, 103 (1971); c) *F. Sondheimer*, Acc. Chem. Res. *5*, 81 (1972).

[7] a) *J. F. Labarre, F. Crasnier*, Fortschr. Chem. Forsch. *24*, 33 (1971); b) G. Binsch, Naturwissenschaften *60*, 369 (1973); c) *R. B. Mallion*, Pure Appl. Chem. *52*, 1541 (1980) and Prog. Nucl. Magn. Reson. Spectrosc. *13*, 303 (1980).

[8] Cf. a) Tri-*tert*-butylcyclobutadiene: *G. Maier, A. Alzérreca*, Angew. Chem. *85*, 1056 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1015 (1973); *S. Masamune, N. Nakamura, M. Suda, H. Ona*, J. Am. Chem. Soc. *95*, 8481 (1973); b) 1,3,5-Tri-*tert*-butylpentalene: *K. Hafner, H. U. Süss*, Angew. Chem. *85*, 626 (1973); Angew. Chem. Int. Ed. Engl. *12*, 575 (1973); c) 1,2-Bis(trimethylsilyl)benzocyclobutadiene: *K. P. C. Vollhardt, L. S. Yee*, J. Am. Chem. Soc. *99*, 2010 (1977); Pure Appl. Chem. *52*, 1645 (1980); d) Methano[12]annulenes: *E. Vogel, H. Königshofen, K. Müllen, J. F. M. Oth*, Angew. Chem. *86*, 229, 231 (1974); Angew. Chem. Int. Ed. Engl. *13*, 281, 283 (1974); e) [16]Annulene: *J. F. M. Oth, J. M. Gilles*, Tetrahedron Lett. *1968*, 6259.

[9] a) Compounds *(2)*—*(4)* were prepared by reductive silylation of the corresponding dimethylpyrazines, and are air-sensitive, yellow liquids, b.p. ≈70°C/0.01 torr; b) *(5)* is obtained by careful hydrogenation of *(1)*; slightly yellow crystals, m.p. =25°C, b.p. =65°C/1 torr; c) *N. C. Cook, J. E. Lyons*, J. Am. Chem. Soc. *88*, 3396 (1966); the NMR data in Table 1 are corrected to $\delta(C_6H_6)=7.27$.

## Organometal-Stabilized 1,4-Dihydropyrazines: Extremely Electron-Rich Heterocycles[**]

By *Wolfgang Kaim*[*]

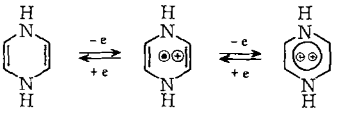
HMO calculations predict that 1,4-dihydropyrazine *(1)* should have a strongly antibonding occupied molecular or-

---

[*] Dr. W. Kaim
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

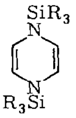
[**] The author thanks the Fonds der Chemischen Industrie for a Liebig-Stipendium.

bital and consequently should be highly reactive[1]. Until now *(1)* has not been synthesized, but the one- and two-electron oxidation products *(1)*$^{+\cdot}$ and *(2)*$^{2+}$ have been detected[2]:

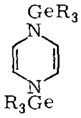


*(1)* *(1)*$^{+\cdot}$ *(1)*$^{2+}$

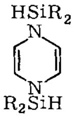
Reductive silylation of pyrazine[3] yields 1,4-bis(trimethylsilyl)-1,4-dihydropyrazine *(2)*, which, in contrast to the highly substituted organic derivatives of *(1)*, exhibits considerable conjugation of *all* eight π-electrons[4] and is a suitable model compound for *(1)*[5]. The photoelectron (PE) spectra of *(2)* and of four other 1,4-dihydropyrazine derivatives *(3)*—*(6)*[6] provide information on the radical cation states of the compounds; these states are advantageously described using molecular orbitals[7]. The first three ionization energies of the compounds *(2)*—*(6)*, together with the corresponding orbital assignments, are shown in Table 1.



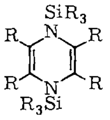
*(2)*



*(3)*



*(4)*



*(5)*

*(6)*

R = $CH_3$

Table 1. PE spectroscopically determined vertical ionization energies $IE^v_{1-3}$ [eV] of the 1,4-dihydropyrazine derivatives *(2)*—*(6)*.

| Compound | $IE^v_1$ | $IE^v_2$ | $IE^v_3$ |
|---|---|---|---|
| *(2)* | 6.16 $b_{3u}(\pi_S^*)$ [a] | 9.5 $b_{1g}(\pi_S)$ | 9.5 $b_{2g}(\pi_A)$ |
| *(3)* | 5.87 $b_{3u}(\pi_S^*)$ | 9.15 $b_{1g}(\pi_S)$ | 9.50 $b_{2g}(\pi_A)$ |
| *(4)* | 6.33 $b_{3u}(\pi_S^*)$ | 9.7 $b_{1g}(\pi_S)$ | 9.7 $b_{2g}(\pi_A)$ |
| *(5)* | 6.48 $b_{3u}(\pi_S^*)$ | 8.10 $b_{2g}(\pi_A)$ | 8.70 $b_{1g}(\pi_S)$ |
| *(6)* | 6.50 $b_1$ | 8.25 $a_2$ | 9.00 $b_1$ |

[a] For denotion of orbitals the symmetry groups $D_{2h}$ and $C_{2v}$, which are valid for planar structures, were used for *(2)*—*(5)* and *(6)* respectively; coordinates according to [8].

The PES data demonstrate:

1) Compounds *(2)*—*(6)* are extraordinarily electron rich[9]; their ionization potentials are similar to those of tetrakis(dialkylamino)ethenes or phosphorus ylides[10]. Of particular note is the extremely low first ionization potential (5.87 eV!) of the trimethylgermyl derivative *(3)* (Fig. 1).

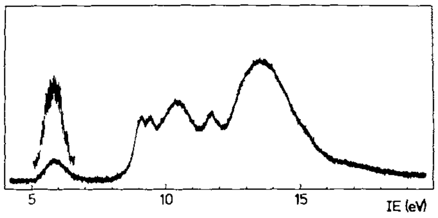


Fig. 1. He(I)-PE spectrum of *(3)* over the region 4 to 20 eV, first band amplified ($R = CH_3$).

2) Variation of the *N*-substituents in *(2)*—*(4)* leads to characteristic shifts of the ionization energies and hence permits assignment of the orbitals to the individual radical cation states. While one ionization remains approximately constant at *ca.* 9.6 eV, and the associated state $\tilde{B} = {}^2B_{2g}$ can therefore be described by a $\pi_A$ molecular orbital[1,8], the first two ionization energies are influenced to approximately the same extent and decrease along the series *(4)*> *(2)*> *(3)* *i.e.* with decreasing "electronegativity" of the nitrogen centers; accordingly these $\tilde{X} = {}^2B_{3u}$ and $\tilde{A} = {}^2B_{1g}$ states correspond to $\pi_S^*$ and $\pi_s$ molecular orbitals[1,8].

3) Unexpectedly, the four methyl groups at the 2,3,5,6-positions do not lead to a reduction[11] but to an increase of the ionization energy of *(5)* relative to *(2)*; apparently, the $CH_3$-electron donor effect is more than compensated by reduction of the cyclic conjugation caused by considerable steric interactions[4]. Benzannulation, as in the quinoxaline derivative *(6)* also increases the ionization potential relative to *(2)*; here, apart from steric interactions, the lowering of the occupied antibonding molecular orbital by a process of charge delocalization[1] into the condensed ring, is also significant[9].

Received: August 27, 1980 [Z 791b IE]
German version: Angew. Chem. *93*, 621 (1981)

---

[1] *A. Streitwieser, Jr.:* Molecular Orbital Theory. Wiley, New York 1961, p. 275ff.; cf. also the correlation diagrams in *E. Heilbronner, H. Bock:* Das HMO-Modell und seine Anwendung. Verlag Chemie, Weinheim 1970, p. 165 and 204.

[2] a) *B. L. Barton, G. K. Fraenkel,* J. Chem. Phys. *41*, 1455 (1964); b) *A. S. Chia, R. F. Trimble,* J. Phys. Chem. *65*, 863 (1961).

[3] *R. A. Sulzbach, A. F. M. Iqbal,* Angew. Chem. *83*, 145 (1971); Angew. Chem. Int. Ed. Engl. *10*, 127 (1971).

[4] *W. Kaim,* Angew. Chem. *93*, 620 (1981); Angew. Chem. Int. Ed. Engl. *20*, 599 (1981).

[5] The cation *(2)*$^{+\cdot}$ has already been reported: *W. Kaim,* Angew. Chem. *92*, 940 (1980); Angew. Chem. Int. Ed. Engl. *19*, 911 (1980).

[6] The compounds were prepared by reductive metalation of 1,4-diazines ($^1H$-NMR in $CDCl_3$/TMS). *(3):* bright red crystals, m.p. = 85 °C; $\delta = 0.30$ (s, 18H), 4.58 (s, 4H); *(4):* yellow liquid, b.p. = 50 °C/0.05 torr; $\delta = 0.12$ (d, 12H), 4.22 (septet, 2H), 4.64 (s, 4H), $^3J_{HSiCH} = 3.2$ Hz; *(5):* colorless crystals, m.p. = 62 °C; $\delta = 0.14$ (s, 18H), 1.69 (s, 12H); *(6):* yellow liquid, b.p. = 80 °C/0.005 torr; $\delta = 0.25$ (s, 18H), 5.28 (s, 2H), 6.52 (m, 4H).

[7] *H. Bock,* Angew. Chem. *89*, 631 (1977); Angew. Chem. Int. Ed. Engl. *16*, 613 (1977).

[8] *R. Gleiter, E. Heilbronner, V. Hornung,* Angew. Chem. *82*, 878 (1970); Angew. Chem. Int. Ed. Engl. *9*, 901 (1970).

[9] Cf. PE spectroscopic investigations on 5,10-dihydrophenazines: *H. J. Haink, J. R. Huber,* Chem. Ber. *108*, 1118 (1975).

[10] a) *B. Cetinkaya, G. H. King, S. S. Krishnamurthy, M. F. Lappert, J. B. Pedley,* J. Chem. Soc. Chem. Commun. *1971*, 1370; b) *K. A. Ostoja Starzewski, H. Bock,* J. Am. Chem. Soc. *98*, 8486 (1976).

[11] Cf. *e.g. H. Bock, W. Kaim,* Chem. Ber. *111*, 3552 (1978).

---

## Model Reactions for the Stereo-Controlled Synthesis of Aminopolyols; Reduction of Isoxazolines with Free or Protected Hydroxy Groups in Position 4 or in Side Chains[**]

By *Volker Jäger, Wilfried Schwab,* and *Volker Buss*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

The γ-aminoalcohol unit is found in many naturally occurring aminopolyols, *e.g.* in hydroxylated amino acids,

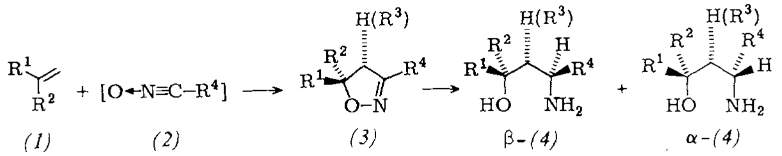
---

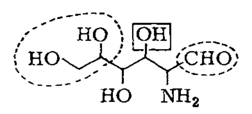
[*] Prof. Dr. V. Jäger [+], Dr. W. Schwab, Dr. V. Buss
Institut für Organische Chemie der Universität Giessen (Germany)

[+] Author to whom correspondence should be addressed; new address: Institut für Organische Chemie der Universität, Am Hubland, D-8700 Würzburg (Germany).

[**] Syntheses with Isoxazolines, Part 9. Part of the Dissertations by *V. B.* (1979) and *W. S.* (1981). This work was supported by the Deutsche Forschungsgemeinschaft.—Part 8: *H. Grund, V. Jäger,* J. Chem. Res. (S) *1979*, 54; (M) *1979*, 649.

sphingolipid bases or amino sugars. *Simple* γ-aminoalcohols *(4)* can be constructed from alkene and nitrile oxide building blocks *(1)* and *(2)* *via* isoxazolines *(3)*, which are equivalent to aldols (β-hydroxyketones)[1]. In addition, the reduction by $LiAlH_4$/ether[2] in many cases can be effected with preparatively useful diastereoselectivity ($\gtrsim 3:1$[3]). In this connection unusually high 1,3-asymmetric induction was stated. In the reduction of *cis/trans*-4,5-dimethylisoxazolines *additivity* of the individual substituent effects ($\Delta\Delta G^{+}$ values) is observed[1].





(5)

It therefore seemed obvious to examine the potential of the isoxazoline route with respect to the synthesis of more complex natural aminoalcohols. With aminodeoxyhexoses such as *(5)* set as a long-term objective, first of all it is required to introduce and carry along further *O*-functions in *(3)*.

The requisite *O*-functions in the *side-chains* of *(3)*—encircled by a dotted line in *(5)*—can be provided in free or protected form by appropriate choice of the cycloaddition components[1d,4]; for derivatives with a *central* hydroxy group—OH group shown in a box in *(5)*—access is given by hydroxylation of isoxazoline-4-anions[5]. In order to solve the problem posed, it then remains essential to determine the influence of free and protected hydroxy groups at the positions stated regarding the stereoselectivity of the reduction step. The most important results relating to this point are listed in Table 1.

Table 1. Aminoalcohols *(4)* from isoxazolines *(3)* by $LiAlH_4$ reduction [a].

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | β-*(4)*/α-*(4)* | $\Delta\Delta G^{+}_{308}$ [kcal/mol] | Yield [%] | M.p. [°C], B.p. [°C/torr] [b] |
|---|---|---|---|---|---|---|---|---|
| *(a)* | $C_{14}H_{29}$ | H | H | $CH_3$ | 88:12 | −1.22 | 96 | 55—59 [c] |
| *(b)* | $C_{14}H_{29}$ | H | H | $CH_2OH$ | 58:42 [d] | −0.38 | 88 | 70—87 |
| *(c)* | $C_{14}H_{29}$ | H | H | $CH_2OTHP$ | 78:22 | −0.78 | 93 [e] | 90—95 [e] |
| *(d)* | $C_{14}H_{29}$ | H | H | $CH_2O$*t*Bu | 77:23 | −0.74 | 97 | 51.5—54 |
| *(e)* | $CH_2OH$ | H | H | $CH_3$ | 37:63 | +0.33 | 69 [f] | 85—105/0.06 |
| *(f)* | $CH_2OTHP$ | H | H | $CH_3$ | 72:28 | −0.58 | 85 | 65—100/*ca.* $10^{-3}$ |
| *(g)* | $CH_2OTrt$ | H | H | $CH_3$ | 92: 8 [g] | −1.50 | 81 [g] | 110—120/0.3 [g] |
| *(h)* | $CH_3$ | $CH_2OH$ | H | $C_6H_5$ | 88:12 | −1.22 | quant. (crude) [h] | 64—75 (β: 83—84.5) |
| *(i)* | H | H | OH | $C_6H_5$ | >90:10 | > +1.35 | 56 [i] | 60—67.5 |

[a] Structure and relative configuration of *(3)* and *(4)* are proven by correct elemental analyses and by IR, $^1H$- and $^{13}C$-NMR spectra; ratios of the diastereomers β-*(4)*/α-*(4)* from $^1H$- and/or $^{13}C$-NMR spectra of the crude products (cf. [1]). For procedure see [1b, c].—Abbreviations: THP = 2-tetrahydropyranyl; Trt = triphenylmethyl (trityl).—The isoxazolines *(3)* were prepared by standard methods (see [1, 4]); A: from nitroalkane according to the *Mukaiyama* method; B: from hydroxamic acid chloride according to *Huisgen*'s *in situ* method.—*(3a):* A, quant. (crude), m.p. 51—51.5 °C; *(3b):* from *(3c)*, 96%, m.p. 74—75 °C; *(3c):* A, 70.5%, m.p. 33—36 °C; *(3d):* A, 74%, m.p. < 5 °C; *(3e):* from *(3f)*, 76%, b.p. 67 °C/0.1 torr; *(3f):* A, 88%, b.p. 95—110 °C/*ca.* $10^{-3}$ torr; *(3g):* from *(3e)*, 60%, m.p. 135—137 °C; *(3h):* B, 79%, m.p. 60 °C; *(3i):* see [5]. [b] Kugelrohr distillation, bath temperature. [c] Main part; rest up to 75 °C. [d] According to the $^{13}C$-NMR spectrum of the hydrochloride; free base: *ca.* 60:40 with some broadened $^{13}C$-NMR signals. [e] After hydrolysis to *(4b)* with $CH_3OH/HCl$, then treatment with basic ion-exchanger Lewasorb A 50. [f] According to $^{13}C$-NMR spectrum still contains impurities. [g] After hydrolysis to *(4e)* with $CH_3OH—CHCl_3/H_2SO_4$, then treatment with $^{\ominus}OH$-form of Lewatit M 600 G-3. [h] Yield of β-*(4h)*: 61%. [i] Not very stable; correct elemental analyses of hydrochloride (m.p. 205—210 °C) and triacetate (m.p. 91—97 °C) were obtained.

$LiAlH_4$-reduction of the 5-tetradecyl derivatives *(3a)*—*(3d)*, which served as models for the synthesis of phytosphingosine[5], for the simplest case *(3a)* afforded an 88 : 12 mixture of the diastereomeric 2-amino-4-octadecanols β-*(4)*/α-*(4)*. A 3-hydroxymethyl group, as in *(3b)*, decreases the diastereoselectivity of the process (Table 1). This could be avoided by blocking the hydroxy group, *e.g.* as 2-tetrahydropyranyl (THP) or *tert*-butyl ether as in *(3c)* or *(3d)*, to the extent that useful diastereomer ratios are achieved once again (Table 1).

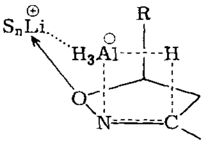
In the reduction of *(3e)* the 5-hydroxymethyl group causes the hydride transfer to occur preferentially from the substituent face of the ring: In the case of *(4e)* we found a β/α ratio of 37 : 63, thus a reversal—even though preparatively unsatisfactory—of the main direction of attack compared to the parent compounds with $R^1 = CH_3$ (β/α = 85 : 15; $\Delta\Delta G^{+}_{308} = 1.06$ kcal/mol[1]). In the THP derivative *(3f)* this hinge effect[6] is still exerted, if only weak (Table 1). The high diastereoselectivity desired is found when the "haptophilicity"[6] of the OH-group is made void by tritylation: After reduction of *(3g)* and deblocking to give *(4e)*, a β/α ratio of 92 : 8 was recorded; the predominant isomer, *erythro*-4-amino-1,2-pentanediol β-*(4g)* could be isolated in 61% yield[7].

The direction of hydride addition to the C═N double bond of *(3h)* is influenced by *both* 5-substituents, methyl *and* hydroxymethyl. The diastereoisomer ratio of β-*(4h)*/α-*(4h)* (88 : 12) again reflects the additivity of the individual substituent effects[8,9]: According to the calculated differences in the free enthalpies of activation for 5-$CH_3$[1] and 5-$CH_2OH$ one would expect a difference of −1.4 kcal/mol, corresponding to a β/α ratio of 90.5 : 9.5 for the hydride transfer from the two different ring faces in *(3h)*. The deviation from the value of 88 : 12 actually observed lies within the limits of experimental error of the $^1H$- and $^{13}C$-NMR spectroscopical determination of diastereomer ratios.

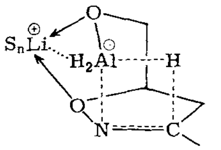
The most powerful directing effect in these reductions was observed in the case of 4-hydroxyisoxazoline *(3i)*[5]: A 69 : 31 mixture of the aminoalcohols was obtained upon reaction of 4-methyl-3-phenylisoxazoline with $LiAlH_4$[1a,c];

in contrast, according to $^1$H-NMR analysis the reduction of *(3i)* furnishes a crude product containing $>90\%$ of one diastereomer of *(4i)*. The relative configuration of the main product could not be deduced from NMR data; however, the inductions stated in the case of 5-methyl- and 5-hydroxymethylisoxazolines suggest formation of the *erythro* diastereomer β-*(4i)*. This interpretation is supported by the results of the phytosphingosine synthesis[5].

The stereochemical outcome of most of these reductions can be satisfactorily accounted for by the following assumptions: in substrates bearing alkyl or phenyl substituents, inducing (*anti*-directing) by size[8] only (cf. *(6)*[10]), solvated lithium cations are coordinated to the free electron pairs of the isoxazoline oxygen atom[1c,d] on both faces of the ring to a different degree. Hence different transition states for the hydride transfer from the respective aluminate counter-ions associated follow.



*(6)* → α-*(4)* (unfavorable)



*(7)* → α-*(4)* (preferred)

In the case of substrates with OR functions, other or additional coordination complexes are involved. If hydroxy groups are present, such as in *(3e)* and *(3i)*, hydride transfer preferably will result from the corresponding intermediate alkoxyaluminate species such as *(7)*; substituents of this kind are *syn*-directing.

The effects described here complement and extend the possibilities to direct cation-assisted nucleophilic additions by means of hydroxy groups, *or* to preclude their action, and thus to exert steric control in the synthesis of acyclic compounds[1d,6,7,11]. In particular, this allows for regio- and stereocontrolled syntheses of *erythro*-aminodiols and many other aminopolyols.

Received: November 7, 1980 [Z 766a IE]
German version: Angew. Chem. *93*, 576 (1981)

CAS Registry numbers:
*(1)* (R′ = $C_{14}H_{29}$, $R^2$ = H), 629-73-2; *(1)* (R′ = $CH_2OH$, $R^2$ = H), 107-18-6; *(1)* (R′ = $CH_2OTHP$, $R^2$ = H), 4203-49-0; *(1)* (R′ = $CH_2OTrt$, $R^2$ = H), 7790-65-9; *(1)* (R′ = $CH_3$, $R^2$ = $CH_2OH$), 513-42-8; *(1)* (R′, $R^2$ = H), 74-85-1; *(2)*, $R^4$ = $CH_3$), 7063-95-8; *(2)* ($R^4$ = $CH_2OH$), 77790-66-0; *(2)* ($R^4$ = $CH_2OTHP$), 77790-67-1; *(2)* ($R^4$ = $CH_2OBu$-*t*), 77790-68-2; *(2)* ($R^4$ = Ph), 873-67-6; *(3a)*, 77790-69-3; *(3b)*, 77790-70-6; *(3c)*, 77790-71-7; *(3d)*, 77790-72-8; *(3e)*, 77790-73-9; *(3f)*, 7790-74-0; *(3g)*, 77790-75-1; *(3h)*, 77790-76-2; *(3i)*, 77790-77-3; β-*(4a)*, 77790-78-4; α-*(4a)*, 77790-79-5; β-*(4b)*, 77790-80-8; β-*(4b)* HCl, 77790-81-9; α-*(4b)*, 77808-87-8; α-*(4b)* HCl, 77790-82-0; β-*(4c)*, 77790-83-1; α-*(4c)*, 77844-48-5; β-*(4d)*, 77790-84-2; α-*(4d)*, 77790-85-3; β-*(4e)*, 77790-86-4; α-*(4e)*, 77790-87-5; β-*(4f)*, 77790-88-6; α-*(4f)*, 77790-49-6; β-*(4g)*, 77790-89-7; α-*(4g)*, 77790-90-0; β-*(4h)*, 77790-91-1; β-*(4h)* HCl, 77790-92-2; β-*4h)* triacetate, 77790-94-4; α*(4h)*, 77790-95-5; α.*(4h)* HCl, 77790-96-6; α-*(4h)* triacetate, 77790-98-8; *(4i)* isomer 1, 77790-99-9; *(4i)* isomer 2, 5817-02-7

---

[1] a) *V. Jäger, V. Buss, W. Schwab,* Tetrahedron Lett. *1978*, 3133; b) *V. Jäger, V. Buss,* Liebigs Ann. Chem. *1980*, 101; c) *V. Jäger, V. Buss, W. Schwab, ibid. 1980*, 122; d) Review: *V. Jäger,* Habilitationsschrift, Universität Giessen 1979.

[2] Reaction sequel: a) hydride addition to C=N, then b) reductive N—O cleavage [1].

[3] *J. W. Scott, D. Valentine, Jr.,* Science *184*, 943 (1974); *D. Valentine, Jr., J. W. Scott,* Synthesis *1978*, 329.

[4] Cf. review: *C. Grundmann, P. Grünanger:* The Nitrile Oxides, Springer, Berlin 1971, p. 96ff. and p. 188ff.

[5] *W. Schwab, V. Jäger,* Angew. Chem. *93*, 578 (1981); Angew. Chem. Int. Ed. Engl. *20*, 603 (1981).

[6] *H. W. Thompson, R. E. Naipawer,* J. Am. Chem. Soc. *95*, 6379 (1973); *H. W. Thompson, E. McPherson,* J. Org. Chem. *42*, 3350 (1977).

[7] Similar reaction control has been observed in disaccharide syntheses: *R. R. Schmidt, M. Reichrath,* Angew. Chem. *91*, 497 (1979); Angew. Chem. Int. Ed. Engl. *18*, 466 (1979).

[8] Cf. Empirical substituent parameters: *H. Förster, F. Vögtle,* Angew. Chem. *89*, 443 (1977); Angew. Chem. Int. Ed. Engl. *16*, 429 (1977); *R. Knorr,* Chem. Ber. *113*, 2441 (1980), and references cited therein.

[9] This additivity also applies in the case of a) 5-$CH_3$ *vs.* 5-$C_6H_5$: *V. Jäger, R. Abt,* unpublished, and b) 5-alkyl *vs. trans*-4-OH: *W. Schwab,* Dissertation, Universität Giessen 1981; see also [5].

[10] In analogy to ketone reductions; review: *J. R. Boone, E. C. Ashby,* Top. Stereochem. *11*, 53 (1979).

[11] For the control of $LiAlH_4$ reductions by coordinating *O*-substituents see, *e.g.*, the following reviews: *J. D. Morrison, H. S. Mosher:* Asymmetric Organic Reactions, Am. Chem. Soc. Washington, D.C. 1976, p. 100ff.; *P. A. Bartlett,* Tetrahedron *36*, 2 (1980); see also *M. W. Lunnon, J. MacMillan,* J. Chem. Soc. Perkin Trans. I *1977*, 2317; *S. Yamaguchi, K. Kabuto,* Bull. Chem. Soc. Jpn. *50*, 3033 (1977); *J. J. Cawley, D. V. Petrocine,* J. Org. Chem. *41*, 2608 (1976).

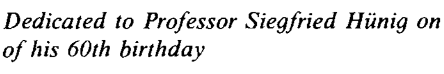
---

# 4-Hydroxylation of Isoxazolines; Synthesis of *rac*-Phytosphingosine (*ribo*-2-Amino-1,3,4-octadecanetriol)[**]

By *Wilfried Schwab* and *Volker Jäger*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

4-Hydroxyisoxazolines are potential precursors for the synthesis of many natural aminopolyols and amino sugars[1]. However, they are not available by nitrile oxide cycloaddition to enol ethers or esters, since 5-alkoxy- and 5-acyloxyisoxazolines are then formed[2]. We have now found an access to *trans*-4-hydroxyisoxazolines by reacting isoxazoline 4-anions[3] with borates, followed by oxidative work-up[4]. The latter constitutes the crucial step of this process: Although anion formation proceeds almost quantitatively[3], incomplete conversion was observed; we attributed this to the competing protolysis of the intermediate boronates. The best results then were achieved by applying concentrated oxidizing agents (hydrogen peroxide or *tert*-butyl hydroperoxide) in the presence of amine or ammonia. *(1)* and *(2)* were thus isolated in yields of 67% (m.p. 96 °C) and 78% (m.p. 102—105 °C), respectively[5]. In the case of *(2)* only the *trans*-isomer ($>90:10$) was formed, according to the $^{13}$C-NMR spectrum of the crude product.



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

1) Lithium diisopropylamide (LDA), tetrahydrofuran (THF)/hexamethylphosphoric triamide (HMPA), -78°C.
2) $B(O\text{-}i\text{-}C_3H_7)_3$ for *(1)*, $B(OCH_3)_3$ for *(2)*, -78 °C.
3) $H_2O_2$, $NEt_3$ für *(1)*, $NH_3$ for *(2)*, -78 °C → RT.

The synthesis of $C_{18}$-phytosphingosine *(6a)*, the long-chain base characteristic of plant sphingolipids[6], was attempted then, with 1-hexadecene and 2-nitroethanol *(3a)* serving as suitable building blocks. For the cycloaddition

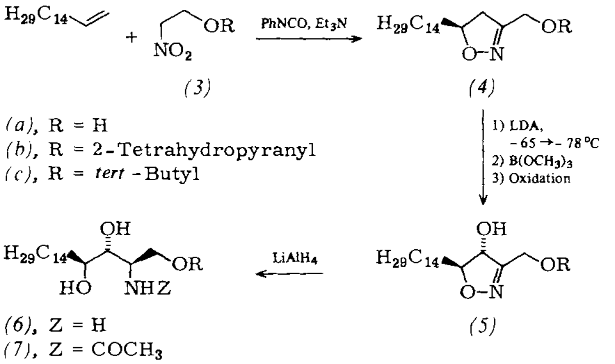
---

[*] Prof. Dr. V. Jäger [+], Dr. W. Schwab
Institut für Organische Chemie der Universität Giessen (Germany)

[+] Author to whom correspondence should be addressed; present address:
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany).

[**] Syntheses *via* Isoxazolines, Part 10. Delivered in part in lectures at Würzburg (3. 7. 1979) and Berlin (GDCh Hauptversammlung, 14. 9. 1979); part of the Dissertation by *W. S.*, Giessen 1981. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 9: [1].

according to the method of *Mukaiyama*[2a], *(3a)* was used as the 2-tetrahydropyranyl ether *(3b)*[1]. The metalation/hydroxylation of the cycloadduct *(4b)* was carried out similarly as with the model compounds. *(5b)* was isolated in up to 55.5% yield, either by lengthy fractional crystallization or by crystallization and chromatographic purification of the mother liquors. Here, too, the hydroxylation proceeded in a highly stereoselective manner: The $^{13}C$-NMR spectra of *(5b)* and of its solvolysis product *(5a)* (with $CH_3OH$/HCl; 98%, m.p. 74—78 °C) did not show any of the signals expected for the *cis*-isoxazoline[7]. Reduction of *(5b)* with $LiAlH_4$[1], followed by removal of the THP group with $HCl/CH_3OH$ produced the hydrochloride of *(6a)*. The broad-band decoupled $^{13}C$-NMR spectrum once again indicated none of the other diastereomers nor impurities to be present. This is consistent with the stereochemical outcome of the reduction of the model compound *(1)*[1]. *rac*-Phytosphingosine *(6a)* was recovered on treatment with basic ion-exchange resin (yield *ca.* 33% with respect to nitroethanol); it was pure according to elemental and $^{13}C$-NMR analyses. The synthetic product *(6a)* was converted into the *N*-acetyl derivative *(7)*; a comparison of its $^{13}C$-NMR spectrum with that of authentic D-*(7)*[8] confirmed the identity of the relative configuration of the synthetic product, as was shown also by GC comparison[9] of the silylated derivatives.



In a modified version of this route, *(6a)* was obtained from the *tert*-butyl ether *(3c)* in similar over-all yield (29%). Here the 4-hydroxyisoxazoline *(5c)* was isolated after crystallization *without* subsequent use of chromatography (oxidative work-up with *tert*-butyl hydroperoxide/triethylamine, or 85% hydrogen peroxide/conc. aqueous ammonia).

Compared with previous syntheses of phytosphingosine (7—9 steps, over-all yields 2—6%[6b,d]), the efficiency of the isoxazoline route for the straightforward synthesis of such aminopolyols is evident. Stereo-controlled syntheses of important amino sugars of this and other configurations are the subject of further work, key steps of which have already been successful[10].

## Procedure

*(6a)*[5] *Cycloaddition:* Hexadecene (14.4 cm³, 50 mmol) and *(3b)* (50 mmol) (crude product of the reaction of *(3a)* with 2 equivalents of dihydropyran/50 mg of *p*-toluenesulfonic acid) are allowed to react as described in Ref. [1]; yield of *(4b)* 13.46 g (70.5%), in fractions with m.p. 28—30 to 34—36.5 °C (mixtures of diastereomers). *(4c)* was obtained analogously as a colorless liquid in 74.1% yield from *(3c)* (20 mmol; crude product of the reaction of *(3a)* with 2-methylpropene/conc. $H_2SO_4$ in $CH_2Cl_2$).—*Hydroxylation: (4b)* (381 mg, 1 mmol), dissolved in THF (2 cm³), was added by means of a syringe to a solution of LDA (1.5 mmol) in 15 cm³ THF/0.7 cm³ (4 mmol) HMPA at −65 °C; 30 min later the mixture was cooled to −78 °C and, after 2 h, treated with $B(OMe)_3$ (0.23 cm³, 2 mmol) and kept for 2.5 h. 0.83 cm³ (6 mmol) $Et_3N$/1 cm³ *tert*-butyl hydroperoxide (10 mmol, 80% with *tert*-butyl peroxide) was then added. The resulting mixture was allowed to warm, stirred at room temperature for 60 h and treated successively with 5 cm³ of $H_2O$, after 30 min with 5 cm³ of conc. $NH_4Cl$ solution and kept for 15 min, then 1 g $NaHSO_3$ was added. After a further 15 min the mixture was extracted four times with ether. Washing (1 N NaOH, half-saturated solution of $NH_4Cl$; three times half-saturated solution of NaCl), drying ($Na_2SO_4$), evaporating and crystallization from cyclohexane/pentane afforded 138 mg of *(5b)* with m.p. 68—73 °C together with a further 79 mg *(5b)*, m.p. 47—50 °C (major part; rest up to 69 °C) after chromatography ($SiO_2$ column, Merck, eluent $CH_2Cl_2/Et_2O$ 4 : 1) and crystallization as above; total yield 55.5%.—*(5c):* From *(4c)* (3 mmol) in an analogous way, however oxidative work-up with 0.9 cm³ (*ca.* 12 mmol) of conc. aqueous ammonia/0.78 cm³ 85% $H_2O_2$; repeated crystallization from cyclohexane afforded analytically pure fractions of 375 mg (m.p. 63—64 °C), 103 mg (m.p. 60—65 °C), and 85 mg (m.p. 60-63 °C; according to $^{13}C$-NMR together with a trace of starting material); total yield 50.8%.—*Reduction:* a) *(5b)* was reduced as detailed in [1]; THP-ether cleavage with $CH_3OH$/HCl in 1.5 h at 60 °C. From 360 mg of *(5b)*, 89.5% of analytically pure *(6a)*·HCl of m.p. (dec.) 200 °C was obtained (isomerically pure according to $^{13}C$-NMR), from which the base *(6a)* (95%) was liberated by means of Lewasorb A 50 ($^{\ominus}$OH form); melting range 68—76 °C (amorphous according to Debye-Scherrer photographs). Recrystallization, from $CH_3CN$/ether gave a product of m.p. 138—144 °C (with sintering above *ca.* 85 °C; lit. m.p. 149—151 °C)[6d]. For identification, 265 mg of *(6a)*·HCl was treated with acetic anhydride/3 N NaOH; after recrystallization from acetone, 250 mg (93%) of *(7)* were obtained as colorless, analytically pure product of m.p. 118—123 °C (sintering at 96—98 °C; lit. m.p. 110—111 °C for D,L-*(7)*[6d]; m.p. 113—123 °C for natural D-*(7)*[8]). $^{13}C$-NMR ($CDCl_3/CH_3OH$ *ca.* 4 : 1; values for D-*(7)* in brackets[8]): $\delta = 33.4$ [C-5 (33.3)], 52.5 [C-2 (52.3)], 61.3 [C-1 (61.3)], 72.8 [C-4 (72.7)], 75.9 [C-3 (75.9)] for the most important signals.—b) Reduction of *(5c)*: From 323 mg of *(5c)*, 308 mg (95%) of colorless crystalline *(6c)* were isolated, m.p. 80—83.5 °C. After removal of the *tert*-butyl group from 115 mg of *(6c)* with 0.4 cm³ of $BF_3 \cdot OEt_2$ in 4 cm³ $CH_2Cl_2$ at room temperature the product was treated and stirred for 15 min each with 2 cm³ of $CH_3OH$, then 3 cm³ of conc. aqueous ammonia, then mixed with 10 cm³ of semi-saturated $NH_4Cl$ solution, and extracted three times with $CH_2Cl_2$. After washing ($H_2O$, then twice with semi-saturated NaCl solution), drying, and removal of the solvent, 77 mg (81%) of *(6a)* was obtained as above.

Received: November 7, 1980 [Z 766b IE]
German version: Angew. Chem. *93*, 578 (1981)

CAS Registry numbers:
*(3a)*, 625-48-9; *(3b)*, 75233-61-3; *(3c)*, 77791-00-5; *(4b)*, 77790-71-7; (±)-*(4c)*, 77791-01-6; (±)-*(5a)*, 77791-02-7; (±)-*(5b)*, 77791-03-8; (±)-*(5c)*, 77791-04-9; (±)-*(6a)*, 22565-81-7; (±)-*(6a)* HCl, 77844-50-9; (±)-*(6c)*, 77791-05-0; (±)-*(7)*, 22565-79-3; 1-hexadecene, 629-73-2;

---

[1] *V. Jäger, W. Schwab, V. Buss*, Angew. Chem. *93*, 576 (1981); Angew. Chem. Int. Ed. Engl. *20*, 601 (1981).

[2] a) *C. Grundmann, P. Grünanger:* The Nitrile Oxides, Springer, Berlin 1971, p. 96ff.; b) *K. Bast, M. Christl, R. Huisgen, W. Mack, R. Sustmann,* Chem. Ber. *106*, 3258 (1973); references cited therein; c) cf. furan cycloadditions: *P. Carmella, G. Cellerino, A. Corsico Coda, A. Gamba Invernizzi, P. Grünanger, K. N. Houk, F. Marinone Albini,* J. Org. Chem. *41*, 3349 (1976).

[3] *V. Jäger, H. Grund,* Angew. Chem. *88*, 27 (1976); Angew. Chem. Int. Ed. Engl. *15*, 50 (1976); *V. Jäger, W. Schwab,* Tetrahedron Lett. *1978*, 3129; see also *H. Grund, V. Jäger,* Liebigs Ann. Chem. *1980*, 80; J. Chem. Res. (S) *1979*, 54; (M) *1979*, 649.

[4] a) Hydroxylation of aryl or allyl anions, see *R. B. Woodward, T. R. Hoye,* J. Am. Chem. Soc. *99*, 8007 (1977) and *M. Schlosser, G. Rauchschwalbe, ibid. 100*, 3258, 6544 (1978) and references cited therein; b) oxidative work-up cf. *R. Köster, Y. Morita,* Angew. Chem. *78*, 589 (1966); Angew. Chem. Int. Ed. Engl. *5*, 580 (1966); *G. W. Kabalka, H. C. Hedgecock, Jr.,* J. Org. Chem. *40*, 1776 (1975); c) literature survey of enolate and similar hydroxylations: *E. Vedejs, D. A. Engler, J. E. Telschow, ibid. 43*, 188 (1978); d) side reactions to be avoided include, among others, the oxidation to yield isoxazoles [2a] and the ring opening to give enoximates [3], which in some cases already takes place at −80 °C.

[5] The compounds described are characterized by correct elemental analyses and IR, $^{1}$H- and $^{13}$C-NMR spectra. Isomeric purity and configurations were determined by $^{13}$C-NMR spectroscopy.

[6] a) Reviews: *W. Stoffel,* Chem. Phys. Lipids *11*, 318 (1973); Rodd's Chemistry of Carbon Compounds, 2nd edit., Vol. I, Part E, Elsevier, Amsterdam 1976, p. 394ff.; b) Syntheses of D-*(6a)* from sugars: *R. Gigg, C. D. Warren, J. Conningham,* Tetrahedron Lett. *1965*, 1303; *J. Gigg, R. Gigg, C. D. Warren,* J. Chem. Soc. *C 1966*, 1872; *J. Gigg, R. Gigg, ibid. 1966*, 1876; c) D-*(6a)* from D-Sphingosine: *M. Proštenik, B. Majhofer-Oreščanin, B. Ries-Lešić, N. Ž. Stanačev,* Tetrahedron *21*, 651 (1965); *B. Weiss,* Biochemistry *4*, 686 (1965). A reinvestigation revealed that a *mixture* of four isomers is formed: *R. J. Kulmacz, G. J. Schroepfer, Jr.,* J. Am. Chem. Soc. *100*, 3963 (1978); d) Syntheses of *rac-(6a): K. Sisido, N. Hirowatari, T. Isida,* J. Org. Chem. *34*, 3539 (1969); *K. Sisido, N. Hirowatari, H. Tamura, H. Kobata, H. Takagisi, T. Isida, ibid. 35*, 350 (1970).

[7] $^{13}$C-NMR of *cis/trans*-4,5-dialkylisoxazolines: *W. Schwab,* Diplomarbeit, Universität Giessen 1978; cf. Habilitationsschrift *V. Jäger,* Universität Giessen 1979.

[8] We are grateful to Prof. Dr. *W. Stoffel,* Köln, for providing a $^{13}$C-NMR spectrum and a reference sample of D-*(6a),* which was obtained from *Hansenula ciferrii.*

[9] *H. E. Carter, R. C. Gaver,* J. Lipid Res. *8*, 391 (1967).

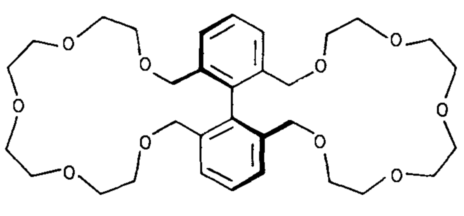
[10] *W. Schwab,* Dissertation, Universität Giessen 1981; *I. Müller,* Diplomarbeit, Universität Würzburg 1980; *R. Schohe,* Diplomarbeit, Universität Würzburg 1980.

## Allosteric Effects: Binding Cooperativity in a Subunit Model[**]

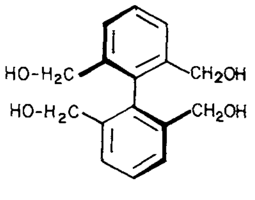
By *J. Rebek, Jr. R. V. Wattley, T. Costello, R. Gadwood* and *L. Marshall*[*]

The binding cooperativity shown by hemoglobin toward oxygen is one of the most intriguing manifestations of allosteric effects. These effects—interactions between remote sites—result from conformational changes induced by binding; in general they provide a means by which the catalytic activity of enzymes can be regulated[1]. We have recently shown that processes involving "small" molecules in solution can also be subjected to such control[2] and we report here the first example of a model system which shows binding cooperativity between two remote sites.

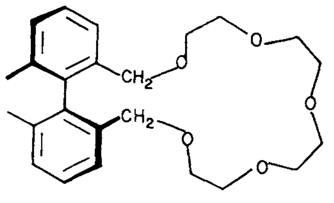
The macrobicyclic structure *(1)* incorporates the minimum requirements for such behavior: symmetrically disposed binding sites and a conformational mechanism by which binding at one polyether site can increase the receptivity of the other. Specifically, that distance between the benzylic C-atoms which is optimum for ion binding to one site is faithfully reproduced at the other site by the rigidity of the biphenyl system. This predictable, mechanical action of *(1)* is precisely the feature which distinguishes it from the host of other known macrobicyclic polyethers.



*(1)*



*(2)*



*(3)*

Polyether *(1)* was obtained as a low-melting solid (m.p. = 70—72 °C)[3] in 20—30% yield, through the action of NaH and tetraethylene glycol ditosylate on the tetra-alcohol *(2)*. The latter is readily available from pyrene through ozonolysis followed by reduction[4]. The monocyclic counterpart *(3)* was also prepared for purposes of comparison.

Analysis of the binding behavior of subunit systems such as *(1)* requires measurements over a large range, *i.e.* from a few percent of the sites occupied to near saturation. High resolution NMR spectroscopy proved to be ideal for this purpose and Figure 1 summarizes the changes observed in the spectra of the downfield aromatic protons, in positions 3,5 and 3′,5′ of the benzyl skeleton, when *(1)* was titrated with $Hg(CN)_2$ in $(CD_3)_2CO/C_6D_6$ (1 : 1, v/v) at 15 °C.

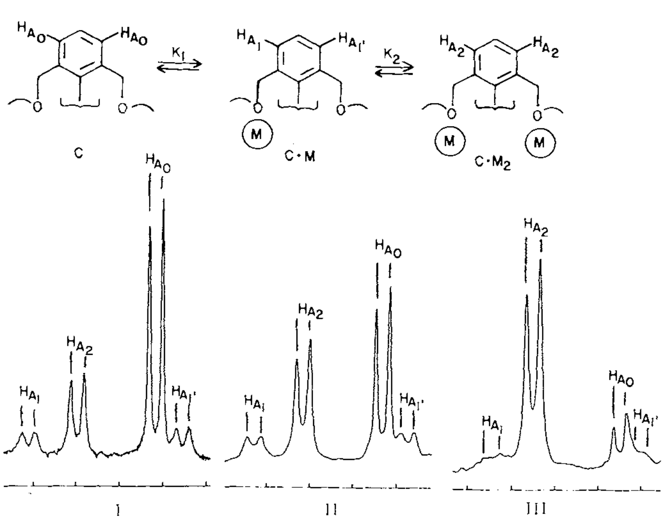


Fig. 1. Changes in the aromatic proton region of the $^{1}$H-NMR spectrum of *(1)* (600 MHz) upon addition of $Hg(CN)_2$. I, 38% sites occupied; II, 50% sites occupied; III, 74% sites occupied.

---

[*] Prof. Dr. J. Rebek, Jr., R. V. Wattley, T. Costello, R. Gadwood, L. Marshall.
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260 (USA)

[**] This research was supported by the National Institutes of Health. Additional funds from the same agency maintain the 600-MHz NMR facility at the Mellon Institute of Carnegie-Mellon University.

The concentration of the various species—free *(1)* (C), the 1 : 1 complex (C·M), and the 2 : 1 complex ($C\cdot M_2$) could be determined by integration of the well resolved 600-MHz $^1H$-NMR spectrum. The excellent resolution is due to the relatively slow rates of exchange involved in complexation of $Hg(CN)_2$ with these ethers. In contrast, alkali metals showed rapid exchange rates and resulted in averaged spectra for the various species.

The ratio $K_2/K_1=[C\cdot M_2]\cdot C/[C\cdot M]^2$ of the macroscopic association constants $K_1=[C\cdot M]/[C]\cdot[M]$ and $K_2=[C\cdot M_2]/[C\cdot M]\cdot[M]$ can be determined directly from the $^1H$-NMR-spectrum. It is found that $K_2=(2.5\pm0.2)\,K_1$. However, these constants must be corrected for statistical effects. The corrected (intrinsic) association constants are $K_2^i\approx 10\,K_1^i$ *i.e.* the system shows *positive cooperativity*. The *Hill* plot of the data[5] produces a slope of $n=1.5$, with mid-point at a free metal concentration of *ca.* 0.03 M. This corresponds to $K_1^i=10\,\text{M}^{-1}$, in good agreement with that observed for the monocyclic polyether *(3)* ($K=13\,\text{M}^{-1}$).

The receptivity of the ether toward a second $Hg(CN)_2$ is enhanced 10-fold by the binding of the first $Hg(CN)_2$. The conformational restrictions imposed on the open site by binding of the first metal are modest—only one of the many internal rotations are removed, yet receptivity is increased by an order of magnitude[6]. This suggests that even greater cooperativity should be available to systems composed of less flexible subunits.

Received: November 7, 1980 [Z 763 IE]
German version: Angew. Chem. *93*, 584 (1981)

CAS Registry numbers:
*(1)*, 77846-54-9; *(2)*, 61358-43-8; *(3)*, 77825-22-0; tetraethylene glycol ditosylate, 37860-51-8

---

[1] *D. E. Koshland, Jr.* in *P. Boyer:* The Enzymes. Vol. 1, Academic Press, New York 1970, p. 341.

[2] *J. Rebek, Jr., R. V. Wattley,* J. Am. Chem. Soc. *102,* 4853—54 (1980); for other systems in which allosteric effects can be invoked see *J.-M. Lehn,* Acc. Chem. Res. *11,* 49 (1978) and *T. G. Traylor, Y. Tatsumo, D. W. Powell, J. B. Cannon,* J. Chem. Soc. Chem. Commun. *1977,* 732.

[3] Satisfactory elemental analysis and anticipated spectroscopic features were obtained for *(1)* and *(3).*

[4] *I. Agranat, M. Rabinovitz, W. Shaw,* J. Org. Chem. *44,* 1936 (1979).

[5] For an excellent discussion of this topic see *A. Levitzki:* Quantitative Aspects of Allosteric Mechanisms, Mol. Biol. Biochem. Biophys. *28,* 15 (1978).

[6] With the larger homologue (22-membered ring) of *(1),* the sites were found to act independently: *J. Rebek, R. V. Wattley, T. Costello, R. Gadwood, L. Marshall,* J. Am. Chem. Soc. *102,* 7398 (1980).

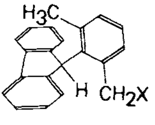
---

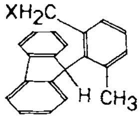
## Contrasting Behavior in the Substitution Reactions of 9-(2-Bromomethyl-6-methylphenyl)fluorene Rotamers[**]

By *Shigeru Murata, Seiichiro Kanno, Yo Tanabe, Mikio Nakamura,* and *Michinori Ōki*[*]

We wish to report that the *sp-* and *ap*-rotamers of 9-(2-bromomethyl-6-methylphenyl)fluorene *(1)* behave quite differently in substitution reactions. *sp-(1)* and *ap-(1)* were prepared by bromination of 9-(2,6-dimethylphenyl)fluorene[1] and separated by preparative high pressure liquid chromatography ($SiO_2$/hexane). Since the activation parameters for interconversion of both rotamers are known ($E_A=27.1$ kcal/mol, $\log A=11.4$), the time necessary for conversion of 5% ($^1H$-NMR detection limit) of one isomer, into the other by internal rotation can be calculated *e.g.* 27.2 h at 62 °C. In order to detect the differences in reactivities of the respective rotamers, the reactions must be carried out under conditions which will not permit isomerization to a detectable degree. At the outset we focused our attention on $S_N2$-type reactions in dimethyl sulfoxide. Preliminary experiments with methanol indicated that, while *sp-(1)* reacted with measurable rates at 57 °C, *ap-(1)* was almost inert. Since methanolysis produces hydrogen bromide, the reaction is autocatalyzed and hence, to compare the rates of clean $S_N2$ reactions, we used 2-methylpyridine as a nucleophile[2]. The pseudo-first order rate constants of the reactions in acetone in the presence of 2-methylpyridine at 34 °C were $1.4\times10^{-2}$ and $4.0\times10^{-4}$ $\text{min}^{-1}$ for *sp-(1)* and *ap-(1),* respectively. Thus *sp-(1)* is *ca.* 35 times more reactive than *ap-(1),* under the conditions used. The products were the corresponding 2-methylpyridinium salts: *sp-(2)* (m.p. = 226—227 °C (decomp.)) and *ap-(2)* (oil)[3]. The poorer reactivity of the *ap*-form may be attributed to the blocking of the back-side of the leaving group $Br^{\ominus}$ by the fluorene moiety.

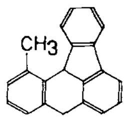
*sp-(1),* X = Br
*sp-(2),* X = $\overset{\oplus}{N}C_5H_4CH_3$



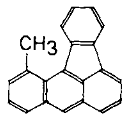


*ap-(1),* X = Br
*ap-(2),* X = $\overset{\oplus}{N}C_5H_4CH_3$

For an investigation of $S_N1$ reactions, we chose trifluoroacetic acid as solvent which has a high dielectric constant but low nucleophilicity. Heating a solution of *ap-(1)* in $CF_3CO_2H/CDCl_3$ (1 : 1) at 61.2 °C caused a decrease in intensity of the methyl and methylene signals in the $^1H$-NMR spectrum of *ap-(1)* from which a rate constant of *ca.* $7\times10^{-4}$ $\text{min}^{-1}$ for the reaction involved was obtained. In sharp contrast, *sp-(1)* did not react with a measurable rate under the same conditions. The enhanced reactivity of the *ap*-form may be ascribed to the interaction of the π-electrons of the fluorene ring with the carbenium ion formed; the inertness of the *sp*-form is due to the lack of such participation.



*(3)*



*(4)*

The product of the reaction of *ap-(1)* in $CF_3CO_2H$/$CDCl_3$ (1 : 1) was a mixture of polymers which could be formed by an intermolecular Friedel-Crafts reaction. However, when the reaction was carried out in dilute solution, identifiable products were obtained *i.e.* heating 33 mg of *ap-(1)* in 1.5 $cm^3$ of $CHCl_3$ and 25 $cm^3$ of $CF_3CO_2H$ afforded 8 mg of 12-methyl-8,12b-dihydrobenz[a]aceanthrene *(3)* (m.p. = 180—181 °C)[5] and 3 mg of 12-methylbenz[a]aceanthrene *(4)* (yellow-orange oil)[6]. The yield of *(4)* decreased if the reaction was carried out under $N_2$, indicating that *(4)* is formed from *(3)* by dehydrogenation of *(2)* by $O_2$. Formation of *(3)* is expected if ionization occurs at the $CH_2$—Br site and intramolecular Friedel-Crafts cy-

---

[*] Prof. Dr. M. Ōki, S. Murata, S. Kanno, Y. Tanabe, Dr. N. Nakamura
Department of Chemistry, Faculty of Science
The University of Tokyo
Bunkyo-Ku, Tokyo 113 (Japan)

[**] Reactivity of Stable Rotamers, Part 5: This work was supported by the Toray Science Foundation.—Part 4: *H. Kikuchi, T. Mitsuhashi, N. Nakamura, M. Ōki,* Chem. Lett. *1980,* 209.

clization follows. The reason why the concentrated solution of *ap-(1)* only gave polymeric product may be, that for the cyclization, rotation about the C9—C1′-bond has to take place: since the barrier to rotation is high, polymerization is preferred.

In conclusion, the rotamers *sp-(1)* and *ap-(1)* exhibit remarkable differences in nucleophilic substitution reactions. In $S_N2$ reactions *sp-(1)* is—predominantly for stereochemical reasons—more reactive, however, in $S_N1$ reactions *ap-(1)* is—predominantly because of electronic interactions—more reactive.

Received: January 25, 1980 [Z 764a IE]
German version: Angew. Chem. *93*, 579 (1981)

CAS Registry numbers:
*(1)*, 52883-19-9; *(2)* bromide, 77825-19-5; *(3)*, 77825-20-8; *(4)*, 77825-21-9

---

[1] *M. Nakamura, M. Ōki*, Tetrahedron Lett. *1974*, 505.

[2] *J. W. Baker*, J. Chem. Soc. *1936*, 1448; *J. W. Baker, C. M. Easty, ibid. 1935*, 519.

[3] $^1$H-NMR ([D$_6$]DMSO) *sp-(2)*, $\delta$ = 1.12 (s, 3 H), 2.96 (s, 3 H), 5.50 (s, 1 H), 6.39 (s, 2 H), 6.8—9.1 (m, 15 H); *ap-(2)*, 1.81 (s, 3 H), 2.83 (s, 3 H), 4.40 (s, 2 H), 5.77 (s, 1 H), 6.6—8.5 (m, 15 H).

[4] *T. W. Bentley, C. T. Bowen, W. Parker, C. I. F. Watt*, J. Am. Chem. Soc. *101*, 2486 (1979) and references cited therein.

[5] *(3)* showed the expected reactions and gave a correct molecular weight in the mass spectrum ($M^{\oplus}$ = 268), as well as a satisfactory elemental analysis. $^1$H-NMR (CDCl$_3$): $\delta$ = 2.48 (s, 3 H), 3.99 (d, 1 H, $J$ = 16.4 Hz), 4.14 (dd, 1 H, $J$ = 16.4 and 2.3 Hz), 4.80 (d, 1 H, $J$ = 2.3 Hz), 6.9—8.1 (m, 10 H). The dehydrogenation of *(3)* with dichlorodicyano-*p*-benzoquinone afforded *(4)*.

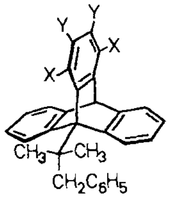
[6] $^1$H-NMR (CDCl$_3$): $\delta$ = 3.17 (s, 3 H) and signals from the aromatic protons; UV, $\lambda_{max}$ (log $\varepsilon$): 430 (3.63), 366 (3.40), and 260 nm (4.54), which is in accord with the spectrum of benz[a]aceanthrylene (*E. Clar, W. Willicks*, J. Chem. Soc. *1958*, 942).

---

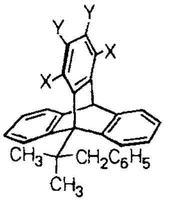
## *peri*-Substituent Effects on the Rotational Barrier of 9-(1,1-Dimethyl-2-phenylethyl)triptycene[**]

By *Gaku Yamamoto, Masahiko Suzuki*, and *Michinori Ōki*[*]

Substitution at the *peri*-position of 9-substituted triptycene derivatives generally raises the barrier to rotation about the 9-substituent-to-bridgehead bond, when the 9-substituent is a primary or a secondary alkyl group[1]. In 9-(1-cyano- or 1-methoxycarbonyl-1-methylethyl)triptycene, introduction of a chloro or a methyl group into the *peri*-position has been found to decrease the rotational barrier[2]. In order to see if this is a general phenomenon in 9-*tert*-alkyl substituted triptycene derivatives, and to investigate the effects of some other *peri*-substituents, we studied the rotational barriers in 9-(1,1-dimethyl-2-phenylethyl)triptycenes with a variety of *peri*-substituents and found an interesting dependence of the barrier on the nature of the substituents.



*ap-(1)-ap-(5)*



*± sc-(1) - ± sc-(5)*

*(1)*, X = H, Y = Cl
*(2)*, X = Y = F
*(3)*, X = OCH$_3$, Y = H
*(4)*, X = Y = Cl
*(5)*, X = CH$_3$, Y = H

Previously we reported the stereoselective synthesis and high rotational stability of 2,3-dichloro-9-(1,1-dimethyl-2-phenylethyl)triptycene *(1)*[3]. Reaction of 9-(1,1-dimethyl-2-phenylethyl)anthracene with dehydrobenzene derivatives gave, stereoselectively, the *ap*-rotamers of *(2)*—*(5)*[4]. A study of the kinetics of the *ap*→ ± *sc* isomerization was carried out by NMR spectroscopy (by $^{19}$F- for *(2)* and $^1$H-NMR for the others) in 1-chloronaphthalene solutions between 160—280°C (Table 1). The ±*sc*-rotamers were isolated upon chromatographic separation of the equilibrated mixture[4].

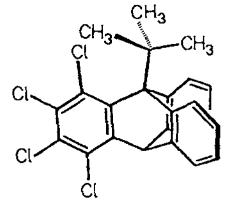
Table 1. Equilibrium and kinetic parameters for *ap*→ ± *sc* isomerization in 1-chloronaphthalene.

$$ap\text{-rotamer} \underset{k_{-1}}{\overset{2k_1}{\rightleftharpoons}} \pm sc\text{-rotamer}$$

$$K = 2k_1/k_{-1} = [\pm sc]/[ap]$$

| Compound | *peri*-Substituent [a] | | $K$ | $T$ [°C] | $\Delta H^{+}$ [kcal/mol] | $\Delta S^{+}$ [eu] | $\Delta G^{+}_{500\,K}$ [kcal/mol] |
|---|---|---|---|---|---|---|---|
| *(1)* | H | (1.2) | 2.0 | (259) | 35.7 | − 9.3 | 40.4 |
| *(2)* | F | (1.35) | 1.42 | (259) | 43.4 | − 1.9 | 44.3 |
| *(3)* | OCH$_3$ | (1.40) [b] | 1.22 | (259) | 42.4 | − 0.1 | 42.4 |
| *(4)* | Cl | (1.80) | 0.48 | (208) | 34.7 | − 7.0 | 38.2 |
| *(5)* | CH$_3$ | (2.0) | 0.41 | (212) | 31.6 | − 13.9 | 38.6 |

[a] In parentheses are the van der Waals radii after Pauling [5] (in Å). [b] van der Waals radius of an oxygen atom.



*(6)*

Table 1 reveals that relatively small *peri*-groups (F or OCH$_3$) considerably increase the barrier relative to that for the *peri*-unsubstituted derivative *(1)*, while bulkier groups (Cl or CH$_3$) *decrease* the barrier. Since the barrier is the energy difference between the ground and the transition states, the effects of *peri*-substitution on both should be examined.

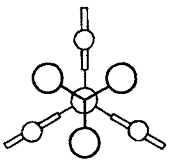
9-*tert*-Butyltriptycene was used as a model compound for these investigations. The crystal structure of its 1,2,3,4-tetrachloro derivative *(6)* reveals the effects of *peri*-substitution on the ground state geometry[6]. The most prominent feature is the tilting of the *tert*-butyl and the *peri*-chloro groups away from each other, due to steric compression. This feature may be found to a greater or less extent in any of the *peri*-substituted derivatives and can be represented by the Newman projection *(8)*; the *peri*-unsubstituted compound is shown in *(7)*. The bulkier the *peri*-group, the greater the degree of tilting of the axis bond and the greater the ground state energy level.

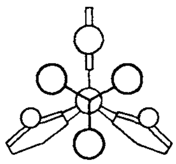
---

[*] Prof. Dr. M. Ōki, Dr. G. Yamamoto, M. Suzuki
Department of Chemistry, Faculty of Science
The University of Tokio
Bunkyo-Ku, Tokyo 113 (Japan)

[**] Restricted Rotation Involving the Tetrahedral Carbon, Part 32. This work was supported by the Japanese Ministry of Education.—Part 31: [2b].

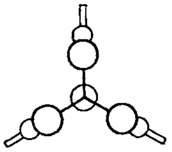
(7)

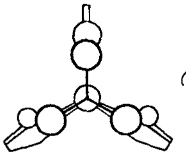




(8)

(9)





(10)

The *peri*-unsubstituted derivative adopts conformation *(9)* as the transition state for rotation, where the $CH_3/H$ eclipsing interaction simultaneously becomes maximal at the three sites, assuming that the geometry of the *tert*-butyl group in the ground state is also maintained in the transition state. In the *peri*-substituted derivatives, however—because of the tilting of the *tert*-butyl group—only one methyl group and the substituent X are eclipsed at a time; the other two methyl groups become eclipsed before or after the maximal $CH_3/X$-interaction. If the *peri*-group is relatively small (F or $OCH_3$), the tilting of the axis-bond is not large and the time lags for the eclipsing process will be small. Since the steric interaction between $CH_3$ and X in *(10)* should be larger than in *(8)*, the destabilization of the transition state should exceed that of the ground state, resulting in an increase of the barrier. Further increase of the bulkiness of the *peri*-substituent causes even larger tilting of the axis-bond and the time lags for eclipsing become larger. Thus, in spite of the large $CH_3/X$-interaction the destabilization of the transition state may be less than that of the ground state, and result in a decrease of the rotational barrier.

It may be argued that the above discussion is an oversimplification of the transition state for rotation, because it neglects the changes in bond lengths and angles. However, we believe that the differential timing of the maximal eclipsing interaction between the *peri*-groups and the side chains of the 9-substituent contributes, at least partially, to the origin of the unusual dependence of the barrier on *peri*-substitution.

Received: March 14, 1980 [Z 764b IE]
German version: Angew. Chem. 93, 580 (1981)

CAS Registry numbers:
*(1)*, 73544-12-4; *(2)*, 73524-75-1; *(3)*, 73524-76-2; *(4)*, 73524-77-3; *(5)*, 73524-78-4

---

[1] *M. Ōki*, Angew. Chem. *88*, 67 (1976); Angew. Chem. Int. Ed. Engl. *15*, 87 (1976).

[2] a) *S. Otsuka, T. Mitsuhashi, M. Ōki*, Bull. Chem. Soc. Jpn. *52*, 3663 (1979); b) *S. Otsuka, G. Yamamoto, T. Mitsuhashi, M. Ōki, ibid.*, *53*, 2095 (1980).

[3] a) *G. Yamamoto, M. Ōki*, J. Chem. Soc. Chem. Commun. *1974*, 713. In this paper, the activation energy for compound *(1)* was misprinted as 33.6 kcal/mol, and should be 36.6 kcal/mol; b) *G. Yamamoto, M. Ōki*, Bull. Chem. Soc. Jpn. *48*, 3686 (1975).

[4] All the new compounds gave satisfactory elemental analyses. Melting points are as follows; *ap-(2)*: 192—194 °C, ±*sc-(2)*: 203—204 °C, *ap-(3)*: 285—288 °C, ±*sc-(3)*: 218—219 °C, *ap-(4)*: 283—285 °C, ±*sc-(4)*: 231—233 °C, *ap-(5)*: 306—308 °C, ±*sc-(5)*: 209—211 °C. Assignment of the rotamers was based on the $^1$H-NMR signal patterns of the *gem*-dimethyl and methylene protons; enantiotopic and isochronous in the *ap*-rotamers and diastereotopic and anisochronous in the ±*sc*-rotamers.

[5] *L. Pauling*, The Nature of the Chemical Bond, 3rd ed., Cornell University Press, New York 1960, p. 260.

[6] *M. Mikami, K. Toriumi, M. Konno, Y. Saito*, Acta Crystallogr. *B31*, 2474 (1975).

## *P*-Functionalized Diferriophosphonium Salts and Complex-Stabilized Derivatives of Phosphinic Acid[**]

By *Hans Schäfer*[*]

A cationic $PH_2$-bridged iron complex *(1)* has been prepared for the first time in the following way:

$$2\ \mathrm{Cp(CO)_2FeX} + \mathrm{Me_3SiPH_2} \xrightarrow[-\ \mathrm{Me_3SiX}]{\mathrm{C_6H_5CH_3},\ 20\,^{\circ}\mathrm{C}} [\mathrm{Cp(CO)_2Fe}]_2\mathrm{PH_2}^{\oplus}\mathrm{X}^{\ominus}$$

*(1a)*, X = Cl; *(1b)*, X = Br; *(1c)*, X = $BPh_4$

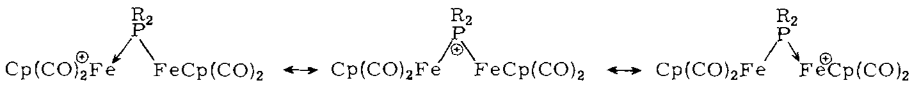
Using similar Si—P cleavage reactions we were previously able to synthesize neutral, open-chain[1] and cyclic[2] $PH_2$-complexes of some transition metals.

$$(1)\ \xrightarrow[\mathrm{CD_3OD}]{\mathrm{D_2O\ or}} [\mathrm{Cp(CO)_2Fe}]_2\mathrm{PD_2}^{\oplus}\mathrm{X}^{\ominus}$$

*(2a)*, X = Cl; *(2b)*, X = Br; *(2c)*, X = $BPh_4$

*(1a)* and *(1b)* can be converted into the tetraphenyl borate *(1c)* by reaction with $NaBPh_4$ in acetone. The salts are air-stable in the crystalline state; *(1a)* and *(1b)* dissolve without decomposition in water and methanol, *(1c)* in acetone, tetrahydrofuran (THF), and dichloromethane. The solutions can be stored indefinitely under an inert gas atmosphere in the dark at room temperature (20 °C). When treated with $D_2O$ or $CD_3OD$ a selective H/D exchange takes place with formation of salts *(2)* containing a *P*-deuterated cation.

The diferriophosphonium ion—the nomenclature corresponds to the central one of the three possible mesomeric resonance formulas—



$$\mathrm{Cp(CO)_2^{\oplus}Fe}\overset{\overset{\mathrm{R_2}}{\mathrm{P}}}{\diagup\ \diagdown}\mathrm{FeCp(CO)_2} \longleftrightarrow \mathrm{Cp(CO)_2Fe}\overset{\overset{\mathrm{R_2}}{\mathrm{P}}}{\diagup^{\oplus}\diagdown}\mathrm{FeCp(CO)_2} \longleftrightarrow \mathrm{Cp(CO)_2Fe}\overset{\overset{\mathrm{R_2}}{\mathrm{P}}}{\diagup\ \diagdown}\mathrm{Fe^{\oplus}Cp(CO)_2}$$

is isoelectronic with the neutral $SiH_2$ complex $[Cp(CO)_2Fe]_2SiH_2$ prepared by *Aylett*[3a]. SiH-[3] and PH-bonds[2a] are so activated by double transition-metal substitution that hydrogen-halogen exchange is observed with

---

[*] Priv.-Doz. Dr. H. Schäfer
Institut für Anorganische Chemie der Universität
Engesserstrasse 30.45, D-7500 Karlsruhe 1 (Germany)

[**] Transition Metal Phosphido-Complexes, Part 5: This work was supported by the Deutsche Forschungsgemeinschaft.—Part 4: [1].

halogenated hydrocarbons even at 20 °C. This enables a gentle halogenation, and thus functionalization of the bridging $PH_2$-group without altering the basic structural moiety. *(1c)* can be converted into salts containing bishalogenated cations using $CBr_4$ or $CCl_4$ in acetone. However, side reactions with the $BPh_4$ anion lead to the formation of a mixture of ionic products. On reaction of *(1a)* or *(1b)* with $CBr_4$ or $CCl_4$ in methanol at 20 °C the hydrogen atoms attached to phosphorus are first replaced by halogen atoms and those consecutively by methoxy groups. The reactions involving several intermediates finally yield the salts *(3a)* and *(3b)* with the first $P(OCH_3)_2$-bridged complex cation, which can be precipitated as the $BPh_4$-salt *(3c)*.

$$(1a,b) + 2\,CX_4 + 2\,CH_3OH \xrightarrow[-2\,CHX_3,\,-2\,HX]{CH_3OH,\ 20\,^\circ C} [Cp(CO)_2Fe]_2P(OCH_3)_2^{\oplus}X^{\ominus}$$

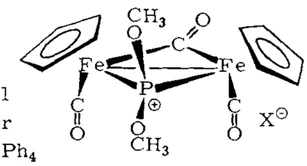
*(3a)*, X = Cl; *(3b)*, X = Br;
*(3c)*, X = $BPh_4$

Reaction of *(1a, b)* with $CBr_4$ in aqueous solutions affords a complex from which *(4c)* can be obtained; *(4c)* is a complex-stabilized derivative of phosphinic acid in which for the first time a $P(OH)_2$ group functions as a bridge.

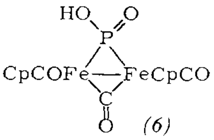
$$(1a,b) + 2\,CBr_4 + 2\,H_2O \xrightarrow[-2\,CHBr_3,\,-2\,HBr]{(CH_3)_2CO,\ H_2O,\ 20\,^\circ C} [Cp(CO)_2Fe]_2P(OH)_2^{\oplus}X^{\ominus}$$

*(4a)*, X = Cl; *(4b)*, X = Br;
*(4c)*, X = $BPh_4$

The IR spectra of solutions of compounds *(1c)*—*(4c)* in acetone each show three CO stretching vibrations of about equal intensity (Table 1). The diferriophosphonium ions of salts *(1)*—*(4)* are presumably sterically fixed in solution and have $C_{2v}$ symmetry[4]. This assumption is supported by the observation that only the salt *(5c)*, in which the cation is present as *cis*-isomer, is formed with cleavage of CO if *(3c)* is irradiated with UV light in acetone.



*(5a)*, X = Cl
*(5b)*, X = Br
*(5c)*, X = $BPh_4$



*(6)*

The structure of the cation of *(5)*, with both Cp groups on the same side of the $Fe_2P$ ring, follows from the $^1H$-NMR spectrum (Table 1), since the two $CH_3O$-groups have a different environment only in this isomer.

A single relatively sharp OH-stretching vibration in the IR spectrum of *(4c)* at 3400 $cm^{-1}$ indicates that the OH-groups of the cation of *(4)* are not associated[5].

*(4c)* is extremely sensitive to light. Upon UV irradiation of an aqueous solution of the bromide *(4b)*, CO is evolved and red crystals are precipitated which, according to the IR spectra, consist of a neutral, cyclic diferriophosphinic acid derivative *(6)*.

In the crystalline state *(6)* is air-stable and only moderately soluble in THF. On addition of bases (NaOH, $NEt_3$), *(6)* is soluble in water, methanol, acetone, THF, and dichloromethane. The IR spectra of the crystals of *(6)* show bands at 2740, 2330 and 1240 $cm^{-1}$ typical for associated P(O)OH-groups. An X-ray structure analysis carried out by *B. Deppisch* on a single crystal shows that *(6)* is associated to give dimers *via* hydrogen bonding of the P(O)OH groups. The two Cp groups are coordinated exclusively in the *cis* position, just as in *(5)*.

### *Procedure*

All reactions up to the isolation of the crystalline products must be carried out under an inert gas atmosphere in anhydrous and degassed solvents and, with the exception of the photolysis, in the absence of light.

*(1b)* and *(1c)*: $Me_3SiPH_2$ (2.34 g, 22 mmol) is condensed under reduced pressure into a mixture of $Cp(CO)_2FeBr$ (10.27 g, 40 mmol) and toluene (100 $cm^3$) cooled with liquid nitrogen. After warming to room temperature (20 °C) the mixture is stirred for 6 h under reduced pressure. The yellow precipitate is filtered, washed with toluene, and dried at $10^{-3}$ torr. This crude product *(1b)* can be used directly for further reactions. Recrystallization from $CH_3OH$ at −78 °C affords 4.76 g (51%) of yellow-brown, air-stable crystals of *(1b)*. Treatment of the crude product with excess $NaBPh_4$ in excess acetone and recrystallization from ace-

Table 1. Characteristic NMR and IR data of the compounds *(1c)*—*(5c)* and *(6)* [a].

| | *(1c)* | *(2c)* | *(3c)* | *(5c)* | *(4c)* | *(6)* |
|---|---|---|---|---|---|---|
| NMR data [b] | | | | | | |
| $\delta(^{31}P)$ [c] | −102 | −103.6 | 312 | 354 | 266 | 168 [h] |
| $\delta(^1H)$ [d] | 5.46 (cp)<br>3.87 ($PH_2$) | 5.46 (cp) | 5.54 (cp)<br>3.77 ($CH_3$) | 5.50 (cp)<br>4.53, 4.27 ($CH_3$) | 5.40 (cp) | — |
| $^3J_{PFeCH}$ [Hz] [e] | 2.05 | 2.05 | 1.7 | 0.8 | 1.9 [g] | — |
| other coupling constants [Hz] [f] | $^1J_{PH}=323$ | $^1J_{PD}=49.5$ | $^3J_{POCH}=12.5$ | $^3J_{POCH}=12.0, 12.5$ | — | — |
| IR data [i] | | | | | | |
| $\nu(CO)$ [$cm^{-1}$] | 2053 vs<br>2035 vs<br>1998 vs | 2053 vs<br>2035 vs<br>1998 vs | 2044 vs (sh)<br>2035 vs<br>1995 vs | 2027 vs, 1956 w<br>1996 s, 1833 s<br>1971 w | 2044 vs (sh)<br>2032 vs<br>1990 vs | 2027 s (sh), 1797 vs [j]<br>1990 vs, 1780 vs<br>1953 vs |
| $\nu$(others) | $\nu(PH_2)=2305$ m [j]<br>$\delta(PH_2)=1065$ s [j] | $\nu(PD_2)=1668$ m [j]<br>$\delta(PD_2)=768$ s [j] | | | $\nu(OH)=3400$ m [j]<br>$\delta(OH)=1240$ m [j] | $\nu(OH)=2740$ m (br), 2330 m (br) [k]<br>$\delta(OH)=1238$ m [k] |

[a] All compounds gave correct elemental analyses. [b] In [$D_6$]acetone. [c] ±1 ppm; $H_3PO_4$ ext. std.; positive sign = downfield. [d] ±0.02 ppm; TMS int. std.; cp = $C_5H_5$. [e] ±0.1 Hz. [f] $\delta(^1H)$ of $BPh_4^{\ominus}$: *o*-phenyl 7.34 (m), *m*-phenyl 6.94 (t), *p*-phenyl 6.78 (t). [g] $T = -60\,^\circ C$. [h] In THF; $T = -60\,^\circ C$. [i] In acetone. [j] Nujol mull. [k] KBr pellet.

tone at $-20\,^{\circ}C$ yields 8.5 g (60%) of golden-yellow, air-stable crystals of *(1c)*.

*(2b)* and *(2c)*: *(1b)* (0.2 g) is recrystallized twice from $CD_3OD$ at $-78\,^{\circ}C$. 0.12 g (60%) of *(2b)* are isolated. *(1c)* (0.5 g) is stirred twice for 1 d with a mixture of acetone and a few drops of $CD_3OD$ or $D_2O$ at $20\,^{\circ}C$ and recrystallized from acetone at $-20\,^{\circ}C$; 0.4 g (80%) of *(2c)* are obtained.

*(3c)*: *(1b)* (1.5 g, *ca.* 3 mmol) is dissolved in $CH_3OH$ (20 $cm^3$), treated with 2.32 g (7 mmol) of $CBr_4$, and the mixture stirred for 8 d. All volatile components are distilled off under reduced pressure at $20\,^{\circ}C$. The residue is re-dissolved in $CH_3OH$ (20 $cm^3$), and the solution is stirred further for 2 d. On addition of excess $NaBPh_4$ *(3c)* precipitates as a yellow powder, which is recrystallized from acetone at $-20\,^{\circ}C$; *(3c)* (1.38 g, *ca.* 60%) is obtained as yellow, air-stable crystals.

*(5c)*: *(3c)* (1 g, 1.3 mmol) is dissolved in acetone and irradiated with UV light (HANAU TQ 150, externally through DURAN 50 glass) for 6 h at $20\,^{\circ}C$ and *ca.* 300 torr. The solution is filtered, concentrated under reduced pressure at $20\,^{\circ}C$, and brought to crystallization at $-78\,^{\circ}C$; *(5c)* (0.62 g, 65%) is obtained as red-brown, air-stable crystals.

*(4c)* and *(6)*: A crude sample of *(1b)* (2.5 g, *ca.* 5 mmol) is dissolved in a mixture of distilled water (100 $cm^3$) and acetone (100 $cm^3$), treated with $CBr_4$ (4 g, 12 mmol) and the final mixture stirred for 24 h. A little more than 100 $cm^3$ of the solution is distilled off (most of the acetone) at $20\,^{\circ}C$. The remaining solution is diluted with 100 $cm^3$ of distilled water, filtered, and divided into two parts. To one half of the solution excess $NaBPh_4$ is added and the resulting yellow powder is filtered off, washed with distilled water, and dried for 12 h at $20\,^{\circ}C$ and $10^{-3}$ torr; *(4c)* (1.48 g, 80%) is isolated as a yellow powder, which is sensitive to light and air.

The other half of the solution is irradiated with UV light (for conditions see above) at $20\,^{\circ}C$ and *ca.* 300 torr until the evolution of CO ceases (*ca.* 6 h). The red crystals are filtered off, washed with acetone, and dried at $20\,^{\circ}C$ under reduced pressure; *(6)* (0.68 g, *ca.* 70%) is obtained as red, air-stable crystals.

Received: October 15, 1980 [Z 773 IE]
German version: Angew. Chem. *93*, 595 (1981)

CAS Registry numbers:
*(1a)*, 78004-87-2; *(1b)*, 78004-88-3; *(1c)*, 78018-41-4; *(2a)*, 78018-42-5; *(2b)*, 78004-89-4; *(2c)*, 78004-91-8; *(3a)*, 78004-92-9; *(3b)*, 78004-93-0; *(3c)*, 78004-95-2; *(4a)*, 78039-74-4; *(4b)*, 78039-71-1; *(4c)*, 78039-73-3; *(5a)*, 78004-96-3; *(5b)*, 78085-88-8; *(5c)*, 78085-90-2; *(6)*, 78039-70-0; $Cp(CO)_2FeBr$, 12078-20-5; $Cp(CO)_2FeCl$, 12107-04-9

---

[1] *H. Schäfer*, Z. Anorg. Allg. Chem. *467*, 105 (1980).

[2] a) *H. Schäfer*, Z. Naturforsch. *B 33*, 351 (1978); b) Z. Anorg. Allg. Chem. *459*, 157 (1979).

[3] a) *B. J. Aylett, H. M. Colquhoun*, J. Chem. Res. (M) *1977*, 1677; b) *W. Malisch, R. Ries*, Angew. Chem. *90*, 140 (1978); Angew. Chem. Int. Ed. Engl. *17*, 120 (1978); Chem. Ber. *112*, 1304 (1979).

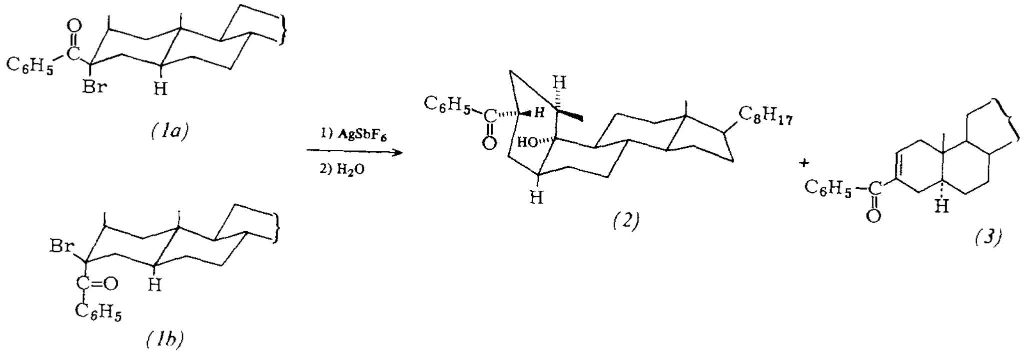
[4] *R. D. Fischer, A. Vogler, K. Noack*, J. Organomet. Chem. *7*, 135 (1967).

[5] Upon exposure to moisture the OH-band is shifted and additional broad OH-bands are observed.

## Regio- and Stereoselective "Long-Range" Hydroxylation of Cholestanes—A Novel Route to 5α-Steroids with *cis*-Coupled A,B-Rings

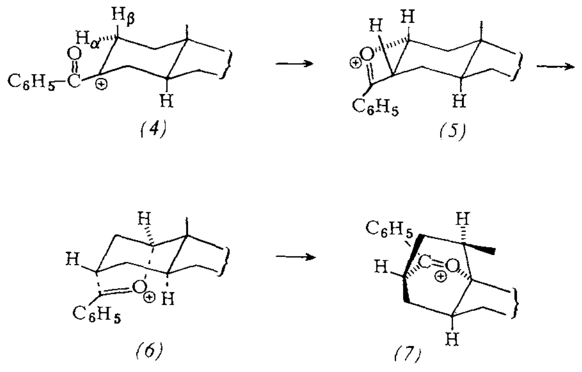
By *Jean-Pierre Bégué*[*]

For some time we have investigated whether compounds can be regio- and stereoselectively hydroxylated, *via* α-acylcarbenium ions, at positions far removed from the carbenium ion center[1]. We have now succeeded in applying this method, which had previously been successfully used on cyclohexane systems, to steroids; the intermediate formation of oxonium ions should prevent backbone rearrangements, and, hence, stereoselective hydroxylation can be anticipated.



The bromides *(1a)* and *(1b)*, prepared from cholestanone[2], were dehalogenated with $AgSbF_6$ (1.5 equivalents) in $CH_2Cl_2$ and, following hydrolysis and thin layer chromatography (silica gel), the hydroxyketone *(2)* [yield: 45 or 32%] and the unsaturated ketone *(3)* [yield: 35 or 25%] were isolated. *(2)* (m.p. = 155 – 160 °C) was identified by means of an X-ray structure analysis[3] and spectroscopic data[4].

The formation of *(2)* and *(3)* can be explained by the initial formation of the α-acylcarbenium ion *(4)*[5]; *(4)* can then undergo two competitive reactions: either by hydride- and methanide-shifts *via (5)* and *(6)* to the oxonium ion *(7)*, resulting in formation of *(2)*, or directly to *(3)* *via* proton elimination. *(3)* is the expected elimination product of a C-3-substituted 5α-steroid[6].



---

[*] Dr. J. P. Bégué
Groupe de Recherche No. 12 (CNRS)
2 rue Henri-Dunant, F-94320 Thiais (France)

The transformation (1)→(2), which is novel for steroids, consists of the following individual steps: (5) is formed by hydride-shift of 2-$H_\beta$ to C-3[7] and successive migration of the 1-H and 19-Me groups—the last step is accompanied by an inversion of the configuration at C-10—leads to the 5-$H_\alpha$ steroid (2).

In educt (1b), the 2-$H_\beta$ and Br are *cis* to each other, this corroborates an earlier observation that dissociation of the C—Br bond and the 1,2-hydride shifts occur sequentially[2]. The fact that in both possible reactions of (4), only 2-H and not 4-H is involved, indicates that analogous intermediate conformations occur in both cases[8].

We have therefore succeeded in the regio- and stereoselective "long-range" hydroxylation of the C-10 position of steroids. Furthermore, the unusual isomerization of an A/B-*trans* to an A/B-*cis* steroid (5-H) has been observed.

Received: May 5, 1980 [Z 774 IE]
German version: Angew. Chem. 93, 597 (1981)

CAS Registry numbers:
*(1a)*, 77825-58-2; *(1b)*, 77825-59-3; *(2)*, 77825-60-6; *(3)*, 77825-61-7

---

[1] a) *J. P. Bégué, M. Charpentier-Morize, C. Pardo*, Tetrahedron *31*, 1919 (1975); *D. Baudry, M. Charpentier-Morize*, Nouv. J. Chim. *2*, 255 (1978); *J. P. Bégué, D. Bonnet-Delpon, M. Charpentier-Morize, C. Pardo*, Tetrahedron *31*, 2505 (1975); b) *J. P. Bégué, M. Charpentier-Morize*, Angew. Chem. *83*, 327 (1971); Angew. Chem. Int. Ed. Engl. *10*, 327 (1971).

[2] *J. P. Bégué, M. Malissard*, Tetrahedron *34*, 2095 (1978).

[3] *F. Baert, J. Lamiot*, unpublished results; the stability of (2) in the presence of bases provides further evidence for the equatorial siting of the benzoyl group.

[4] $^1$H-NMR: $\delta=0.75$ (s, 3H, 18-Me), 1.39 (d, 3H, 19-Me, $J=8$ Hz), 3.67 (t, 1H, 3-H); $^{13}$C-NMR: $\delta=12.8$ (C-18), 43.0 (C-13), 74.3 (C-10), 128.3, 128.7, 132.8, 136.6 ($C_6H_5$), 203.6 ($C{=}O$); MS: $m/z=492$ ($M^\oplus$), 474 ($M^\oplus-18$), 450, 369, 133, 105; IR: $\nu$(CO) = 1690 cm$^{-1}$; $\nu$(OH) = 3630 cm$^{-1}$.

[5] The structure of the α-acylcarbenium ions is not yet known; however, they could exist as carbenium or oxirenium ions; see: *J. P. Bégué, M. Charpentier-Morize*, Acc. Chem. *13*, 207 (1980) and literature cited therein.

[6] *W. Klyne:* The Chemistry of the Steroids, Wiley, New York 1957, p. 69.

[7] It can be shown that successive 1,2-hydride shifts occur in the reaction of *cis*- and *trans*-isomers of (1-bromo-4-*tert*-butyl)cyclohexyl(phenyl)ketone with $AgSbF_6$ after formation of the α-acylcarbenium ion [8].

[8] *R. Bucourt*, Top. Stereochem. *8*, 207 (1974).

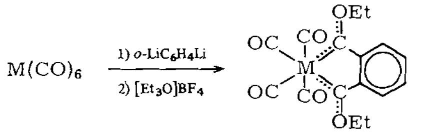
---

## Synthesis of a Novel Biscarbene Type of Complex[1]

By *Ernst Otto Fischer, Werner Röll, Ulrich Schubert*, and *Klaus Ackermann*[*]

The direct reaction of carbonyl transition metal monocarbenes with nucleophiles LiR to give biscarbene complexes is, with few exceptions[2], thwarted by the strong electrophilic character of the carbene carbon atom; the addition does not take place at one of the CO ligands, but at the carbene carbon.

We have now succeeded in synthesizing 1,4-chelated *cis*-bis[alkoxy(aryl)carbene] complexes by reaction of *o*-dilithiobenzene[3] with hexacarbonylchromium, -molybdenum or -tungsten and alkylation of the adducts with triethyloxonium tetrafluoroborate.



(1), M = Cr
(2), M = Mo
(3), M = W

IR spectra in the $\nu_{CO}$-region (cm$^{-1}$, hexane)

| | | | |
|---|---|---|---|
| *(1)*: 2018 (m), | 1953 (vs), | 1947 (sh), | 1898 (m) |
| *(2)*: 2035 (m), | 1963 (vs), | 1953 (sh), | 1905 (m) |
| *(3)*: 2032 (m), | 1957 (vs), | 1947 (sh), | 1896 (m) |

$^1$H-NMR spectra in [$D_6$]acetone (ref. to $\delta_{CD_2HCOCD_3}=2.1$)

| | | |
|---|---|---|
| *(1)*: 1.8 (T), | 5.25 (Q), | 7.75 (S) |
| *(2)*: 1.8 (T), | 5.2 (Q), | 7.75 (S) |
| *(3)*: 1.75 (T), | 5.05 (Q), | 7.8 (S) |

$^{13}$C{$^1$H}-NMR spectra in $CD_2Cl_2$ (ref. to $\delta_{CD_2Cl_2}=54.2$)

| | $C_{Carb.}$ | $CO_{trans}$ | $CO_{cis}$ | $C_{1,2}$ | $C_{3-6}$ | | $OCH_2$ | $CH_3$ |
|---|---|---|---|---|---|---|---|---|
| *(1)*: | 337.97 | 240.69 | 224.76 | 155.40 | 133.75 | 116.90 | 77.92 | 15.54 |
| *(2)*: | 329.52 | 228.16 | 215.34 | 155.89 | 134.12 | 118.20 | 79.70 | 15.54 |
| *(3)*: | 312.31 | 220.21 | 209.49 | 158.48 | 134.12 | 119.01 | 81.00 | 15.22 |

The biscarbene complexes (1)—(3) are stable in the solid state at room temperature, crystallize from pentane as permanganate-colored to black leaflets, and dissolve in most common organic solvents to give dark-red solutions.

If the complex is assumed to have quasi-octahedral structure, then the four $\nu_{CO}$ bands of the IR spectra are in agreement with theory; the short-wavelength vibration corresponds to the species $A_1^{(2)}$, the long-wavelength vibration to the species $B_2$.

The insertion of a second carbene function leads to a significant shielding of the carbene carbon atom compared to in $(CO)_5M[C(OR^1)R^2]$[4], whereas a downfield shift is observed for $^{13}$C{$^1$H}-NMR signals of the CO groups, in agreement with investigations by *Todd et al.*[5]. The resonances of the remaining aromatic and aliphatic carbon atoms of (1)—(3) lie in the usual range for carbene complexes.

The X-ray structure analysis[6] of (1) shows that the presence of two *cis*-carbene ligands in the complex has only a

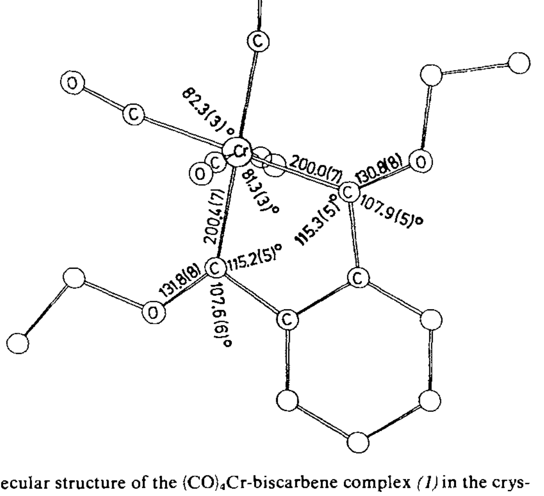


Fig. 1. Molecular structure of the $(CO)_4$Cr-biscarbene complex (1) in the crystal.

---

[*] Prof. Dr. E. O. Fischer, Dipl.-Chem. W. Röll, Priv.-Doz. Dr. U. Schubert, Dipl.-Chem. K. Ackermann
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

slight effect on the bonding of the carbene carbon atom, but that the coordination octahedron of the metal is markedly distorted. The $C_{carbene}$—Cr and $C_{carbene}$—$C_{phenylene}$ bond lengths are comparable with those found in other alkoxy(aryl)carbene complexes of chromium, only $C_{carbene}$—O is slightly shorter (cf.[7]). The angles at $C_{carbene}$ are not unduly affected by the ring formation. The phenylene ring is essentially coplanar with the atoms of the two carbene groups and, within the standard deviations, shows no bond-length alternation.

The coordination octahedron is distorted in two respects by the chelate effect of the biscarbene ligand ($C_{carbene}$—Cr—$C_{carbene}$ angle of 81.3°) (cf. [8]): 1. Since the *trans*-$C_{carbene}$—Cr—$C_{CO}$ groups in the plane of the carbene ligands with 179.0 and 178.5° are almost linear and no bending of this plane takes place, the $C_{CO}$—Cr—$C_{CO}$ angle of 82.3° is likewise very small, while the *cis*-$C_{carbene}$—Cr—$C_{CO}$ angles of 98.5 and 97.9° are distinctly widened.—2. The CO ligands perpendicular to the carbene plane are bent in towards the chelate ring and form an angle of 171.7(3)° with each other.

## *Procedure*

A suspension of $Cr(CO)_6$ (2.5 g, 11.3 mmol) in 150 ml tetrahydrofuran is treated at 0 °C with 80 ml of a 0.15 M solution of *o*-dilithiobenzene in ether and the mixture stirred for 1 h. The solvent is then removed and the residue is taken up in 100 ml of dichloromethane (−10 °C). A solution of triethyloxonium salt in $CH_2Cl_2$ is now added dropwise until the mixture no longer reacts alkaline, and, after 15 minutes' stirring, the mixture is evaporated to dryness. The crude product is chromatographed at −25 °C with pentane/$CH_2Cl_2$ (5 : 1) on silica gel. The eluate of the almost black zone is evaporated down, dissolved in pentane, and allowed to crystallize at −78 °C; m.p. 115 °C *(1)*. *(2)* and *(3)* are obtained analogously; m.p. 104 °C and 114 °C, respectively.

Received: December 23, 1980 [Z 776 IE]
German version: Angew. Chem. *93*, 582 (1981)

CAS Registry numbers:
*(1)*, 78128-66-2; *(2)*, 78128-67-3; *(3)*, 78128-68-4; $Cr(CO)_6$, 13007-92-6; $Mo(CO)_6$, 13939-06-5; $W(CO)_6$, 14040-11-0; *o*-$LiC_6H_4Li$, 51241-56-6; $[Et_3O]BF_4$, 368-39-8

---

[1] Transition metal-Carbene Complexes, Part 116.—Part 115: *E. O. Fischer, W. Kleine*, J. Organomet. Chem. *208*, C 27 (1980).

[2] *E. O. Fischer, F. R. Kreissl, C. G. Kreiter, E. W. Meineke,* Chem. Ber. *105*, 2558 (1972); *P. B. Hitchcock, M. F. Lappert, P. L. Pye*, J. Chem. Soc. Dalton Trans. *1977*, 2160.

[3] *G. Wittig, F. Bickelhaupt*, Chem. Ber. *91*, 883 (1958).

[4] *C. G. Kreiter, V. Formáček*, Angew. Chem. *84*, 155 (1972); Angew. Chem. Int. Ed. Engl. *11*, 141 (1972).

[5] *L. J. Todd, J. R. Wilkinson*, J. Organomet. Chem. *77*, 1 (1974).

[6] Monoclinic, $P2_1/n$ ($Z=4$), $a=716.5(5)$, $b=2256(3)$, $c=1087.5(6)$ pm, $\beta=114.14(5)°$, $V=1604\times10^6$ pm$^3$, $\rho_{calc}=1.47$ g/cm$^3$ (−10 °C); 1722 structure factors ($I \geqq 3.9\sigma$, $2° \leqq 2\Theta \leqq 48°$), $Mo_{K\alpha}$ ($\lambda=71.069$ pm graphite monochromator), $R_1=0.078$, $R_2=0.070$ (Syntex $P2_1$/XTL).

[7] *U. Schubert*, J. Organomet. Chem. *185*, 373 (1980).

[8] *U. Schubert, A. Rengstl*, J. Organomet. Chem. *166*, 323 (1979).

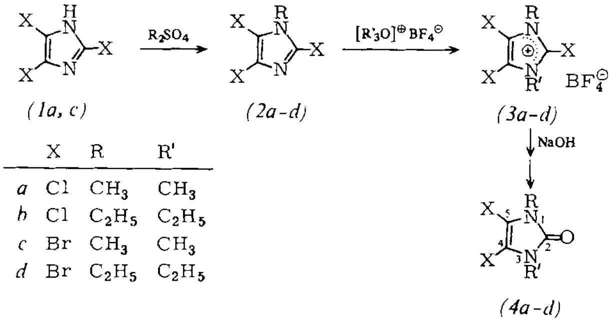
---

# Simple Synthesis of 1,3-Dialkyl-4,5-dihalo-2(3*H*)-imidazolones[**]

*By Heinrich Wamhoff, Wolfgang Kleimann, Gerhard Kunz, and Christoph H. Theis*[*]

*Dedicated to Professor Rolf Appel on the occasion of his 60th birthday*

Maleic acid anhydrides and imides[2a] as well as vinylene carbonates[2b] and their dihalo derivatives[1,3], 4-oxazolin-2-ones[4a], 1,3-dioxoles and 1,4-dioxene[4b] have, as cyclophilic molecules, already been the subject of several investigations, but an efficient synthesis of the potentially cyclophilic 4,5-dihalo-2(3*H*)-imidazolones has so far not been reported[5].



| | X | R | R' |
|---|---|---|---|
| *a* | Cl | $CH_3$ | $CH_3$ |
| *b* | Cl | $C_2H_5$ | $C_2H_5$ |
| *c* | Br | $CH_3$ | $CH_3$ |
| *d* | Br | $C_2H_5$ | $C_2H_5$ |

We have now found a simple access to the title compounds *(4)*. Trichloro- *(1a)*[6] and tribromoimidazole *(1c)*[7] are alkylated with dialkyl sulfate to the alkylimidazoles *(2a—d)* and then quaternized with trialkyloxonium tetra-

Table 1. Some spectroscopic data of the compounds *(3a—d)*, *(4a—d)* and *(8)*. $^1H$- and $^{13}C$-NMR spectra with TMS as internal standard, δ values, coupling constants [Hz]; IR spectra [cm$^{-1}$].

| | |
|---|---|
| *(3a)*, | $^1H$-NMR [a]: 3.95 (s, $CH_3$); $^{13}C$-NMR [b]: 135.2 (C-2), 119.1 (C-4,5), 34.9 ($CH_3$) |
| *(3b)*, | $^1H$-NMR [a]: 4.39 (q, $CH_2$), 1.46 (t, $CH_3$, $J=6$); $^{13}C$-NMR [b]: 132.5 (C-2), 120.7 (C-4,5), 45.5 ($CH_2$), 13.5 ($CH_3$) |
| *(3c)*, | $^1H$-NMR [a]: 3.86 (s, $CH_3$); $^{13}C$-NMR [b]: 124.8 (C-2), 112.4 (C-4,5), 38.1 ($CH_3$) |
| *(3d)*, | $^1H$-NMR [a]: 4.30 (q, $CH_2$), 1.39 (t, $CH_3$, $J=6$); $^{13}C$-NMR [b]: 121.7 (C-2), 111.6 (C-4,5), 48.0 ($CH_2$), 13.9 ($CH_3$) |
| *(4a)*, | $^1H$-NMR [c]: 3.29 (s, $CH_3$); $^{13}C$-NMR [d]: 150.5 (C-2), 106.7 (C-4,5), 47.48 ($CH_3$); IR (KBr): 1720 (C=O) |
| *(4b)*, | $^1H$-NMR [c]: 3.75 (q, $CH_2$), 1.20 (t, $CH_3$, $J=7.0$); $^{13}C$-NMR [d]: 150.4 (C-2), 106.2 (C-4,5), 37.0 (C-6), 14.6 (C-7); IR (KBr): 1700 (C=O), 1605 (C=C) |
| *(4c)*, | $^1H$-NMR [c]: 3.24 (s, $CH_3$); $^{13}C$-NMR [d]: 151.7 (C-2), 96.4 (C-4,5), 29.4 (C-6); IR [e]: 1690 (C=O), 1580 (C=C) |
| *(4d)*, | $^1H$-NMR [c]: 3.75 (q, $CH_2$), 1.22 (t, $CH_3$, $J=7.5$); $^{13}C$-NMR [d]: 151.0 (C-2), 96.0 (C-4,5), 38.5 (C-6), 14.6 (C-7); IR [e]: 1740, 1795 (C=O) |
| *(8)*, | $^1H$-NMR [c]: 7.29 (dd, $H^c$), 6.38 (dd, $H^a$, $J_{ab}=14.1$), 6.14 (dd, $H^b$, $J_{bc}=14.1$), 5.81 (d, $H^d$, $J_{cd}=7.5$), 4.20 (q, 2 $H^f$, $J_{fg}=7.5$), 3.79 (q, 4 $H^h$, $J_{hi}=7.5$), 1.84 (d, 3 $H^e$, $J_{ae}=6.0$), 1.18–1.36 (m, 9 H, $H^{g+i}$) |

Solvents: [a] $[D_6]$acetone, [b] $CD_3OD/CD_2Cl_2$ 1 : 1, [c] $CDCl_3$, [d] $[D_6]$benzene, [e] $CHCl_3$.

---

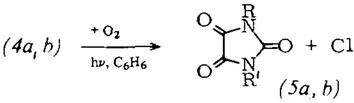
[*] Prof. Dr. H. Wamhoff, Dipl.-Chem. W. Kleimann, Dipl.-Chem. G. Kunz, Dr. C. H. Theis [***]
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

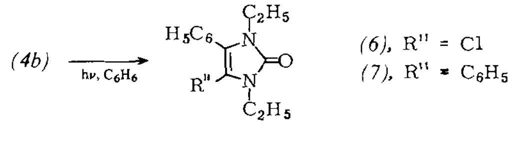
[**] Photochemistry of Heterocycles, Part 12. This work was supported by the Deutsche Forschungsgemeinschaft, the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen, and the Fonds der Chemischen Industrie.—Part 11: *G. Szilágyi, H. Wamhoff*, Angew. Chem. and Angew. Chem. Int. Ed. Engl. in press.

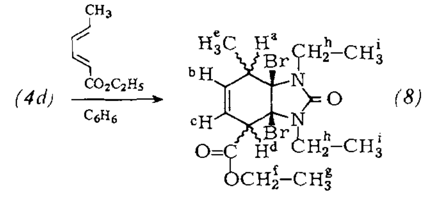
[***] Present address: Dynamit Nobel AG, Hauptabteilung Forschung und Entwicklung, D-5210 Troisdorf (Germany)

fluoroborate in high yields to the crystalline, stable, high-melting imidazolium salts *(3a—d)*. On treatment with dilute sodium hydroxide the salts *(3a—d)*, readily soluble in dimethylformamide, exchange their 2-halogen substituents for hydroxy groups selectively and almost quantitatively. With NaOH the intermediary 2-hydroxyimidazolium salts in turn split off $NaBF_4$ to afford the 4,5-dihalo-2(3*H*)-imidazolones *(4a—d)* (cf. Table 1)[8]. The chloro-derivatives *(4a, b)* are stable, whereas the bromo-derivatives *(4e, d)* decompose even with traces of moisture or on exposure to light.

UV irradiation (benzene, filter $\lambda = 350$ nm) of *(4a, b)* without carefully excluding oxygen (or far more rapidly on passing through $O_2$) leads in high yields to the dialkylparabanic acids *(5a, b)*[9a], most probably *via* the intermediary endoperoxides[10], which spontaneously eliminate chlorine. If oxygen is completely excluded, *e.g.* in argon atmosphere, *(4b)* is photoarylated (benzene, filter $\lambda = 320$ nm); *(6)* and *(7)* can be detected (each 3% yield) with the aid of mass spectrometry.







The sole isolable Diels-Alder adduct *(8)* of *(4d)* is formed with ethyl sorbate on heating for 8 h in benzene under inert gas. Careful work-up affords colorless crystals which rapidly decompose. *(8)* is characterized spectroscopically (see Table 1); the mass spectrum shows a molecular ion (triplet) of weak intensity at $m/e = 436$.

### *Procedure*

*(2a—d):* A suspension of anhydrous potassium carbonate in a solution of *(1a, c)* (100 mmol) in anhydrous acetone (300 $cm^3$) is treated with 100 mmol dialkyl sulfate and the mixture heated for 2 h under reflux. After filtration, evaporation of the filtrate to dryness, and treatment of the residue with ethanol, *(2a—d)* are precipitated with water. Yield/m.p. (b.p.): *(2a):* 78%/79 °C; Ref. [6] 75 °C. *(2b):* 83%/56 °C/0.07 torr; Ref. [6] 53 °C/0.05 torr. *(2c):* 75%/93 °C; Ref. [9b] 93—94 °C. *(2d):* 87%/61—62 °C; Ref. [9b] 61—62 °C.

*(3a—d):* *(2a—d)* (60 mmol) are suspended in anhydrous $CH_2Cl_2$ (50 $cm^3$). After addition of trialkyloxonium tetrafluoroborate (60 mmol) the mixture is briefly refluxed. The crystals which precipitate on cooling are recrystallized from a little methanol. Yield/m.p.: *(3a):* 84%/305 °C. *(3b):* 81%/268 °C. *(3c):* 76%/293—296 °C (dec.). *(3d):* 81%/285—288 °C (dec.).

*(4a—d):* A solution of *(3a—d)* (10 mmol) in dimethylformamide (40 $cm^3$) is stirred into 40 $cm^3$ of 2 N NaOH. The reaction mixture is immediately extracted with *n*-hexane and filtered through sodium sulfate. The products *(4a—d)* are isolated by evaporating down in a stream of inert gas. Yield/m.p.: *(4a):* 88%/88—91 °C. *(4b):* 82%/35—37 °C. *(4c):* 93%/87—88 °C (dec.). *(4d):* 94%/105—106 °C (dec.).

Received: August 7, 1980 [Z 777 IE]
German version: Angew. Chem. *93*, 601 (1981)

CAS Registry numbers:
*(1a)*, 7682-38-4; *(1c)*, 2034-22-2; *(2a)*, 873-25-6; *(2b)*, 59800-51-0; *(2c)*, 1003-91-4; *(2d)*, 31250-75-6; *(3a)*, 77944-08-2; *(3b)*, 77944-10-6; *(3c)*, 77944-12-8; *(3d)*, 77944-14-0; *(4a)*, 77944-15-1; *(4b)*, 77944-16-2; *(4c)*, 77944-17-3; *(4d)*, 77944-18-4; *(5a)*, 5176-82-9; *(5b)*, 10319-61-6; *(6)*, 77944-19-5; *(7)*, 77944-20-8; *(8)*, 77944-21-9; ethyl sorbate, 2396-84-1

---

[1] *G. Szilágyi, H. Wamhoff,* Angew. Chem. 92, 1066 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1026 (1980).

[2] a) *D. Bryce-Smith,* Pure Appl. Chem. *16*, 47 (1968); *34*, 193 (1973); *D. Bryce-Smith, R. R. Deshpande, A. Gilbert,* Tetrahedron Lett. *1975*, 1627; *W. Hartmann, H. G. Heine, L. Schrader, ibid. 1974,* 883, 3101; b) *W. Hartmann, R. Steinmetz,* Chem. Ber. *100*, 217 (1967); *W. Hartmann, ibid. 101*, 1643 (1968); *J. Tancrede, M. Rosenblum,* Synthesis *1971*, 219; *R. H. Grubbs,* J. Am. Chem. Soc. *92*, 6693 (1970).

[3] *H. D. Scharf,* Angew. Chem. *86*, 567 (1974); Angew. Chem. Int. Ed. Engl. *13*, 520 (1974); *H. D. Scharf, F. Korte,* Chem. Ber. *98*, 764, 3672 (1965); *99*, 1289 (1966); Angew. Chem. *77*, 452 (1965); Angew. Chem. Int. Ed. Engl. *4*, 429 (1965); *G. Szilágyi, H. Wamhoff, P. Sohár,* Chem. Ber. *107*, 1265 (1974); *H. Wamhoff, H. J. Hupe, ibid. 111*, 2677 (1978); *K. M. Wald, A. A. Nada, G. Szilágyi, H. Wamhoff, ibid. 113*, 2884 (1980).

[4] a) *K. H. Scholz, H. G. Heine, W. Hartmann,* Justus Liebigs Ann. Chem. *1976*, 1319; *1977*, 2027; Tetrahedron Lett. *1978*, 1467; b) *J. Mattay, H. Leismann, H. D. Scharf,* Chem. Ber. *112*, 577 (1979).

[5] Photoreactions of the 1,3-diacetyl- and 1,3-diphenyl-4-imidazolin-2-ones: *G. Steffan, G. O. Schenk,* Chem. Ber. *100*, 3961 (1967); *G. Steffan, ibid. 101*, 3688 (1968): bromination/dehydrobromination of 1,3-diacetyl-4-imidazolin-2-ones: *W. Thünker,* Dissertation, Technische Hochschule Aachen 1977; *H. D. Scharf,* private communication.

[6] *K. H. Büchel, H. Erdmann,* Chem. Ber. *109*, 1625, 1637 (1976); *A. W. Lutz, S. Lorenzo,* J. Heterocycl. Chem. *4*, 399 (1967).

[7] *I. E. Balaban, F. L. Pyman,* J. Chem. Soc. *1922*, 947.

[8] 2-Chlorobenzothiazolium tetrafluoroborate is similarly capable of smooth Cl/OH exchange: *H. Balli,* Justus Liebigs Ann. Chem. *647*, 11 (1961); quaternized 2-aryl-4,5-dichloroimidazoles are extremely sensitive to bases and readily decompose: *D. Günther, D. Bosse,* Angew. Chem. *92*, 138 (1980); Angew. Chem. Int. Ed. Engl. *19*, 130 (1980).

[9] a) *(5a):* 50% yield, m.p. 152—153 °C; *(5b):* 71% yield, m.p. 50—52 °C; *H. Biltz, E. Topp,* Ber. Dtsch. Chem. Ges. *46*, 1387 (1913): 154 and 49—51 °C, respectively; b) *O. Wallach, ibid. 15*, 644 (1882); *16*, 543 (1883).

[10] *Note added in proof:* Similar endoperoxides have been obtained on UV irradiation of 4,5-diaryl-4-oxazolin-2-ones (*F. S. Guziec, Jr., E. T. Tewes,* J. Heterocycl. Chem. *17*, 1807 (1980).

---

## The Unusual Stereochemistry of the Cycloaddition of Vinyl Ethers with Sulfonyl Isothiocyanates

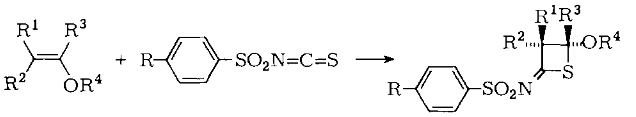
By *Ernst Schaumann, Hans-Günther Bäuch,* and *Gunadi Adiwidjaja*[*]

The stereochemistry of the products formed in synchronous reactions can be predicted on the basis of the rules for the conservation of orbital symmetry[1]. In the case of two-step cycloadditions a knowledge of the conformation of the intermediate would be necessary. The reaction of vinyl ethers *(1)* with the isothiocyanates *(2)* has now opened an insight into this otherwise difficultly accessible area of research.

---

[*] Prof. Dr. E. Schaumann, Dr. H.-G. Bäuch
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)
Dr. G. Adiwidjaja
Mineralogisch-petrographisches Institut der Universität
Grindelallee 48, D-2000 Hamburg 13 (Germany)

*(1a)*, $R^1 = R^2 = R^3 = H$, $R^4 = C_2H_5$
*(1b)*, $R^1 = R^3 = H$, $R^2 = CH_3$, $R^4 = C_2H_5$
*(1c)*, $R^1 = CH_3$, $R^2 = R^3 = H$, $R^4 = C_2H_5$
*(1d)*, $R^1 = R^2 = CH_3$, $R^3 = H$, $R^4 = C_2H_5$
*(1e)*, $R^1 = R^2 = H$, $R^3 = C_6H_5$, $R^4 = CH_3$



*(2a)*, R = H
*(2b)*, R = $CH_3$
*(3)*

Table 1. Ylides and physical data of the 2-thietaneimines *(3)*.

| *(3)* | R¹ | R² | R³ | R⁴ | R | Yield [%] | M.p. [°C] | IR (KBr) $\tilde{\nu}$(C=N) |
|---|---|---|---|---|---|---|---|---|
| *(a)* | H | H | H | $C_2H_5$ | $CH_3$ | 60 | 71–72.5 | 1600 |
| *(b)* | H | $CH_3$ | H | $C_2H_5$ | $CH_3$ | 76 | – | 1590 |
| *(c)* | $CH_3$ | H | H | $C_2H_5$ | $CH_3$ |  | 76–78 | 1590 |
| *(d)* | $CH_3$ | $CH_3$ | H | $C_2H_5$ | $CH_3$ | 69 | 73–74 | 1595 |
| *(e)* | H | H | $C_6H_5$ | $CH_3$ | H | 50 | 90–92 | 1595 |

The alkenes *(1)* react with the heteroallenes *(2)* at 50 °C to give 1 : 1 adducts (Table 1). Intense $\tilde{\nu}_{C=N}$ bands in the IR spectrum and signals at $\delta = 180.7$ *(3a)* and 190.2 *(3d)* in the $^{13}$C-NMR spectrum are indicative of the 2-thietane imine structure of the products and hence of a [2+2]-cycloaddition of the vinyl ethers *(1)* with the C=S double bond of *(2)*. The X-ray structure analysis[2] provides final proof of the structure of *(3c)* (Fig. 1). In contrast to the parent compound[3] and other thietanes with sp²-hybridized C2[4], the four-membered ring in *(3c)* is completely planar. Also remarkable for a four-membered ring is the extremely long S1—C4 distance.

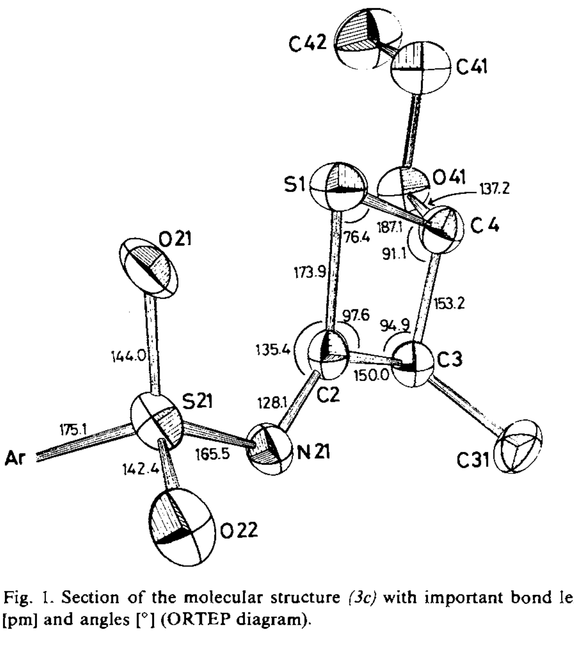
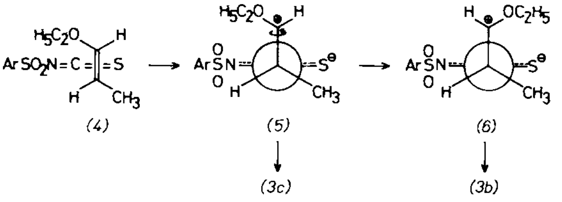


Fig. 1. Section of the molecular structure *(3c)* with important bond lengths [pm] and angles [°] (ORTEP diagram).

The cycloaddition of *(1)* with *(2)* can be readily monitored and kinetically evaluated by means of ¹H-NMR spectroscopy. The slight influence of solvent on the rate of the reaction of *(1d)* with *(2b)* $[k(CD_3CN)/k(CCl_4) = 24\,(37\,^{\circ}C)]$ could indicate a concerted cycloaddition. Inconsistent with this, however, is the finding that the cycloaddition with *(2b)* is only threefold faster on going from the *trans*-vinyl ether *(1c)* to the *cis*-compound *(1b)*; thus, the effect is of the same order of magnitude as in the reaction of *(1)* with tetracyanoethylene, the example *par excellence* for a cycloaddition with zwitterionic intermediate[5].

The configuration of the cycloadducts obtained from *(1b)* and *(1c)* can—on the basis of the X-ray crystallographically determined stereochemistry of *(3c)*—be determined *via* the vicinal ¹H-NMR coupling constants of the protons on the four-membered ring. As in the case of 2-azetidinones[6] $^2J_{cis}$ with a value of 6 Hz is greater than the value of $^2J_{trans}$ of 2.5 Hz. It thus follows that the *cis*-vinyl ether *(1b)*—otherwise especially susceptible to change of configuration—affords 98±2% of the *cis*-product *(3b)*; isomerization to the *trans*-product *(3c)* occurs only secondarily, thus affording evidence for a kinetically controlled reaction. Surprisingly, however, when the *trans*-vinyl ether *(1c)* is used as starting material (in $CCl_4$), the *cis*-cycloadduct *(3b)* is formed, depending upon the temperature, in 33 to 42% yield.



*(4)* *(5)* *(6)*
*(3c)* *(3b)*

The difference in the selectivity of the cycloaddition of the *cis*- and the *trans*-vinyl ethers *(1b)* and *(1c)* cannot be explained in terms of a concerted multicenter process or a dipolar intermediate in "U conformation"[7]. We therefore assume, in analogy to the $[_{\pi}2_s+_{\pi}2_a]$-process[1], an orthogonal approach of the reactants as in *(4)*, in which the steric interactions of *(2)* with the substituents on the β-C atom of *(1)* are slight. With the *trans*-vinyl ether *(1c)* as starting compound the zwitterion *(5)* is formed, in which, however, the orientation of ethoxy- and sulfonyl-groups to each other is sterically and electrostatically unfavorable. Hence, rotation about the original π-bond of *(1)* competes with ring closure to the *trans*-product *(3c)*; *(6)* is formed as intermediate and, hence, finally the *cis*-product *(3b)*. This model could be of general importance for dipolar cycloadditions of heteroallenes[8], whereas for two-step cycloadditions between cumulated π-electron systems the orientation corresponding to a $[_{\pi}2_s+_{\pi}2_s]$-process is theoretically required[9] and has been proven experimentally[5].

Received: August 14, 1980 [Z 778 IE]
German version: Angew. Chem. *93*, 600 (1981)

---

[1] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).

[2] $a = 1113.1(2)$, $b = 1756.3(3)$, $c = 873.5(1)$ pm, $\beta = 121.45(2)^{\circ}$, space group $P2_1/c$, $Z = 4$; 1771 symmetry independent structure amplitudes; $R = 0.055$. Measurements in the $\vartheta < 22^{\circ}$ region on a four-circle single-crystal diffractometer (Hilger & Watts) with monochromatorized $Mo_{K\alpha}$ radiation. Solution by direct methods (Multan).

[3] *D. O. Harris, H. W. Harrington, A. C. Luntz, W. D. Gwinn,* J. Chem. Phys. *44*, 3467 (1966).

[4] *C. D. Shirrell, D. E. Williams,* Acta Crystallogr. *B 29*, 2128 (1973); *V. Bertolasi, G. Gilli, ibid. 34*, 3403 (1978).

[5] *R. Huisgen,* Acc. Chem. Res. *10*, 117 (1977).

[6] *F. Effenberger, P. Fischer, G. Prossel, G. Kiefer,* Chem. Ber. *104*, 1987 (1971).

[7] *R. Huisgen, R. Schug, G. Steiner,* Angew. Chem. *86*, 48 (1974); Angew. Chem. Int. Ed. Engl. *13*, 81 (1974).

[8] Cf. *E. Schaumann, J. Ehlers,* Chem. Ber. *112*, 1000 (1979); *H. M. Frey, N. S. Isaacs,* J. Chem. Soc. *B 1970*, 830.

[9] *N. D. Epiotis, R. L. Yates, D. Carlberg, F. Bernardi,* J. Am. Chem. Soc. *98*, 453 (1976).

## BOOK REVIEWS

**Comprehensive Biochemistry.** By *M. Florkin* and *E. H. Stotz.* Section VI: A History of Biochemistry, Part V: The Unravelling of Biosynthetic Pathways. Vol. 33 A, xx, 433 pp., 45 figs.; Vol. 33 B, xix, 320 pp., 30 figs. Elsevier Scientific Publishing Company, Amsterdam 1979. Vol. 33 A, bound, Dfl. 140.00, Vol. 33 B, bound, Dfl. 108.00.

After more than 15 years this monumental work[*] which has itself become almost historical, is now alledgedly approaching its conclusion. As its crowning achievement, a wide-ranging history of biochemistry was intended to form a historical finale summarizing all the developments. But both it, and therefore the whole work, will remain incomplete—Professor *Florkin* died shortly after these two volumes had appeared, and whether the material collected for the last volume, containing the physiological and biological ideas on the origin of life, can be properly synthesized by a different hand without the experienced and systematizing driving force of the original author remains an open question. Indeed, even now one can discern an increasing uncertainty and disinclination for this overwhelming self-imposed task. Though far-reaching, the account given of how and by whom our present generally accepted knowledge on the biosynthetic steps and chains that lead to the building blocks of cells have come about is an aggregation of isolated facts rather than a synoptic whole. In contrast to the preceding volumes, which presented the origins of biochemical thinking stretching back to chemistry and biology, the development of the concept of integrating cellular reactions into general physical chemistry, and the investigation of the material world side by side with organic chemistry, and in which the authors' personal involvement with these developments and investigations and their personal knowledge of the research workers, circumstances, and controversies made the course of development clear, here we have a bare account, subdivided in accordance with the chapter titles, of the events up to around the mid-sixties. It is a textbook of intermediate metabolism, with emphasis on the development of methods and theorems, after an entrance into the cell interior had been achieved near the turn of the century by processes for the preparation of active cell extracts and, with glycolysis as an example, the foundations of the isolation of enzymes and of their chemistry and thermodynamics had been laid. The beginning consists of the energetics of biosyntheses and the activation of substrates by phosphates and thiols. Sugsequently there is a critical description of the possibility—discovered and considered to be effective on the basis of simplified ideas concerning the influence of the law of mass action on the cell situation—of obtaining peptides and polysaccharides, without sufficient reference to the serious fallacy and without a sufficiently clear treatment of the concepts of regulation, compartmentalization, and circumvention of energetically unfavorable equilibria by the synthesis of labile intermediates. Then follow alternative pathways of the glucose metabolism, photosynthesis with a hint of the (truly "revolutionary") concept of multienzyme complexes, and the formation of complex carbohydrates, fatty acids, isoprenoids, tetrapyrroles, heterocycles, and amino acids of various genealogies. All this is well-considered and excellently done, although the compilation is on the dull side and bloated with facts. The treatment is thoroughly competent, and often adopts a remote standpoint to distribute merit and priority, with a critical detachment from tales of favor and hatred. All this is very fitting and proper for the doyen of comparative biochemical research. And yet the whole has a certain lifelessness and mere dutifulness about it—after all, this should be an epic history of a heroic period of biochemistry, a period dominated by personalities. What does become impressively clear is that for a generation the investigation of biosynthetic metabolic pathways was one of the most successful domains of biochemical research, which was made possible by the methods acquired in connection with catabolic reactions and by the reductionistic concepts of chemists who had devoted themselves to this promising field. With their tendency to strive toward an over-all view, medics and biologists had given a picture of the details with a blurred outline, but had pointed out earlier the necessity for regulation and integration. Here again it is clear that only the interplay of all life sciences can give us a picture approximating to reality. The work is illustrated by portraits of many of the protagonists and is thus made more personal, perhaps not always justifiably.

These two volumes have not only increased the long Russian green series by two handsome and comprehensive parts, but have transformed it into an interesting and valuable work of history. Regretfully, we must now wait long for the conclusion, for who is there—precisely for what remains to be done—to replace *Florkin*, the co-founder of comparative biochemistry, a man who was as interested in the biological substrate as in the chemical product?

It is almost superfluous to mention that in both production and form the books do credit to the publishers (though this is reflected in their price) and that they may be recommended to any scientist interested in history both as a collection of material and as an aid in the formulation of his own opinions.

*L. Jaenicke* [NB 541 IE]

*0570-0833/81/0707-0615 $ 02.50/0*

## Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Molecular Electronic Structures. An Introduction.** By *C. J. Ballhausen* and *H. B. Gray*. Benjamin/Cummings Publishing, Reading 1980. viii, 133 pp., bound, $ 14.50.—ISBN 0-8053-0452-5

**The Heterocyclic Chemistry of Phosphorus. Systems Based on the Phosphorus-Carbon Bond.** By *L. D. Quin*. John Wiley & Sons, Chichester 1981. xiii, 434 pp. bound, £ 27.05.—ISBN 0-471-06461-0

**The Inorganic Chemistry of Biological Processes.** By *M. N. Hughes*. John Wiley & Sons, Chichester 1981. 2nd edit. ix, 338 pp., bound, £ 9.90.—ISBN 0-471-27815-7

**Annual Reports on Fermentation Processes.** Vol. 4. Edited by *G. T. Tsao*. Academic Press, New York 1980. xiv, 319 pp., bound, $ 28.50.—ISBN 0-12-040304-8

**Chromatographic Science Series. Vol. 14.** Introduction to Analytical Gas Chromatography. History, Principles, and Practice. By *J. A. Perry*. Marcel Dekker, Basel 1981. xviii, 426 pp., bound, SFr. 74.00.—ISBN 0-8247-1537-3

**Electron Spin Resonance.** Vol. 6. Senior Reporter: *P. B. Ayscough*. The Royal Society of Chemistry, London 1981. xiii, 359 pp., bound, £ 49.00.—ISBN 0-85186-810-0.—A volume in the series "Specialist Periodical Reports"

**Pergamon Series in Analytical Chemistry. Vol. 1.** An Introduction to Chemical Equilibrium and Kinetics. By *L. Meites*. Pergamon Press, New York 1981. xiii, 549 pp., bound, $ 19.95.—ISBN 0-08-023803-3

**Advances in Heterocyclic Chemistry.** Vol. 27. Edited by *A. R. Katritzky* and *A. J. Boulton*. Academic Press, New York 1980. ix, 331 pp., bound, — 49.50.—ISBN 0-12-020627-7

**Analytical Sciences Monographs No. 8.** The Sampling of Bulk Materials. By *R. Smith* and *G. V. James*. The Society of Chemistry, London 1981. viii, 191 pp., bound, £ 16.50.—ISBN 0-85186-810-X

**Transport Across Biological Membranes.** By *M. Höfer*. Pitman Books, London 1981. xiii, 184 pp., bound, £ 15.00.—ISBN 0-273-08480-1

**Structure and Bonding. Vol. 43. Bonding Problems.** Edited by *J. B. Goodenough, P. Hemmerich, J. A. Ibers, C. K. Jørgensen, J. B. Neilands, D. Reinen,* and *R. J. P. Williams*. Springer-Verlag, Berlin 1981. v, 220 pp., bound, DM 98.00.—ISBN 3-540-10407-0

**Molecular Interactions.** Vol. 2. Edited by *H. Ratajczak* and *W. J. Orville-Thomas*. John Wiley & Sons, Chichester 1981. xxiii, 627 pp., bound, £ 39.00.—ISBN 0-471-27681-2

**Advances in Organometallic Chemistry.** Vol. 19. Edited by *F. G. A. Stone* and *R. West*. Academic Press, New York 1981. ix, 318 pp., bound, $ 42.00.—ISBN 0-12-031119-4

**Advances in Chromatography.** Vol. 19. Edited by *J. C. Giddings, E. Grushka, J. Cazes,* and *P. R. Brown*. Marcel Dekker, Basel 1981. xv, 312 pp., bound, SFr. 98.00.—ISBN 0-8247-1246-3

**Terpenoids and Steroids.** Vol. 10. Senior Reporter: *J. R. Hanson*. The Royal Society of Chemistry, London 1981. xi, 284 pp., bound, £ 45.00.—ISBN 0-85186-336-1.—A volume in the series "Specialist Periodical Reports"

**Inorganic Reaction Mechanisms. Vol. 7.** Senior Reporter: *A. G. Sykes*. The Royal Society of Chemistry, London 1981. xxi, 442 pp., bound, £ 72.00.—ISBN 0-85186-315-9.—A volume in the series "Specialist Periodical Reports"

**Mathematics for Physical Chemistry.** By *R. G. Mortimer*. Macmillan Publishing, New York 1981. x, 405 pp., bound, $ 10.95.—ISBN 0-02-384000-5

**Advances in Quantum Chemistry. Vol. 12.** Edited by *P.-O. Löwdin*. Academic Press, New York 1980. x, 325 pp., bound, $ 48.00.—ISBN 0-12-034812-8

**The Alkaloids. Vol. 10.** Senior Reporter: *M. F. Grundon*. The Royal Society of Chemistry, London 1981. xii, 263 pp., bound, £ 49.00.—ISBN 0-85186-337-X.—A volume in the series "Specialist Periodical Reports"

---

**Editorial office:** Boschstrasse 12, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

**Editor:** *O. Smrekar*, **Translation Editors:** *I. G. Neil* and *A. Stimson*.

**Publishers:** Verlag Chemie GmbH. (Managing Director *Dr. Helmut Grünewald*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany, Telephone Weinheim (06201) 14031 (602-1), Telex 465516 vchwh d.

ANGEWANDTE CHEMIE

Volume 20 · Number 8
August 1981
Pages 617–702

International Edition in English

# The Philosophy of Science: Its Possibilities and Limits[**]

By Wolfgang Wieland[*]

Science in the modern world has long since become a factor in the production and reproduction of goods and a condition of life in this world. At the same time, however, it is more than this. Science has therefore become caught-up in an orientation crisis ever since scientists became aware that science can no longer be pursued merely for the sake of pure knowledge, the ideal from ancient times which had been held to be the proper guide for science in its quest for self-understanding. Is the philosopher of science capable of providing the researcher with an answer to the questions what it is he does, and whether or not he is deceiving himself in regard to science and his relationship to it? The philosophy of science has revealed areas which demonstrate that our science is never the smooth and elegant construction composed of observation, experiments, and mathematical and formal techniques which it has often been held to be. It is not the least of the modern philosophy of science's achievements to have demonstrated that science cannot teach man what he should do with it and its results.

Upon being requested to expound upon the possibilities and limits of the philosophy of science[1-3], a professional philosopher does well to begin by considering the fact that the modern philosophy of science has met with a growing interest which has long since ceased to be restricted to specialized institutes. Nowadays one speaks of the falsification principle, of scientific revolutions, of paradigms and their shifts, even outside professional circles; and the conviction is that an approach has been found which might enable scientists to adequately understand and represent what they do. Of course, this manner of speaking often remains at the level of mere slogans, but it must also be taken seriously. Whenever a certain discipline's basic concepts have finally crossed the threshold to becoming mere slogans, the reasons behind this symptom are worth investigating.

Just twenty-five years ago, the situation was very different. The philosophy of science was cultivated in Germany only in a few, seemingly almost esoteric circles. The general public no more took notice of it than did the specialized academic public. An information deficit existed, which was difficult to overcome. The German edition of the book, which is without doubt the most important in the modern philosophy of science, *Popper*'s "The Logic of Scientific Research"[6], published in 1934, had long since been out of print and there was no prospect of a new edition. There is, then, all the more reason to inquire how a general interest came to be directed towards those who had begun to make scientific methods and science itself the object of their inquiry and research.

In order to understand this, one must recall that, during the past two decades, the role that science has played, in the eyes of the general public and in its own eyes, has

---

[*] Prof. Dr. W. Wieland
Philosophisches Seminar, Abteilung I, der Universität
Werthmannplatz, D-7800 Freiburg (Germany)

[**] Originally given as a lecture at the presentation of the Goedecke-Preis der Universität Freiburg i. Br. on December 5, 1980.

*0570-0833/81/0808-0617 $ 02.50/0*

changed. It has ceased to play a role which, within the functional context of the modern world, might be compared with that of a mere ecological niche. The military use of knowledge gained in nuclear physics had, at an earlier date, precipitated a clear and general awareness that science is not as harmless with respect to human life on earth as had long been presumed. Nonetheless, this instance in particular seemed at first to indicate that this had basically been just a regrettable accident in the history of science and its application. The conviction at the time—a conviction which is often still expressed—was that what appeals to the scientist's sense of responsibility could prevent similar mishaps in the future[4]. Such appeals are usually well-meant and ill-founded. They proceed for the most part from a false estimation of the nature of scientific work and of the opportunities an individual scientist has to exercise his influence. Certainly, every person is responsible to a certain degree for the remote consequences and side-effects of his actions, even if he did not intend them. But there is hardly another area in which the possible consequences of human actions are less predictable and more difficult to calculate than in the realm of science and of cognitive conduct in general. Knowledge, especially as the result of scientific research, takes its own course once it has been expressed and published. The initiator has no more influence upon this course than anyone else.

Today, it is at least evident that an old dream has come to an end. For, the founders of modern science in the seventeenth century had hoped that their new science might one day be so highly developed that it would be able to provide man with a clear answer to the ancient question: what must be done in order to optimally further both the well-being of each individual and the common good? A radical change in attitude has occurred here. Modern science has perhaps transformed human life to a degree for which there is no comparable example in history, but this has taken place in a manner which no one could have predicted. Today, science can provide man with counsel concerning a multitude of special problems. Nevertheless, in the essential questions of life, it is far from able to provide guidance or instruction for our actions. On the contrary, we have suddenly realized that the reliable guides, which we need in order to deal with science and its consequences, are lacking.

It is a platitude to say that science today has become a political issue. Certainly, the individual scientist must still, just as always, cultivate the attitude of theoretical aloofness; he must have learned to disregard himself, his wishes, expectations, and hopes in his work. At the same time, however, science as a whole has been integrated into the system of human needs, their administration, and satisfaction. Science encounters great difficulties in attempting to maintain or to obtain anew a small portion of that latitude without which it never could have originated or developed. Today, all over the world, science is no longer supported by the state and society in just a few areas and is thus confronted with obligations. A rough estimate has indicated that there are more scientists living in the world today than during the whole development of science over the past few millenia. Science has long since paid the price for the possibilities of expansion which it has been granted. It is also confronted with the demand to relinquish an increasing portion of that freedom which was taken for granted by researchers before science became enmeshed in the system of human needs, as one of its functional elements. If the scientist nevertheless demands a certain degree of freedom, this is, in contrast to a popular prejudice, no defence of a position which is now untenable. It is not a struggle for special privileges. Whoever wishes to paralyze science and its work could accomplish this most effectively by allowing it to be perfectly administrated and completely regulated. If, then, in spite of everything, there is still a willingness to grant science a certain degree of freedom, then this is less an act of generosity than the consequence of an insight into an elementary necessity for scientific work.

This necessity is based on the fact that the results of scientific research can never be exactly predicted. Expressed in this manner, this is obviously common knowledge. If the results could be prognosticated in every detail, the researcher's painstaking labor would be superfluous. However, in reality scientific research is constantly subject to the law of trial and error. Every scientific activity worthy of the name, therefore, entails the risk of possible failure, and the only guarantee for science's freedom is the impossibility of banishing risk. Truth can never be a secure, incontrovertible possession for all time. A modern scientist's dilemma becomes apparent here. Unless he is extremely naive, he knows that he is integrated into the modern world's system of needs and their satisfaction; he also knows that he is hardly granted the opportunity to undertake research in his particular field just because of an interest in a fundamentally unavailable and functionless truth for its own sake. But, at the same time, he is well aware of another fact: if he abandoned his science as science, then he would allow himself to be integrated into this system of needs with no reservations whatsoever.

In the modern world, science has long since become a factor in the production and reproduction of goods and a condition of the possibility of living in this world. At the same time, however, it is more than this; the question is where to draw the line. In any case, science has become caught up in an orientation crisis ever since scientists became aware that science is no longer pursued solely for its own sake. In previous eras, scientists believed that this ideal could serve as a guide in their self-interpretation. But when the discrepancy between science's traditional self-interpretation and its factual existence under the conditions of the modern world became apparent, it is not surprising that there is a search for bearing-points.

Can the modern philosophy of science provide such bearing-points? The researcher who concerns himself with the philosophy of science's questions cannot expect any assistance in fulfilling the tasks which present themselves to him within his specific field. His concern with the philosophy of science, then, cannot be motivated by a purported optimization of his daily work, but by the aspiration to gain an insight into what he really does and whether or not he is deceiving himself with respect to science and his relationship to it. Thus, it is no mere coincidence that the philosophy of science, a discipline which has been in existence for a long time, succeeded in gaining the attention of a large public at that moment in which the entanglement of science in the modern world's system of needs and their satisfaction became apparent.

**What is the philosophy of science?** I shall characterize this discipline by tracing the **major stages of its development.**

**The first stage** in this development was marked by the already legendary **"Vienna Circle"**[5]. This circle included a number of prominent researchers who had come together in the period immediately after the First World War and collaborated with each other closely. Their intention was to bring philosophy into a close and lasting union with the exact sciences. Especially important among them were *Moritz Schlick* and, after his violent death, *Rudolf Carnap.* It was only after the political situation had forced the majority of its members to emigrate that the circle began to exercise a greater influence. At first, it attracted little attention; wherever it was taken notice of, it was not usually taken very seriously. In the final analysis this may have arisen since the members of this circle often exhibited a certain awkwardness whenever they departed from the philosophy of science proper and became involved in polemics with the representatives of other contemporary philosophical movements.

The Vienna Circle intended, above all, to apply the principle of empiricism. Their plan to base all valid knowledge upon experience had, of course, been proclaimed repeatedly throughout the history of human thought and knowledge: beginning with *Epicurus* and his school in ancient times up to *John Stuart Mill.* The Vienna Circle, however, dedicated itself to the task of also finally realizing the principle of empiricism in detail. Thus, the members of the Vienna Circle were not content with the application of mere fundamental theoretical considerations aimed at emphasizing the role of experience in the construction of human knowledge. Rather, they attempted to demonstrate something in detail that no one had ever been able to show before, *i.e.*, the way in which a certain particular piece of knowledge, for instance, the insight into the validity of a natural law, can be traced back step by step to experience and conclusively founded on this.

Whenever the members of this circle dealt with the knowledge found in the empirical sciences, they were less interested in the way in which such knowledge is discovered in a particular instance. Instead, they inquired how knowledge, which was already factually present, can be provided with a foundation, legitimized, and systematized. But here they encountered difficulties of a special nature. These are related to the indisputable fact that natural science, in the end, aims to find and found propositions with a high degree of universality. In this respect, singular real facts, as such, are less important than the universally valid laws to which these facts are subject. However, in natural science the pathway to these laws always proceeds from observations and experiments, and observations and experiments are always immediately directed to singular facts. Natural laws—one might consider, for instance, the laws of conservation in physics cannot, at least as such, be observed. The problem presented here is whether there is a method which makes it possible to base an insight into the existence of universally valid natural laws upon the observation of singular facts at all. This difficulty is involved in every empirical science: inasfar as it is founded upon experience, it refers to particular facts; inasfar as it is a science, it orients itself upon the ideal of supra-individual, universal validity. The difficulty that is known as the problem of "induction" presents itself here. Is there a methodologically incontestable way to proceed from singular facts to the deduction of propositions which can lay claim to strict universal validity, such as the natural laws?

The Vienna Circle attempted to find the pathway which leads from singular observable facts to universal natural laws, and then to survey and map it out, so to speak. That such a pathway must exist at all, is by no means obvious; nevertheless, the success of modern natural science seems to guarantee the existence of a corresponding pathway. The first step upon the way has far-reaching consequences but seems at first to be quite insignificant. The point of departure was not sense-data, not observations and experiments as such, but rather statements concerning them. At first, the Vienna Circle viewed the foundation of empirical science to be these statements and not the observations to which they refer. These are the famous "protocol sentences" which only contain what has actually been perceived. For instance, "The researcher $R$ observed at time $t$ using the measuring apparatus $A$ that the needle moved $x$ units." An extensive discussion dealt with the question: what kind of information it is that a protocol sentence must or may contain? Without proceeding any further on this point, we should emphasize the basic thought involved here: protocol sentences should be such that, if one wishes to attain those universally valid statements of laws which are the goal of natural sciences, the only additional requirement should be the techniques supplied by logic and mathematics.

This is without doubt a new approach that takes seriously the idea that the foundation of all scientific knowledge must be sought in experience. In spite of this, logic and mathematics are by no means interpreted as empirical sciences. Although formal logic occupied a central position in the work of the Vienna Circle, experience remained the essential basis for all knowledge of reality. It thus became necessary to redefine the boundaries between these domains; for, if one does not wish to accept anything as well-founded knowledge that is not based upon experience, and if, on the other hand, one must admit that logic and mathematics are not founded upon experience, then the only alternative is simply to deny these two disciplines the ability to provide knowledge. In this case, one need only stipulate the proper normative connotations for the concept of knowledge. In accordance with the view developed by the original Vienna Circle, logic and mathematics consequently cannot lead to knowledge in the normative sense of the word indicated above because they purportedly deal only with analytical statements, with tautologies. They were thus interpreted as mere organizational systems consisting of signs and symbols; their function was to regulate the operations and transformations within the realm of these symbolic systems. According to the presuppositions of such an interpretation, the high estimation of logic and mathematics within the Vienna Circle was not necessarily impaired by the fact that both of these disciplines were denied the capability to provide knowledge in the normative sense of the word.

Only those statements that can be empirically verified or falsified were recognized as meaningful sentences, again in a sense determined by a suitable normative definition of the term. This is the Vienna Circle's famous criterion of meaning. A statement's ability to be empirically verified and falsified is, according to this norm, not only a condition for recognizing the correctness or falsity of the statement itself, but also for its having any meaning at all. According to this criterion, the meaning of a sentence can only be understood by someone who knows what must be done in order to verify or falsify it through experience. If this criterion is not fulfilled, then the statement is meaningless.

We have thus established the following: according to the conception of a philosophy of science originally developed by the Vienna Circle, certain observational statements, the protocol sentences, are the foundation of all empirical knowledge. It is from them, and only from them, that more general statements up to and including natural laws may be deduced by means of mathematical and logical techniques. More general statements are to be verified as well as falsified on the basis of these statements.

**Karl R. Popper**, in his earlier mentioned book [6], marks the beginning of **the second stage** in the development of the modern philosophy of science. He called attention to the fact that those statements which scientific research is most interested in discovering, the statements of laws, can and must be repeatedly corroborated by experience, but that it is never possible for them to be verified in a strict sense by experience. It is trivial to say that natural laws, as such, are never the objects of direct observation; however, according to *Popper*'s thesis, they can also never be deduced by means of formal techniques if our only available basis is composed of observational statements. Of course, the problem of induction is then irresolvable if the universal validity which science aims at in general statements cannot be attained on the sole basis of observation and experimentation. *Popper* realized that no logical or mathematical procedure can exist which would allow one to proceed from singular observational statements and lead to the deduction of natural laws which would fulfill a claim to strict universal validity thereby passing the final test, so to speak, of enabling events that will occur in the future to be prognosticated.

The considerations upon which *Popper* bases his theory are surprisingly simple. In fact, he did nothing other than consider the formal difference between singular, empirical statements, on the one hand, and universal, law-like statements, on the other. A natural law is universal precisely because, according to its very idea, it is valid for an indefinite, unlimited number of single cases, as long as certain initial conditions are fulfilled. The unlimited number of singular cases can never be exhausted by observation. On the other hand a claim to universal validity, which is made by a general statement and holds for an indefinite number of cases, can be rejected even if only one counter-example is found. Similarly, textbooks of logic used to cite the statement "All swans are white", which can be refuted by the discovery of a single black swan. This illustrates the meaning of *Popper*'s famous falsification principle. This principle holds that statements concerning the validity of a natural law can never be verified in a strict sense, though they can indeed be falsified. Precisely in the case of general statements of law, the symmetry between verification and falsification, that was often presupposed earlier, does not exist.

Of course, one does not have to forego searching for natural laws on this account. *Popper*'s solution, or better, his dismissal, of the problem of induction by no means prevents researchers from orienting themselves upon natural laws and the statements which express them. *Popper*'s new turn affects only the formal status of laws. Under the presupposition of the falsification principle, the only function they can ever fulfill is that of a hypothesis. Regardless of how well and how often they have been corroborated anew, they still never cease to function as hypotheses, as far as their fine logical structure is concerned. They are suppositions which are never valid for more than the time being, so to speak, which are always subject to revocation; for, they are constantly accompanied by a risk that can never be completely overcome, the risk that they might someday be falsified after all by future experiments or observations. Hence, complete security can never be attained in this area. At the very most, within the restrictions of ordinary language, where there are no clear-cut boundaries, one may say that a hypothesis has been proved whenever it has been corroborated in a great number of instances. In truth, all general statements of law, as far as their logical status is concerned, are suppositions which, on principle, can never be absolved from the compulsion to succeed. In accordance with this status, they can never clearly represent the final goals of science's efforts for knowledge. Their character is like that of a tool, in that their construction demonstrates the researcher's ingenuity. To this extent, there can be no final decision about their "truth", though one can indeed say something about their ability to perform certain tasks. For, by means of them, observations and experiences should be able to be explained, but it is impossible to deduce the assumptions, which are presupposed in the explanation, from the state of affairs they are supposed to explain.

*Popper*'s conception does much more justice to the unique dynamics proper of scientific research than does the Vienna Circle's conception. His theory is based on the idea of an open-ended science, which in principle can never come to an end in its work, since the supply of hypotheses which can be tested is and remains inexhaustable. For, at any moment there are only a finite number of hypotheses which have been eliminated by falsification, that is, by counter-examples from experience. *Popper*'s philosophy of science also accounts for the risk of failure which is inseperable from any research enterprise. It is no coincidence that *Popper*'s main work is entitled "The Logic of Scientific Discovery"[6]. The theme here is not merely logical relationships such as those that may hold between propositions. The question is not just how statements that express universally valid knowledge can be founded and deduced, that is, how their validity can be legitimized; but also how such statements can be found at all and how they are to be dealt with. Here, we have a conception that is not content merely to organize and provide a foundation for knowledge that is already present. For, this conception is oriented to the same degree upon the scientific researcher's concrete activity. *Popper*'s conception also attempts to do it justice.

If statements of law are such that they cannot be verified, but, at most, falsified, then there is of course always the possibility that one and the same empirical finding may be interpreted and explained on the basis of very different hypotheses that compete with one another. Therefore, the question arises whether there are rules which enable us to make a reasonable choice between such competing hypotheses. For what reason does one explanatory model prevail over the other, when there are a number of models available that have not yet been falsified? There is no answer to such questions which could be satisfactorily explained by *Popper*'s conception.

**Thomas S. Kuhn,** however, has proposed an answer in his essay on "The Structure of Scientific Revolutions"[7], which appeared in 1962 and marks the **beginning of the third stage** in the modern philosophy of science. This work is a challenge not only to the contemporary philosophy of science, but also to the modern scientist's whole self-understanding, and it is no mere coincidence that, at first, it provoked some reactions which were primarily emotional. *Kuhn* proposes a conception according to which the competition among theories and the competition among hypotheses is ultimately decided by situations whose estimation and evaluation lie less within the domain of the logician and epistemologist, than in that of the historian and sociologist. The occurrences which define an epoch in the history of science are precisely the ones which no longer permit an explanation that is purely scientific in nature, at least according to this conception. In this case, the only answer that remains for the theorist of science is: "This can only be explained historically". *Popper* had defended the thesis that it is impossible to verify general statements of laws; he had not called into doubt the possibility of falsifying them. *Kuhn* now goes a decisive step further. He asserts that, in the history of science until now, there has not been a single instance in which a general hypothesis has been falsified in a manner corresponding to *Popper*'s model of falsification. By means of a number of case studies from the history of physics and astronomy, as well as from chemistry and biology, *Kuhn* tries to illustrate that theories and hypotheses of laws are not discarded as soon as a particular experience cannot be brought into agreement with them. *Kuhn* demonstrates that, according to all historical experience, theory prevails when a collision between theory and individual experience occurs. As a rule, the purported counter-example is reinterpreted so that it fits into the theory from which one proceeded in the first place.

On a smaller scale, we are familiar with similar experiences from the course of everyday experimental research: if a certain measurement or observation deviates too strongly from the general context, no researcher will immediately conclude that hei on the track of previously undiscovered laws. At first, he supposes instead that the particular result which deviates from the general context is due to a measuring error that must be recognized as such and corrected. The hypotheses from which one proceeds thus possess a unique capability to persevere. The stability which *Kuhn* ascribes to established theories is of a similar nature. It merely seems that such theories are tested by experience. In reality, experience is from the outset interpreted or, if necessary, reinterpreted so that it is commensurable to a theory which from the outset is assumed to be valid.

*Kuhn* himself has peculiar reservations in regard to the term "theory". He prefers to speak instead of "paradigms", which refer to theoretical patterns that determine whole directions of research and even whole scientific epochs. Geocentric and heliocentric astronomy, phlogiston and oxygen chemistry may illustrate what *Kuhn* means by paradigms. These paradigms are most closely comparable to the precedent-setting or model cases upon which a lawyer orients himself in his work. They establish the framework within which specialized research takes place. They specify within their domain what can be accepted as a possible object of experience. In view of them, a decision is often made about which questions can be meaningly posed within a science and which ones cannot. Whenever conflicts between paradigms and experience arise—according to *Kuhn*'s findings, which are not discovered by the philosophy but rather by the history of science—experience will, as a rule, be disregarded. In spite of this, a paradigm's power is not completely unlimited. After all, *Kuhn* must account for the fact that scientific theories one day come to be replaced by other theories. There are phases in the development of a science during which experience is no longer merely adjusted to the paradigm dominant at the time; in such phases, paradigms compete with one another. These are the phases *Kuhn* calls scientific revolutions. But even here, he is not prepared to grant rational criteria a decisive influence; the explanatory ability of a new paradigm is generally of a different sort, but not always greater than that of the paradigm it replaces. The competition among theories, up until now, has never been resolved in a manner which would fulfill the requirements of rational foundation. Logic and experience may play a role in the shifts from an old theory to a new one, but they do not suffice by themselves to explain the dynamics of a theory. The only fact that can be registered is that one theory has prevailed over other competing theories. According to *Kuhn*'s conception, it is a mere myth that successful theories distinguish themselves over the theories they replace by a greater capability to explain and interpret phenomena. A theory's performance can only be spoken of in a very different sense; its performance can be measured only historically by the number of adherents it has been able to find who are committed to it. *Max Planck* coined the phrase that scientific theories do not cease to be discussed because they have been refuted, but because their proponents finally die out. Basically, what *Kuhn* does is merely to provide a theoretical conception that is a skillful variation of this statement.

*Kuhn*'s conception not only renounces the possibility of verifying the statements of laws, as *Popper*'s conception does, but also of falsifying them. For *Kuhn*, the researcher's painstaking labor based on observation and experimentation is by no means absurd; but he believes he has demonstrated that observation and experimentation alone can neither prove nor disprove a certain theory. Nor would *Kuhn* deny that there is a connection between experience, on the one hand, and theory on the other; however, according to his conception, this connection is much looser than the practicing researcher or the philosopher of science has previously supposed.

The way in which *Kuhn* interprets scientific research shows very little similarity to the ideals which were traditionally attached to it. At times, it may even seem as if he wished to deprive the researcher of his self-confidence in the rationality of his actions. But at least his conception is able to account for the conditions in which science is actually pursued. If the faith in an absolutely certain "method" for science, which would be capable of providing indisputable decisions, is an illusion, then the human side of the scientific enterprise appears in a completely different light. It becomes understandable that, within science, certain schools emerge which orient themselves upon particular methods or models of explanation and that scientists try to gain recognition for them. It is understandable that the researcher strives for recognition and that this endeavour is by no means merely the result of personal vanities which have no bearing upon science. It is understandable that there are conflicts concerning priorities in science—in short, it is understandable that science is regularly pursued by groups of people and that the internal structure of these groups is not fundamentally different from that of other groups. That scientific labor is tied to and oriented upon a group, remains ultimately a kind of organizational principle which is capable of regulating this work. In the end, it is symptomatic that *Kuhn* avoids the term "truth" except in quoting others.

This third stage in the modern philosophy of science might represent a temporary conclusion to its history, but, as is proper for a genuine trilogy, a satire follows. Its author is **Paul K. Feyerabend,** the bold warrior "Against Method"[8], which is the title of one of his works. In reading his recent publications, one occassionally has the impression that *Palmström*[*] has landed among the philosophers of science. Fortunately, *Feyerabend,* who has long since proven himself as a philosopher and as a historian of science, can allow himself the luxury of an ironically aloof attitude. Besides, he is only drawing the final conclusion in the development traced here when he rejects *Kuhn*'s group principle as the organisational principle's last gasp, so to speak, and propagates total methodological anarchy, in which each approach initially has equal justification. This first principle in his theory rapidly gained fame; it is: "Anything goes." Here modern science appears as one of many forms of mythical thought if there is no sure method of giving scientific statements a foundation and allowing them to distinguish themselves from other statements. According to this conception, it is categorically impossible to clearly delineate the realm of science from other realms of human activity. Whoever performs scientific work in the usual sense can claim no superiority over those who try to cure illnesses by faith-healing or to influence the weather by rain dances, at least in *Feyerabend*'s estimation. According to this conception, science has at its disposal no rules or results that a free person is obliged to recognize.

These very brief comments suffice to indicate what high demands are placed upon the reader's sense of irony here. Regardless of how one might judge *Feyerabend*'s attempt, it can be instructive for everyone who comes to deal with it. There is no doubt that the image of science sketched here sometimes exhibits the traits of a caricature, but a good caricature does not consist merely in the distortion of its object; instead, it renders certain characteristics extremely prominent and distinct compared to others. *Feyerabend* basically draws the final conclusion in a development whose turning point must be sought at that point where the orientation upon the concept of truth is abandoned as a guide for comprehending the meaning and task of the scientific enterprise. *Feyerabend*'s conception is especially suited to illustrate the extent to which modern science has already become a functional part of a comprehensive system for mastering and transforming reality. Contemporary science is indeed confronted with obligations both with regard to truth and to its role in helping master our existence, without being able to resolve the tension between these two obligations or merely establish an equilibrium between them.

It would be a misunderstanding to suppose that this sketch intends to reduce the modern philosophy of science to absurdity regarding its development. On the contrary, much can be learned from this development because it is so logically consistent, and with the onesidedness characteristic of self-consistent thought, it carries things to an extreme. Certain elements of science are screened out of this development; extrapolations are made possible on this basis, and these allow traits of science to be illustrated which might otherwise easily be overseen. For this reason, other important developments which are closely related to the modern philosophy of science have not been dealt with. These include hermeneutics, which concerns itself with problems that are especially relevant to the human sciences; as well as evolutionary epistemology, a conception from which much can be expected as soon as it has gone through the teething stage in which it now finds itself. A further conception, the so-called Critical Theory, has not been dealt with because up until now it has been unable to attain the minimal degree of conceptual clarity and distinctness necessary for a productive occupation with any philosophical proposal. The ambiguity with which critical theory still amalgamates political wishes and epistemological claims makes it impossible to accept its representatives as partners in a philosophical discussion oriented towards the ideal of conceptual clarity.

At the outset, we spoke of the orientation crisis which afflicts current science. This crisis reveals itself, among other things, in the fact that faith in science, a sceptical attitude towards science, and even a certain superstition towards science all find proponents; and that these proponents include many who live and work within the charmed circle of science. However, the philosophy of science, which encounters such a great interest today, cannot resolve this orientation crisis, although it can contribute something else. It can develop concepts which are necessary to represent the crisis and it can, above all, illustrate

---

[*] A poem from "Galgenlieder" by Christian Morgenstern.

the great extent to which science as it is actually undertaken in our world conflicts with the projections and ideals with which it is often confused.

**The lessons which can be learned from the development of the philosophy of science** do not make it possible to define precisely and finally what science is. But it can provide an indication what science certainly is not. Hence, first of all, science's work does not consist merely in the accumulation of knowledge about facts or laws. It is simply not the case that science's business consists in reaping new harvests which, so to speak, can be stored up in its warehouses for all time. In the domain of science, one must always reckon with the possibility that a result which seemed to be completely certain may be reinterpreted and relativized during the further course of research, and perhaps even declared invalid. The basic, epoch-making discoveries, are those which compel us ever anew to reinterpret that which was previously known and only apparently secure for all times. The accumulation model is obviously not suited to the true development of science. The science we possess is an open-ended science which permits no predictions regarding its further course.

Secondly, the philosophy of science, in contrast to the original intentions it attached to its work, has been forced to place a stronger emphasis upon the active role played by the thought and conduct of the researcher. Whatever scientific research might achieve does not just consist in a simple copy of reality. Whatever confronts us as the result of research is no mere image of reality; it is the result of our intervention into reality and our processing of it. The philosophy of science has shown that the researcher not only intervenes in reality with his experiments and measuring apparatus, but also in a much more subtle but effective manner with his entire theoretical and mental arsenal, that is, with his concepts and questions, with his definitions and hypotheses. Obviously, no discovery which deserves the name is exclusively the object of convention. It would nonetheless be impossible to make such discoveries if one did not settle upon conventions at a variety of levels. The philosophy of science, in any case, has rightfully and persistently put its finger on those points which illustrate that science, even in the ideal case, is never the smooth and elegant construction composed of observation, experimentation, and mathematical and formal techniques which it is often held to be. Here, one cannot even take recourse to the well-known argument that everyone who utilizes the technical applications of modern science has implicitly, by means of his action, recognized the underlying theory's correctness; at most, the mere possibility that it may be correct has been recognized. If an effect can be explained by a certain theory, the possibility is still not excluded that it might perhaps be explained just as well by another, completely different theory. This is due to a simple logical fact: theories are, by their very nature, at best sufficient, but never necessary conditions for the effects and applications which are subsumed under them. As far as the technical applications of science are concerned, the factual possibility of things always has priority over the theories that are offered as their explanation.

Thirdly, the philosophy of science has also had to account for the fact that the scientist's actions always remain enmeshed in the organization of the human community in general. The researcher is also a part of modern society's system of needs; nonetheless, he can exercise his activities meaningfully and with good prospects of success only if he is at least practically suspended from this system. For this reason, the latitude which a scientist claims for his work is not a superaddition or special privilege but rather an elementary necessity for science's very existence.

The question still remains what we wish to do with science and its results and what we should do with them. Furthermore the question of whether or not we can determine which of those knowable objects science deals with are at the same time worth knowing about, also remains. But these are questions of practical nature and cannot be answered within the realm of science itself. A great portion of science's success in its work is due to the fact that it ignores such questions before it has begun its work. In any case, it is not the least of the modern philosophy of science's achievements to have demonstrated that science cannot instruct man what he should do with it and its results.

Received: February 12, 1981 [A 377 IE]
German version: Angew. Chem. *93*, 627 (1981)
Translated by *Thomas Nenon*, Freiburg

---

[1] *E. Ströker:* Einführung in die Wissenschaftstheorie, 2nd ed., Wissenschaftliche Buchgesellschaft, Darmstadt 1977; cf. also: Denkwege der Chemie. Elemente ihrer Wissenschaftstheorie, Alber-Verlag, Freiburg 1967.

[2] *F. von Kutschera:* Wissenschaftstheorie I und II. Grundzüge der allgemeinen Methodologie der empirischen Wissenschaften, W. Fink-Verlag, München 1972.

[3] *W. Stegmüller:* Probleme und Resultate der Wissenschaftstheorie und Analytischen Philosophie, Vol. I, II, IV, Springer-Verlag, Berlin 1969.

[4] Cf. *H. Mohr*, Angew. Chem. *90*, 651 (1978); Angew. Chem. Int. Ed. Engl. *17*, 670 (1978).

[5] *V. Kraft:* The Vienna Circle, the Origin of Neo-Positivism, Greenwood Press, London 1953.

[6] *K. R. Popper:* Logic of Scientific Discovery, Harper and Row, New York 1974.

[7] *T. S. Kuhn:* The Structure of Scientific Revolutions, University of Chicago Press, Chicago, Ill. 1962.

[8] *P. Feyerabend:* Against Method. Outline of an Anarchistic Theory of Knowledge, New Left Books, London 1975.

# Mass Spectrometry of Negative Ions[**]

**New analytical methods (22)**

By Herbert Budzikiewicz[*]

"It appears that negative ion mass spectra measured with a commercial instrument and the electron energies used (20—70 eV) are not suitable either for molecular weight or for structure determination—". This was the conclusion of a paper appearing in 1965 which expressed the then almost universal opinion on the importance of negative ion mass spectrometry in the structure analysis of organic compounds[8]. The fact that quinones and aromatic nitro compounds were exceptions to this rule was rather taken as substantiation of this opinion. The potential value of the work originating from the laboratories of *Manfred von Ardenne* was first realized with the development of chemical ionization. This technique gave a firm foundation to negative ion spectrometry in the area where it is complementary to that of positive ions.

## 1. Introduction[***]

Whereas positive ion mass spectrometry is an integral part of modern instrumental analysis, the importance of its negative ion counterpart is still considered with some uncertainty. Statements like "unimportant in structure analysis of organic molecules", "important complementary method to positive ion mass spectrometry", or "much more sensitive than the positive ions", indicate that, since only a few research groups are investigating this area systematically, the subject is still not widely understood or appreciated. However, this did influence the instrument manufacturers. Whereas in the sixties several mass spectrometers had dual polarity facilities, these were abandoned and have only recently been reintroduced.

In this paper we shall discuss the principal differences between positive and negative ion mass spectrometry as well as the importance of the latter in structure elucidation and the analysis of mixtures. Since our knowledge in certain areas is incomplete, in particular as regards chemical ionization, general conclusions are not warranted. We shall not consider the details of instrumentation here[****], nor purely physical aspects, *e.g.* the determination of electron affinities[2], electron capture cross sections[3], or appearance potentials[4].

## 2. Theoretical Foundations

### 2.1. Definitions and Units

Like in many areas of physics, there is a problem of sign here too. According to modern definition, ionization is a transition in which the number of negative charges decreases or that of the positive charges increases. This means, that not the formation of the molecular anion [eq. (a)],

$$\mathrm{AB} + \mathrm{e} \rightarrow \mathrm{AB}^{\ominus} \qquad \text{(a)}$$

but rather the reverse process [eq. (b)]

$$\mathrm{AB}^{\ominus} \rightarrow \mathrm{AB} + \mathrm{e} \qquad \text{(b)}$$

is considered as ionization.

All energy expressions are based on this definition.

The electron affinity *(EA)* of AB is defined as the minimum energy required for an electron to be released from the system $\mathrm{AB}^{\ominus}$. Consequently, this is also the first ionization potential of $\mathrm{AB}^{\ominus}$, *i.e.* $I(\mathrm{AB}^{\ominus})$[*]. From this it is possible to define the appearance potentials of fragment ions, $A(\mathrm{A}^{\ominus})$, for dissociative electron capture according to eq. (c), and for ion pair formation according to eq. (d), where $D(\mathrm{AB})$ is the dissociation energy and $E$ the excitation energy (vibration and rotation energy) of $\mathrm{A}^{\ominus}$, which, for example, are determined from the activation energy for decomposition (see Section 2.2)

$$\mathrm{A}^{\ominus} \rightarrow \mathrm{AB} - \mathrm{B} + \mathrm{e} : A(\mathrm{A}^{\ominus}) = EA(\mathrm{A}) - D(\mathrm{AB}) - E \qquad \text{(c)}$$

$$\mathrm{A}^{\ominus} \rightarrow \mathrm{AB} - \mathrm{B}^{\oplus} : A(\mathrm{A}^{\ominus}) = EA(\mathrm{A}) - I(\mathrm{B}) - D(\mathrm{AB}) - E \qquad \text{(d)}$$

Unfortunately, even in the recent literature, there is no agreement on sign usage. It should be made clear, however, that in bond homolysis, energy must be consumed, like in the process $\mathrm{B} \rightarrow \mathrm{B}^{\oplus}$. In the formation of stable negative ions ($\mathrm{A}^{\ominus}$) from A, energy must be released[**].

### 2.2. Ionization Processes

#### 2.2.1. Resonance Capture ($\mathrm{AB} \rightarrow \mathrm{AB}^{\ominus}$)

Resonance capture is a prerequisite for the formation of molecular anions ($\mathrm{AB}^{\ominus}$) capable of detection by mass spectrometry. This is possible only if $EA(\mathrm{AB}) > 0$. Thereby an electron is accepted by a low lying unoccupied orbital. The electron capture cross-section, *i.e.* the probability of ioni-

---

[*] Prof. Dr. H. Budzikiewicz
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

[**] Mass Spectrometry of Negative Ions, Part 3.—Part 2: [36].

[***] Abbreviations: EI = electron impact ionization, CI = chemical ionization, NCI = negative chemical ionization, NI = negative ionization, $EA$ = electron affinity, $I$ = ionization potential, $A$ = appearance potential.

[****] See [1] and the construction details of modern apparatus. The problem of high negative entry voltage of secondary electron multipliers, which prevent negative ions of too low acceleration voltage from reaching the first dynode has meanwhile been solved by the introduction of a conversion dynode. The latter works at a potential of +2—4 kV, transforming $M^{\ominus}$ into $M^{\oplus} + 2\mathrm{e}$.

[*] Definitions commonly used in mass spectrometry are to be found in [5].

[**] Conversion factors for energy units: 1 eV = 23.0 kcal = 96.14 kJ.

zation, can vary over a wide range for organic compounds (*e.g.* by a factor of $10^6$ between hexane and $CCl_4$)[*]. The phenomenon of resonance capture is also used with electron capture detectors in gas chromatography.

During resonance capture $AB^\ominus$ is formed as an excited species with an excitation energy of at least $EA$(AB). Provided that this species ($AB^\ominus$) is not deactivated by radiative emission of its excess energy[7], or through collision at higher pressures, then it can lose the electron again (autoionization). In small molecules this process occurs very rapidly ($\approx 10^{-13}$ s). In larger molecules, where the excess energy can be distributed over many internal degrees of freedom, the process is slow enough ($> 10^{-6}$ s) for $AB^\ominus$ to be observed in the mass spectrometer. If the excitation energy is sufficient according to eq. (c) (see Fig. 1a), then fragments can be formed (cf. Section 2.2.2). In general, resonance capture is observed at electron energies of 0 to a maximum of 2 eV (*e.g.* for $SF_6^\ominus$, the ion yield curve has its maximum at 0 eV and falls to zero again at 0.3 eV).

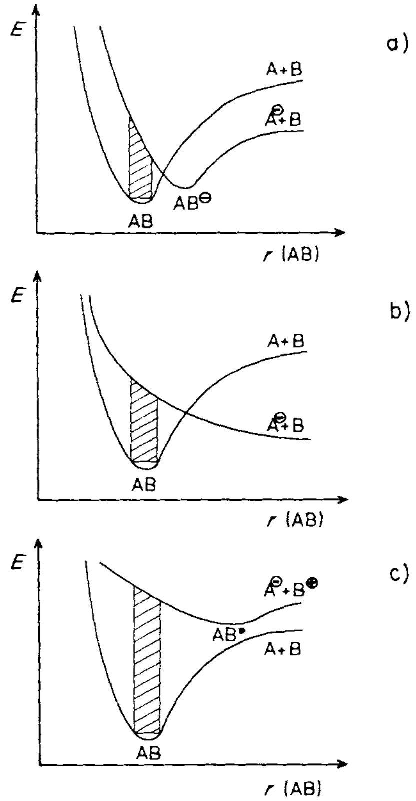


Fig. 1. Typical potential curves for the formation of negative ions from diatomic molecules. a) Resonance capture, b) dissociative resonance capture, c) ion-pair formation.

2.2.2. Dissociative Resonance Capture ($AB \rightarrow A^\ominus + B$)

During electron capture, $AB^\ominus$ attains either a repulsive (Fig. 1b) or an attractive state, in which the dissociation threshold is lower than that of AB by at least the amount of $EA$(B): $AB^\ominus$ decomposes within the subsequent vibrational period. This process is observed at energies between 2 and 15 eV. The ion yield curve for $A^\ominus$ is normally structured (Fig. 2); the maxima correspond to different excited states (see Section 3.4.1).

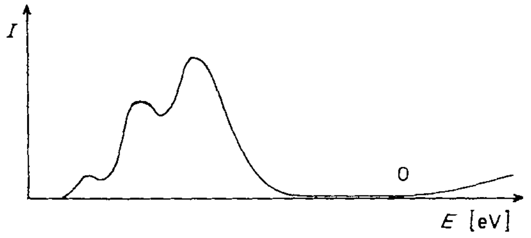


Fig. 2. Typical ion-yield curve for negative fragment ions; $I$ = ion current.

2.2.3. Ion Pair Formation ($AB \rightarrow A^\ominus + B^\oplus$)

In the majority of cases, no intermediate of the type $AB^\ominus$, but rather an excited molecule AB* is formed which then dissociates heterolytically (Fig. 1c). Ion pair formation begins at energies above *ca.* 15 eV (the point marked by 0 on the ion yield curve in Fig. 2).

## 3. Electron Impact Ionization

### 3.1. General

It follows from the discussion in Section 2.2 that molecular ions ($M^\ominus$) are formed only at the lowest electron energies. Under normal electron impact conditions (70 eV), therefore, one would expect only fragment ions to be formed under NI-conditions. Investigation of a series of typical organic compounds[8] appeared to confirm this (Fig. 3)[*], though there is some evidence, in particular in the work of *Bowie*[9], that intensive $M^\ominus$ ions can also be observed at 70 eV. In the case of nitrobenzene[10], it was even found that the relative intensity of $M^\ominus$ with respect to $NO_2^\ominus$ increased by a factor of 150 when increasing the electron energy from a nominal value of 3 to 20 eV. This apparent contradiction can be explained[11-13]: The generation of positive ions is accompanied by thermal secondary elec-

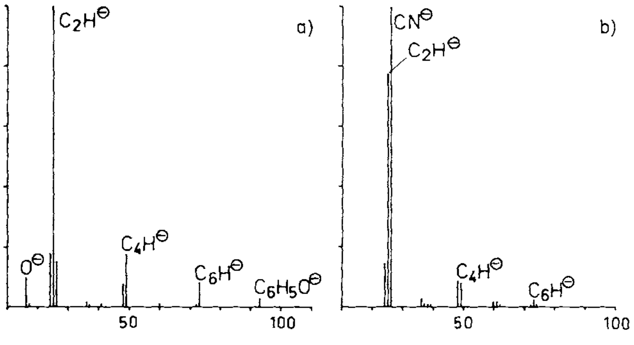


Fig. 3. NI spectra of a) anisole, b) aniline (CH-4, 70 eV).

---

[*] A table of the most important classes of compounds is found in ref. [6].

[*] It has been suggested that the mass spectra of negative ions (negative spectra) be represented in icicle form [8] (mass scale on top, ion intensities toward the bottom). This has been followed up by only a few authors and so will not be considered here.

trons ($e_s$), which then allow the formation of $M^{\ominus}$ ions [eq. (e)]. This makes it understandable that the formation of $M^{\ominus}$ commences at the ionization potential of $C_6H_5NO_2$ and that the ion yield curve of $M^{\ominus}$ follows that of $M^{\oplus}$. Further proof is found in the observation that in the addition of $SF_6$, which has a high electron capture cross section for thermal electrons, the formation of $M^{\ominus}$ at higher electron energies is suppressed. Thus we are dealing with a secondary process, as confirmed by the observed pressure dependence (see the following Section).

$$M + e_p \rightarrow M^{\oplus} + e_s + e'_p \qquad \text{(e1)}$$
$$M + e_s \rightarrow M^{\ominus} \qquad \text{(e2)}$$

### 3.2. Dependence of Spectra on Ionization Energy, Temperature, and Pressure

The typical energy ranges for the various ionization processes have been mentioned already in Section 2.2, those for the formation of energy deficient secondary electrons according to eq. (e) in Section 3.1. The special importance of the ionization energies for dissociative resonance capture will be treated in Section 3.4.1.

The excitation energy $E$ of an ion depends on the energy of the ionizing electron as well as the internal energy of the molecule to be ionized; it follows from the discussion in Section 2 that the extent of fragment formation will increase with the inlet or source temperature, as is indeed observed[14].

The pressure dependence of the various ion-source processes is more complicated. Here, only the rate of formation of the ions will be considered and not their further reactions. At higher pressures it is possible that, *e.g.* through ion-molecule reactions, the ion current becomes independent of the sample pressure. Occasionally, one uses this situation to achieve more reproducible spectra[14].

The simplest case is that of ion pair formation, since (see Section 2.2.2) the electrons only supply energy for the excitation of the molecule (AB*), which is the rate determining step. The rate of formation, and hence the intensity of the ion current of $A^{\ominus}$ is linearly dependent on the sample pressure and the density of emitted primary electrons $Ne_p$ [eq. (f)].

$$AB + e_p \rightarrow AB^* + e'_p; \quad AB^* \rightarrow A^{\ominus} + B^{\oplus} \qquad \text{(f1)}$$
$$\frac{d[A^{\ominus}]}{dt} = k[AB]\,Ne_p \qquad \text{(f2)}$$

By analogy, eq. (f2) applies to the dissociative capture at low pressures and electron energies, when the primary electrons are responsible for the formation of $AB^{\ominus}$. At higher pressures and electron energies, capture of secondary electrons takes place according to eq. (e2). The number of these electrons is also a function of the pressure of AB according to eq. (g1)[*]. Thus, the final equation shows a second order pressure dependence [eq. (g2)]. Similar considerations apply to slowed down primary electrons, $e'_p$.

$$Ne_s = k' \cdot Ne_p \cdot [AB] \qquad \text{(g1)}$$
$$\frac{d[A^{\ominus}]}{dt} = k'' \cdot Ne_s \cdot [AB] = k \cdot Ne_p \cdot [AB]^2 \qquad \text{(g2)}$$

The resonance capture of $e_p$ to give $AB^{\ominus}$ is described analogously by eq. (f2) that of $e_s$ by eq. (g2). If, however, the life of the molecular anions is sufficiently long only when they can be deactivated through two-body collisions we have again second-order pressure dependence, according to eq. (h1). If at higher primary electron energies, secondary electrons are captured, then it follows from eq. (g1) that the pressure dependence rises to the third power [eq. (h2)].

$$2\,AB + e_p \rightarrow AB^{\ominus} + AB^*: \frac{d[AB^{\ominus}]}{dt} = k \cdot Ne_p \cdot [AB]^2 \qquad \text{(h1)}$$
$$\frac{d[AB^{\ominus}]}{dt} = k \cdot Ne_p \cdot [AB]^3 \qquad \text{(h2)}$$

If the pressure is high enough that the deactivation step is no longer rate determining, then the exponent decreases by one (pseudo-$(n-1)^{th}$ order). Of course, fractional orders can be found at intermediate pressures; this is also borne out by measurement[15].

In this section we have shown in a comprehensive manner the critical dependence of the spectra on instrumental parameters as compared to the spectroscopy of positive ions. In situations where it is impossible to find reaction conditions where only single processes can be selected (see Section 3.4), chances are that the spectra obtained are barely reproducible.

### 3.3. Stability of Molecular Anions[16]

The question of structural requirements for the existence of long-lived molecular anions has inspired a whole range of studies and hypotheses. What is surely essential is the presence of a low-lying unoccupied molecular orbital (this explains why, for example, alkanes cannot form stable $M^{\ominus}$ ions). An attempt at correlating the probability of the occurrence of long-lived molecular anions with the dipole moments measured in the gas phase[17] met without success in this case: Acetone ($\mu = 2.84\,D$) afforded no $M^{\ominus}$ ion[8] whereas *p*-benzoquinone ($\mu = 0\,D$) furnished an intense $M^{\ominus}$ ion[18]. In particular through the work of *Bowie et al.*, supported by the theoretical studies of *Christophorou et al.*, it became clear that intense molecular anions can be expected when, after resonance capture the system can stabilize itself through resonance *via* a π-system. Some typical examples are quinones such as *(1)*[18-21], simple diketones such as *(3)*[18] and their monoximes[22], as well as compounds such as maleic anhydride and its derivatives[23], aromatic nitro compounds such as *(5)*[24,25] and related systems like aromatic azoxy compounds[26], aryl-$SO_2$—X compounds[27], and highly conjugated nitriles[28,29].

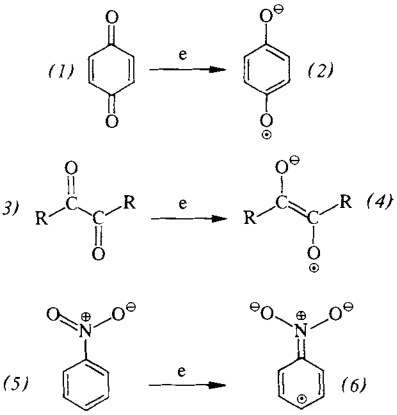
Substituent effects have been investigated, in particular, in the case of aromatic nitro compounds. It would appear that it is inductive effects (apart from possible *ortho*-effects

---

[*] Eq. (g1) holds for the stationary state in which the capture of $e_s$ in the reaction $AB + e_s \rightarrow AB^{\ominus}$ [Eq. (e2)] is independent of [AB], *i.e.* the capture step is not rate determining ($e_s$ is formed according to Eq. (e1)).

$$\frac{dNe_s}{dt} = k_p \cdot [AB] \cdot Ne_p - k_s \cdot Ne_s = 0$$

in the fragmentation[30]) rather than mesomerism which play an important role[31,32]. Resonance stabilization involving an aromatic system is, however, essential in many cases: aliphatic nitro compounds[33], as well as ketones[8], show no $M^{\ominus}$ ions, whereas $C_6H_5NO_2$ and benzophenone do[34].

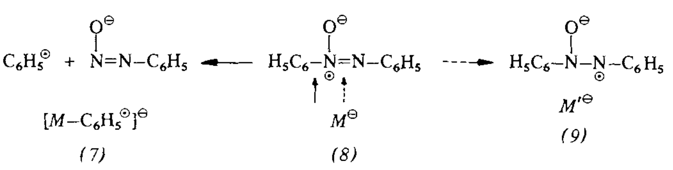


Phosphoric acid derivatives[35] and thiocarboxylic acid esters[36] can be counted in this group. So far, it has not been possible to clarify just how important a role the unoccupied d-orbitals play in this case. Owing to lack of complete data the discussion concerning sulfur compounds[18,37-39] as well as compounds containing other heteroatoms such as Si[40], is not yet closed. It is possible to obtain stable anions from unsubstituted arenes[41] and fluorocarbons[42]. One particularly interesting group is that of the metal complexes, in which the electron can be bound by the metal cation by changing the valence (see Section 3.4.3). It can be concluded that—apart from quinone systems and metal complexes—only nitrobenzene derivatives are expected with certainty to give intense $M^{\ominus}$ ions. Thus, nitrobenzoic acid derivatives are recommended for the analysis of alcohols[43] and of amino acid esters[44]. The importance of NI-mass spectrometry in the analysis of explosives should also be mentioned[45].

### 3.4. Fragment Formation

#### 3.4.1. General Considerations

Over the years there has been no lack of attempts deriving general rules from the diverse observations made on the fragmentation of negative ions. One attempt[46], applying the concept of localized charge also to molecular anions, led to rather general rules (*e.g.* "slow electrons prefer to position themselves at the positive end of a dipole"; "if, due to excess energy, a π bond adjacent to a negative center is ruptured with electron pairing [*(8)*→*(9)*], then $M^{\ominus}$ is stabilized. If, however, rupture of a σ-bond occurs [*(8)*→*(7)*], then fragmentation rapidly follows", *etc.*).



$$C_6H_5^{\bullet} + \overset{O^{\ominus}}{\overset{|}{N}}{=}N{-}C_6H_5 \longleftarrow H_5C_6{-}\overset{O^{\ominus}}{\overset{|}{\underset{\oplus}{N}}}{=}N{-}C_6H_5 \dashrightarrow H_5C_6{-}\overset{O^{\ominus}}{\overset{|}{N}}{-}\underset{\oplus}{N}{-}C_6H_5$$

$[M-C_6H_5^{\bullet}]^{\ominus}$ *(7)* $M^{\ominus}$ *(8)* $M'^{\ominus}$ *(9)*

Two observations were the prerequisite for a more detailed discussion: a) some exothermic processes $AB \rightarrow A^{\ominus} + B$ require an activation energy[47,48]; b) orbital symmetry arguments play an important role[48,49]. This means, for example, that formation of $Cl^{\ominus}$ from $C_6H_5Cl^{\ominus}$ in the lowest excited state does not simply correspond to the reverse of the approach of $Cl^{\ominus}$ to $C_6H_5^{\bullet}$, because the lowest unoccupied orbital of $C_6H_5Cl$ is an aromatic π* orbital, whereas in $C_6H_5^{\bullet}$ the unpaired electron occupies a σ orbital. Hence, dissociation must take place either from a state in which the added electron occupies a non-bonding orbital of the Cl (this requires higher excitation)[*], or after reorientation (*e.g.* by two body collision)[48]. Thus, different mass spectra are obtained at different ionizing energies (cf. the structured ion yield curve in Section 2.2.2). For example, at 1 eV $CH_3SCH_3$ gives only $CH_3S^{\ominus}$ ions, at 4.5 eV both $S^{\ominus}$ and $CH_3^{\ominus}$ but no $CH_3S^{\ominus}$ ions, at 7.5 eV all three types of ion *etc.*[49]. Further examples may be found in a review article[50]. These results led *Khvostenko et al.*[51] to formulate some rules which we shall consider in a somewhat extended form:

1) Whereas in positive ion spectrometry each fragment can carry the charge, in the case of NI a prerequisite for this is a positive *EA*. That is why, for example, no $N^{\ominus}$ or $N_2^{\ominus}$ ions are formed from azo compounds. Similarly, no $C_2H_5^{\ominus}$ ions are observed (even when $[M-C_2H_5]^{\ominus}$ is formed); anions which would have to be formed by simple breakage of a non-activated σ bond of a longer alkyl chain are usually absent.

2) Other factors being equal, the probability of anion formation roughly parallels the *EA* of the uncharged species in question. This is seen in the often observed very intense halogen ions, $CN^{\ominus}$, $O^{\ominus}$, $HC{\equiv}C^{\ominus}$, *etc.* (see Fig. 3).

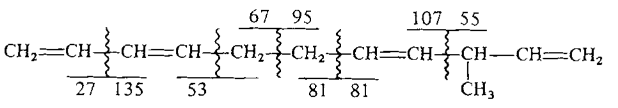
3) It should be possible to correlate the orbital symmetries of the daughter and parent ions. Even so, distinguishable mass spectra, at different excitation energies are only obtainable when one employs monoenergetic electrons. Otherwise, (*e.g.* using a hot filament or secondary electrons according to Eq. (e1)) the decompositions arising from the various energy levels will overlap. Their importance depends on the energy distribution of the electrons concerned.

4) The fact that, in the case of anions, autoionization (emission of e) competes with fragment formation, means that rapid decay reactions (in particular those involving simple bond cleavages) are preferred over more complex rearrangements. The portion of ions formed by rearrangement increases with increasing lifetime of the decaying ion (see Section 2.2.1). This is true for molecular as well as for fragment ions. Thus, in the case of negative ion spectra, it should be easier to make a simple correlation with the structure of the substrate molecules. For example, the two compounds 9-methylundeca-1,3,7,10-tetraene *(10)* and 3,8-dimethyldeca-1,4,6,9-tetraene *(11)*, have positive ion spectra which are almost indistinguishable. In their NI spectra (Fig. 4), all fragments can be interpreted in terms of simple bond breakages. Similarly the negative ion spec-

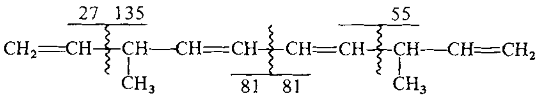
---

[*] Using the values given in Ref. [47-48], $EA(Cl) = 3.7$ eV and $D(C_6H_5Cl) = 2.9$ eV, the formation of $Cl^{\ominus}$ according to Eq. (c) is calculated to be exothermic by −0.8 eV. However, the $E_a$ was measured as 0.76 eV.

trum of 1-heptene contains an ion at $m/z=27$ ($CH_2{=}CH^{\ominus}$) which is absent in the case of 2-heptene[52].



$CH_2{=}CH{-}CH{=}CH{-}CH_2{-}CH_2{-}CH{=}CH{-}\underset{CH_3}{CH}{-}CH{=}CH_2$ *(10)*



$CH_2{=}CH{-}\underset{CH_3}{CH}{-}CH{=}CH{-}CH{=}CH{-}\underset{CH_3}{CH}{-}CH{=}CH_2$ *(11)*

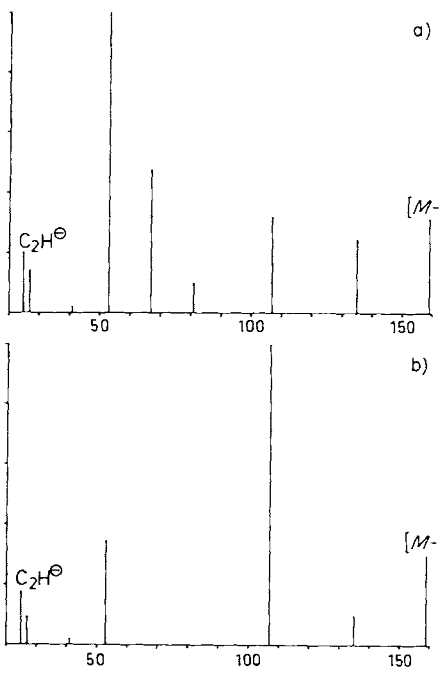


Fig. 4. NI spectra of a) 9-methylundeca-1,3,7,10-tetraene and b) 3,8-dimethyl-deca-1,4,6,9-tetraene (MKh 13-03, 2.5—8 eV) (after [59]).

5) The fact that autoionization can occur, thereby causing only those ions with a relatively low energy and thus a long enough lifetime to be recorded ($>10^{-6}$ s), leads to a very important difference from that of the fragmentation processes in the case of positive ions. In particular, ions requiring a high activation energy are formed. Thus, 1,2-diphenylethane *(12)* affords $C_6H_5CH{=}CH^{\ominus}$; this ion, however, is not present in the spectrum of 1,2-diphenylethylene *(14)*, despite the fact that it could arise here through simple bond breaking. Instead, the ion formed after $H_2$ elimination is in fact $H_5C_6C{\equiv}C^{\ominus}$[51]. $H_2$-Elimination of this kind is very frequently observed in the case of negative ions.

$$\underset{(12)}{H_5C_6{-}CH_2{-}CH_2{-}C_6H_5} \xrightarrow{e} \underset{(13)}{H_5C_6{-}CH{=}CH^{\ominus}} + H_2 + C_6H_5^{\odot}$$

$$\underset{(14)}{H_5C_6{-}CH{=}CH{-}C_6H_5} \xrightarrow{e} \underset{(15)}{H_5C_6{-}C{\equiv}C^{\ominus}} + H_2 + C_6H_5^{\odot}$$

The rules outlined above explain several important observations:

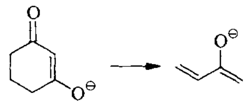
a) The 70-eV spectra of compounds which cannot form stable molecular anions frequently consist of merely "molecular debris", *i.e.* particularly stable species such as acetylide ions, ($C_2^{\ominus}$, $C_2H^{\ominus}$, $C_4H^{\ominus}$ *etc.*), or $O^{\ominus}$, $CN^{\ominus}$, $NO_2^{\ominus}$ *etc.* (Fig. 3)[8].

b) In particular, when using electrons of lower energy (see Section 3.4.2), an $[M-H]^{\ominus}$ ion is frequently observed in place of $M^{\ominus}$ (Fig. 4). The relatively high dissociation energy of, *e.g.*, C—H and O—H bonds plus the high *EA* of the resulting anions, explains these observations.

c) Fragments specific to the substrate structure can be expected for compounds forming stable $M^{\ominus}$ ions. Fragments can also be formed in rearrangement reactions. "Molecular debris" will not occur in such cases (cf. Fig. 7). The rule that consecutive elimination of two radicals will not occur[24] applies particularly to these ions. This often cited rule is the pendant to the "even electron rule" for positive ions[53]. There are, however, many exceptions[18,54], *e.g.*, *p*-methylbenzoic acid methyl ester (see Section 3.4.3).

A comparison of biacetyl, 1,2- and 1,3-cyclohexanedione may serve as an illustration[18,39]: in biacetyl the negative charge is well stabilized—as shown in *(4)* (Section 3.3); only minor amounts of $C_2H^{\ominus}$ ($m/z=25$) and $HC{\equiv}C{-}O^{\ominus}$ ($m/z=41$) ions are formed in addition to $M^{\ominus}$. 1,3-Cyclohexanedione can form a resonance stabilized enolate ion *(16)*; as a result $[M-H]^{\ominus}$ furnishes the base peak (Fig. 5a).

*(16)*



*m/z* 69

1,2-Cyclohexanedione, on the other hand, exists largely as the enol. Therefore, resonance stabilization of $M^{\ominus}$, as was the case for biacetyl, will not occur here, and furthermore the enolate ion is less stabilized than in the case of the 1,3-dione. The result is $M^{\ominus}$ and $[M-H]^{\ominus}$ ions of low intensity, as well as $H_2$-elimination from the latter, and intense peaks at $m/z=25$ and 41 (Fig. 5b).

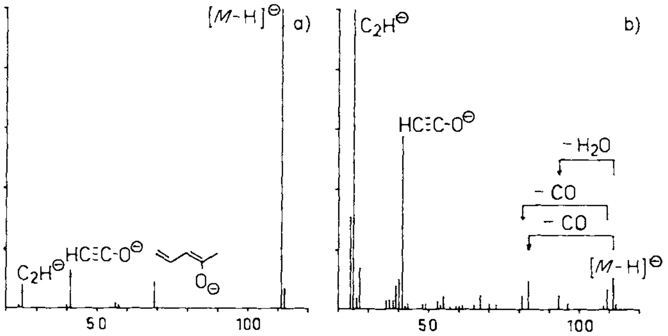


Fig. 5. NI-spectrum of a) 1,3-cyclohexanedione, b) 1,2-cyclohexanedione (CH-4, 70 eV).

### 3.4.2. Stable Molecular Anions

The importance of stable molecular anions for the interpretation of negative ion spectra has been emphasized by *Bowie et al.* (see Section 3.3) as well as *Rullkötter et* *al.*[18,39]. The concentration of the thermal electrons may be increased by appropriate adjustment of experimental parameters in cases where no stable molecular ions are obtained under normal electron impact ionization conditions (70 eV, $10^{-4}$ Pa)[8]. There are several such possibilities:

1) *Decreasing the electron energy.* The work of *Khvostenko et al.*[50] has shown that characteristic negative ion spectra can be obtained using low excitation energies. Natural products such as sugars, steroids, or glycosides also furnish intense $[M-\mathrm{H}]^{\ominus}$ ions under such conditions[55] (see Section 3.4.1). Yet, the electron energies required ( < 10 eV) are not always accessible with commercial mass spectrometers. The use of energies of above 10 eV is of no advantage but rather causes a decrease of ion intensities compared to 70 eV spectra[39].

2) *Decreasing of the drawout potentials*[18,39]. This effect is illustrated in Figure 6. Whereas methyl propyl sulfide *(17)* gives mainly $C_2H^{\ominus}$, $S^{\ominus}$, and $SH^{\ominus}$ ions under the normal operating conditions of 6—8 V of the Varian CH-4 mass spectrometer, these ions are superceded by the structurally significant $CH_2S^{\ominus}$ and $CH_3S^{\ominus}$ ions at 0 V.

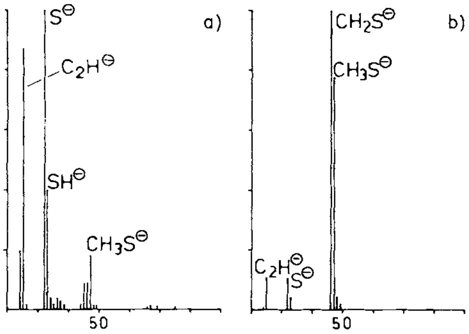


Fig. 6. NI-spectra of methyl propyl sulfide *(17)*; drawout potential a) 8 V, b) 0 V (CH-4, 70 eV).

*(17)* $CH_3—S—CH_2—CH_2—CH_3 + e \longrightarrow$
$[CH_3—S—CH_2—CH_2—CH_3]^{\ominus} \longrightarrow CH_3S^{\ominus}$ *m/z* 47

3) *Increasing the source pressure.* In this case too, the number of low-energy electrons increases; this holds for both secondary (Eq. (e1)) and slowed down primary electrons arising from plasma discharges. In the case of nitrobenzene a pressure increase by a power of ten causes a corresponding increase in the relative intensity of $M^{\ominus}$[10]. The usual electron impact sources limit the increase in sample pressure attainable. Therefore *Knof et al.* constructed a source capable of supporting pressures of up to $10^{-1}$ Pa[56]. Since almost all modern commercial mass spectrometers are equipped with CI sources, such modifications of the EI source are no longer necessary. An increase in sample pressure in the source can result in ion-molecule reactions; thus alcohols, aldehydes, acids, amines, *etc.* form cluster ions of the composition $[n\cdot M-\mathrm{H}]^{\ominus}$ ($n$=2—4). Furthermore, so-called auto-CI can occur (see Section 3.5) as in the formation of $CHCl_4^{\ominus}$ from $CHCl_3$. In order to circumvent such difficulties, it has been suggested the source pressure be increased by introduction of an additional gas ($N_2$, Ar, $H_2$, $CH_4$)[57-58]. At any rate, this is an area bordering on CI which is true also of the work of *Manfred von Ardenne* as discussed in Section 3.5.

### 3.4.3. Special Classes of Compounds

This section presents a selection of results where simple structure fragment correlations are possible. The following abbreviations are used: N = normal conditions spectrometery ($\approx$70 eV, $10^{-4}$ Pa), L = low electron energy, P = increased source pressure.

1) Aliphatics and Cycloaliphatics

*Olefins:* $[M-\mathrm{H}]^{\ominus}$, single bond breakage. There is no simple correlation between ion intensity and the nature of the bond to be cleaved (*e.g.* alkylic, vinylic, *etc.*) (L)[52,59].

*Alcohols:* $[M-\mathrm{H}]^{\ominus}$, $[M-3\,\mathrm{H}]^{\ominus}$; an unambiguous correlation between fragments and substrate structure is not possible. Cluster formation may occur (P)[56,60].

*Ethers:* $RO^{\ominus}$ (L)[52].

*Mercaptans:* $[M-\mathrm{H}]^{\ominus}$, $S^{\ominus}$, $SH^{\ominus}$. NI Mass spectrometry of mercaptans is of importance in crude oil analysis (P)[60]. *Thioethers:* $RS^{\ominus}$, $S^{\ominus}$ (L)[49-50]. $RS^{\ominus}$ becomes uncharacteristic in the case of long chain compounds (N)[18,39].

*Aldehydes, Ketones:* $[M-\mathrm{H}]^{\ominus}$, $HC{\equiv}C—O^{\ominus}$, $CH_3COCH_2^{\ominus}$ or the corresponding homologs (L)[50-52]. $[M-\mathrm{H}]^{\ominus}$ (P)[60]. *1,2-Diketones:* $M^{\ominus}$ (cf. Sections 3.3 and 3.4.1). *1,3-diketones:* $[M-\mathrm{H}]^{\ominus}$ (N)[18,34,39].

*Acids:* $[M-\mathrm{H}]^{\ominus}$ (P)[60]. *Dicarboxylic acids;* $[M^{\ominus}]$, $[M-\mathrm{H}]^{\ominus}$, $[M-\mathrm{COOH}]^{\ominus}$ and when sterically possible $[M-\mathrm{H_2O}]^{\ominus}$ (N)[61].

*Esters:* In some unsaturated esters $[M-\mathrm{H}]^{\ominus}$, $CH_3O^{\ominus}$, $^{\ominus}CH_2COOCH_3$, as well as $[M-\mathrm{CH_3OH}]^{\ominus}$ were found (L)[62-63]. $CH_2(COOC_2H_5)_2$ similarly gave $[M-\mathrm{H}]^{\ominus}$ and $^{\ominus}CH_2COOC_2H_5$ (P)[60]. Dithiocarboxylic acid methyl esters give $M^{\ominus}$ and $[M-\mathrm{CH_3}]^{\ominus}$ (N)[36].

*Dinitriles:* $[M-\mathrm{H}]^{\ominus}$, $^{\ominus}CH_2CN$, $CN^{\ominus}$ (N)[64].

*Nitrites:* $RO^{\ominus}$, $[M—NO—H_2]^{\ominus}$, $HNO^{\ominus}$ L[157].

2) Aromatic Compounds.

*Unsubstituted aromatics:* $C_6H_6$ gives $[M-\mathrm{H}]^{\ominus}$, whereas in higher annelated aromatics the importance of $M^{\ominus}$ increases. The situation is analogous for heteroaromatic compounds (L)[16,41,50,55,65]. $[M]^{\ominus}$ and $[M-\mathrm{H}]^{\ominus}$ are observed in higher condensed aromatics and heteroaromatics in particular; occasionally $[M-2\,\mathrm{H}]^{\ominus}$ (thermally) is also observed (P)[57,60,66,67].

*Aralkanes and heteroaralkanes* show $[M-\mathrm{H}]^{\ominus}$ together with $[M-\mathrm{C}_n\mathrm{H}_{2n+1}]^{\ominus}$. Either aryl$^{\ominus}$ or aryl-$CH_2^{\ominus}$ may predominate depending on the nature of the compound. Different structures are discussed for the ion $C_7H_7^{\ominus}$ depending on the precursor. In view of the discussion in Section 3.4.1 it is interesting to note that the $C_7H_7^{\ominus}$ ion is virtually absent in the spectrum of *tert*-butylbenzene, from which it cannot be formed without rearrangement (L)[50,68].

*Ketones:* $[M-\mathrm{H}]^{\ominus}$, $C_6H_5^{\ominus}$ (both weak) for acetophenone and its homologs; $M^{\ominus}$, $[M-2\,\mathrm{H}]^{\ominus}$, $C_6H_5CO^{\ominus}$, $C_6H_5^{\ominus}$ have a high to medium intensity for benzophenone (N)[18,34,39].

*Benzoic acids and thiobenzoic acid esters:* $[M-H]^\ominus$, $[M-R]^\ominus$, $[M-COOR]^\ominus$ and to an important extent $C_2H^\ominus$ and $C_4H^\ominus$ for benzoic acid alkyl esters. $C_6H_5COO^\ominus$ is apparently formed through ion pair formation. Thioesters and dithioesters give rise to $M^\ominus$ and $[M-CH_3]^\ominus$ (the latter ion has a relative intensity of 100% when a COSR group in contrast to a CSOR group is present) as well as $RS^\ominus$ (N)[18,36]. $[M-H]^\ominus$, $[M-COOCH_3]^\ominus$, $OCH_3^\ominus$ as well as an intense $[M-H-CH_3]^\ominus$ (splitting off of two radicals!) for $p$-$CH_3$—$C_6H_4COOCH_3$ (L)[54]. Multiply unsaturated aliphatic esters give complicated spectra[141,142].

*Quinones:* Unsubstituted quinones give rise to intense $M^\ominus$; anthraquinone esters fragment by elimination of $^\circ R$ and $^\circ COOR$ radicals. In 1-alkoxycarbonyl derivatives $^\circ OR$ is also lost as a result of an *ortho* effect (N)[18,19].

*Nitrobenzene and Derivatives* (N): As a result of the extensive work carried out by *Bowie et al.*[9], these compounds are among the most thoroughly studied. However, since they are not of general importance they will only be dealt with here in a limited manner. Apart from $NO_2^\ominus$, intense $M^\ominus$ and $[M-NO]^\ominus$ are observed. In compounds with an *ortho* substituent containing an H atom ($CH_3$, $NH_2$ *etc.* by operation of an "*ortho*-effect"[30]) $[M-OH]^\ominus$ is also found[13,69]. Whereas $p$-nitrobenzoic acid methyl ester hardly fragments at all[18], esters of longer chain alcohols give $O_2N$—$C_6H_4$—$COO^\ominus$ ions[43]. Neighboring group interactions between the $NO_2$ group and an *ortho* substituent is also important in the isomeric nitrobenzoic acid phenyl esters[31]: only the *ortho* isomer *(18)* easily eliminates $C_6H_5O^\ominus$, leading to the formation of a cyclic structure. (The subsequent elimination of $CO_2$ supports the presence of such a structure (Fig. 7).)

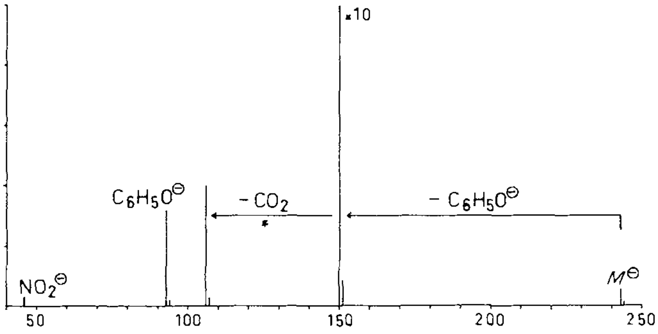
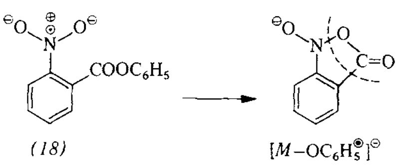


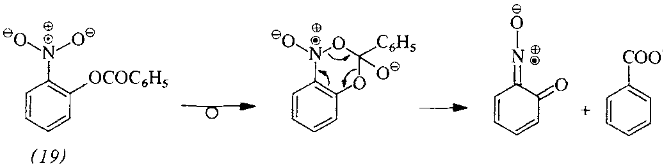
Fig. 7. NI-spectrum of $o$-nitrobenzoic acid phenyl ester *(18)* (RMU-6D, 70 eV) (after [31]).

More complicated rearrangement reactions are also observed: whereas $p$-nitrophenyl benzoate gives $[M-C_6H_5CO]^\ominus$ as the principal fragment, the $o$-isomer *(19)* eliminates $C_6H_4NO_2^\ominus$. $^{18}O$-labeling shows that one of the O atoms in $C_6H_4NO_2^\ominus$ comes from phenol. Neighboring group interaction is important here too[31].

*Silyl Compounds* (N): Benzoic acid trimethylsilyl esters give a weak $M^\ominus$; the base peak is $C_6H_5COO^\ominus$. The analogous $p$-nitrobenzoic acid ester gives almost only $M^\ominus$[18,70], whereas for the $m$-compound, $[M-(CH_3)_3Si]^\ominus$ is the base peak. The $o$-compound is again special in that it shows $[M-(CH_3)_3SiOH]^\ominus$[70]. *Ortho* effects are also found for the trimethylsilyl ether of $o$-nitrophenol[70].



*(18)*



*(19)*

3) Organometallic Compounds (N)

Intense $M^\ominus$ peaks are usually obtained from β-alkenedionates[71,135,136], dithiocarbonates[72], salicylaldehyde derivatives[73,74] and metallocenes[75,76]. The ligand anion is usually also observed. In general, further fragmentation is of little importance and, therefore, in contrast to the situation for positive ion spectra, the question whether valence changes of the metals influence the fragmentation pattern cannot be studied[77,78]. The high intensities of $M^\ominus$ have, however, been used in the trace analysis of metals[138].

4) Natural Products

Nitrobenzamides of glycine and alanine give intense $M^\ominus$ peaks. Poorer ion yields are obtained from the trifluoroacetates. The fragments observed in these two examples are more characteristic of the derivative groups than of the amino acids themselves. The paucity of data available gives no indication of a special advantage of the NI technique (N)[44]. The situation is similar for the $N$-acetyl-$p$-nitrobenzyl esters of alanine, valine and proline which give $[M-{}^\circ CH_2C_6H_4-NO_2]^\ominus$ ions (L)[79]. Alkylated itaconic acid anhydrides give intense $M^\ominus$ ions; elimination of the alkyl groups with concomitant hydrogen migration also occurs (N)[23].

Two acetylated diterpene diols give $[M-H]^\ominus$, cleavage of the acetoxy group, and $CH_3COO^\ominus$ as the most intense ion (L)[80]. The preferred formation of carboxylate ions permits identification of the esterified acids in a diterpene of the *Euonymus* family; furthermore, small amounts of homologs are seen; these are indicated by arrows in Figure 8a. The corresponding $RCO^\oplus$ ions in the positive spectra (Fig. 8b) are obscured by the large number of fragment ions in this region (L)[55]. $[M-H]^\ominus$ ions were obtainable from some hydroxysteroids (L)[55]. Arabinose also yields an $[M-H]^\ominus$ together with $O{=}CH$—$CH{=}CH$—$O^\ominus$ ($m/z=71$) as the base peak (L)[55]. Sugar acetates form $[M-CH_3CO]^\ominus$ (cf. Fig. 8a) and eliminate $CH_3COOH$ as well as $CH_2CO$ (L)[81].

5) Pesticides

A series of carbamates of aromatic hydroxy compounds has been examined; the phenolate ion usually appears with high intensity. Some thiophosphoric acid esters and chlorinated compounds were also studied (N)[82].

6) Inorganic Compounds

NI-spectra may be obtained from inorganic compounds as well (regarding $SF_6$ see Section 2.2.1) when they are sufficiently volatile and their *EA* is positive. The investigations are not so much of importance for analyses but rather for the determination of physical data[162].

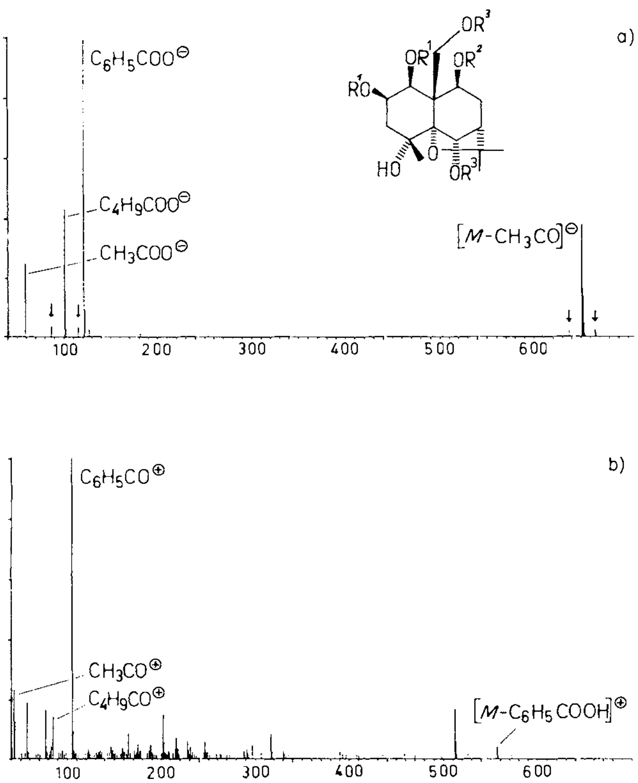


Fig. 8. a) NI-spectrum of Euolaline (ester B-5) from *Euronymus europaeus* (MAT-731, 5 eV). $R^1=C_6H_5CO$; $R^2=C_2H_5CHCH_3CO$, $R^3=CH_3CO$; b) positive spectrum (MAT-731, 100 eV).

### 3.5. The Work of *Manfred von Ardenne*

For many years the majority of the NI spectra relevant to the structure analysis of organic molecules came from the research institute Dresden-Weisser Hirsch. In the apparatus constructed by *Manfred von Ardenne,* the primary electrons are deprived of most of their energy through collision with Ar at a pressure of *ca.* 1 Pa. The electrons produced in this way give rise to $M^\ominus$ or, more frequently, $[M-H]^\ominus$ ions, which often undergo subsequent characteristic decomposition. Before the introduction of field desorption mass spectrometry, *Ardenne*'s instrument was the only one allowing usable spectra of involatile compounds to be obtained. This method played an important role in *Reichstein*'s work on cardenolide glycosides. The literature up to 1968 is reviewed in [83]; accordingly, only a short overview and description of newer work is given here. It appears that only one instrument of the *Ardenne* type is in existence in Dresden. Nevertheless, many of the results are relevant in studies using CI mass spectrometry, and in some areas can even be considered as pionieering work (see Section 4).

Inasmuch as this technique involves pure electron attachment (see also Section 4.2.1), the results extend those in Section (3.4.3); aromatics give $[M-H]^\ominus$ together with $M^\ominus$, the latter increasing with the number of rings. Acids give $[M-H]^\ominus$ but may also undergo fragmentation; thus phenylacetic acid gives $C_7H_7^\ominus$ as the base peak. In esters, both $[M-H]^\ominus$, $RCOO^\ominus$, and $R'O^\ominus$ are to be expected although the relative intensities may vary; thus for butyl butyrate the ratio of carboxylate to alcoholate ion equals *ca.* 3 : 1; in ethyl benzoate the carboxylate ion predominates; in phenyl benzoate the alcoholate ion. More complicated fragments may also be observed, however: butyl butyrate gives $[M-29]^\ominus$. Aliphatic alcohols give $[M-H]^\ominus$ and intense $[M-3H]^\ominus$, and ketones give $[M-H]^\ominus$ ions. The three isomeric nitrobenzoic acids give widely different negative ion spectra (*p:* $[M-NO]^\ominus$, $[M-HNO_2]^\ominus$; *m:* $[M-OH]^\ominus$; *o:* a combination of the *m* and *p* spectra.

Natural product studies are also important: usually, $M^\ominus$ or $[M-H]^\ominus$ are of high intensity. Steroid glycosides lose their sugar moiety with the formation of alcoholate ions[83]; esters behave as described above[83,84]. Gibberellins split off $H_2O$, HCOOH, and CO, but show only few skeletal fragments[85]. Amino acids give rise to $[M-H]^\ominus$, $[M-R]^\ominus$ and $R^\ominus$[86]. Glucose esters[87], terpenes[133] and lichen constituents[134] have also been throughly studied.

*von Ardenne* systematically examined the occurrence of ion-molecule reactions[83], a problem also relevant to CI mass spectrometry (several of these processes are discussed in Section 4). Molecular ions react either with the residual gases $H_2O$ and $O_2$ or with non-ionized molecules of the same material (auto-CI). The most important processes are presented in Table 1.

Table 1. Ions in the $M^\ominus$ region formed in ion-molecule reactions (ionization with electrons slowed down by collision with an auxiliary gas).

| Ion | Class of compound | Remarks |
|---|---|---|
| $[M+OH]^\ominus$ | alkanes, cycloalkanes<br>alkenes | only ion in $M^\ominus$ region |
| $[M+O]^\ominus$ | aromatics | |
| $[M-H+O]^\ominus$ | hydrocarbons | |
| $[M-2H+O]^\ominus$ | compounds with allylic $CH_2$-group | $[M+14]^\ominus$ can be confused with homologous compounds [85]. |
| $[nM-H]^\ominus$ | alcohols, acids | see Section 3.4.2 |
| $[M+CF_3]^\ominus$ | trifluoroacetates | |
| $[M+Cl]^\ominus$ | chlorine compounds | [88], see text. |

Apparently, traces of halogen compounds are easily retained in the source so that $[M+Cl]^\ominus$ ions may be found in later measurements[83]. All these reactions may complicate the analysis of unknown substances.

## 4. Chemical Ionization (CI)

### 4.1. General

The principles and instrumental techniques of CI are described in refs.[89] and [90], respectively. The reactant gas can have three functions:

1) Slowing down the primary electrons to give thermal electrons.
2) Charge transfer; this requires that *EA* (reactant gas) < *EA* (substance).
3) True CI; here, there is a chemical reaction between an ion of the reactant gas and a molecule of the substance to be examined[164].

The first two processes lead to resonance capture with or without dissociation. The findings of *von Ardenne* (Section

3.5) and the possibility of raising the source pressure using an auxiliary gas could be included here[57,58] (Section 3.4.2). For practical reasons, in this section we shall discuss those studies carried out using commercially available CI sources.

Similarly as in work with EI sources (see Section 3.2), instrumental parameters play an important role here also. General problems related to CI such as the influence of the repeller potential on the residence time in the source, optimum reactant gas pressure, *etc.*, will not be further dealt with here (for further information see [89,90] and references cited therein). In this case also, it is true that with increasing source temperature, the relative proportion of $M^{\ominus}$ and quasi-$M^{\ominus}$ decreases while the fragment ions increase or even in some cases appear for the first time[83,91]. In extreme cases, this can lead to a situation where quasi-$M^{\ominus}$ is formed only when the source is cold, *e.g.* $[M+OH]^{\ominus}$ for alkanes (see Section 4.2.4)[55]. Because of the high pressure of the reactant gas (up to $10^2$ Pa), processes such as the formation of low energy electrons and collisional deactivation of excited ions occur exclusively by way of reactant gas molecules, *i.e.* eqs. (g1) and (h1) no longer play a role. One could expect, therefore, that as a first approximation, there is a linear dependence of ion formation on substance pressure (see, however, Section 4.3).

## 4.2. Specific Reactant Gases

### 4.2.1. Formation of low energy electrons ($CH_4$, $i$-$C_4H_{10}$, $NH_3$, $H_2$, and occasionally $CH_2Cl_2$)

(Compare also Section 3.5 and ref. [57,58] as well as Section 4.2.2 regarding $H^{\ominus}$ and 4.2.3 regarding $CH_2Cl_2$.)

In general, the results of *von Ardenne* (Section 3.5) apply here also. Studies using $CH_4$ and $i$-$C_4H_{10}$[55] have shown that alkanes give no $M^{\ominus}$ ions, whereas benzil does, and esters fragment to carboxylate ions; aromatic nitro compounds behave as expected from the results of *Bowie et al.* (Section 3.4.3). Oligosaccharides give $M^{\ominus}$ ions of moderate intensity[92]. Bile acids give $[M-H]^{\ominus}$ from which water splits off[93]. First results[55] indicate that the use of different reactant gases gives rise to electrons of varying energy content. Thus, for a chloro compound (aldrin) it was found that, when $i$-$C_4H_{10}$ is used, fewer fragments are formed than with $CH_4$[94]. Systematic studies are still called for in this area.

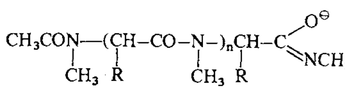
Because of their importance as pesticides and also following the Seveso catastrophy, chlorinated cycloaliphatic and aromatic compounds have been particularly well investigated[91,94-96]. $M^{\ominus}$ ions, and occasionally $[M-H]^{\ominus}$, are almost always observed. The most important fragmentation reactions are those where Cl, HCl, and possible combinations of these, are lost. $RO^{\ominus}$ is observed in ethers but often only at higher source temperatures. By auto-CI, $[M+Cl]^{\ominus}$ is formed, as well as smaller amounts of $[M+Cl_3]^{\ominus}$. When $CH_2Cl_2$ is used the formation of the former ion is somewhat lower. It would appear that this is due to $CH_2Cl_2$ having a greater affinity for $Cl^{\ominus}$; $CH_2Cl_3^{\ominus}$ appears at the expense of $[M+Cl]^{\ominus}$[94]. Traces of $O_2$ and/or $H_2O$ (see Section 3.5) in the source lead to nucleophilic displacement of Cl by $O^{\ominus}$ ($[M-Cl+O]^{\ominus}=[M-19]^{\ominus}$ and $[M-HCl-Cl+O]^{\ominus}=[M-55]^{\ominus}$). This occurs to a greater extent with $CH_4$ than with $i$-$C_4H_{10}$[94]. It has been suggested, because of the bad reproducibility of the intensities of these ions, that some $O_2$ be added to the reactant gas ($CH_4$) in order to achieve constant ratios[91,96]. When hydrocarbons are used as reactant gases, one occasionally observes addition of alkyl residues giving $[M+CH_3]^{\ominus}$, $[M+C_2H_5]^{\ominus}$ and $[M-H+CH_3]^{\ominus}$. Since the ions $CH_3^{\ominus}$ and $C_2H_5^{\ominus}$ do not occur in the plasma, it may be assumed that alkylation precedes ionization[55,139,140,163].

A series of alkylated cyclic pharmaceuticals (phenothiazines, barbiturates and others) was examined[97-100,156]. Whereas the use of $N_2$[97], $NH_3$[98] and $i$-$C_4H_{10}$[156] normally allows the observation of $[M-H]^{\ominus}$ ions, the use of $CH_4$[98] can lead to $H^{\ominus}$ transfer giving intense $[M+H]^{\ominus}$ ions (see Section 4.2.2). Important fragments are always formed by elimination of the whole side chain; longer chains are preferred over smaller, and unsaturated over saturated ones.

A series of chelates has been reported to give abundant $M^{\ominus}$ (or $[M—H]^{\ominus}$) as well as the ligand anions[163]. Several derivatives of primary amines have also been investigated[155].

### 4.2.2. Acid-Base Reactions

Several reactant gases give anions which can abstract $H^{\oplus}$ from another molecule in an acid-base reaction. For example, $CH_3O^{\ominus}$ can be used as the reagent anion (obtained from a reactant gas mixture consisting of *ca.* 0.1% of $CH_3ONO$ in $CH_4$). $CH_3O^{\ominus}$ reacts with ketones abstracting the α-H-atom, yielding intense $[M-H]^{\ominus}$ ions. The formation of $[M-H]^{\ominus}$ and ions of the type *(20)* from the reaction of an acetylated tripeptide ester with $CH_3O^{\ominus}$ has also been described[97].


*(20)*

$$CH_3CO\underset{\underset{CH_3}{|}}{N}—(\underset{\underset{R}{|}}{C}H-CO-\underset{\underset{CH_3}{|}}{N}-)_n\underset{\underset{R}{|}}{C}H-C\genfrac{}{}{0pt}{}{\nearrow O^{\ominus}}{\searrow\!\!\!= NCH_3}$$

Using $H_2$ as the reaction gas the stronger base $H^{\ominus}$ may be obtained[101,102]. Ketones, acids and esters possessing α-H-atoms, as well as acids, amines, alcohols and phenols give $[M-H]^{\ominus}$; fragment ions are absent or of low intensity except when strongly stabilized species such as $RCOO^{\ominus}$ can be formed, *e.g.* from esters. Nitroarenes give rise to $M^{\ominus}$ ions. Compounds which do not form stable $M^{\ominus}$ or $[M-H]^{\ominus}$ ions, *e.g.* aliphatic ethers, give intense fragment ion peaks (*e.g.* $RO^{\ominus}$ and $ROCH_2^{\ominus}$).

However, $H^{\ominus}$ can also add as a nucleophile to neutral molecules. Thus, ketones give $[M+H]^{\ominus}$ ions, especially when α-H-atoms are lacking (*e.g.* benzophenone)[102]. It should be mentioned that $H^{\ominus}$ can also be formed from both $CH_4$ at 10 eV[97] and isobutane[94], thus giving rise to formation of $[M+H]^{\ominus}$ ions (see Section 4.2.1). $H^{\ominus}$ reacts with traces of $H_2O$ to give $OH^{\ominus}$, which then leads to $[M+OH]^{\ominus}$ and $[M+H_2O+OH]^{\ominus}$ ($[M+35]^{\ominus}$) (particularly with alcohols and ketones; cf. also the formation of cluster ions $[ROH_n+RO]^{\ominus}$, Section 3.4.1). 1-Pentanol is reported to give $[M-H]^{\ominus}$ (15%), $[M+OH]^{\ominus}$ (44%), and $[M+H_2O+OH]^{\ominus}$ (40%)[102]. Less basic reactant gas ions can be generated from the plasma of $H^{\ominus}$ or $CH_3O^{\ominus}$ by addition of $CH_3NO_2$, $CH_3COCH_3$, $C_6H_5CH_3$, $C_2H_2$, $CH_3CN$, cyclopentadiene, *etc.*, until the original ions disappear[97,101]. However, a practical use of such ions of varying base strength has not yet been studied.

### 4.2.3. Cl$^{\ominus}$ and F$^{\ominus}$ as Plasma Ions

$CH_2Cl_2$ forms Cl$^{\ominus}$ together with some $HCl_2^{\ominus}$ and $CH_2Cl_3^{\ominus}$. The ratio of the three ions is strongly dependent on pressure and temperature. Reasonably constant values are, however, obtained at a pressure of $\approx$100 Pa and 210 °C[103]. Intense $[M+Cl]^{\ominus}$ ions are obtained from compounds capable of forming strong hydrogen bonds (acids, amides, amino acids, aromatic amines and phenols[103], but also polyols[104] and thiophosphoric acid esters[137]). Aliphatic amines and alcohols give low intensity $[M+Cl]^{\ominus}$ ions. This is also observed for ketones, esters, and ethers where attack of Cl$^{\ominus}$ on a substituted carbon atom in $S_N$-like transition states has been postulated. Cl$^{\ominus}$ is of little importance as a reactant ion for this group of compounds. Hydrocarbons, tertiary amines, and nitriles do not react at all. Nitroarenes give $M^{\ominus}$ and sometimes $[M+HCl]^{\ominus}$. Alkyl bromides and iodides give Br$^{\ominus}$ and I$^{\ominus}$, respectively[103].

Apart from the addition of Cl$^{\ominus}$, one may also add $HCl_2^{\ominus}$ and $CH_2Cl_2^{\ominus}$, especially at low source temperatures. When Cl$^{\ominus}$ is just weakly bound in a quasi-M$^{\ominus}$, drastic temperature effects are observed. Thus, the intensity ratio of $[M+Cl]^{\ominus}$ to Cl$^{\ominus}$ decreases by $10^2$ when increasing the temperature from 65 °C to 200 °C.

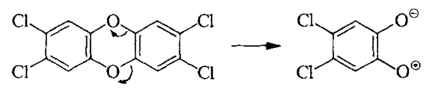
$CF_2Cl_2$ gives only Cl$^{\ominus}$. $[M+Cl]^{\ominus}$ and, more rarely $[M-H]^{\ominus}$ ions have been observed in a series of natural products (oligosaccharides, testosterone, reserpine, tetracycline); apart from the elimination of water there are hardly any fragments observed[92,93]. The Cl$^{\ominus}$ spectra should find application in particular in trace analysis, *e.g.* of acids, in materials which are not easily ionized with Cl$^{\ominus}$[103].

Little is known about F$^{\ominus}$. As reactant gases $CHF_3$, $CF_4$, $NF_3$, and perhaps also $SF_6$ may be used. Cyclic diols give $[M+F]^{\ominus}$[104]. $RSi(CH_3)_3$ can undergo cleavage of activated C—Si bonds with the formation of R$^{\ominus}$ and $FSi(CH_3)_3$[105]. Furthermore, the behavior of a series of metal complexes with Schiff bases toward reactant gases such as $CF_4$, $SO_2F_2$ and $SF_6$ has been investigated[106].

### 4.2.4. O$^{\ominus}$, $O_2^{\ominus}$, OH$^{\ominus}$ and $S_x^{\ominus}$ as Plasma Ions

When used as a reactant gas, $O_2$ leads to the formation of O$^{\ominus}$, $O_2^{\ominus}$ and a large number of low-energy electrons although it is somewhat aggressive toward the hot filament[97,101,102,107,108]. Alcohols, even tertiary ones, and free acids give $[M-H]^{\ominus}$ and $[M+O_2]^{\ominus}$ ions although few fragments. Polycyclic aromatic hydrocarbons give rise to $M^{\ominus}$ and $[M-H+O]^{\ominus}$ (phenolate ions), sulfur containing aromatic compounds (*e.g.* dibenzothiophene) $M^{\ominus}$ and intensive $[M+O_2]^{\ominus}$ (sulfone?). Of importance in pollution analysis is the formation of *(22)*, $m/z=176$ (80% TIC) ($M^{\ominus}$ from dichloro-*o*-benzoquinone, cf. Section 3.3), from tetrachlorodibenzodioxine *(21)*, which permits its detection in the presence of other chloro compounds.

*(21)*



*(22)*

O$^{\ominus}$ is also formed through decay of $N_2O^{\ominus}$; the observed formation of NO$^{\ominus}$ ($O^{\ominus}+N_2O\rightarrow NO^{\ominus}+NO$), particularly at high pressures, can be suppressed by addition of inert gases. Alkyl substituted aromatic compounds give $[M-H+O]^{\ominus}$, usually together with $[M-H]^{\ominus}$; $[M-R]^{\ominus}$ and $[M-R+O]^{\ominus}$ are formed with varying intensities. $[M-H+N_2O]^{\ominus}$ ($[M+43]^{\ominus}$), and $[M-H+N_2O-H_2O]^{\ominus}$ ($[M+25]^{\ominus}$) may be very intense[98,100,109]. Aliphatic alcohols give $[M-H]^{\ominus}$ (loss of the hydroxyl-H) and/or $[M-3H]^{\ominus}$ (elimination of hydrogen from both the α- and the β-position whereby an enolate anion $R-CH=CH-O^{\ominus}$ or $R-CH=CR'-O^{\ominus}$ is formed; this explains why $[M-3H]^{\ominus}$ is found only with primary and secondary alcohols). Characteristic fragments are formed by α-cleavage (bigger residues are lost preferentially) and additional loss of two H-atoms, one of which stems from the carbon of the second chain neighboring the hydroxylated carbon atom, thus yielding again an enolate anion[158]. $[M-17]^{\ominus}$ is thus $[M-CH_3-H_2]^{\ominus}$ in the case of 2-alkanols![100,109]. Acid chlorides give besides $[M+O-Cl]^{\ominus}$, $[M+O-Cl-H_2]^{\ominus}$[110]. As regards $[M-H]^{\ominus}$ and $[M-2H]^{\ominus}$ from ketones, unsaturated hydrocarbons, nitriles and some aromatics see refs.[111-114].

OH$^{\ominus}$ can be obtained from $H_2O$[158]. More frequently, however, it is generated by a different process: If $N_2O$ is mixed with $H_2$, $CH_4$, $i$-$C_4H_{10}$ and similar gases, then the primary product O$^{\ominus}$ reacts further to give OH$^{\ominus}$, which in turn can react with a whole range of compounds. The formation of OH$^{\ominus}$, side-reactions, and pressure and temperature dependence have been throughly studied[109] and have shown that the highest proportion of OH$^{\ominus}$ in the overall ion current is obtained at pressures of *ca.* 100 Pa, temperatures above 150 °C, and a mixing ratio of *ca.* 1:1. On the other hand, a high source temperature can be critical in measurements: only when the source is cold do alkanes give $[M+OH]^{\ominus}$, $[M-H]^{\ominus}$ and $[M-3H]^{\ominus}$ ($C_4H_{10}/N_2O$); in addition, $[M+NO]^{\ominus}$ and $[M+N_2O]^{\ominus}$ ($CH_4/N_2O$) are formed. At higher temperatures absolutely no ions are obtained from the hydrocarbons[55]. The stability of $[M+OH]^{\ominus}$ increases with increasing molecular size[115]. In general, it is possible to say that, alkenes[55,116], acids, alcohols, ketones, and esters give $[M-H]^{\ominus}$ as an intense ion (frequently accompanied by $[M-3H]^{\ominus}$)[109,117]; in the case of alcohols one H comes from the α- and one from the β-position[158]. This is also true for steroids and terpenoids, which have been examined in detail[118,160]. Fragmentation is usually of little importance; RCOO$^{\ominus}$, and to some extent R'O$^{\ominus}$, is found for esters (RCOOR'). Ethers and amines give hardly any quasi-molecular ions; RO$^{\ominus}$ and $[RO-H_2]^{\ominus}$ dominate for ethers; the fragment ($m/z=42$) formed from aliphatic amines seems to be independent of the structure[109]. Acid chlorides give similar results with OH$^{\ominus}$ and O$^{\ominus}$; however, the subsequent loss of $H_2$ is less apparent in the former case[110]. Alkyl substituted aromatics give $[M-H]^{\ominus}$ together with $[M+43]^{\ominus}$ and $[M+25]^{\ominus}$[109]. In general, the formation of these ions formed by attack of $[M-H]^{\ominus}$ on $N_2O$ is of lesser significance when $i$-$C_4H_{10}$ (or higher alkanes)/$N_2O$ is employed as the reactant gas[55]. See also the results reported in refs. [109] and [119]. The fact that OH$^{\ominus}$ does not give any ions with saturated hydrocarbons, particularly at higher tempera-

Table 2. Summary of the possible Uses of NCI.

| Reactant gas | Reagent ions | Class of compound | Ios in the $M$ region | Remarks |
|---|---|---|---|---|
| Ar, $N_2$ | | various | $M^{\ominus}$, $[M-H]^{\ominus}$ | traces of $H_2O$, $O_2 \rightarrow$ $[M-H+O]^{\ominus}$, $[M+O]^{\ominus}$, $[M+OH]^{\ominus}$<br>traces of Cl cpds.$\rightarrow [M+Cl]^{\ominus}$ |
| $CH_4$, $i$-$C_4H_{10}$<br>$NH_3$, $(CH_2Cl_2)$ | — | various | $M^{\ominus}$, $[M-H]^{\ominus}$<br>$[M+CH_3]^{\ominus}$, $[M-H+CH_3]^{\ominus}$, $[M+C_2H_5]^{\ominus}$ | $+O_2$ in the case of polyhalo cpds.$\rightarrow$ $[M-Cl+O]^{\ominus}$, $[M+ClO]^{\ominus}$ |
| $CH_3ONO$ | $CH_3O^{\ominus}$ | cpds. with acidic H | $[M-H]^{\ominus}$ | ev. + $C_2H_2$, $CH_3CN$, $CH_3NO_2$, *etc.* $\rightarrow$weaker bases |
| $H_2$ ($CH_4$, $i$-$C_4H_{10}$) | $H^{\ominus}$ | cpds. with acidic H | $[M-H]^{\ominus}$ | traces of $H_2O \rightarrow OH^{\ominus} \rightarrow$ $[M+OH]^{\ominus}+[M+H_2O+OH]^{\ominus}$ |
| | | nitroarenes | $M^{\ominus}$ | |
| | | cpds. without acidic H | $[M+H]^{\ominus}$ | |
| $CF_2Cl_2$ | $Cl^{\ominus}$<br>$(HCl_2^{\ominus})$ | RCOOH, $RCONH_2$, ArOH, $ArNH_2$, perchloro cpds., polyols | $[M+Cl]^{\ominus}$, $[M-H]^{\ominus}$ (little) | traces of $O_2$ in the case of polyhalo cpds. |
| $CH_2Cl_2$ | $(CH_2Cl_3^{\ominus})$ | ROH, $RNH_2$, carbonyl cpds. | $[M+Cl]^{\ominus}$, $[M+HCl_2]^{\ominus}$ | vide supra<br>weak, decreases with increasing temperature |
| | | nitroarenes | $M^{\ominus}$, $[M+HCl]^{\ominus}$ | (weak) |
| | | RBr(I) | $Br^{\ominus}(I^{\ominus})$ | |
| | | multifunctionel natural proucts | $[M+Cl]^{\ominus}$, $[M-H]^{\ominus}$ | |
| | | hydrocarbons, *tert*-amines, nitriles | no $[M+Cl]^{\ominus}$ | |
| $CHF_3$ | $F^{\ominus}$ | alcohols | $[M+F]^{\ominus}$, $[M-H]^{\ominus}$ | |
| $CF_4$<br>$NF_3$ | $(CF_3^{\ominus})$ | $RSi(CH_3)_3$ | $R^{\ominus}$ | when $R^{\ominus}$ is a stable anion |
| $N_2O$ | $O^{\ominus}$ | unsaturated hydrocarbons, acetone, nitriles | $[M-H]^{\ominus}$, $[M-2H]^{\ominus}$<br>$[M-H+O]^{\ominus}$ | |
| | | RCOCl | $[M-Cl+O]^{\ominus}$, $[M-H_2Cl+O]^{\ominus}$ | |
| | | phenothiazines | hardly any ions | |
| | | ROH | $[M-H]^{\ominus}$, $[M-3H]^{\ominus}$ | |
| | | alkylarenes | $[M-H]^{\ominus}$, $[M-H+O]^{\ominus}$,<br>$[M-H+N_2O]^{\ominus}$,<br>$[M-H+N_2O-H_2O]^{\ominus}$ | $M+43$ or $M+25$ |
| $O_2$ | $O^{\ominus}$, $O_2^{\ominus}$ | ROH, RCOOH | $[M-H]^{\ominus}$, $[M+O_2]^{\ominus}$ | |
| | | polycyclic arenes | $M^{\ominus}$, $[M-H+O]^{\ominus}$ | |
| | | S-arenes | $[M+O_2]^{\ominus}$ | sulfones? |
| | | chlorinated arenes | $M^{\ominus}$, $[M-Cl+O]^{\ominus}$, $[M-H+O]^{\ominus}$ | |
| $N_2O+$ $H_2$, $CH_4$, $i$-$C_4H_{10}$ and others | $OH^{\ominus}$ | alkanes | $[M+OH]^{\ominus}$, $[M-3H]^{\ominus}$ (little)<br>$[M+NO]^{\ominus}$, $[M+N_2O]^{\ominus}$ | only at lower temperatures<br>$(CH_4)$, only at lower temperatures |
| | | akenes | $[M-H]^{\ominus}$, $[M-3H]^{\ominus}$ (little)<br>"$M+25$", "$M+43$" | |
| | | alkylarenes | $[M-H]^{\ominus}$<br>"$M+25$", "$M+43$" | $(CH_4)$ |
| | | ROH, RCOOH, ketones, esters | $[M-H]^{\ominus}$, also $[M-3H]^{\ominus}$ | |
| | | ethers | $[M-3H]^{\ominus}$ | |
| | | amines | scarcely ions | |
| | | RCOCl | $[M-Cl+O]^{\ominus}$, $[M-H_2Cl+O]^{\ominus}$ | |
| S | $S_x^{\ominus}$ | alkanes | $[M-H+S_x]^{\ominus}$ | intense $S_x^{\ominus}$-spectrum |
| | | dinitriles | $[M-H]^{\ominus}$, $[M+S_x]^{\ominus}$, | |
| | | ferrocene | $C_5H_5S_x^{\ominus}$ | |

tures, means that it is possible to determine the presence of aromatics in crude oil fractions[119].

If a mixture of $N_2O$ and $D_2$ is used, one can observe an interesting exchange reaction: in simple alcohols neither $[M-H]^{\ominus}$ nor $[2M-H]^{\ominus}$ exchange, whereas this is observed for both ion types in diols. A special bridging mechanism is conceivable in this case[143].

Alkanes react with sulfur to give intense ions of the composition $C_nH_{2n+1}S_x^{\ominus}$ ($x=1-4$)[83] (besides of course the normal sulfur spectrum up to $S_8^{\ominus}$). Dinitriles give, in addition to $[M-H]^{\ominus}$, also $[M+S_x]^{\ominus}$ ions[64]; ferrocene gives $[C_5H_5S_x]^{\ominus}$[76].

### 4.2.5. Pulsed Positive-Ion Negative-Ion Chemical Ionization (PPINICI)

With quadrupole instruments it is possible to quickly switch the measuring set-up for positive and negative ions, thus making it possible to measure both spectra alternately[97]. In this way, it is easy to get complementary information; *e.g.* since aromatic compounds give $M^{\oplus}$ and $[M-H+O]^{\ominus}$ when $O_2$ is used as reactant gas, and sulfur-containing arenes give $M^{\oplus}$ and $[M+O_2]^{\ominus}$ (see Section 4.2.4), it is possible to distinguish very quickly between these two classes. Reactant gas mixtures such as $CH_4$ with $CH_3ONO$ (which give $CH_5^{\oplus}$ and $CH_3O^{\ominus}$) can be employed[97]. This procedure will prove useful in cases where both positive and negative ion spectra cannot separately be measured owing to lack of either substance or time. The price to be paid for this advantage is that the same reactant gas must be used for both methods; consequently the possible range of CI is curtailed. Furthermore, the time required for the double scan, together with that of switching systems, is critical since the time available is limited by the width of the gas chromatography peaks, and finally the optimal adjustment of the source is not possible for both types of ionization.

### 4.3. Sensitivity of the Method

On the whole, only scattered data are available here. For barbiturates, anthracene and benzil, for example, it is reported that the total ion current (TIC) for NCI is about equal to that for positive EI but up to a factor of 50 higher than that for positive CI. For chlorinated dibenzodioxins the NCI sensitivity is higher by a factor of about 1000 than that for either positive EI or positive CI. In addition, quasi-molecular ions carry the major part of the total ion current in NCI[100, 145, 159].

In an analysis of the problem *Hunt et al.*[120] established the formation of $M^{\ominus}$ should occur about 400 times more frequently than that of $[M+H]^{\oplus}$ on using $CH_4$ as the reactant gas ($\approx 100$ Pa) and low substance pressures, causing the ionization to be diffusion controlled (addition of $H^{\oplus}$ or capture of a thermal electron). This value was experimentally verified for some highly fluorinated compounds. A requirement is, however, that each collision leads to a stable (quasi) molecular ion, *i.e.* processes such as autoionization of $M^{\ominus}$, dissociative resonance capture, *etc.* could lead to a drastic decrease in the yield of $M^{\ominus}$.

Furthermore, impurities, particularly halogen compounds (*e.g.* solvents), which might be retained in the source (see Section 3.5) can lead to a strong reduction in the number of thermal electrons. *Hunt et al.* suggested derivatization with *e.g.* $C_6F_5COOH$ or $C_6H_5CHO$, which, using single ion detection, allows access to the fg-region ($10^{-15}$ g). One should be aware, however, that the derivatization of a pure substance and the preparation of dilution series is not the same as the identification of a trace impurity.

## 5. Further Ionization Methods and Techniques

As in all ionization methods giving mainly (quasi) molecular ions, the collision induced fragment formation[121] has been used, whereby charge reversal can also occur ($M^{\ominus} \rightarrow M^{\oplus} \rightarrow$ positive fragments)[122]. The opposite process, namely the formation of $M^{\ominus}$ from $M^{\oplus}$ through collision, has likewise been observed[123]. Negative ions both from organic and inorganic compounds can also be obtained using special methods such as atmospheric pressure ionization (API)[124], laser desorption[125, 144, 161], secondary ion mass spectrometry (SIMS)[126], or $^{252}Cf$ plasma desorption[127, 144]. All these methods are confined to specialized laboratories and will not, therefore, be further treated here. Judging from the few results available, two methods of ionization may develop into generally applicable procedures, namely the direct chemical ionization (DCI) and field desorption (FD). Under DCI conditions, substances of low volatility or thermal sensitivity are placed directly in the reactant gas plasma with the aid of a special probe. It is still an open question whether ionization takes place in the condensed phase, followed by emission of ions from the surface, or whether ionization follows the vaporization of the molecules. At any rate, examples have shown that negative ions can also be produced in this manner. Thus, an $OH^{\ominus}$ plasma ($CH_4+N_2O$, see Section 4.2.4) interacts with glycosides to give $[M-H]^{\ominus}$ as well as the sugar sequence[146], and with non-derivatized glucuronides to give, in part $[M-H]^{\ominus}$ and in part, by electron capture, $M^{\ominus}$, together with the anions of the glycosidic alcohols. The general appearance of the spectra is strongly dependent on the recording conditions; *e.g.* at strong heating currents, the $[M-H]^{\ominus}$ peak is barely visible[147]. Using $CH_4$ as a retarding gas (cf. Section 4.2.1) it was possible to observe $M^{\ominus}$ or $[M-H]^{\ominus}$ as well as a series of fragment ions of some penicillin derivatives[148]. Using field desorption (FD), the $M^{\ominus}$ ion of a ubiquinone, and the $[M-H]^{\ominus}$ ions (often accompanied by $[nM-H]^{\ominus}$) of sulfonic acids and oligopeptides could be generated[153]. The $[M-H]^{\ominus}$ ions of compounds possessing acidic hydrogen atoms can be generated by placing a mixture of the substance with water and polyethylene oxide on an FD-emitter. The addition of LiCl can lead to $[M+Cl]^{\ominus}$ ions, as observed, for example, in the case of cholesterol[128].

Using the same procedure, the anions of organic and inorganic salts can be identified, often together with cluster ions, *e.g.* $LiCl_2^{\ominus}$ and $Li_2Cl_3^{\ominus}$ (organic examples are sodium naphthalenesulfonate and the salts of fatty acids; in the case of dibasic inorganic acids the anions are obtained only after cation exchange)[128, 154]. Alternatively, a freshly broken tungsten rod has been employed as the field desorption cathode for inorganic salts, and polyvinyl alcohol was used as the electrolyte (this, however, undergoes partial fragmentation of its own to give ions such as $CH^{\ominus}$, $C_2H^{\ominus}$, *etc.*)[149]. Chloride[150], bromide[151], and less easily fluoride ions[152] can be liberated from their salts using thermal ionization (hot rhenium ribbon). This procedure is useful in the trace analysis of halides in minerals according to the isotope dilution method[150], and in environmental analysis[152].

## 6. Closing Remarks

The possibilities offered by modern CI sources will probably restrict in future the practical use of the generation of negative ions from organic molecules using electron impact ionization to some special classes of compounds and to studies on the formation and decomposition of ions, determination of physicochemical data, *etc.* Usually, the generation of thermal electrons by slowing down of the primary electron current in CI sources leads to characteristic and more reproducible spectra. Examples are known where the fragmentation pattern of the negative ion spectrum gives information not available from the positive ion spectrum. The major importance appears, however, to lie in the paucity of fragments, which—given the necessary sensitivity—facilitates the analysis of mixtures, particularly when using single or multiple ion detection. The advantages and disadvantages compared with fragment poor positive CI spectra—obtained by specific ionization of certain compound classes—must be evaluated from case to case. Only a first step towards the use of reactant gases in the identification of particular structural elements has been taken. A vast area remains to be explored.

When using NI mass spectrometry in practice it should not be forgotten that it is much easier to interpret the spectra of a known compound than to derive structurally relevant information from the spectrum of an unknown substance. In particular, the numerous ion-molecule reactions observed in NCI lead, among other things, to several different quasi-molecular ions, the interpretation of which requires some experience.

It cannot be the purpose of a review article to give a complete evaluation of the literature. Instead, an attempt has been made to select from the available data those aspects which are of special importance for a general understanding of the special features of NI mass spectrometry, in particular those of interest to the organic and analytical chemist. The literature has been surveyed up to the middle of 1981 in so far as the journals have been directly available. It was considered important to select references which facilitate the location of further information (older reviews[50,83,129-132], tabulated works[2,4,16], and recent contributions in series publications[9,71]). Also less widely available publications and those indicating research groups specializing in NI mass spectrometry have been quoted.

*I wish to thank Dr. J. Rullkötter (now at KFA Jülich) and D. Stöckl, Dipl.-Chem., who in their doctoral theses collected and sorted extensive literature material. The Landesamt für Forschung Nordrhein-Westfalen is gratefully acknowledged for generous support of our work on negative ions.*

Received: October 1, 1980 [A 375 IE]
German version: Angew. Chem. *93*, 635 (1981)
Translated by Edeline Wentrup-Byrne, Marburg

---

[1] *Ch. E. Melton:* Principles of Mass Spectrometry and Negative Ions, Marcel Dekker, New York 1970.

[2] *F. H. Field, J. L. Franklin:* Electron Impact Phenomena, Academic Press, New York 1970, p. 147ff.; cf. [1], p. 222 and *H. M. Rosenstock, K. Draxl, B. W. Steiner, J. T. Herron,* J. Phys. Chem. Ref. Data, Suppl. 1, *6*, 736 (1977).

[3] Cf. *e.g. D. L. McCorkle, A. A. Christodoulides, L. G. Christophorou, I. Szamrej,* J. Chem. Phys. *72*, 4049 (1980).

[4] *J. D. Dillard,* Chem. Rev. *73*, 589 (1973).

[5] *H. Budzikiewicz:* Massenspektrometrie - Eine Einführung, 2 edit. Verlag Chemie, Weinheim 1980.

[6] *E. D. Pellizzari,* J. Chromatogr. *98*, 323 (1974).

[7] *R. L. Woodin, M. S. Foster, J. L. Beauchamp,* J. Chem. Phys. *72*, 4223 (1980).

[8] *R. T. Aplin, H. Budzikiewicz, C. Djerassi,* J. Am. Chem. Soc. *87*, 3180 (1965).

[9] Part 131 of the series, which is mainly concerned with with negative ions: *V. C. Trenerry, J. H. Bowie,* Org. Mass Spectrom. *15*, 367 (1980).

[10] *J. Yinon, H. G. Boettger,* Int. J. Mass Spectrom. Ion Phys. *10*, 161 (1972/73).

[11] *J. C. J. Thynne,* Chem. Commun. *1968*, 1075.

[12] *T. McAllister,* J. Chem. Soc. Chem. Commun. *1972*, 245.

[13] *R. G. Alexander, D. B. Bigley, R. B. Turner, J. F. J. Todd,* J. Chem. Soc. Faraday Trans. I *1974*, 1212.

[14] *D. R. Dakternieks, I. W. Fraser, J. L. Garett, I. K. Gregor,* Org. Mass Spectrom. *12*, 370 (1977).

[15] *G. Albers, H. Knof,* Org. Mass Spectrom. *13*, 258 (1978).

[16] *V. A. Mazunov, V. I. Khvostenko,* VINITI 200-76 (Engl. summary in High Energy Chem. (USSR) *10*, 253 (1976)). Extensive data on *EA*, dipole moments and lifetimes of $M^{\ominus}$ are given here, as well as pertinent references.

[17] *O. H. Crawford,* Mol. Phys. *20*, 585 (1971).

[18] *J. Rullkötter, H. Budzikiewicz,* Int. J. Mass Spectrom. Ion Phys. *20*, 269 (1976).

[19] *A. C. Ho, J. H. Bowie, A. Fry,* J. Chem. Soc. B *1971*, 530.

[20] *L. G. Christophorou, J. G. Carter, A. A. Christodoulides,* Chem. Phys. Lett. *3*, 237 (1969).

[21] *J. G. Dillard, J. H. O'Toole, M. Ogliaruso,* Org. Mass Spectrom. *10*, 728 (1975).

[22] *J. H. Bowie, S. Janposri,* Org. Mass Spectrom. *11*, 1290 (1976).

[23] *A. Selva, P. Traldi, L. Camarda, G. Nasini,* Biomed. Mass Spectrom. *7*, 148 (1980).

[24] *J. H. Bowie,* Aust. J. Chem. *24*, 989 (1971).

[25] *A. Hadjiantoniou, L. G. Christophorou, J. G. Carter,* J. Chem. Soc. Faraday Trans. II *69*, 1691 (1973).

[26] *G. A. Vaglio, R. P. Ferrari, V. Mortarini, A. Gasco, R. Calvino,* Org. Mass Spectrom. *14*, 668 (1979).

[27] *C. Nolde, J. Ø. Madsen, S.-O. Lawesson, J. H. Bowie,* Ark. Kemi *31*, 481 (1969).

[28] *C. E. Brion, L. A. R. Olsen,* Int. J. Mass Spectrom. Ion Phys. *9*, 413 (1972).

[29] *G. Holzmann, H. W. Rotkopf,* Org. Mass Spectrom. *13*, 636 (1978).

[30] *H. Schwarz,* Top. Curr. Chem. *73*, 232 (1978).

[31] *J. H. Bowie, B. Nussey,* Org. Mass Spectrom. *6*, 429 (1972).

[32] *J. P. Johnson, D. L. McCorkle, L. G. Christophorou, J. G. Carter,* J. Chem. Soc. Faraday Trans. II *71*, 1742 (1975).

[33] *S. Tsuda, A. Yokohata, M. Kawai,* Bull. Chem. Soc. Jpn. *42*, 607 (1969).

[34] *G. A. Vaglio,* Ann. Chim. Rome *69*, 139 (1979).

[35] *H. J. Meyer, F. C. V. Larsson, S.-O. Lawesson, J. H. Bowie,* Bull. Soc. Chim. Belg. *87*, 517 (1978).

[36] *J. Rullkötter, H. Budzikiewicz,* Org. Mass Spectrom. *11*, 44 (1976); references to further sulfur compounds cited therein.

[37] *I. Kh. Aminev, V. I. Khvostenko,* Khim. Geterotsikl. Soedin. *1971*, 1631.

[38] *J. H. Bowie, F. Duus, S.-O. Lawesson, F. C. V. Larsson, J. Ø. Madsen,* Aust. J. Chem. *22*, 153 (1969).

[39] *J. Rullkötter,* Dissertation, Universität Köln 1974.

[40] *R. S. Gohlke,* J. Am. Chem. Soc. *90*, 2713 (1968).

[41] *A. Hajiantoniou, L. G. Christophorou, J. G. Carter,* J. Chem. Soc. Faraday Trans. II *69*, 1704 (1973).

[42] *W. T. Naff, C. D. Cooper, R. N. Compton,* J. Chem. Phys. *49*, 2784 (1968).

[43] *J. H. Bowie, B. J. Stapleton,* Aust. J. Chem. *28*, 1011 (1975).

[44] *B. J. Stapleton, J. H. Bowie,* Org. Mass Spectrom. *11*, 429 (1976).

[45] *J. Yinon, H. G. Boettger, W. P. Weber,* Anal. Chem. *44*, 2235 (1972).

[46] *R. G. Alexander, D. B. Bigley, J. F. J. Todd,* Org. Mass Spectrom. *7*, 643 (1973).

[47] *W. E. Wentworth, R. S. Becker, R. Tung,* J. Phys. Chem. *71*, 1652 (1967).

[48] *D. D. Clarke, C. A. Coulson,* J. Chem. Soc. A *1969*, 169.

[49] *V. I. Khvostenko, I. Kh. Aminev, I. I. Furlei,* Teor. Eksp. Khim. *9*, 99 (1973).

[50] *V. I. Khvostenko, G. A. Tolstikov,* Usp. Khim. *45*, 251 (1976); Russ. Chem. Rev. *45*, 127 (1976).

[51] *V. I. Khvostenko, S. R. Rafikov,* Dokl. Akad. Nauk SSSR *220*, 892 (1975); Proc. Acad. Sci. USSR *220*, 107 (1975).

[52] *V. I. Khvostenko, V. S. Falko, I. Kh. Aminev,* Zh. Org. Khim. *11*, 665 (1975).

[53] *M. Karni, A. Mandelbaum,* Org. Mass Spectrom. *15*, 53 (1980).

[54] *V. I. Khvostenko, V. V. Takhistov, V. S. Falko, O. S. Sokolova,* Izv. Akad. Nauk SSSR, Ser. Khim. *1978*, 1547.

[55] Unpublished results.

[56] *H. Knof, V. Hausen, D. Krafft,* Z. Naturforsch. *A 27*, 162 (1972).

[57] *R. C. Dougherty, C. R. Weisenberger,* J. Am. Chem. Soc. *90*, 6570 (1968).

[58] *J. E. Szulejko, I. Howe, J. H. Beynon, U. P. Schlunegger,* Org. Mass Spectrom. *15*, 263 (1980).

[59] *V. I. Khvostenko, V. P. Yuve'ev, I. Kh. Aminev, G. A. Tolstikov, S. R. Rafikov,* Dokl. Akad. Nauk SSSR *202*, 861 (1972); Proc. Acad. Sci. USSR *202*, 128 (1972).

[60] *R. Large, H. Knof,* Org. Mass Spectrom. *11*, 582 (1976).

[61] *A. Ito, K. Matsumoto, T. Takeuchi,* Org. Mass Spectrom. *7*, 1279 (1973).

[62] *A. Sh. Sultanov, U. M. Dzhemilev, V. I. Khvostenko, G. A. Tolstikov, R. I. Khusnutdinov, S. R. Rafikov,* Dokl. Akad. Nauk SSSR *238*, 367 (1978); Proc. Acad. Sci. USSR *238*, 32 (1978).

[63] *V. I. Khvostenko, E. G. Galkin, U. M. Dzhemilev, G. A. Tolstikov, V. S. Falko,* Izv. Akad. Nauk SSSR, Ser. Khim. *1980*, 1663.

[64] *Y. Hirata, K. Matsumoto, T. Takeuchi,* Org. Mass Spectrom. *9*, 913 (1974).

[65] *I. K. Aminev, V. I. Khvostenko, V. P. Yuve'ev, G. A. Tolstikov,* Izv. Akad. Nauk *1973*, 1885.

[66] *G. Albers, H. Knof,* Org. Mass Spectrom. *12*, 698 (1977).

[67] *G. Albers, H. Knof,* Z. Naturforsch. *A 32*, 641 (1977).

[68] *V. I. Khvostenko, I. I. Furlei, V. A. Mazunov, S. R. Rafikov,* Dokl. Akad. Nauk SSSR *213*, 1364 (1973); Proc. Acad. Sci. USSR *213*, 1134 (1973).

[69] *J. H. Bowie, T. Blumenthal, I. Walsh,* Org. Mass Spectrom. *5*, 777 (1971).

[70] *J. H. Bowie, B. A. Hale,* Org. Mass Spectrom. *11*, 1105 (1976).

[71] *D. R. Dakternieks, I. W. Fraser, J. L. Garnett, I. K. Gregor,* Org. Mass Spectrom. *14*, 676 (1979), (part XIV of the series *M. R. Blake, J. L. Garnett, I. K. Gregor, S. B. Wild, ibid. 15*, 369 (1980)).

[72] *I. W. Fraser, J. L. Garnett, I. K. Gregor, K. J. Jessop,* Org. Mass Spectrom. *10*, 69 (1975).

[73] *Y. Hirata, K. Matsumoto, T. Takeuchi,* Org. Mass Spectrom. *13,* 264 (1978).

[74] *W. C. Gilbert, L. T. Taylor, J. G. Dillard,* J. Am. Chem. Soc. *95,* 2477 (1973).

[75] *G. M. Begun, R. N. Compton,* J. Chem. Phys. *58,* 2271 (1973).

[76] *Y. Hirata, K. Matsumoto, T. Takeuchi,* Org. Mass Spectrom. *10,* 698 (1975).

[77] *C. G. McDonald, J. S. Shannon,* Aust. J. Chem. *19,* 1545 (1966).

[78] *H. Budzikiewicz, E. Plöger,* Org. Mass Spectrom. *3,* 709 (1970).

[79] *C. L. Brown, C. L. Chan,* J. Am. Chem. Soc. *98,* 2682 (1976).

[80] *L. A. Baltina, I. I. Furlei, P. F. Vlad, V. I. Khvostenko, G. A. Tolstikov, V. S. Falko,* Khim. Prir. Soedin. *1978,* 454.

[81] *G. A. Tolstikov, V. S. Falko, L. A. Baltina, V. I. Khvostenko,* Izv. Akad. Nauk SSSR, Ser. Khim. *1977,* 1051.

[82] *P. C. Rankin,* J. Assoc. Off. Anal. Chem. *54,* 1340 (1971).

[83] *M. von Ardenne, K. Steinfelder, R. Tümmler:* Elektronenanlagerungsmassenspektrographie organischer Substanzen, Springer, Berlin 1971.

[84] *H. Budzikiewicz, Ch. Horstmann, K. Pufahl, K. Schreiber,* Chem. Ber. *100,* 2798 (1967).

[85] *D. Voigt, G. Adam, J. Schmidt, K. Schreiber,* Org. Mass Spectrom. *12,* 169 (1977); *D. Voigt, G. Adam, P. Franke, ibid. 15,* 587 (1980).

[86] *D. Voigt, J. Schmidt,* Biomed. Mass Spectrom. *5,* 44 (1978).

[87] *D. Voigt, H. Lehmann,* J. Prakt. Chem. *321,* 243 (1979).

[88] *G. Adam, D. Voigt, K. Schreiber, M. von Ardenne, K. Tümmler, K. Steinfelder,* J. Prakt. Chem. *315,* 125 (1973).

[89] *W. J. Richter, H. Schwarz,* Angew. Chem. *90,* 449 (1978); Angew. Chem. Int. Ed. Engl. *17,* 424 (1978).

[90] *R. E. Mather, J. F. J. Todd,* Int. J. Mass Spectrom. Ion Phys. *30,* 1 (1979).

[91] *K. L. Busch,* Å. Norström, M. M. Bursey, *J. R. Hass, C. A. Nilsson,* Biomed. Mass Spectrom. *6,* 157 (1979).

[92] *A. K. Ganguly, N. F. Cappuccino, H. Fujiwara, A. K. Bose,* J. Chem. Soc. Chem. Commun. *1979,* 148.

[93] *A. K. Bose, H. Fujiwara, B. N. Pramanik,* Tetrahedron Lett. *1979,* 4017.

[94] *R. C. Dougherty, J. Dalton, F. J. Biros,* Org. Mass Spectrom. *6,* 1171 (1972).

[95] *R. C. Dougherty, J. D. Roberts, F. J. Biros,* Justus Liebigs Ann. Chem. *47,* 54 (1975).

[96] *K. L. Busch, J. R. Hass, M. M. Bursey,* Org. Mass Spectrom. *13,* 604 (1978).

[97] *D. F. Hunt, G. C. Stafford, F. W. Crow, J. W. Russel,* Anal. Chem. *48,* 2058 (1976).

[98] *R. Ryhage, H. Brandenberger,* Biomed. Mass Spectrom. *5,* 615 (1978).

[99] *H. Brandenberger, R. Ryhage,* Recent Dev. Mass Spectrom. Biochem. Med. *1,* 327 (1978).

[100] *H. Brandenberger,* Recent Dev. Mass Spectrom. Biochem. Med. *2,* 227 (1979).

[101] *D. F. Hunt,* Finnigan Spectra *6,* No. 1. (1976).

[102] *T. M. Harvey,* Ph. D. Thesis, University of Virginia (University Microfilms, Ann Arbor, Michigan, No. 75-28067).

[103] *H. P. Tannenbaum, J. D. Roberts, R. C. Dougherty,* Anal. Chem. *47,* 49 (1975).

[104] *F. J. Winkler, D. Stahl,* J. Am. Chem. Soc. *101,* 3685 (1979).

[105] *C. H. DePuy, V. M. Bierbaum, L. A. Flippin, J. J. Grabowski, G. K. King, R. J. Schmitt,* J. Am. Chem. Soc. *101,* 6443 (1979).

[106] *E. Baumgartner, J. G. Dillard,* Org. Mass Spectrom. *14,* 360 (1979).

[107] *D. F. Hunt, T. M. Harvey, J. W. Russel,* J. Chem. Soc. Chem. Commun. *1975,* 151.

[108] *D. F. Hunt, Ch. N. McEwen, T. M. Harvey,* Anal. Chem. *47,* 1730 (1975).

[109] *A. L. C. Smit, F. H. Field,* J. Am. Chem. Soc. *99,* 6471 (1977).

[110] *J. R. Lloyd, W. C. Agosta, F. H. Field,* J. Org. Chem. *45,* 1614 (1980).

[111] *J. H. J. Dawson, A. J. Noest, N. M. M. Nibbering,* Int. J. Mass Spectrom. Ion Phys. *30,* 189 (1979).

[112] *J. H. J. Dawson, Th. A. M. Kaandorp, N. M. M. Nibbering,* Org. Mass Spectrom. *12,* 330 (1977).

[113] *J. H. J. Dawson, N. M. M. Nibbering,* Int. J. Mass Spectrom. Ion Phys. *33,* 3 (1980).

[114] *A. P. Bruins, A. J. Ferrer-Correira, A. G. Harrison, K. R. Jennings, R. K. Mitchum,* Adv. Mass Spectrom. *7,* 355 (1978).

[115] *C. Kajdas,* Rocz. Chem. *45,* 1771 (1971).

[116] *C. H. DePuy, V. M. Bierbaum, G. K. King, R. H. Shapiro,* J. Am. Chem. Soc. *100,* 2921 (1978).

[117] *F. J. Winkler, D. Stahl,* J. Am. Chem. Soc. *100,* 6779 (1978).

[118] *T. A. Roy, F. H. Field, Y. Y. Lin, L. L. Smith,* Anal. Chem. *51,* 272 (1979).

[119] *L. W. Siek,* Chem. Br. *16,* 38 (1980).

[120] *D. F. Hunt, F. W. Crow,* Anal. Chem. *50,* 1781 (1978).

[121] *G. Klass, J. H. Bowie,* Aust. J. Chem. *30,* 1249 (1977); *C. V. Bradley, I. Howe, J. H. Beynon,* Biomed. Mass Spectrom. *8,* 85 (1981).

[122] *J. H. Bowie, Th. Blumenthal,* Aust. J. Chem. *29,* 115 (1976); *J. E. Szulejko, I. Howe, J. H. Beynon,* Int. J. Mass Spectrom. Ion Phys. *37,* 27 (1981).

[123] *T. Keough, J. H. Beynon, R. G. Cooks,* J. Am. Chem. Soc. *95,* 1695 (1973).

[124] *E. C. Horning, D. I. Carrol, I. Dzidic, S.-N. Lin, R. N. Stillwell, J.-P. Thenot,* J. Chromatogr. *142,* 481 (1977); cf. also *T. W. Carr,* Anal. Chem. *49,* 828 (1977).

[125] *M. A. Posthumus, P. G. Kistemaker, H. L. C. Meuzelaar, M. C. Ten Noever de Brauw,* Anal. Chem. *50,* 985 (1978).

[126] *A. Benninghoven* in *H. S. Hertz, S. N. Chesler:* Trace Organic Analysis, U. S. Department of Commerce, Washington, D.C., 1979, p. 627, see also *A. Eicke, W. Sichtermann, A. Benninghoven,* Org. Mass Spectrom. *15,* 289 (1980); *L. K. Lin,* S. U. Unger, *R. G. Cooks,* Tetrahedron *37,* 1067 (1981).

[127] *R. D. McFarlane* in *G. R. Waller, O. C. Dermer:* Biochemical Applications of Mass Spectrometry, 1. Suppl. Vol., Wiley, New York 1980, p. 1209; see also *B. Schueler, F. R. Krueger,* Org. Mass Spectrom. *15,* 295 (1980).

[128] *K. H. Ott, F. W. Röllgen,* J. J. Zwinselman, R. N. Fokkens, N. M. M. Nibbering, Org. Mass Spectrom. *15,* 419 (1980), and references cited therein.

[129] *S. Pignataro,* Chim. Ind. (Milan) *57,* 25 (1975).

[130] *Ch. E. Melton* in *G. R. Waller:* Biochemical Applications of Mass Spectrometry, Wiley, New York 1972, Chap. 28.

[131] *J. G. Dillard* in *G. R. Waller, O. C. Dermer:* Biochemical Applications of Mass Spectrometry, 1. Suppl. Vol., Wiley, New York 1980, Chap. 28.

[132] Mass Spectrometry, Specialist Periodical Rep., Chem. Soc., London, also always contains short sections on the newest aspects of NI mass spectrometry.

[133] *D. Voigt, G. Adam, W. Schade,* Org. Mass Spectrom. *16,* 85 (1981).

[134] *S. Hunek, J. Schmidt,* Biomed. Mass Spectrom. *7,* 301 (1980).

[135] *S. R. Prescott, J. E. Campana, T. H. Risby,* Anal. Chem. *49,* 1501 (1977).

[136] *D. R. Dakternieks, I. W. Fraser, J. L. Garnett, I. K. Gregor, M. Guilhaus,* Org. Mass Spectrom. *15,* 556 (1980).

[137] *R. C. Dougherty, J. D. Wander,* Biomed. Mass Spectrom. *7,* 401 (1980).

[138] *T. H. Risby,* Environ. Health Perspect. *36,* 39 (1980).

[139] *K. L. Bush, C. E. Parker, D. J. Harvan, M. M. Bursey, J. R. Hass,* Appl. Spectrosc. *35,* 85 (1981).

[140] *Ch. N. McEwen, M. A. Rudat,* J. Am. Chem. Soc. *101,* 6470 (1979).

[141] *I. I. Furley, V. N. Odinikov, V. I. Khvostenko, G. A. Tolstikov, N. Ya. Grigoreva, I. M. Avrutov,* Izv. Akad. Nauk SSSR, Ser. Khim. *1981,* 330.

[142] *V. I. Khvostenko, E. G. Galkin, U. M. Dzemilev, G. A. Tolstikov, V. C. Falko,* Izv. Akad. Nauk SSSR, Ser. Khim. *1980,* 1663.

[143] *J. R. Lloyd, W. C. Agosta, F. H. Field,* J. Org. Chem. *45,* 3483 (1980).

[144] *B. Schueler, F. R. Krueger,* Org. Mass Spectrom. *15,* 295 (1980).

[145] Cf. manufacturer's brochure: Kratos Data Sheet for MS30 (1977).

[146] *A. P. Bruins,* Adv. Mass Spectrom. *8,* 246 (1980).

[147] *A. P. Bruins,* Biomed. Mass Spectrom. *8,* 31 (1981).

[148] *J. L. Gower, C. Beaugrand, C. Sallot,* Biomed. Mass Spectrom. *8,* 36 (1981).

[149] *M. Anbar, G. A. St. John,* J. Am. Chem. Soc. *97,* 7195 (1975).

[150] *K. G. Heumann, F. Beer, R. Kifmann,* Talanta *27,* 567 (1980) and references cited therein.

[151] *K. G. Heumann, K. Baier, F. Beer, R. Kifmann, W. Schindlmeier,* Adv. Mass Spectrom. *8,* 318 (1980).

[152] *K. G. Heumann,* Toxicol. Environ. Chem. Rev. *3,* 111 (1980).

[153] *T. Higuchi, E. Kubota, F. Kunihiro, Y. Hagaki,* Adv. Mass Spectrom. *8,* 1061 (1980).

[154] *K. H. Ott, F. W. Röllgen, J. J. Zwinselman, R. H. Fokkens, N. M. M. Nibbering,* Angew. Chem. *93,* 96 (1981); Angew. Chem. Int. Ed. Engl. *20,* 111 (1981); see also *J. J. Zwinselmann, R. H. Fokkens, N. M. M. Nibbering, K. H. Ott, F. W. Röllgen,* Org. Mass Spectrom; in press (1981); *K. H. Ott, F. W. Röllgen, P. Dähling, J. J. Zwinselmann, R. H. Fokkens, N. M. M. Nibbering,* Org. Mass Spectrom. in press (1981).

[155] *E. A. Bergner, R. C. Dougherty,* Biomed. Mass Spectrom. *8,* 204, 208 (1981).

[156] *L. V. Jones, M. J. Whitehouse,* Biomed. Mass Spectrom. *8,* 231

[157] *A. J. Noest, N. M. M. Nibbering,* Adv. Mass Spectrom. *8,* 227 (1980).

[158] *G. Boand, R. Houriet, T. Gäumann,* Adv. Mass Spectrom. *8,* 238 (1980).

[159] *J. R. Hass, M. D. Friesen, D. J. Harvan, C. E. Parker,* Anal. Chem. *50,* 1474 (1978).

[160] *A. P. Bruins,* Anal. Chem. *51,* 967 (1979).

[161] *H. J. Heinen,* Int. J. Mass Spectrom. Ion Phys. *38,* 309 (1981).

[162] *D. Wecker, A. A. Christodoulides, R. N. Schindler,* Int. J. Mass Spectrom. Ion Phys. *38,* 391 (1981).

[163] N. B. H. Henis, K. L. Busch, M. M. Bursey, Inorg. Chimica Acta *53,* L 31 (1981).

[164] For a review on mechanistic studies by ion cyclotron resonance spectroscopy see: *N. M. M. Nibbering,* Recl. Trav. Chim. Pays-Bas, in press (1981).

# Structure and Decay of Gaseous Organic Radical Cations Studied by Their Radiative Decay, Exemplified by the 1,3-Pentadiyne Cation

By John P. Maier[*]

*Dedicated to Professor Edgar Heilbronner on the occasion of his 60th birthday*

The radiative decay of over a hundred open-shell organic radical cations has now been established. As a result, the spectral structure of such cations in their ground and excited electronic states can be probed with resolutions of the order of $\leqslant 1\ \mathrm{cm}^{-1}$. This is achieved by means of emission and laser-induced fluorescence techniques. The analysis of the emission and excitation spectra provides the vibrational frequencies of many of the totally symmetric fundamentals of the cations in the two electronic states. In order to study the relaxation behavior of these cations under "isolated conditions", the lifetimes and fluorescence quantum yields can be obtained by means of photoelectron-photon coincidence measurements. These data yield the radiative and non-radiative rate constants as a function of the internal energy of the cations. The structural and decay information obtained from each of these techniques is illustrated using the 1,3-pentadiyne radical cation as example.

## 1. Introduction

Molecular ions have attracted a great deal of interest in the past decade. This has arisen with the realization of their importance in various environments and physicochemical phenomena. These include stellar, cometary and interstellar media as well as plasma, laser and radiation chemistry[1]. The application of spectroscopic methods enables the species to be identified and, for example, the physical conditions (*e.g.* temperature, particle densities) prevailing in the medium to be inferred. Furthermore, the dynamic aspects (*e.g.* radiative lifetimes, collision-cross-sections) are essential for the quantitative evaluation of the pertinent chemical processes. A good example of these aspects is the key role ions and ion-molecule reactions appear to play in interstellar space[2], producing large organic species (*e.g.* cyanopolyacetylenes)[3].

For all these investigations and evaluations, the spectroscopic structure and relaxation behavior of ions have to be well characterized in the laboratory. The knowledge acquired for polyatomic species is, however, still nevertheless scarce. The present article deals with our contributions in obtaining the spectroscopic and relaxation data for open-shell organic cations.

Open-shell, or radical cations of organic molecules in the gas phase have, for some time, only been experimentally accessible by mass-spectroscopic techniques. In the latter, however, neither the internal energy nor the state of the cations can usually be specified. The first generally applicable technique to provide a detailed insight into the energetics and electronic structure of radical cations was photoelectron (PE) spectroscopy[4]. By means of this technique ionization energies leading to the doublet states of radical cations, which could be reached in the photoionization process, can be measured. An example of this is given in Figure 1, which shows how the ground and lowest excited states of an organic cation are located with respect to the ground state of the molecular species. These results can be viewed on two levels; simply as a means of locating the doublet cationic states $^2\tilde{X}$ (ground), $^2\tilde{A}$ (first excited state), $^2\tilde{B}$, $^2\tilde{C}$..... $^2\tilde{J}$..... (*i.e.* successive excited states) or the symmetry of the states can be deduced as well, by associating each with a configuration based on the molecular orbital description. These aspects have been extensively discussed and reviewed[5].

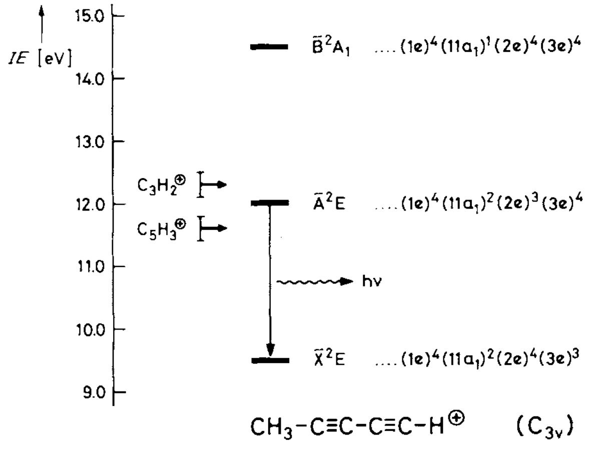


Fig. 1. Location and assignments of the lowest doublet electronic states of the 1,3-pentadiyne radical cation (under assumed $C_{3v}$ symmetry) taken from the PE study [14]. Adiabatic ionization energies (I.E.) are used. The appearance potentials of the $C_5H_3^{\oplus}$ and $C_3H_2^{\oplus}$ fragment-ions are also indicated [19]. The detected radiative decay of the 1,3-pentadiyne cation enables the $\tilde{X}^2E$ and $\tilde{A}^2E$ states to be probed in detail using the techniques described in the text.

In order to observe the finer spectroscopic structure, and to follow the relaxation dynamics of such radical cations under collision-free conditions, other approaches, or tech-

---

[*] Dr. J. P. Maier
Physikalisch-Chemisches Institut der Universität
Klingelbergstrasse 80, CH-4056 Basel (Switzerland)

0570-0833/81/0808-0638 $ 02.50/0

niques, had to be developed or applied. These invariably involve the absorption or emission of electromagnetic radiation. Historically the most important high resolution technique for molecular systems[6] and radicals[7] was emission spectroscopy. This is also the case for di- and triatomic cations[8]. With the advent of tunable lasers alternative methods, often leading to even finer details, have flourished.

Complementary studies on polyatomic organic radical cations in the gas phase are only now beginning to follow. The purpose of this article is to present an overview of the structural and dynamic data that is obtained from methods relying on the radiative decay of such electronically excited cations[9]. The techniques used are emission, laser-induced excitation and photoelectron-photon coincidence spectroscopy[10].

Emission (or fluorescence) spectroscopy is one of the oldest techniques for molecular structure investigations, whereby photons emitted following electron impact, as in a discharge tube (or photon impact excitation), are wavelength dispersed while their intensity is measured[8].

In the laser-induced fluorescence technique on the other hand, the wavelength of a tunable narrow bandwidth light source (dye-laser) is scanned and the excitation spectra are obtained by monitoring the resultant fluorescence[11]. The latter is detected, provided the exciting laser wavelength coincides with a molecular transition (*i.e.* resonance) and the excited species decays radiatively. Thus, the technique is specific and the resolution is given by the bandwidth of the laser. In addition it is rather sensitive, since ion densities of $10^6-10^9$ cm$^{-3}$ are adequate for such measurements. The photoelectron-photon coincidence method[12] is also specific, as it is partly based on the principle of PE spectroscopy and selects the internal energy of an electronically excited cation. If such a "prepared" cation decays by emission of a photon, this will yield a true coincidence if the sampled electron and photon both originate from the same level and from the same cation.

Table 1. Summary of the characteristics of the three techniques used to study the structure and decay of radical cations in the gas phase.

| Technique | Information | Resolution |
|---|---|---|
| Electron impact induced emission spectroscopy | Ground state vibrational frequencies, rotational structure, lifetimes of lowest levels of excited states | 0.004 nm<br>6 ns |
| Laser-induced fluorescence spectroscopy | Excited state vibrational frequencies, rotational structure, lifetimes of excited state levels | 0.02 or 0.002 nm<br>5 ns |
| Photoelectron-photon coincidence spectroscopy | Fluorescence quantum yields and cascade-free lifetimes of excited state levels. | 50-100 meV<br>10-15 ns |

Table 1 summarizes the information provided by these measurements, as well as the energy and time characteristics of the techniques. As can be seen for the cations decaying radiatively, the structure of the two electronic states involved in the transition ($^2\tilde{X}$ and $^2\tilde{A}$ or $^2\tilde{B}$) can be probed with a resolution $10^2-10^3$ better than can be achieved with PE spectroscopy, because photons can be wavelength-selected much more precisely than it is possible to energy-analyze photoelectrons. On the other hand, the coincidence determinations are necessarily carried out with lower resolution because electron energies have to be analyzed. The essence of the coincidence experiment is that the energy of the outgoing photoelectron serves to define the internal energy of the cation. Since the electrons and photons can be individually counted, absolute measurements of fluorescence quantum yields of radical cations in selected vibrational levels are possible.

The starting point of such studies was the search for the radiative decay of electronically excited radical cations, because prior to 1973 only a handful of open-shell triatomic radical cations[8] and the butadiyne radical cation[13] were known to yield emission spectra. Thus, in our earliest experiments, the emission spectra of organic radical cations were studied using an electron beam apparatus. As a result, the emission spectra of over a hundred such cations have now been reported[9, 10]. In all cases, the band systems were assigned to the $^2\tilde{A}$(or $^2\tilde{B}$)$\rightarrow$$^2\tilde{X}$ electronic transitions of these cations on the basis of their PE spectra, and lie in the 300—800 nm wavelength region.

Table 2. Main classes of organic radical cations found to decay radiatively: $\tilde{A}$ (or $^2\tilde{B}$)$\rightarrow$$^2\tilde{X}$. For a complete listing see [10].

| | |
|---|---|
| $X-C\equiv NNQ^{\oplus}$<br>$X-C\equiv C-H^{\oplus}$<br>$X-C\equiv C-X^{\oplus}$ | X = Cl, Br, I |
| $X(C\equiv C)_2H^{\oplus}$ | X = Cl, Br, I, CN, $CH_3$, $C_2H_5$ |
| $X(C\equiv C)_2X^{\oplus}$ | X = Cl, Br, I, CN, F, $CF_3$, $C_2H_5$ |
| $H_3C-C\equiv C-X^{\oplus}$ | X = Cl, Br, CN |
| $H_3C(C\equiv C)_2X^{\oplus}$ | X = Cl, Br, CN, $CH_3$, H |
| $H(C\equiv C)_nH^{\oplus}$ | n = 2, 3, 4 |
| $H(CH=CH)_nH^{\oplus}$ | n = 3, 4 |
| Fluorobenzenes$^{\oplus}$, Chlorobenzenes$^{\oplus}$, Chlorofluorobenzenes$^{\oplus}$, Bromofluorobenzenes$^{\oplus}$, Fluorophenols$^{\oplus}$ | |

Table 2 summarizes the main classes of organic cations which undergo radiative decay. Rather than try to present a comprehensive review of the emission, laser-induced fluorescence and photoelectron-photon coincidence studies of radical cations, the 1,3-pentadiyne cation (and its deuterated derivatives) will be taken as an example. This will serve to illustrate the structural and decay data that can at present be obtained.

## 2. Electronic States

The electronic states of the 1,3-pentadiyne radical cation were first investigated by *Heilbronner et al.* using He(Iα) PE spectroscopy[14]. The bands were attributed to various ionization processes by means of which a link to the molecular orbital description of 1,3-pentadiyne was established. This is summarized in Figure 1, where the measured energetic data for the lowest electronic states of 1,3-pentadiyne cation, their symmetries and corresponding configurations are depicted. The configurations shown are those which, by far, dominate these lowest electronic states. On the other hand at higher levels in the energy manifold such a simple description is often inadequate, as configurational interaction can be considerable. A consequence of this is the appearance of additional PE bands in the higher valence ionization region[15].

It should again be pointed out that the labelling

$^2\tilde{X}, {}^2\tilde{A}, {}^2\tilde{B}, \ldots {}^2\tilde{J} \ldots\ldots$

of the states of radical cations, inferred in conjunction with the PE spectral data, is not entirely a true sequence of the doublet states. The "non-Koopmans' states", *i.e.* those differing in the location of two electrons from the molecular ground state configuration, are usually not accessible by the photoionization process. The lowest of these may, in favorable cases, be located using techniques such as matrix absorption-[16] or photodissociation-[17] spectroscopy where the cation in its ground state is the absorbing species. Nevertheless, the $^2\tilde{A}$ state of organic radical cations labelled according to their photoelectron spectra is, with a few exceptions, the lowest excited electronic state. The corresponding quartet states of organic radical cations

$^4\tilde{a}, {}^4\tilde{b}, {}^4\tilde{c}, \ldots {}^4\tilde{j} \ldots\ldots$

have, to date, not been experimentally located; however, in most cases the lowest state of this multiplicity, $^4\tilde{a}$, is expected to lie energetically above that of $^2\tilde{A}$, having a similar geometry to the cationic ground state.

Further structural information suggested by the PE spectrum of 1,3-pentadiyne is that the linear configuration of the carbon atoms is probably retained for the $\tilde{X}^2E$ and $\tilde{A}^2E$ cationic states. This is based on the Franck-Condon profile of the first two bands (cf. Fig. 2) for which the adiabatic, $(0_0^0)$, transitions are intense. On the basis of the separation of the ionization energies leading to the $\tilde{X}^2E$ and

$$H_3C{-}C{\equiv}C{-}C{\equiv}C{-}H^{\oplus}\ \tilde{A}^2E \longrightarrow \tilde{X}^2E(C_{3v})$$

$\tilde{A}^2E$ states, the emission band system detected on electron impact excitation of 1,3-pentadiyne could be identified as the electronic transition of its radical cation[18]. The radiative decay is manifested in spite of the fact that the $C_5H_3^{\oplus}$ fragment ion appearance potential lies about 0.5 eV below the lowest level of the $\tilde{A}^2E$ state (cf. Fig. 1)[19].

## 3. Vibrational Frequencies

In this section the vibrational structural data which can be deduced from the emission and laser-induced excitation spectra of radical cations in their $^2\tilde{X}$ and $^2\tilde{A}$ (or $^2\tilde{B}$) states will be discussed. Previously, the only source of vibrational frequencies of organic cations in the gas phase has been PE spectroscopy[4], and in a few cases photoionization mass spectroscopy or spectroscopy of Rydberg states[20]. These techniques, however, provide only a few values for larger organic cations and are of limited accuracy. To illustrate these aspects, a "high resolution" recording (electron band pass of 160 cm$^{-1}$) of the first two photoelectron bands of 1,3-pentadiyne is reproduced in Figure 2. Discernible are vibrational peaks corresponding to the excitation of two, and three, modes of the $\tilde{X}^2E$ and $\tilde{A}^2E$ cationic states, respectively. The accuracy of the frequencies deduced from such measurements is, at best, ±40 cm$^{-1}$. The inferred values are included in Table 3, where they can be compared with the emission and excitation data.

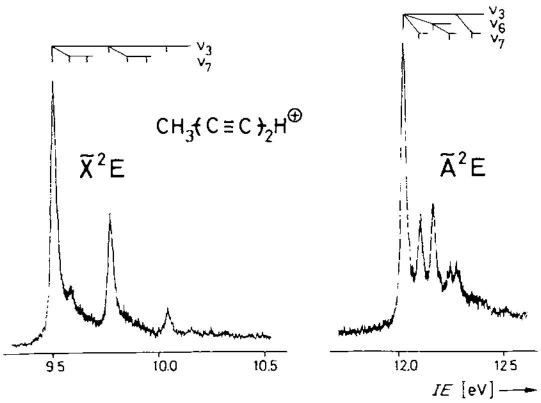


Fig. 2. The first two bands in the He(Iα)-PE spectrum of 1,3-pentadiyne recorded with a band pass of ≈20 meV. A vibrational assignment is indicated (cf. Table 3).

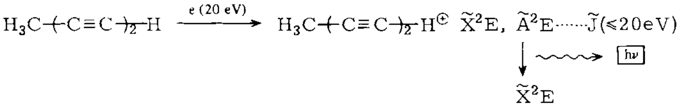
### 3.1. Emission Spectra

The emission spectra of the 1,3-pentadiyne cation and of its three deuterated derivatives are shown in Figure 3.

Table 3. Vibrational frequencies of the totally symmetric fundamentals ($A_1$) of the 1,3-pentadiyne and of 5,5,5-trideutero-1,3-pentadiyne cations (under $C_{3v}$ classification) in their $\tilde{X}^2E$ and $\tilde{A}^2E$ states, inferred from their emission (em) and excitation (ex), spectra; values ±10 cm$^{-1}$. The PE spectral (PE) values are ±40 cm$^{-1}$. The ground molecular state frequencies and the approximate description of the modes are taken from [22].

| Species | State | $\nu_1$ $\nu(\equiv C{-}H)$ | $\nu_2$ $\nu_s(CH_3)$ | $\nu_3$ $\nu(C{\equiv}C_c)$ | $\nu_4$ $\nu(C{\equiv}C_H)$ | $\nu_5$ $\delta(CH_3)$ | $\nu_6$ $\nu_a(C{-}C)$ | $\nu_7$ $\nu_s(C{-}C)$ | $\nu_{13}$ $\delta(CCC)$ |
|---|---|---|---|---|---|---|---|---|---|
| $H_3C(C{\equiv}C)_2H$ | $X^1A_1$ | 3316 | 2919 | 2257 | 2072 | 1375 | 1152 | 686 | 320 |
| $H_3C(C{\equiv}C)_2H^{\oplus}$ | $\tilde{X}^2E$ | | | | | | | | |
| | em | | | 2205 | | 1340 | 1190 | 685 | 320 |
| | ex | | | | | | | 695 | 325 |
| | PE | | | 2160 | | | | 650 | |
| | $\tilde{A}^2E$ | | | | | | | | |
| | ex | | | 2135 | 2000 | 1270 | 1130 | 665 | 305 |
| | em | | | | | | 1140 | 670 | 305 |
| | PE | | | | 2000 | | 1140 | | |
| $D_3C(C{\equiv}C)_2H$ | $X^1A_1$ | 3315 | 2113 | 2252 | 2071 | 1023 | 1182 | 652 | 308 |
| $D_3C(C{\equiv}C)_2H^{\oplus}$ | $\tilde{X}^2E$ | | | | | | | | |
| | em | | | 2205 | | 1025 | 1210 | 645 | 305 |
| | ex | | | | | | | 650 | 305 |
| | $\tilde{A}^2E$ | | | | | | | | |
| | ex | | | 2180 | 1990 | 980 | 1160 | 620 | 285 |
| | em | | | | | | | 630 | 290 |

These spectra were recorded with an optical resolution of 7 $cm^{-1}$ using a crossed electron sample beam apparatus[18]. Using this apparatus, the radical cations are produced under clean and reasonably well-defined conditions. A collimated electron beam of chosen energy is directed at an effusive sample beam entering the interaction region at right angles to it, and the sample is efficiently removed by means of a liquid nitrogen trap. In the case of the 1,3-pentadiynes, the electron beam energy was tuned to about 20 eV, which in general is an advantageous energy range for the ionization cross section and yet the excitation of fragments is still not overwhelming. Thus, the various accessible states of the 1,3-pentadiyne cation are produced, *e.g.*:



$$H_3C\text{-}(C\equiv C)_2\text{-}H \xrightarrow{e\,(20\,eV)} H_3C\text{-}(C\equiv C)_2\text{-}H^{\oplus}\ \tilde{X}^2E,\ \tilde{A}^2E\cdots\cdots\tilde{J}(\leq 20\,eV)$$

$$\downarrow \rightsquigarrow \boxed{h\nu}$$

$$\tilde{X}^2E$$

as well as excited molecular states of 1,3-pentadiyne, and of some of its fragments (*e.g.* $C_2^*$, CH*, H*) as a result of inelastic electron processes. The photons emitted from the ionization region are wavelength-dispersed and detected by a single photon counting technique. Computerized on-line data acquisition is used[21].

The primary information that can be inferred from the structure of the emission spectra, such as shown in Figure 3, are vibrational frequencies, mainly the totally symmetric modes of the cationic ground states. Usually these can be obtained with an accuracy of 5—10 $cm^{-1}$, limited usually by the width of the bands. In addition, when the resolution is reduced to about 1 $cm^{-1}$, or better, the bands are often split into sub-bands, which are usually attributed to sequence transitions. Excited vibrational levels in the $^2\tilde{A}$ states are known to decay radiatively, in view of the excitation spectra and the photoelectron-photon coincidence measurements *(vide infra).*

In the 1,3-pentadiyne cation, excitation of four of the totally symmetric fundamentals, $A_1$ (under $C_{3v}$ symmetry classification), in the $\tilde{X}^2E$ state is indicated from the emission spectra (Fig. 3). In addition, a degenerate mode ($\nu_{13}$) is doubly excited.

The assignment of most of the intense bands of the emission band systems is shown in Figure 3. The numbering of the fundamentals follows the ground state molecular values[22] given in Table 3. Most of the assignments are to transitions from the lowest vibrational level of the $\tilde{A}^2E$ state to the various excited levels in the $\tilde{X}^2E$ state, which possess $A_1$ symmetry. A few bands are also observed at higher energy than the $0_0^0$ bands, the emitting levels corresponding to the excitation of the $\nu_5$-, $\nu_6$- and $\nu_7$-modes in the $\tilde{A}^2E$ electronic state. The study of the isotopically labeled derivatives serves as a means of corroborating the assignments, as is usual in other forms of spectroscopy. The inferred vibrational frequencies for the 1,3-pentadiyne and 5,5,5-trideuterio-1,3-pentadiyne cations are summarized in Table 3.

In a similar fashion, the ground state vibrational frequencies of many of the cations listed in Table 2 have been obtained. For the smallest, or high symmetry species, the frequencies of all the totally symmetric modes could often be inferred. In contrast, for the largest, or low symmetry species, the number of vibrations that can be excited is large but usually only a few of the modes are strongly excited.

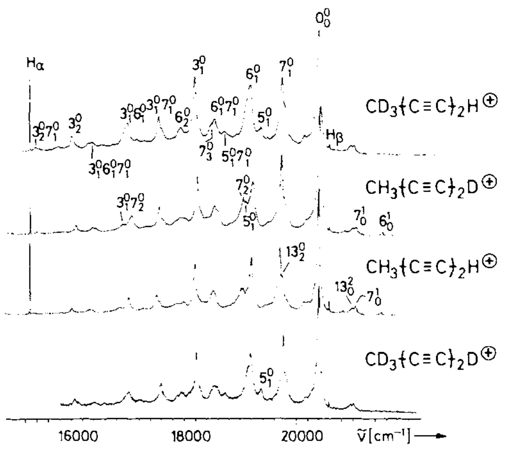


Fig. 3. The $\tilde{A}^2E \rightarrow \tilde{X}^2E$ emission band system of the 1,3-pentadiyne radical cation recorded with an optical resolution of 0.16 nm. The vibrational assignment of the bands was made using the numbering in Table 3.

### 3.2. Laser-Induced Excitation Spectra

One method of obtaining the complementary vibrational frequency data for the cations in their excited electronic states is *via* their absorption or excitation spectra. Although the primary excitation process in the absorption and excitation techniques is the same, the principle of monitoring the induced changes differs. In the absorption experiment the change in intensity of the incident light is measured, whereas for the excitation spectra the total (*i.e.* wavelength-undispersed) fluorescence is detected. Consequently, the latter technique is much more sensitive but depends on the excited species decaying radiatively. The relative intensities of the bands in the absorption and excitation spectra will naturally differ but the same spectroscopic information (vibrational, or rotational) is available.

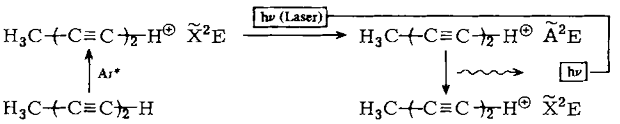
As yet, absorption spectra of organic radical cations in the gas phase have not been measured due to the inherently low densities associated with their generation. However, the excitation spectra can be obtained for the radical cations which relax by emission of photons (cf. Table 2) even at low cation concentrations because of the availability of tunable dye-lasers.

The laser-induced fluorescence technique is well established for spectroscopic studies on molecular systems[23], but only in recent years has its application to cations evolved. The technique was first applied to the $N_2^+$ cation[24], and since then has been used to probe a few of the organic radical cations whose radiative decay has been observed (Table 2)[25]. Table 4 summarizes the results obtained to date on the organic cations investigated by this approach, usually using a laser bandwidth of the order of 1 $cm^{-1}$. A large part of the effort has been devoted to the study of Jahn-Teller effects (*i.e.* of the spectroscopic consequences of the removal of the degeneracy of electronic states, which according to the Jahn-Teller theorem, are inherently unstable) in the ground states of the hexafluoro-, 1,3,5-trifluoro-, and 1,3,5-trichlorobenzene cations[29,30]. Conventional high resolution emission spectroscopy has also been applied to the latter problem[33].

Table 4. Organic radical cations studied by the laser-induced fluorescence technique in the gas phase. The isotopic species are not listed.

| Cation | | Ref. |
|---|---|---|
| $Cl{+}C{\equiv}C{+}X^{\oplus}$ | X = H, Cl | [26] |
| $H_3C{+}C{\equiv}C{+}_2H^{\oplus}$ | | [27] |
| $H_3C{+}C{\equiv}C{+}_2CH_3^{\oplus}$ | | [27, 28] |
| Fluorobenzenes$^{\oplus}$ | | [29] |
| 1,3,5-trichlorobenzene$^{\oplus}$ | | [30] |
| 1,3,5-trichlorotrifluorobenzene$^{\oplus}$ | | [31] |
| Fluorophenols$^{\oplus}$ | | [32] |

The laser-induced excitation spectra of the $\tilde{A}^2E \leftrightarrow \tilde{X}^2E$ transition of the cations of 1,3-pentadiyne and of 5,5,5-trideuterio-1,3-pentadiyne are reproduced in Figure 4[27]. The process whereby the spectra are obtained is shown in Scheme 1.



Scheme 1

In essence, the apparatus used to record the spectra consists of a source of rare gas metastables which on collision with the sample molecules yield the molecular radical cations (*i.e.* Penning ionization), a nitrogen pumped dye-laser, a detection system and on-line data accumulation. The latter consists of a micro-computer controlled transient digitizer which samples the photo-multiplier signals[27]. Thus, the total fluorescence is monitored as a function of the laser wavelength, which is driven by the computer. The spectra shown consist of three separate recordings using appropriate dye solutions. Due to the relatively high pressure of the rare gas carrier, the radical cations formed in the Penning ionization process are thermalized by collisions. By this means, a sufficient concentration of radical cations in the lowest vibrational level of the $\tilde{X}^2E$ state is produced.

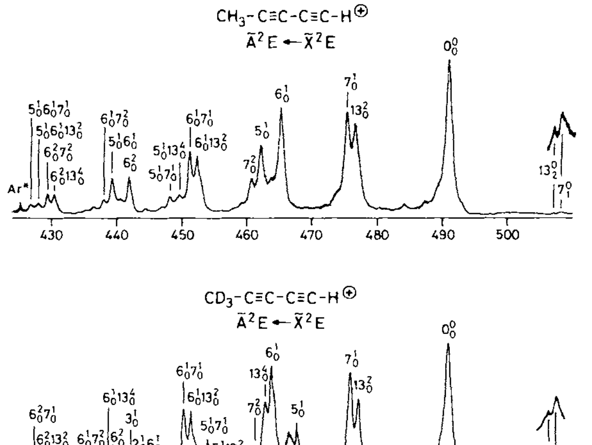


Fig. 4. The $\tilde{A}^2E \leftrightarrow \tilde{X}^2E$ laser-induced excitation spectra of 1,3-pentadiyne and 5,5,5-trideuterio-1,3-pentadiene radical cations recorded with a 0.02 nm bandwith. The vibrational numbering of the assigned bands corresponds to the modes listed in Table 3.

Analysis of the excitation spectra of the 1,3-pentadiyne cations (Fig. 4) yields the vibrational frequencies of five $A_1$ modes, as well as of the $\nu_{13}$ mode of the excited state. The sequence bands are not resolved, though asymmetry for most of the bands is apparent.

The inferred vibrational frequencies are also given in Table 3. Thus, sets of frequency values are available for these radical cations in the $\tilde{X}^2E$ and $\tilde{A}^2E$ states, and can be compared to the molecular state values. The respective changes can in turn be related to the molecular orbital description of the structure (cf. Fig. 1) as the electrons are removed from orbitals of different nodal characteristics. The $\tilde{X}$ and $\tilde{A}$ cationic states are generated by removal of electrons from π-molecular orbitals, $2e^{-1}$ and $1e^{-1}$, which are antibonding and bonding between the triple bands, respectively[14]. These features are reflected to an extent in the changes in frequencies of the various vibrations (cf. Table 3).

## 4. Non-Radiative Decay

The preceding sections have been concerned with structural aspects of radical cations which have become accessible using the described spectroscopic techniques. The dynamic features, that is the relaxation behavior of electronically excited radical cations under collision-free conditions, will now be briefly considered. The discussion is restricted to those cations decaying radiatively, albeit that the numerous studies of cations which do not reveal a detectable radiative relaxation provide ancillary information about the rates of the non-radiative decay pathways. The implications of such "negative" observations have already been previously summarized[9].

The non-radiative pathways open to organic radical cations in their lowest excited electronic states are internal conversion, $[^2\tilde{A} \rightsquigarrow {}^2\tilde{X}]$, isomerization and fragmentation $[^2\tilde{A} \rightsquigarrow \cdots \rightarrow F_1^{\oplus}, F_2^{\oplus} \ldots]$ if the latter are allowed energetically. In the majority of cations listed in Table 1, only the radiative and internal conversion channels to the $^2\tilde{X}$ state are accessible. Fragmentation thresholds usually lie higher in energy[34] (but for exceptions see Section 4.2), as do the lowest states of higher multiplicity, $^4\tilde{a}$, as discussed earlier. Thus, the study of the internal conversion process is simpler than with molecular species, for which the $S_1 \rightsquigarrow T_1$ (intersystem crossing) process is always a competing, and sometimes dominant decay process[35]. Furthermore, for molecular systems the determinations of absolute fluorescence quantum yields are fraught with difficulties, relying on comparison with suitable standards and careful calibration of the apparatus[36]. In contrast, flourescence quantum yields, $\phi_F(\upsilon')$ of state selected levels, *e.g.* $^2\tilde{A}(\upsilon')$, can be directly determined for radical cations using the photoelectron-photon coincidence technique.

### 4.1. Lifetimes

The lifetime $\tau(v')$ of an electronically excited cation in a selected vibrational level can be determined by following the intensity of the emitted photons as a function of time. Thus, if the bands in the emission spectrum have been assigned, the decay curves corresponding to the various levels in the excited state, from which the emission bands originate, can be obtained.

However, in practice, such determinations are mainly restricted to the lowest vibrational level, 0°, of the excited state as most of the strong bands identified originate from this level (cf. Fig. 3). The lifetimes of some of the low excited levels can sometimes be obtained because of the weak bands at higher energy levels of the $0_0^0$ bands. These limitations are dictated in the emission experiment by the necessary compromise between optical resolution and practical measuring times. Clearly, the way to obtain the lifetimes of such cations in excited vibrational levels at high resolution is by the laser-induced fluorescence technique. This is one of the aims for the near future.

In the case of the emission technique, the lifetimes are deduced from decay curves accumulated using the single photon delayed coincidence approach (*i.e.* by measuring the time interval between formation of the cation and the arrival of the fluorescence photon) when the electron beam is pulsed, typically at frequencies up to 500 kHz[21]. The level is selected by tuning the monochromator to an appropriate emission band. The advantage of this method is that high quality statistics can be reasonably rapidly obtained[37]. An example of such a decay curve is given in Figure 5 for the 1,3-pentadiyne cation in the $\tilde{A}^2E$ $0^0$ state. The inferred $\tau(0^0)$ value is $48 \pm 3$ ns.

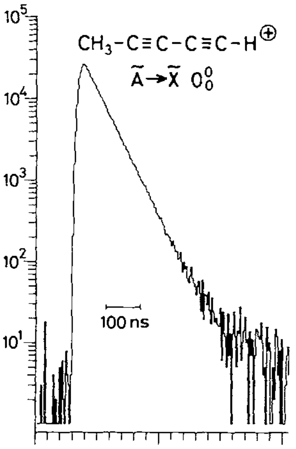


Fig. 5. Decay curve for the $\tilde{A}^2E$ $0^0$ level of the 1,3-pentadiyne cation accumulated using pulsed electron beam excitation and a 0.8 nm band pass for the $0_0^0$ band. The data are plotted using a semilogarithmic scale and the background has been subtracted.

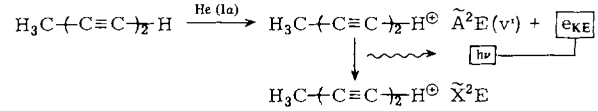
The measured lifetime, $\tau(v')$, yields the overall rate constant, $k_T(v')$, for the selected level. It is composed of the sum of the rate constants of the radiative channel, $k_r(v')$, and of all the non-radiative channels, $k_{nr}^i(v')$, accessible *i.e.*

$$\tau(v')^{-1} = k_T(v') = k_r(v') + \sum_i k_{nr}^i(v') .$$

On the other hand, when the radiative decay is not detected, a lower limit for the non-radiative rate can be given. Typical $k_r(v')$ values for organic radical cations are $\approx 10^7$ $s^{-1}$, the sensitivity of the apparatus implies that $\sum_i k_{nr}^i(v') \geq 10^{12}$ $s^{-1}$.

### 4.2. Photoelectron-Photon Coincidences

The principle of the measurements relies on the detection of energy selected photoelectrons in coincidence with undispersed photons following photoionization with a monochromatic source, *e.g.*, He(Iα)[12] or synchrotron radiation[38]. This is again illustrated by the recent results on 1,3-pentadiyne cations in the $\tilde{A}^2E$ state[39] (Scheme 2).



Scheme 2

Thus, the internal energy (or vibrational level) $v'$ within the $\tilde{A}^2E$ state is determined by the kinetic energy, $e_{KE}$, of the ejected photoelectron. The spread in the electron energy, typically 100 meV for 10 eV electrons, means that, in effect, internal energies within this bandwidth are sampled. The detection of true photoelectron-photon coincidences proves that the fluorescence process occurs only when the cations are initially prepared in the selected state, *i.e.* if they themselves decay to a lower electronic state or if an excited isomer cation or fragment relaxes by photon emission. Since in the case of the cations investigated, the radiative decay has been established, there is no ambiguity.

The fluorescence quantum yield is obtained from the coincidence statistics[40]. The rate of true coincidences, $N_T$, obtained from the area encompassed by the decay curve superimposed on the background of random coincidences (cf. Fig. 6), and the rate of detection of energy selected electrons, $N_e$, are required since it can be shown that

$$N_T / N_e = f_{h\nu} \, \phi_F(v')$$

In this relationship $f_{h\nu}$ is the photon detection probability (determined entirely by experimental factors) and this can be absolutely calibrated as a function of wavelength using cations for which $\phi_F(v') = 1$. These include $N_2^{\oplus}(\tilde{B}^2\Sigma_u^+ \, v' = 0)$, $N_2O^{\oplus}(\tilde{A}^2\Sigma^+ \, 0^0)$ and $CO_2^{\oplus}(\tilde{A}^2\Pi_u \, 0^0)$. The nature of the experiment is such that long counting periods are required, typically a day for each curve, in order to infer the $\phi_F(v')$ and $\tau(v')$ values with an error of 5%.

Figure 6 shows the relevant part of the He(Iα) PE spectrum of 1,3-pentadiyne, recorded under the coincidence conditions, showing the four energy locations within the $\tilde{A}^2E$ state (arrows) where coincidences were detected. Qualitatively, these observations show directly, as does the excitation spectrum (Fig. 4), that the radiative channel depletes vibrational levels up to $\approx 0.5$ eV above the zeroth level in the $\tilde{A}^2E$ state. One such photoelectron-photon coincidence curve is depicted in Figure 6; in this case for

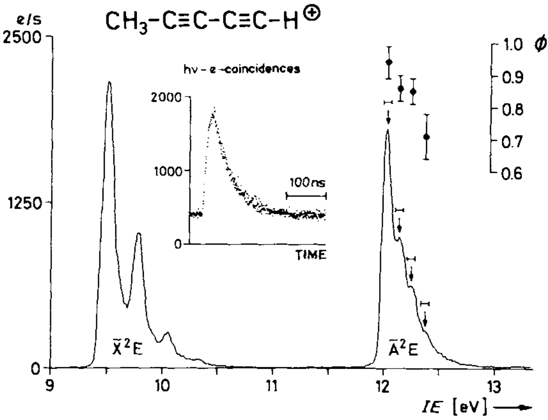


Fig. 6. Photoelectron-photon coincidence curve for the $\tilde{A}^2E$ $0^0$ level of the 1,3-pentadiyne cation accumulated over 17 h. The decay curve of true coincidences is superimposed on the background of random coincidences. The lifetime is extracted from the decay-part of the curve and the fluorescence quantum yield from the rate of true coincidences and the electron count rate. The He(Iα)-PE spectrum was recorded under the coincidence conditions. The fluorescence quantum yields determined are plotted at the internal cation energies selected.

the $\tilde{A}^2E$ $0^0$ level of the 1,3-pentadiyne cation. This consists of a uniform background of random coincidences upon which is superimposed a curve whose decay-part is characteristic of the excited state and from which the cascade-free lifetime is extracted. The determined $\phi_F(v')$ values are plotted above the vibrational bands in the photoelectron spectrum.

The radiative, $k_r(v')$, and non-radiative, $k_{nr}(v')$ $(\equiv \sum_i k^i_{nr}(v'))$, rate constants can then be evaluated from the measured quantities *via*

$$k_r(v') = \phi_F(v')/\tau(v')$$

and

$$k_{nr}(v') = [1-\phi_F(v')]/\tau(v').$$

For the 1,3-pentadiyne cation and its isotopic derivatives it is found that, within the error limits, the radiative rates are the same and constant over the internal energy sampled. In contrast, the $k_{nr}(v')$ rates increase with excess energy and vary among the isotopes. Similar trends in the $k_{nr}(v')$ dependence on excess energy are apparent for the isotopic cations as well as other organic radical cation studied hitherto (Table 5).

The availability of such data enables one to consider the decay of organic cations in terms of the developed theoretical models of radiationless transitions[35,44]. In the example of 1,3-pentadiyne cation, the $^2\tilde{A}\rightsquigarrow{}^2\tilde{X}$ internal conversion process falls within the statistical limit category, since the density of vibrational levels of the $^2\tilde{X}$ state is sufficiently high $(\rho(\tilde{X}) \approx 10^{10}/\text{cm}^{-1})$. This situation, $\tau(\tilde{A}) \ll \hbar\rho(\tilde{X})$, is characterized by non-unity fluorescence quantum yields, mono-exponential decay and, for a large energy gap situation, by a decrease in the $k_{nr}(0^0)$ rate on deuteration[35,44]. In addition, with excess vibrational energy the $k_{nr}(v')$ rates often increase either exponentially, or linearly, depending on the cation. The applications of the radiationless decay models to organic cations have already been considered in some detail in connection with the average fluorescence quantum yields and lifetimes for the excited state[45]. Such data have been obtained by the photoion-photon coincidence approach for the cations of the fluorinated benzenes[46] and of chloro- and dichloro-acetylene[47].

Table 5. Organic radical cations for which fluorescence quantum yields and lifetimes of selected levels have been obtained by the photoelectron-photon coincidence technique. All the isotopic species are not included.

| Cation | | Ref. |
|---|---|---|
| $H(C\equiv C)_2H^{\oplus}$ | $\tilde{A}^2\Pi_u$ | [41] |
| *cis*-1,2-$C_2H_2F_2^{\oplus}$ | $\tilde{A}^2A_1$ | [42] |
| $Cl(C\equiv C)_2X^{\oplus}$, X = H, (Cl) | $\tilde{A}^2\Pi_{(u)}$ | [26] |
| $H_3C(C\equiv C)_2H^{\oplus}$ | $\tilde{A}^2E$ | [39] |
| $H_3C(C\equiv C)_2CH_3^{\oplus}$ | $\tilde{A}^2E_u$ | [39] |
| Fluorobenzenes$^{\oplus}$ | $\tilde{B}(\pi^{-1})$ | [43] |

The non-radiative decay of 1,3-pentadiyne cations in the $\tilde{A}^2E$ state leads ultimately to the $C_5H_3^{\oplus}$ fragment ion[18]. As depicted in Figure 1, the appearance potential of this fragment ion is found at about half an electron volt below the lowest level of the $\tilde{A}^2E$ state[19]. This species thus belongs to the relatively small category of organic radical cations for which both the radiative $(^2\tilde{A}\rightarrow{}^2\tilde{X})$ and fragmentation $(^2\tilde{A}\rightsquigarrow\cdots\rightarrow M^{\oplus}, F_1^{\oplus}, F_2^{\oplus}\cdots)$ pathways occur, following their preparation in an excited state[9]. The organic cations for which this decay behavior has been demonstrated are collected together in Table 6. Because fragment ions are produced, mass spectroscopic approaches can be used to probe this decay channel of state selected cations. Two such methods are photoelectron-photoion coincidence[53] and photodissociation spectroscopies[17].

Table 6. Organic radical cations for which the radiative $(^2\tilde{A}\rightarrow{}^2\tilde{X})$ and fragmentation $(^2\tilde{A}\rightsquigarrow\cdots\rightarrow M^{\oplus}, F_1^{\oplus}\cdots)$ decay channels are both detected. The isotopically labeled derivatives studied are not listed.

| Cation | | Ref. |
|---|---|---|
| *cis*-$C_2H_2F_2^{\oplus}$ | | [48] |
| $H_3C-C\equiv C-X^{\ominus}$ | X = Cl, Br | [49] |
| $H_3C(C\equiv C)_2X^{\oplus}$ | | [49] |
| $H_3C(C\equiv C)_2H^{\oplus}$ | | [18] |
| $H_3C(C\equiv C)CH_3^{\oplus}$ | | [50] |
| $H_5C_2(C\equiv C)_2R^{\oplus}$, R = H, $C_2H_5$ | | [18, 50] |
| *trans,cis*-1,3,5-Hexatriene$^{\oplus}$ | | [51] |
| all-*trans*-1,3,5-Heptatriene$^{\oplus}$ | | [51] |
| all-*trans*-1,3,5,7-octatetraene$^{\oplus}$ | | [52] |

The fragmentation processes of 1,3-pentadiyne cations have consequently been studied by *Heilbronner et al.* using the photoelectron-photoion coincidence technique[19]. In these measurements, mass-selected ions are detected in coincidence with energy-selected photoelectrons, and yield the branching ratios of the ions detected as a function of the internal energy of the parent cation. For example, the branching ratio of the $C_5H_4^{\oplus}$ parent ion decreases in a parallel fashion to the $\phi_F(v')$ value (cf. Fig. 6) across the PE band corresponding to the $\tilde{A}^2E$ state. Furthermore, it was concluded on the basis of the results on the deuterated derivatives that prior to the loss of H (or D) extensive scrambling and/or ionic carbon skeletal isomerization takes place[19]. This is consistent with the interpretation, that the $k_{nr}(v')$ rates determined from the photoelectron-photon coincidence data correspond to the $\tilde{A}^2E \rightsquigarrow \tilde{X}^2E$ internal conversion process[40]. The 1,3-pentadiyne cations are then highly vibrationally excited, and in due course fragment. The results and inferences from all the different measurements are summarized schematically in Figure 7.

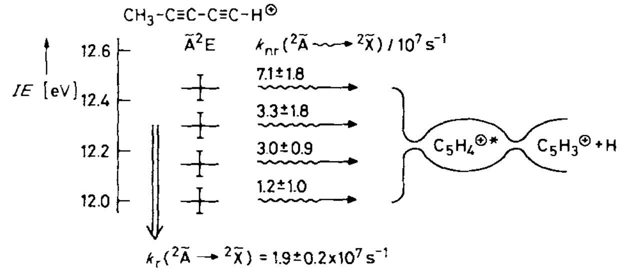


Fig. 7. Schematic view of the relaxation behavior of the $\tilde{A}^2E$ state of the 1,3-pentadiyne cation. The radiative and non-radiative rate constants as a function of the vibrational excitation have been obtained from the photoelectron-photon coincidence measurements. The radiationless decay leads ultimately to the $C_5H_3^{\oplus}$ fragment ions but prior to that, sufficient time is available for structural rearrangements of the vibrationally excited $C_5H_4^{\oplus *}$ cation.

Such a mechanism can be quantitatively followed for some of the cations listed in Table 6 because the slowest step in the fragmentation rate could also be determined. An example is the *cis*-1,2-difluoroethylene cation in the lowest level of the $\tilde{A}^2A_1$ state; the fragmentation rate is an order of magnitude slower than the non-radiative rate (presumably $^2\tilde{A} \rightsquigarrow {}^2\tilde{X}$ step), which competes directly with the radiative decay ($^2\tilde{A} \rightarrow {}^2\tilde{X}$)[42,48].

## 5. Concluding Remarks and Outlook

In this article, the recent spectroscopic studies on 1,3-pentadiyne radical cation in its ground and first excited doublet states have been chosen to illustrate the sort of structural and dynamic information that has become accessible. The techniques developed for this purpose rely on the radiative decay of the excited cations, which is also their limitation. However, since to date the emission spectra of over a 100 organic radical cations have been recorded, these approaches can be applied to them.

The advantage of the emission and laser-induced fluorescence methods is that the states of the cations involved in the transition can be probed with resolutions of 1 $cm^{-1}$. Improvements in resolution by a further factor of ten have already been achieved (cf. Table 1) and in the future this should enable not only more precise data on the vibrational frequencies of cations to be obtained, but also the resolution of rotational fine structure in smaller species[10].

It is fair to say that the spectroscopic data from electronic spectra are usually invaluable in ultra-high resolution studies which probe details such as hyperfine interactions. This has already been demonstrated by the recent laser-ion beam experiments on some diatomic and triatomic cations[54]. A further step in this direction will undoubtedly be the development of double resonance techniques (*e.g.* microwave-optical) relying on the laser-induced fluorescence decay of such organic cations. The latter property is also of potential interest in monitoring ion-molecule collisions and as a diagnostic tool for the investigation of internal energy partitioning. Knowledge of the energetic and dynamic processes of the open-shell cation is a prerequisite for this purpose.

Complementary data on the relaxation characteristics of radical cations can be obtained from studies of their lifetimes and from fluorescence quantum yields. To this end the photoelectron-photon coincidence technique is employed. Consequently, the rates of the radiative and non-radiative relaxation channels can be followed as function of excess internal energy of the cation. Observations of this type will be extended to individual vibrational levels, and in some cases to rotational levels, when their lifetimes have been measured by the laser-induced fluorescence approach. As sets of such data become available on structurally related cations, a more detailed description of the relaxation behavior of organic radical cation should emerge.

Undoubtedly the understanding of the interdependence between the spectroscopic features and relaxation characteristics of molecular species and their ions will, in time, become more firmly established. One of the ultimate goals of studies of this sort is, of course, the investigation of "state to state chemistry" and as outlined in this article there are some advantages in also trying to achieve these aims *via* studies of open-shell organic cations.

*I would like to take this opportunity of thanking Professor E. Heilbronner, not only for his continual support throughout but also for providing a congenial environment for me in Basel. Furthermore, the work described in this article was only made possible by the efforts of my co-workers over the past few years; Dr. Michael Allan, Fritz Burger, Dr. Oskar Marthaler, Dr. Manijeh Mohraz, Liubomir Misev and Fritz Thommen, and by the continual financial support of the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project No. 2-622-0.80). Ciba-Geigy, Sandoz and F. Hoffmann-La Roche, Basel are also thanked for financial support.*

Received: February 25, 1981 [A 362 IE]
German version: Angew. Chem. 93, 649 (1981)

---

[1] For reviews of the various specialized topics see *P. Ausloos:* Kinetics of Ion-Molecule-Reactions, Plenum Press, New York 1979.

[2] *W. D. Watson,* Acc. Chem. Res. *10,* 221 (1977) and references therein.

[3] Cf. *e.g. R. H. Gammon,* Chem. Eng. News *56,* Oct. 2, p. 21 (1978); *H. W. Kroto,* New Sci. *86,* Aug. 10, p. 400 (1978).

[4] *D. W. Turner, C. Baker, A. D. Baker, C. R. Brundle:* Molecular Photoelectron Spectroscopy, Wiley-Interscience, London 1971, and references therein.

[5] Cf. also *E. Heilbronner,* IUPAC XXIII, *7,* 9 (1971); *E. Heilbronner, J. P. Maier,* Organic Photoelectron Spectroscopy, in *C. R. Brundle, A. D. Baker:* Electron Spectroscopy: Theory, Techniques and Applications, Academic Press, London 1976; *H. Bock,* Angew. Chem. *89,* 631 (1977); Angew. Chem. Int. Ed. Engl. *16,* 613 (1977).

[6] *G. Herzberg:* Molecular Spectra and Molecular Structure, Vol. I - Spectra of Diatomic Molecules; Vol. III - Electronic Spectra of Polyatomic Molecules, van Nostrand, New York 1950 and 1966, respectively.

[7] *G. Herzberg:* The Spectra and Structure of Simple Free Radicals, Cornell University Press, Ithaca, New York 1971.

[8] *G. Herzberg,* Q. Rev. Chem. Soc. *25,* 201 (1971); *S. Leach* in *B. DiBartolo:* Spectroscopy of the Excited State, Plenum Press, New York 1979.

[9] Cf. *J. P. Maier* in [1], p. 437; *J. P. Maier,* Chimia *34,* 219 (1980), and literature cited therein.

[10] Cf. *J. P. Maier, O. Marthaler, L. Misev, F. Thommen* in *J. Berkowitz:* Molecular Ions, Plenum Press, New York 1981, for some more details regarding the techniques.

[11] Cf. *e.g. R. N. Zare, P. J. Dagdigian*, Science *185*, 739 (1974).

[12] *M. Bloch, D. W. Turner*, Chem. Phys. Lett. *30*, 344 (1975).

[13] *J. H. Callomon*, Can. J. Phys. *34*, 1046 (1956).

[14] *F. Brogli, E. Heilbronner, V. Hornung, E. Kloster-Jensen*, Helv. Chim. Acta *56*, 2171 (1973).

[15] *L. S. Cederbaum, W. Domcke, J. Schirmer, W. von Niessen, G. H. F. Diercksen, W. P. Kraemer*, J. Chem. Phys. *69*, 1591 (1978), discuss such effects for hydrocarbons.

[16] Cf. *e.g. E. Haselbach, T. Bally, R. Gschwind, U. Klemm, Z. Lanyiova*, Chimia *33*, 405 (1979).

[17] *R. C. Dunbar* in *M. T. Bowers:* Gas Phase Ion Chemistry, Vol. II, Academic Press, London 1979 and references cited therein.

[18] *J. P. Maier, O. Marthaler, E. Kloster-Jensen*, J. Chem. Phys. *72*, 701 (1980).

[19] *J. Dannacher, E. Heilbronner, J.-P. Stadelmann, J. Vogt*, Helv. Chim. Acta *62*, 2186 (1979).

[20] *M. B. Robin:* Higher Excited States of Polyatomic Molecules, Vol. 1 and 2, Academic Press, London 1973.

[21] *M. Allan*, Dissertation, Universität Basel 1976; *O. Marthaler*, Dissertation, Universität Basel 1980.

[22] *J. Lamotte, J.-C. Lavalley, R. Romanet*, J. Chim. Phys. Phys. Chim. Biol. *70*, 1077 (1973).

[23] *J. L. Kinsey*, Annu. Rev. Phys. Chem. *28*, 349 (1977), and references cited therein.

[24] *P. Engelking, A. L. Smith*, Chem. Phys. Lett. *36*, 22 (1975).

[25] Review: *T. A. Miller, V. E. Bondybey*, J. Chim. Phys. *77*, 695 (1980) and references cited therein.

[26] *J. P. Maier, O. Marthaler, L. Misev, F. Thommen*, Discuss. Faraday Soc. *71*, No 15 (1981).

[27] *J. P. Maier, L. Misev*, Chem. Phys. *51*, 311 (1980).

[28] *T. A. Miller, V. E. Bondybey, B. R. Zegarski*, J. Chem. Phys. *70*, 4982 (1979).

[29] *V. E. Bondybey, T. A. Miller*, J. Chem. Phys. *70*, 138 (1979); *T. A. Miller, V. E. Bondybey*, Chem. Phys. Lett. *66*, 165 (1979); *T. Sears, T. A. Miller, V. E. Bondybey*, J. Chem. Phys. *72*, 6749 (1980).

[30] *T. A. Miller, V. E. Bondybey, J. H. English*, J. Chem. Phys. *70*, 2919 (1979); *71*, 1088 (1979).

[31] *T. J. Sears, T. A. Miller, V. E. Bondybey*, J. Am. Chem. Soc. *102*, 4864 (1980).

[32] *J. P. Maier, L. Misev*, Helv. Chim. Acta *63*, 1920 (1980).

[33] *C. Cossart-Magos, D. Cossart, S. Leach*, Chem. Phys. *41*, 363, 345 (1979).

[34] *H. M. Rosenstock, K. Draxl, B. W. Steiner, J. T. Herron*, J. Phys. Chem. Ref. Data *6*, Suppl. 1 (1977) contains a compilation of fragment ion appearance potentials.

[35] *P. Avouris, W. M. Gelbart, M. A. El-Sayed*, Chem. Rev. *77*, 793 (1977) and references cited therein.

[36] *W. E. Howard, E. W. Schlag*, Chem. Phys. *17*, 123 (1976).

[37] *M. Allan, E. Kloster-Jensen, J. P. Maier*, J. Chem. Soc. Faraday Trans. II *73*, 1406 (1977).

[38] *E. W. Schlag, R. Frey, B. Gotchev, W. B. Peatman, H. Pollak*, Chem. Phys. Lett. *51*, 406 (1977).

[39] *P. Forster, J. P. Maier, F. Thommen*, Chem. Phys. *1981*, in press.

[40] *J. P. Maier, F. Thommen*, Chem. Phys. *51*, 319 (1980).

[41] *J. P. Maier, F. Thommen*, J. Chem. Phys. *73*, 5616 (1960).

[42] *J. P. Maier, F. Thommen*, J. Chem. Soc. Faraday II *77*, 845 (1981).

[43] *J. P. Maier, F. Thommen*, Chem. Phys. *57*, 319 (1981).

[44] *K. F. Freed*, Top. Appl. Phys. *15*, 23 (1976); *W. M. Gelbart*, Annu. Rev. Phys. Chem. *28*, 323 (1977) and references cited therein.

[45] *S. Leach, G. Dujardin, G. Taieb*, J. Chim. Phys. Phys. Chim. Biol. *77*, 407 (1980).

[46] *G. Dujardin, S. Leach, G. Taieb*, Chem. Phys. *46*, 407 (1980).

[47] *G. Dujardin, S. Leach, G. Taieb, J. P. Maier, W. M. Gelbart*, J. Chem. Phys. *73*, 4987 (1980).

[48] *J. P. Maier, O. Marthaler, G. Bieri*, Chem. Phys. *44*, 131 (1979).

[49] *J. P. Maier, O. Marthaler, E. Kloster-Jensen*, J. Electron Spectrosc. Relat. Phenom. *18*, 251 (1980).

[50] *M. Allan, J. P. Maier, O. Marthaler, E. Kloster-Jensen*, Chem. Phys. *29*, 331 (1978).

[51] *M. Allan, J. P. Maier*, Chem. Phys. Lett. *43*, 94 (1976); *M. Allan, J. Dannacher, J. P. Maier*, J. Chem. Phys. *71*, 3114 (1980).

[52] *T. B. Jones, J. P. Maier*, Int. J. Mass Spectrom. Ion Phys. *31*, 287 (1979).

[53] *T. Baer* in *M. T. Bowers:* Gas Phase Ion Chemistry, Vol. I, Academic Press, New York 1979 and references cited therein.

[54] *A. Carrington*, Proc. R. Soc. London *A 367*, 433 (1979) and references cited therein.

# Methods of Fluorination in Organic Chemistry

By Michael R. C. Gerstenberger and Alois Haas[*]

Since the days of the "Manhattan Project" our knowledge of the chemistry of fluorine-containing compounds has increased tremendously. At first only considered out of curiosity, this area of research bordering between inorganic and organic chemistry has developed from modest beginnings to such a complexity of interesting ramifications that it would be very difficult to review all aspects in detail. The motivating force behind the developments in this field were, above all, the unusual properties the numerous compounds acquire on introduction of fluorine substituents. The spectrum of unusual modes of behavior extend from extreme stabilization in fluorine-containing polymers and blood-substitutes to drastic increases in reactivity in pharmacologically and phytomedicinally active substances and in dyes. Moreover, one physical peculiarity of the fluorine atom, its magnetic moment, opens a new route to the decyphering of metabolic processes.—Parallel to the ever increasing number of fluorinated compounds there has been a concomitant increase in the variety of methods of synthesis and reagents, which is frequently difficult to overview in entirety, even for the specialists. Older, simple methods such as halogen metathesis with metal fluorides and electrofluorination are being refined as far as higher selectivity is concerned, and completely new, very reactive substances such as hypofluorites and noble-gas fluorides enable fascinating reactions on complex substrates, *e.g.* steroids and nucleobases. The present review is an attempted documentation and classification of the methods as well as a critical appraisal, not least from the standpoint of efficiency and economic aspects.

## 1. Historical Note

The entire course of development of the chemistry of fluorinating agents for organic compounds has been determined and motivated by the industrial importance of the resulting products. *F. Swart's* studies of simple metathesis reactions[1]

$$R{-}X + MF \rightarrow R{-}F + MX\,; \quad X = Cl,\ Br,\ I$$

mainly with $SbF_3$ and $HgF_2$, have led to the use of $CCl_2F_2$ as an inert, nontoxic, and readily accessible coolant that could replace $NH_3$ and $SO_2$. The usefulness of highly fluorinated compounds as resistant materials was first recognized during the Manhattan Project in the manipulation of the extremely aggressive $UF_6$[2]. The prerequisite for the synthesis of substances of this kind had been provided a few years earlier with the introduction of $CoF_3$ as a reagent for the exhaustive fluorination of hydrocarbons[3] and by the discovery of polytetrafluoroethylene[4]. The development of electrofluorination aimed in the same direction[5,6]. The significance of low-fluorinated compounds for biochemistry was initially based on toxicological research with fluoroacetic acid and the concept of "lethal synthesis" that developed from it[7], and also on the use of fluorinated nucleic acids as cytostatics[8].

## 2. Uses of Fluorinated Compounds

Two classes of fluorine-containing substances must essentially be distinguished, on the basis of their preparation and their uses. The first class comprises compounds in which all or at least most of the hydrogens initially bonded to carbon atoms have been replaced by fluorine (highly fluorinated compounds); in the second class this applies to only some of the hydrogen atoms (low-fluorinated compounds). In what follows we shall present a selection of fields in which these two classes are used[9].

### 2.1. Highly Fluorinated Compounds

#### 2.1.1. Coolants for Cooling Systems and Aerosol Propellants

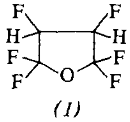
Chlorofluoroalkanes and cycloalkanes are used in these two domains, especially the short-chain ones, on account of the low boiling points required, for example $CCl_2F_2$, $CF_2Cl{-}CFCl_2$, $CFCl_3$, and *cyclo*-$C_4F_8$.

#### 2.1.2. Fire Extinguishers

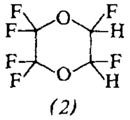
The compounds of choice here are the bromine-containing fluoroalkanes, *e.g.* $CF_3Br$ and $CF_2ClBr$.

#### 2.1.3. Inhalation Anaesthetics

The best known example is halothane, $CF_3{-}CHClBr$, although oxygen heterocycles such as the tetrahydrofuran derivative *(1)* and the dioxane derivative *(2)* have given very promising results.



*(1)*



*(2)*

---

[*] Prof. Dr. A. Haas, Dr. M. R. C. Gerstenberger
Lehrstuhl für Anorganische Chemie II der Ruhr-Universität
Postfach 102148, D-4630 Bochum (Germany)

0570-0833/81/0808-0647 $ 02.50/0

### 2.1.4. Surfactants

Typical examples in this field are the perfluoroalkanesulfonic acids $R_fSO_3H$ ($R_f$ = *e.g.* $C_7F_{15}$ to $C_{10}F_{21}$) and their derivatives. Because of its extremely low surface energy, the perfluorinated chain reduces the surface tension in aqueous systems at concentrations at which analogous non-fluorinated compounds are practically ineffective. These compounds are used as fire-extinguishing foams, as emulsifiers in polymerization reactions, and as wetting and dispersing agents.

### 2.1.5. Polymers

The best known example is of course polytetrafluoroethylene, whose unusual properties (high melting point, form stability (lack of flow) above the melting point, insolubility in all conventional solvents, and high thermal and chemical resistance) make this class of compounds suitable for a wide range of applications. Further developments have led to copolymers of tetrafluoroethylene (TFE) and perfluoropropylene (reduced tendency toward crystallization in spite of shorter chain lengths), of TFE and ethylene (better mechanical strength), and of TFE and perfluorinated alkyl vinyl ethers (better thermal resistance).

### 2.1.6. Blood Substitutes[10]

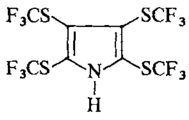
Although this sphere of application is still in its infancy, spectacular results have already been achieved with some classes of compounds (perfluorinated cycloalkanes, amines, and oxygen heterocycles). The specific requirements are: similarity to normal blood as regards osmotic pressure, rheological properties, transport, and exchange of $CO_2$ and $O_2$, as well as the possibility of new production of erythrocytes and other blood constituents.

### 2.1.7. Summary of the Uses of Highly Fluorinated Compounds

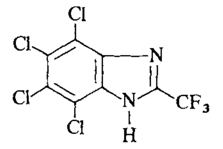
The fundamental precondition for all the above-mentioned spheres of application is high chemical (and by extension biological) inertness of the compounds used. This requirement is very largely satisfied by substances containing C—F bonds, a lack of any chemical interaction with biological systems being observed above all in the perhalogenated compounds. The absence of interaction means that the compounds have a very low toxicity, a property required particularly for the blood substitutes. Interestingly enough, the common structural feature of anaesthetics, *i.e.* substances that must interact with the organism to some extent (weakly) if they are to fulfill their function, is an incomplete replacement of the H-atoms by the halogen. The specific action of these compounds correlates with the remaining *C*-bonded hydrogens[11,12]. Pronounced biological activity is thus encountered predominantly in the compounds with a low fluorine content. Examples behaving contrary to this rule, such as the perfluoroalkylsulfonyl-substituted urea *(3)* (strongly hypocholesterolemic and anorectically active)[13], the highly substituted pyrrole *(4)* (strong fungicidal and insecticidal action)[14], and benzimidazole *(5)* (strongest known respiratory-chain decoupler)[15] are exceptions.

$C_8F_{17}SO_2NHCONH_2$

*(3)*



*(4)*



*(5)*

## 2.2. Low-Fluorinated compounds

### 2.2.1. Pharmaceuticals

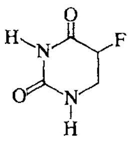
As a rule, a specific interaction of a fluorinated compound with a living organism is only possible when not all the *C*-bonded hydrogen atoms have been replaced by halogens. This may be attributed to the fact that a biologically active substance must bear a certain similarity to the structures with which it is to interact. Many of the fluorine-containing drugs do in fact show a close analogy to natural products, *e.g.* nucleobases, steroids, and amino acids. The future significance of such classes of compounds, which can hardly be overestimated, stems from the following properties of elementary fluorine[16]:

1. The highest electronegativity of all the elements in the periodic table. The difference between fluorine and chlorine, the closest homolog, is substantially greater than the differences between any other two successive halogens, and is reflected in the term "superhalogen"[17] used to describe fluorine. The unusually strong polarization of the C—F bond is explained by a strong negative inductive effect which can gradually alter and even invert the reaction behavior of adjacent centers.

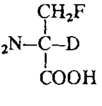
2. Fluorine is the halogen whose van der Waals radius is most like that of hydrogen (F = 1.35; H = 1.1 Å). The steric requirements of the two atoms are so similar that formal replacement of H by F can be regarded as an "isogeometric transformation".

3. The high energy of the C—F bond (107 kcal/mol) is responsible for the difficult metabolization of fluorine-containing compounds which can lead to competitive enzyme inhibition. The term "lethal synthesis" is used[18] if an intermediate stage of this kind is produced in the organism from a precursor (*e.g.* fluoroacetic acid → fluorocitric acid, competitive inhibition of aconitase in the tricarboxylic acid cycle, and its inactivation by fluoroacetic acid[19]).

This last point in particular has given rise to the concept of "antimetabolites", *i.e.* fluorine analogs of natural products which are incorporated in their stead and give rise to lethal synthesis. An important example is 5-fluorouracil *(6)*[20], which as a competitive inhibitor of thymidylate synthetase constitutes one of the most potent antineoplastic agents. 5-Fluorouracil is used in particular in the treatment of breast cancer, leukemia and Hodgkin's disease.

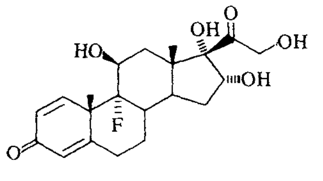


*(6)*



$$H_2N-\overset{\displaystyle CH_2F}{\underset{\displaystyle COOH}{C}}-D$$

"DFA" *(7)*



*(8)*

2-Deuterio-3-fluoro-D-alanine (DFA) *(7)*[21] belongs to the group of "cell-wall active antibiotics". As an inhibitor of alanine racemase, in combination with cycloserine it represents a broad-spectrum bactericidal agent with a pronounced activity against virtually all microorganisms known to be pathogenic in man[22].

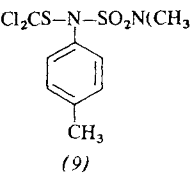
A very different situation prevails in another group of pharmacologically active substances, the fluorinated corticosteroids. Whereas the preparations discussed so far are antagonists of their H-analogs, the antiphlogistic and antirheumatic activity common to the corticosteroids is intensified or modified in the fluorinated derivatives. Triamcinolone *(8)*[23] has a markedly stronger action than cortisone in the treatment of rheumatic arthritis; on the other hand, the undesirable sodium retention (mineralocorticoid activity) observed with many halogenated steroids is suppressed.

### 2.2.2. Study of Metabolic Processes
### ("Reporter Group Technique")

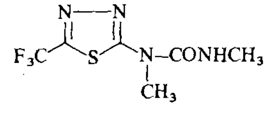
The fluorine atom has a nuclear spin ($I = 1/2$), and $^{19}$F-NMR studies[24] are therefore possible. They are facilitated by the fact that fluorine is an element of 100% natural abundance; the apparatus necessary resembles that customary in proton resonance spectroscopy. The spectra-accumulation technique with the use of the Fourier transformation allows reliable detection of even very small concentrations. The substantially greater absorption range of several hundred ppm in comparison with the $^{1}$H-NMR spectrum and the comprehensive and well-systematized literature on reference compounds[25] are further factors favoring the use of fluorinated compounds in biochemistry. The bonding behavior of inhibitors such as *N*-trifluoroacetyltryptophan and *N*-trifluoroacetylphenylalanine on chymotrypsin has thus been examined[26]. The prosthetic group of the xanthine oxidase of milk could be discerned by $^{19}$F-NMR spectroscopy[27]; similar investigations have been carried out on the enzyme-inhibitor complex of thymidylate synthetase with fluorodeoxyuridine monophosphate[28].

### 2.2.3. Pesticides

Fluorine-containing compounds have also gained application in the realm of plant protection, *i.e.* some of them are distinguished by fungicidal, insecticidal, and herbicidal action. There is no universal theory on the significance of fluorine in these compounds; the mere heterogeneity of the structures is enough to make this difficult.



*(9)*



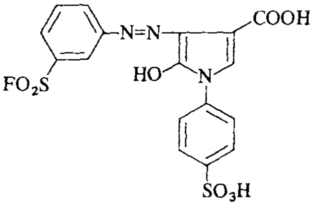
*(10)*

Two arbitrarily cited examples are *N*-dichlorofluoromethylsulfenyl-*N*-dimethylaminosulfonyl-4-methylaniline *(9)*[29] (tradename Euparen), a broad-spectrum fungicide, and *N,N'*-dimethyl-*N*-(5-trifluoromethyl-1,3,4-thiadiaz-2-yl)urea *(10)*[30] (Thiazafluron), a herbicide.

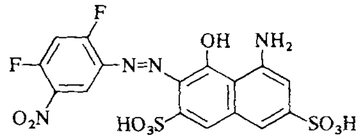
### 2.2.4. Dyes

Fluorine-containing components are used in reactive dyes for two essential reasons:

Fluorine acts as a nucleofugal group in the process of fixing the dye to the fibers, *e.g.* in the azo compounds *(11)* and *(12)*[31,32].



*(11)*



*(12)*

Fluorine increases the dye's reactivity with respect to the nucleophilic groups of the fibers without itself being the leaving group. Examples are found in the series of halogenated pyrimidine derivatives[33].

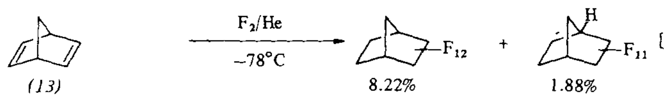
## 3. Production of Highly Fluorinated Compounds

Essentially there are three possible methods for the synthesis of this class of compounds: fluorination with elementary fluorine or with fluorine-active metal fluorides, and electrofluorination.

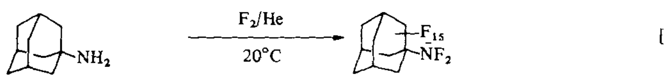
In all these techniques oxidative fluorination (*i.e.* fluorination of CC double and triple bonds; increase of the oxidation number of hetero-atoms such as sulfur and phosphorus) and metathesis (replacement of other halogens and hydrogen with fluorine) take place side by side. The common characteristic feature of these methods, their lack of selectivity, is rather regarded as positive in view of the high degree of fluorination desired.

### 3.1. Elementary Fluorine

Fluorinations with gaseous fluorine are among the oldest methods. Originally the reactions were carried out at several hundred degrees Celsius; the reaction partners, *e.g.* longer-chain, branched, or ring alkanes, were thus present in the gas phase. However, the heat of reaction released gave rise to fragmentations, *i.e.* product mixtures difficult to sort out were frequently produced. More recently the process has been modified[34] in that the fluorine is diluted with $N_2$ or He; the fluorine fraction of the gas mixture should be well below 10% at the start. Careful control of the reaction temperature in specially designed reactors is a further important condition. Highly fluorinated products are obtained in all cases. The reactions are metathetic as regards the H-atoms and oxidative in the presence of multiple bonds and hetero-atoms in low oxidation stages. Functional groups remain partly intact. The fluorinations of the compounds *(13)*—*(23)* can serve as examples.



(13) [35]



(14) [36]

$$\underset{(15)}{(CH_3)_2SO_2} \xrightarrow[20^\circ C]{F_2/He} \underset{34\%}{(CF_3)_2SO_2} + \underset{15\%}{CF_3SO_2F} + \underset{40\%}{SO_2F_2} \qquad [37]$$

$$\underset{(16)}{(CH_3)_4Ge} \xrightarrow[-100 \rightarrow -20^\circ C]{F_2/He} \underset{63.5\%}{(CF_3)_4Ge} \qquad [38]$$

$$\underset{(17)}{(CH_3)_2Hg} \xrightarrow[-78^\circ C]{F_2/He} \underset{6.5\%}{(CF_3)_2Hg} \qquad [39]$$

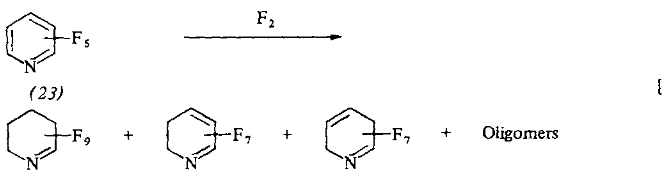
$$\underset{(18)}{(CH_3)_4Si} \xrightarrow[-100 \text{ bis } -110^\circ C]{F_2/He} \underset{\text{(mixture)}}{\text{Polyfluorinated tetramethylsilanes}} \qquad [40]$$

$$\underset{(19)}{CS_2} \xrightarrow[-120^\circ C]{F_2/He} \underset{60\%}{F_3S{-}CF_2{-}SF_3} \qquad [41]$$

$$\underset{(20)}{ICF_2{-}CF_2I} \xrightarrow[-78^\circ C]{F_2/CFCl_3} F_2ICF_2{-}CF_2IF_2 \qquad [42]$$

$$\underset{(21)}{CH_3COOC_2H_5} \xrightarrow[-78^\circ C]{F_2/He} \underset{5\%}{CF_3COOC_2F_5} + \underset{20\%}{CF_3COOCHFCF_3} \qquad [43]$$

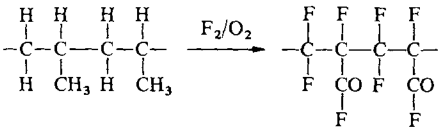
$$\underset{(22)}{CH_3(OCH_2CH_2)_nOCH_3} \xrightarrow[-78^\circ C]{F_2/He} CF_3(OCF_2CF_2)_nOCF_3,\ n = 1,2 \qquad [44]$$



(23) [45]

The majority of these reactions were performed at low temperatures. Fragmentation took place in the reactions carried out close to room temperature with the formation of secondary products[46,47].

Reactions of this kind proceed by a radical mechanism, as has been demonstrated by studies at low temperatures[48]. The simultaneous fluorination and functionalization of polypropylene surfaces is of potential industrial significance[49]:



$$-CH_2-CH(CH_3)-CH_2-CH(CH_3)- \xrightarrow{F_2/O_2} -CF_2-CF(COF)-CF_2-CF(COF)-$$

The fluorination of polyesters and polyamides with elementary fluorine improves the wetting characteristics[50] of the products.

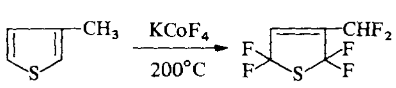
## 3.2. Fluorine-Active Metal Fluorides

At elevated temperature fluorides of metals in the highest oxidation state release a part of their fluorine in free form, the metal thus being reduced. Familiar examples are $AgF_2$, $MnF_3$, $CeF_4$, $PbF_4$, and $BiF_5$. $CoF_3$ and $KCoF_4$ are used most often. The fluorination can be described by the following simple equation:

$$CoF_3 \rightleftharpoons CoF_2 + 0.5\,F_2$$

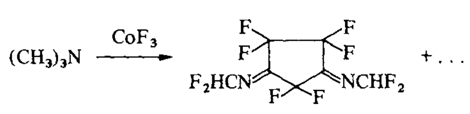
$CoF_3$ can be prepared[51] by the reverse reaction, the equilibrium being displaced to the left. Fluorides of this kind are thus generally regarded as the solid "transport form" of elementary fluorine. The reaction is therefore related to that of free fluorine: metathesis and oxidation take place side by side, resulting in highly fluorinated compounds. Complex product mixtures are isolated even from the fluorinations of ethane[52] and 2-methylpropane[53], but the percentage distribution of the products is clearly temperature-dependent, allowing a measure of control over the reaction.

The oxidative fluorination of double bonds likewise does not yield consistent products[52]; the stereospecificity is low, as has been demonstrated on cycloalkenes[54]. The use of aromatic substrates, *e.g.* naphthalene, shows that even with the relatively mild $CsCoF_4$ some saturated systems are formed[55]. The theory of the fluorination of arenes[56] with the fluorine-active metal fluorides assumes intermediary formation of radical cations, whose rearrangement then leads to a wide variety of products. A reaction with a clearly defined course, such as that of *(24)*→*(25)*, is therefore an exception[57]:



*(24)* *(25)*

The presence of functional groups in the reactants does not cause any fundamental change in this picture. Fluorinations of linear[58] and ring[59-61] ethers give the usual wide ranges of products, the corresponding dioxolane derivatives[59] being regarded as potential inhalation anaesthetics. For the oxygen heterocycles studied, ring-opening reactions have not been described. Conversely, the reaction of trimethylamine leads to ring products such as *(26)*[62].



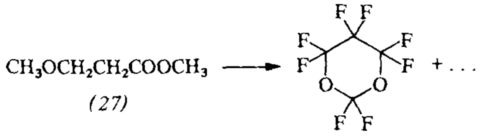
*(26)*, 13%

Short-chain nitriles ($CH_3CN$, $C_2H_5CN$) are largely monosubstituted in the α position, both with $CoF_3$ and with $KCoF_4$; the C≡N group remains intact. Longer-chain and unsaturated compounds react less specifically[63].

## 3.3. Electrofluorination

Like the two methods described in the preceding sections, electrofluorination is regarded as a classical technique[5], although it is also cited frequently in more recent publications. The substrate to be fluorinated is introduced into liquid hydrogen fluoride to which a small percentage of water or a conducting salt (*e.g.* $NH_4F$) has been added to increase the electrical conductivity. The electrolysis vessel is made of steel or copper, the cathode is iron or copper, and the anode is usually nickel. The voltage used for the electrolysis must be below the discharge potential of elementary fluorine to avoid its evolution. The organic substrate serves as a depolarizer[6,64], reacting with the $F^-$ probably in the form of radical cations. The anodic current density must be adjusted to the individual reaction; a high anodic current density favors ring-cleavage products in the fluorination of tertiary aromatic amines[65], a low one increases the yield of the five-membered ring product in the fluorination of *N*-alkylated piperidines[66].

Electrochemical fluorination is in many respects the least selective process compared with the processes in Sections 3.1 and 3.2, and this applies above all to the compounds containing functional groups. Thus, while the conversion of $CH_3CN$ into $CF_3CN$ takes place without destruction of the nitrile group[67], in trifluoromethylbenzonitriles this group is split off as $NF_3$[68]. Aromatic carbocycles[68] and heterocycles[69] are "fluorinated up" oxidatively. Ring cleavage is likewise observed, as in the saturated or partially saturated ring compounds: from oxane derivatives[70] perfluorinated linear ethers are produced; sulfolane[71] is converted into $C_4F_9SO_2F$ in a high yield (30 to 50%). Conversely, in the electrofluorination of methyl β-methoxypropionate *(27)*[72] a ring product is isolated in addition to many others[73].


(27)

In the reaction of carboxylic acids[74-76] elimination of $CO_2$ is observed above all, resulting in the formation of fluorinated alkanes. Alcohols give carboxylic acid fluorides[77] or cyclic ethers[78]. Hetero-elements, *e.g.* sulfur, are raised by fluorination to the highest state of oxidation[79,80]. Exclusive halogen exchange has not been observed[81]. In conclusion, reference may be made to a more recent finding, that the selectivity may be favorably influenced, at least in the fluorination of arenes, by the choice of a different anode material (platinum) and a different solvent ($CH_3CN$)[82]. Directed *p*-substitution[83] and disubstitution[84] in substituted benzenes is thus made possible. In the case of 1,1-diphenylethylene the fluorine can be added smoothly to the olefinic double bond[85], whereas with 1,2-isomers[86] several products are obtained.

The above three methods have the common feature that they give rise to mixtures of highly fluorinated compounds, *i.e.* their selectivity is low. Their usefulness therefore stands or falls with the availability of appropriate separation methods, such as fractional condensation and distillation or chromatographic techniques.

## 4. Preparation of Low-Fluorinated Compounds

The reactions leading to substances of this class represent the true domains of fluorination agents. Three such compounds have already been mentioned in Section 2.2.1: 5-fluorouracil *(6)*, 2-deuterio-3-fluoro-D-alanine *(7)*, and triamcinolone *(8)*, all potent fluorine-containing pharmaceuticals. There are two fundamentally different ways in which the fluorine atom can be introduced:

1. Fluorination at an early stage of conventional synthesis with possible modification of subsequent steps while adhering to the basic principle. This method requires much time and effort, because fluorine often produces a drastic change in the reaction, especially in the case of small molecules. The laborious development of a completely new synthetic sequence is thus frequently necessary[87].

2. Incorporation of the F-atom into the compound in question at the end of conventional synthesis, which in the above examples *(6)*, *(7)*, and *(8)* amounts to the fluorination of a nucleobase, an amino acid, and a corticosteroid, respectively. During this process any functional groups and multiple bonds already present in the molecule should as far as possible remain undisturbed, unless the intention is to substitute one of them deliberately.

Given the availability of suitable fluorination agents and techniques, the second method is more elegant than the first, quicker, and more economic. The demands on a fluorinating agent are thus clearly defined:

*selectivity,* the most important condition;
*efficiency, i.e.* high conversions and yields in as short a time as possible; this requirement is often directly associated with the first;
*Simplicity of the technical implementation of the preparation* and *economy* of the process.

Reactions with extremely aggressive gaseous substances, reactions under pressure, and difficultly accessible reagents must be regarded as less favorable.

In what follows, the classical and modern reagents and methods will be compared with one another. The three aspects of selectivity, efficiency, and simplicity underlie the emphasis on the preparational aspect in this review. Mechanistic considerations will be taken into account only insofar as they prove indispensable for understanding a reaction or if they occupy a large area in the researched literature; nevertheless, they provide a simple scheme of ordering for the very heterogeneous group of fluorinating agents in the confusing host of publications.

Fundamentally, two possibilities are available for classification purposes:

1. Classification by the *mode of fluorination.* The key question is: "Which function in the molecule is altered?"

   The most important reaction types are as follows:

   *Metathetic fluorination*

   $-H_{\text{aliphat.}} \rightarrow -F$
   $-H_{\text{aromat.}} \rightarrow -F$
   $-H_{\text{aldehyd.}} \rightarrow -F$
   $-Cl$, $-Br$ or $-I \rightarrow -F$
   $-OH \rightarrow -F$
   $-SH \rightarrow -F$
   $>C{=}O \rightarrow >CF_2$
   $-COOH \rightarrow -CF_3$
   $-NH_2 \rightarrow -F$

   Special cases: $-NO_2$, —tosyl, or $-O-SO_2CF_3 \rightarrow -F$
   Epoxide and aziridine ring opening.

*Oxidative Fluorination*

$—CH{=}CH— \rightarrow —CHF—CHX—$ $X = H, Cl, Br, I, NO_2, F$

$—C{\equiv}C— \rightarrow —CF{=}CX—$

$\gtreqless E \rightarrow \gtreqless EF_2$ E = heteroatom *e.g.* phosphorus

2. Classification by *fluorinating agents*. The key question is: "What can the fluorinating agents do?"
The most important reaction types and reagents are as follows:

*Nucleophilic F-transfer*
metal fluorides, $MF_n$
hydrogen fluoride, HF
tetrafluoroboric acid, $HBF_4$
halogen fluorides, $XF_n$
sulfur tetrafluoride, $SF_4$
fluorophosphoranes, $R_nPF_{5-n}$

*Electrophilic F-transfer*
perchloryl fluoride, $ClO_3F$

*Nucleophilic and electrophilic F-transfer*
fluorine-containing nitrogen compounds

*Electrophilic and radical F-transfer*
fluorine, $F_2$
trifluorofluoroxymethane, $CF_3OF$
noble-gas fluorides

In what follows the second type of classification will be used, for the purpose of clarity and to illustrate the order of importance.

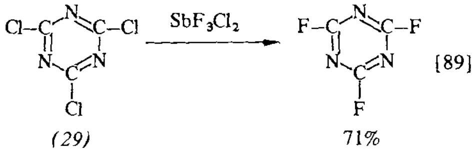
## 4.1. Nucleophilic F-Transfer

### 4.1.1. Metal Fluorides

*Classical process:* Of the reactions with metal fluorides, two well known metatheses will first be presented: Because of the easy availability of the metal fluorides, this type of substitution of chlorine, bromine, or iodine by fluorine continues to enjoy great popularity, in spite of the lower activity in comparison with more modern variants, which gives rise to lower conversions and, owing to the high temperatures required, to a variety of side reactions. Insensitive compounds thus constitute favorable substrates: highly fluorinated aliphatics[90] and arenes[91], hexachlorobenzene[92], and highly halogenated pyridines[93]. Metal fluorides are also used for halogen exchange on heteroelements such as silicon ($KF$[94], $AgF$[95]), germanium ($PbO/SbF_3$[96]), phosphorus (in cyclic phosphazenes with Swarts' reagent $SbF_3/SbCl_5$[97]), sulfur ($SO_2Cl_2$: $PbF_2$[98], aminosulfenic acid halides: $CsF$[99]), tungsten ($AsF_3$[100]), and osmium (tridodecylammonium fluoride[101]).

$$CH_3(CH_2)_5\text{—}Cl \xrightarrow[175\text{–}185°C]{KF/Glycol} CH_3(CH_2)_5\text{—}F \qquad [88]$$

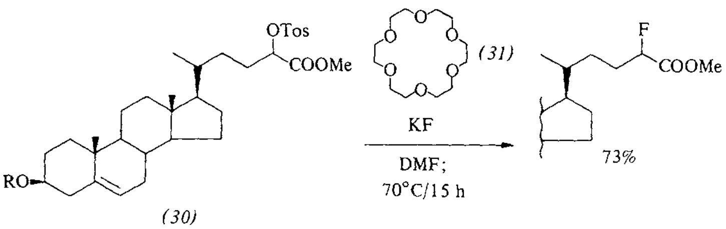
*(28)* 54%



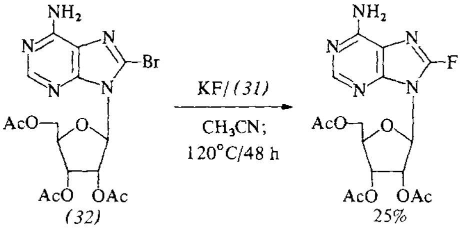
*(29)* 71% [89]

This simple method can also prove successful with complicated derivatives of natural products, as shown by the examples of prostaglandins ($KHF_2$[102], $(C_4H_9)_4N^+F^-$[103], sugars ($CuF$[104]), and nucleosides ($KF$[105]). In all these cases it is not a halogen that is exchanged but, for reasons of the easier accessibility, a tosyl group (obtained from the alcohol by esterification). The unusual substitution of a chlorine atom in the vinyl position with $AgF$[106] and the exchange of an $NO_2$ group in the aromatic ring for F with $KF$[107] are noteworthy special cases.

*Activation by crown ethers:* In the overwhelming majority of the above reactions an aprotic polar solvent such as sulfolane or $CH_3CN$ was used as the medium. By an exclusive solvation of the cations a degree of anion activation is assured, without which nucleophilic substitution takes place only slowly. The process is enhanced by the use of a chelating crown ether whose solvate complex with the cation of the metal fluoride has a high formation constant. The unsolvated fluoride ion ("naked fluoride") is strongly nucleophilic. In this way the substitution of Cl, Br, or I by F on singly or multiply bound carbons can take place in acceptable yields under mild conditions. Two examples of the use of [18]crown-6 *(31)* in the reaction of the steroid *(30)*[108] and the nucleoside *(32)*[109] may serve as an illustration of this method (DMF = dimethylformamide, R = tetrahydropyranyl).



*(30)*



*(32)*

The action of the crown ether *(31)* can be seen from comparisons on less spectacular examples: without an addition of *(31)* halogen-fluorine-substitutions in aliphatics and aromatic carbocycles proceed under mild conditions (boiling acetonitrile) to an extent of less than 5%; in the presence of catalytic quantities of *(31)* the degrees of conversion are between 40 and 90%[110]. The nucleophilic substitution on pentachloropyridine with *(31)* at 65 °C leads in 2 hours quantitatively to 3,5-dichloro-2,4,6-trifluoropyridine[111]; in the absence of *(31)* the same reaction proceeds at 200 °C in 6 h to an extent of only 65%[112]. Similarly clear results have been obtained with other crown ethers[113, 114].

The method has been used successfully on a variety of substrates, among them pyrimidine derivatives (nucleophilic exchange in the ring)[115], 2,3-dichloro-1,4-dioxane[116], carbonic esters, and carbamoyl compounds (substitution of chlorine on sp$^2$-hybridized carbon of the C=O group)[117], substitution of chlorine in the difficultly accessible vinyl position[118,119], on a β-oxolactone (tertiary position)[120], and in nitroamines (74—85% yields; no reaction in the absence of catalyst!)[121,122]. The method also finds application for metathesis reactions on a heteroatom (silicon[123], sulfur[124]). In virtually all cases [18]crown-6 *(31)* is selected as the catalyst, owing to its excellent complexing properties for the potassium ion and its commercial availability. The molar ratio of the substrate to the catalyst *(31)* is *e.g.* 10 : 1[125,126].

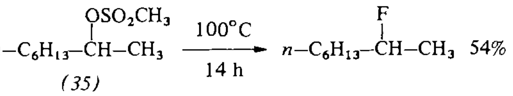
*Phase-transfer catalysis:* In the halogen-fluorine exchange reactions this popular method of preparative organic chemistry offers the particular technical advantage of the use of readily separable aqueous fluoride solutions. In addition, the yields may be high and the selectivity good, as in the reactions of *(33)—(35)*[127] (using $(KF)_{aq}/(C_{16}H_{33})(C_4H_9)_3P^+Br^-$).

$$n\text{-}C_8H_{17}Cl \xrightarrow[7\text{ h}]{160^\circ C} n\text{-}C_8H_{17}F \qquad 82\%$$

*(33)*

$$PhCH_2Cl \xrightarrow[7\text{ h}]{120^\circ C} PhCH_2F \qquad 95\%$$

*(34)*



$$n\text{-}C_6H_{13}\text{-}\overset{OSO_2CH_3}{CH}\text{-}CH_3 \xrightarrow[14\text{ h}]{100^\circ C} n\text{-}C_6H_{13}\text{-}\overset{F}{CH}\text{-}CH_3 \qquad 54\%$$

*(35)*

The reaction of the diazomethane derivative *(36)* constitutes a special application[128].

$$Ph_2C{=}N_2 \xrightarrow[(KHF_2)_{aq}]{Bu_4N^{\oplus}ClO_4^{\ominus}} Ph_2CHF \quad 50\%$$

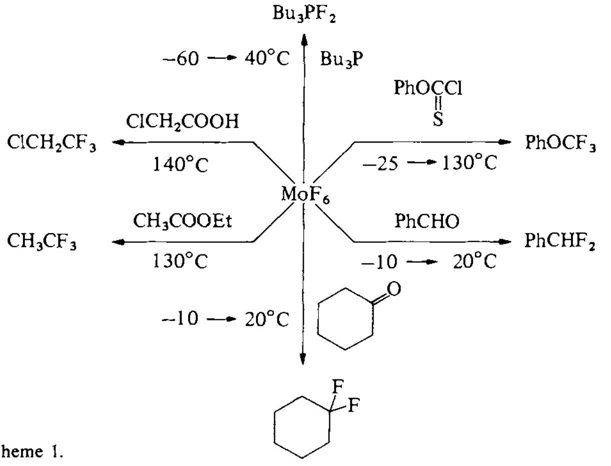
*(36)*

*Polymer-supported reagents:* In this case a basic ion-exchanger is charged with fluoride ions and reacted with the compound to be fluorinated in an organic solvent. Examples of this method are offered by the reactions of *(33)—(35)* to the corresponding fluorine compounds with resin-$\overset{+}{N}(CH_3)_3F^-$ in *n*-pentane under reflux (30, 24, and 20 h).

Noteworthy about these examples are the very mild reaction conditions and the outstanding yields (92, 100, and 70%). A further preparative advantage lies in the ease of removal of the exchanged halide which, being fixed to the resin, is simply filtered off. Other applications[130] have recently been reported.

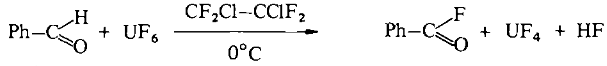
*New metal fluorides:* For some years now, molybdenum hexafluoride has found a variety of applications both for the metathetic and for the oxidative fluorinations (Scheme 1)[131-136].

The many known reactions also permit an estimation of the relative reactivities in multifunctional molecules.

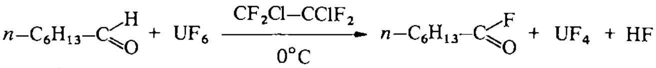


Scheme 1.

Uranium hexafluoride is an unusual fluorinating agent. This strongly aggressive substance, whose handling on a large scale made it necessary to develop highly resistant perfluorinated polymers[2], can substitute fluorine for aldehyde hydrogen under mild conditions, *e.g.* in *(37)* and *(38)*, with a high degree of selectivity[137]. This reaction does not take place with any other fluorinating agent.



*(37)* 40%



*(38)* 47%

*Organo-substituted metal fluorides:* The substitution of some of the fluorines bound to a metal atom by organic groups (*e.g.* phenyl groups) reduces the reactivity of the original fluorinating agent, as shown by the following sequence[138], found experimentally for antimony compounds:

$$PhSbF_4 > Ph_2SbF_3 > SbF_3 > Ph_3SbF_2$$

The phenylantimony compounds were obtained as follows:

$$Ph_2SbF \xrightarrow{XeF_2} Ph_2SbF_3 \quad [139] \quad 98\%$$

$$Ph_3Sb \xrightarrow{XeF_2} Ph_3SbF_2 \quad [139] \quad 95\%$$

$$PhSb(O)(OH)_2 \xrightarrow{SF_4} PhSbF_4 \quad [140] \quad 87\%$$

An example of the use of $Ph_2SbF_3$ is the partial fluorination of benzotrichloride *(39)*.

$$PhCCl_3 \xrightarrow[CH_2Cl_2/50^\circ C]{Ph_2SbF_3} PhCClF_2 \quad [138] \quad 65\%$$

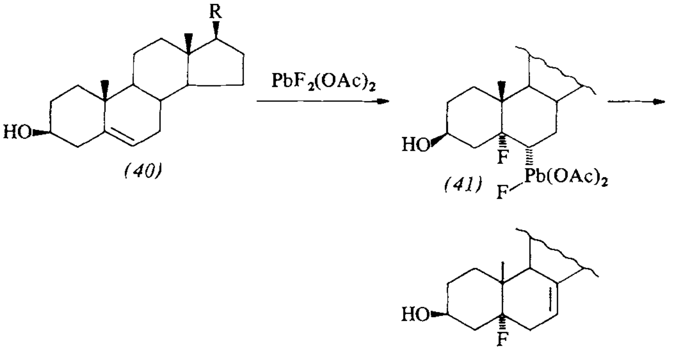
*(39)*

Diphenylantimony(III) fluoride has also been carefully studied[141], but so far nothing is known of its properties as a fluorinating agent. It will probably prove to be less active than $SbF_3$. This has been demonstrated for PhHgF, whose fluorinating power is too low for the reaction with 1-bromopentane. In contrast, the adduct $PhHgF \cdot HF$ permits the fluorination of $PhCCl_3$ *(39)* to $PhCFCl_2$ or $PhCF_3$, depending on the reactant ratios used[142].

The combination $Tl(OCOCF_3)_3/KF$[143] is suitable for the introduction of fluorine into activated arenes:

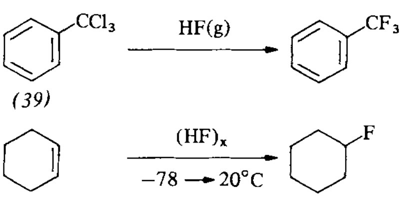
$$\text{Aryl-H} \xrightarrow{Tl(OCOCF_3)_3} \text{Aryl-}Tl(OCOCF_3)_2 \xrightarrow{KF} \text{Aryl-}TlF_2 \xrightarrow{BF_3} \text{Aryl-F}$$

In this reaction the thallium(III) reagent exerts an oxidizing and fluorinating action.—A parallel from the field of aliphatic chemistry is represented by the fluorination of a steroid of the type of *(40)* with $PbF_2(OCOCH_3)_2$[144,145]. The intermediate *(41)* has been isolated ($R = CH_3CO—$).



### 4.1.2. Hydrogen Fluoride

*Classical reactions:* HF can both replace a halogen on $sp^3$-hybridized carbon by fluorine and add to double or triple bonds; examples are the reactions with *(39)* and *(42)*.

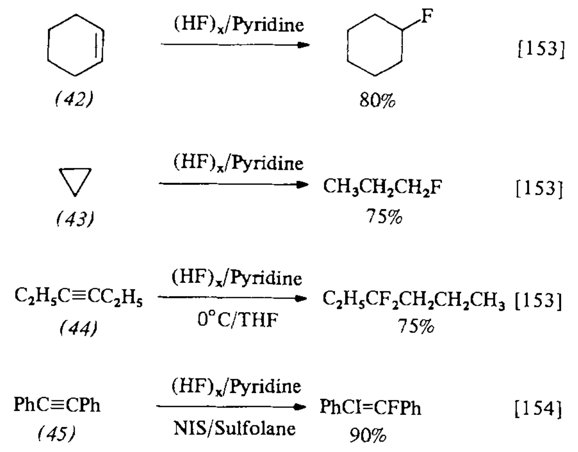


95% [147]

70% [146]

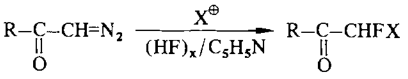
The use of anhydrous HF is also significant with complicated substrates. The exchange of esterified OH-groups in various sugars[148,149] can be carried out in this way, but the ionic mechanism leads to rearrangements[150]. Pure hydrogen fluoride is also used for the fluorination of small molecules such as KOCN or KSCN (formation of $H_2N—CXF$; $X = O, S$)[151], and in steroid chemistry[152]. However, the tendency to alkyl shifts in the protonated substrate is a constant perturbing factor.

*$(HF)_x$/pyridine:* A clear improvement of the situation has been brought about by *Olah*[153,154] with the introduction of the HF/pyridine mixture. Pyridine is an excellent solvent for hydrogen fluoride: a 70% solution does not lose any HF up to 50 °C, which obviously facilitates the handling of the reagent. Moreover HF is a weaker acid in pyridine than in the pure form, so that cationically induced polymerizations and rearrangements are strongly suppressed. On the other hand, the nucleophilic activity of the fluoride ion is enhanced. The reactions with *(42)*—*(45)* have been selected as examples (THF = tetrahydrofuran, NIS = *N*-iodosuccinimide).



The last of these reactions, the combined addition of fluorine and another halogen to a double-bond, is an example of "halofluorination". In alkenes the reaction follows Markovnikov's rule[155], but it can also be performed selectively in the presence of other functional groups (*e.g.* aryl[156] and ester groups[157]), and subsequent HX elimination permits the production of vinyl fluorides[158].

Nucleophilic substitution also proceeds with $(HF)_x$/pyridine. OH-groups are exchanged above all, *e.g.* in steroids[159] or in organosilicon and organogermanium compounds[160]. Interestingly, in a chlorinated alcohol reacting with Olah's reagent the halogen remains intact[161]. α-Diazoketones of the type *(46)* can likewise be used as educts[162]. This reaction has a very wide applicability. For procedural details and for the preparation of the HF/pyridine mixture, reference is made to a comprehensive recent publication[163].



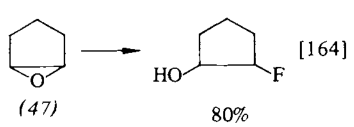
$$\underset{\underset{O}{\|}}{R-C}-CH{=}N_2 \xrightarrow[(HF)_x/C_5H_5N]{X^{\oplus}} \underset{\underset{O}{\|}}{R-C}-CHFX$$

*(46)*

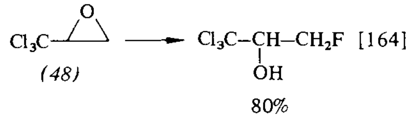
$R = C_6H_5, c\text{-}C_6H_{11}, C_2H_5, OC_2H_5$; $X = H, Cl, Br, I$

*Ring-opening reactions:* Olah's reagent makes it possible to open epoxide and aziridine rings as in *(47)*—*(49)* at 20 °C by nucleophilic attack and to arrive selectively at fluorinated alcohols and amines in high yields.

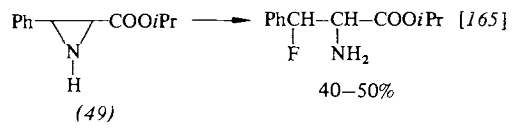
The ring opening in *(49)* shows that fluorinated amino acids are also accessible in this way. Further examples of the epoxide reactions are the fluorinations of "glycerol entities" for the synthesis of potential cancerostatics[166], of epoxidized sugars[167], and of simple oxiranes, although in the latter case with the similarly active reagent $(HF)_x/(CH_3)_3N$[168]. There are also other applications with aziridines[169,171]. Under the given conditions azirines react in a similar fashion; the product is an α-fluoroketone[170].



(47)



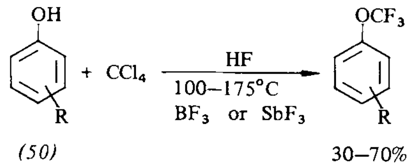
(48)



(49)

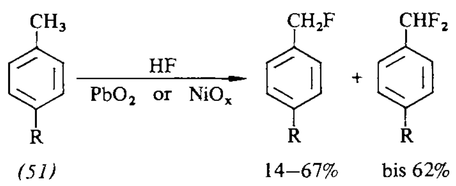
*Special processes:* The aim of this section is to present a few "spectacular" processes and some special features.

There are few proven methods for the introduction of the $CF_3O$ group (cf. Section 5.3) into arenes. Multistage syntheses are generally performed, but these can be used only on a very limited number of substrates. One recently published[172] method is based on phenols such as *(50)*. The



(50)

reaction is a "single-vessel process", which reduces the expenditure on apparatus. A variety of groups with different inductive and mesomeric effects have been tried as the substituent R. Although the yields are different, the basic process remains practicable. The reaction of *(51)* could be of similar significance[173,174].



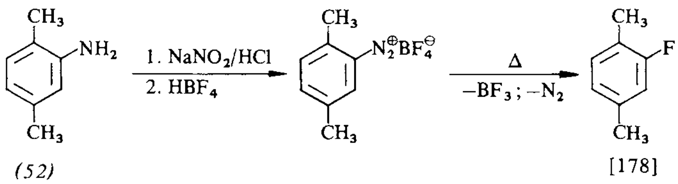
(51)

R *e.g.* $NO_2$, CN

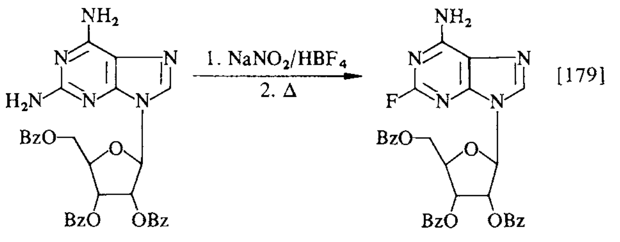
Other interesting reactions are fluorination in the *p*-position to an azide group in arenes (from amino groups by diazotization and reaction with $NaN_3$)[175], the conversion of aryltriazenes into aryl fluorides[176], and the monofunctional diazotization of 2,3-diaminosuccinic acid in the presence of HF, in which one $NH_2$ group is replaced by fluorine[177].

### 4.1.3. Boron Trifluoride, Tetrafluoroboric Acid and Their Salts

*Classical reactions:* The most common process in this group is the "Balz-Schiemann" reaction, in which an aromatic $NH_2$ group as in *(52)* and *(53)* is replaced by fluorine. The $NH_2$ group is first diazotized in the presence of tetrafluoroboric acid, and this is followed by thermal decomposition of the isolated intermediate product, diazonium tetrafluoroborate (Bz = benzyl).



(52)

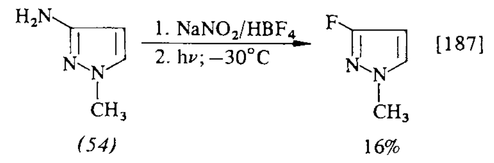


(53)

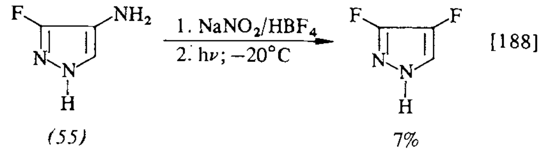
Other interesting more recent applications are the fluorination of the carcinogenic benz[*a*]anthracene[180] and of some aminopyrimidine derivatives used in the treatment of leukaemia[181]. The latter example also demonstrates the high decomposition temperature of the intermediate stage: 225 °C.

*Modifications of the classical reactions:* In a number of cases catalysis with crown ethers dramatically reduces the decomposition temperature of the intermediate tetrafluoroborate[182]. Within certain limits the $HBF_4$ can be replaced by $HPF_6$[183,184]. Fluorine can be introduced into alkyl compounds *e.g.* with $NO^+BF_4^-$ (substitution of the azide group)[185] and with $AgBF_4$ (substitution of bromine α to the keto group)[186].

*"Photo-Schiemann reaction":* If, for example, the aromatic carbocycle *(52)* is replaced by heterocycles such as *(54)* and *(55)*, the intermediate diazonium salt becomes so unstable that its isolation, the precondition for controlled thermal decomposition, becomes impossible. Here the answer lies in the "photo-Schiemann reaction", in which the intermediate is not isolated but decomposed photolytically *in situ*.



(54)



(55)

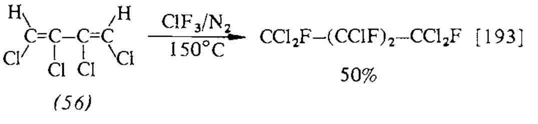
The method has also proven successful in the conception of antiviral agents, namely in the fluorination of an imidazole ring bound to a ribose molecule[189].

*Fluorinations with $BF_3$:* Similarly to hydrogen fluoride, boron trifluoride can split epoxide rings nucleophilically.

A vicinal fluoroalcohol is formed during the subsequent hydrolysis. This reaction has so far been used only in a few instances in steroid chemistry[190–192]; it has proved not to be very selective.

### 4.1.4. Halogen Fluorides

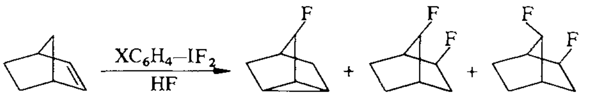
*Classical reactions:* Some interhalogen compounds were tried out early as fluorinating agents, *e.g.* for *(56)* and *(57)*. The reactions are metatheses, although additions to double bonds have also frequently been observed[195,196], especially with reactive reagents such as $BrF_3$. This ambivalent behavior is of course synonymous with low selectivity. In the classical methods halogen fluorides are thus more successful with simple substrates, *e.g.* for the preparation of $SeF_4$ from $SeCl_4$ (ClF)[197]. The addition of "IF" (AgF + $I_2$) to the double bond of a nucleoside sugar[198] is highly selective, but this is not a typical example.



*(56)*

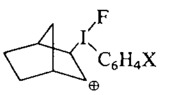
$$(57)\ CI_4 \xrightarrow[90-100°C]{IF_5} CF_3I\ [194]$$

*Organohalogen fluorides:* During the systematic further development of the halogen fluorides the effect of substituting one or more fluorines by organic groups has been studied, just as in the metal fluorides. The whole has so far been limited to iodine. The common intermediate stage in the reaction of norbornene *(58)* is the cation *(59)*. $CH_3IF_2$ has similar fluorinating properties to those of $XC_6H_4$—$IF_2$[201]; a noteworthy point here[202], as in the case of the phenyl derivatives[203], is the careful product analysis. All the organo-derivatives mentioned fluorinate double bonds on an exclusive basis. Metathesis occurs only with the compound *(60)*. The reaction of *(60)* with PhMgBr affords PhF in 90% yield.



*(58)* 6–18% 74–88% 5–13%

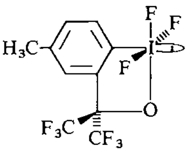
X = *p*–$OCH_3$, *m*–$OCH_3$, H, *m*–Cl, *m*–$NO_2$ [199]



*(59)*

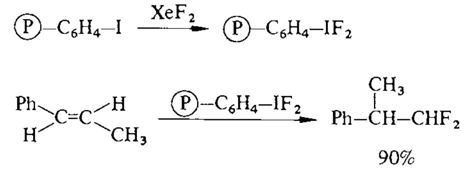
$$R{-}I \xrightarrow[R = C_6H_5,\, C_6F_5,\, C_3F_7]{XeF_2} R{-}IF_2 \xrightarrow[R = C_6F_5]{XeF_2} R{-}IF_4\ [200]$$

60–82% 100%



*(60)*

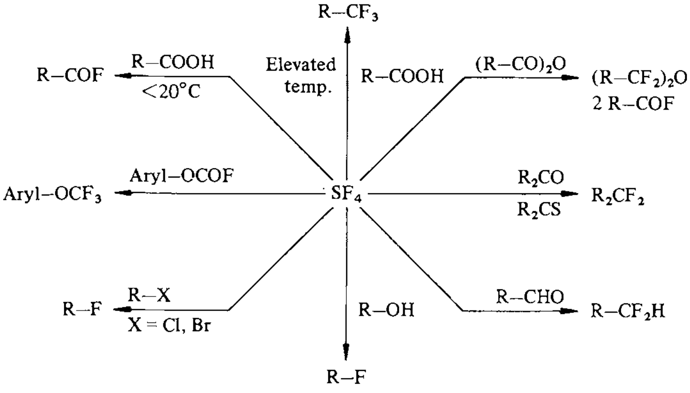
*Polymer-supported reagents*[205]: Again as in the case of the metal fluorides, it is possible with iodine fluorides to make use of the preparative advantage of the easy separation of a polymeric resin by appropriate derivatization:



However, the distinctly cationic reaction mechanism in all organoiodine fluorides leads to a predominance of rearranged products.

### 4.1.5. Sulfur Tetrafluoride and Analogues

*Classical reactions:* $SF_4$ is one of the most common fluorinating agents. Its action mechanism is metathetic in character (Scheme 2[206]).



$$R{-}OH + SF_4 \xrightarrow{(\text{Lewis acid})} R{-}OSF_3 + HF$$
$$R{-}OSF_3 \longrightarrow R{-}F + SOF_2$$

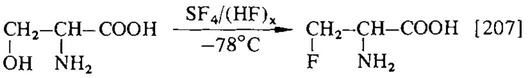
Scheme 2.

The above reaction path[207] can be regarded as definite. Although the manipulation of the sulfur tetrafluoride is not without problems (boiling point −40 °C, toxicity like that of phosgene), the reagent is still often used, especially with more inert substrates. A popular application is for the conversion of carboxyl groups into the $CF_3$ or the acid fluoride. Acetylenedicarboxylic acid is converted smoothly into the acid fluoride[208]. Fluorocarbonic esters are converted into the $CF_3O$-substituted compounds by $SF_4$[209]. $SF_4$ plays a particularly outstanding role in the introduction of the $CF_3$ group into aromatic systems. This applies both to carbocycles[210] and to heterocycles like thiazoles[211], and even to the very sensitive furans[212-214]. It is also possible to replace COOH by $CF_3$ in perfluorinated adamantanes[215].

The likewise customary conversion of a keto group into $CF_2$ has been demonstrated on anthraquinone[216] and on adamantanones[217,218]. Biologically active compounds (*e.g.* lysine derivatives[219]) frequently contain amino groups that are sufficiently nonreactive in the case of tertiary perfluorinated compounds[220] or have to be protected *e.g.* by the $CF_3CO$ group[221]. The carbonyl groups of acid amides are inert[222]. The replacement of the OH-group by F is possible in 3-*O*-acetyldigitoxigenin in moderate yields, with KF as an HF-receptor. An interfering competitive reaction in this process is the elimination of $H_2O$ with the formation of a double bond in the steroid skeleton[299].—$SF_4$ can also replace Cl, Br, or I with F, as shown by an example from adamantane chemistry[223]. The reaction conditions are mild (85—140 °C; 3—8 h). The epoxide ring is already opened at room temperature, though in rather uncontrolled fashion[224]. Even tertiary hydrogens have been substituted by fluorine with the aid of $SF_4$ (substrate: adamantane)[225].

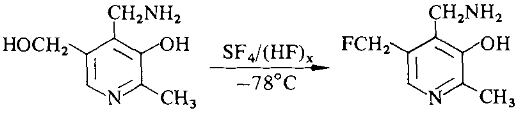
*Hydrogen fluoride as a catalyst and a solvent:* In the reactions with $SF_4$ hydrogen fluoride is primarily used as a catalyst, allowing the reaction temperature to be reduced and thus preventing side reactions from taking place. In addition, the reaction times become shorter and the conversions more complete. In many cases the applications are covered by the examples already cited: replacement of the COOH bound to the benzene ring by a $CF_3$-group[226,227] and analogous reactions on the furan[228-230] and adamantane[231] skeletons, tertiary H-atoms being also exchanged for F, apparently owing to the high temperature. The CO-group in aromatic trifluoroacetic acid esters is smoothly fluorinated to $CF_2$[232-234].

Hydrogen fluoride plays a particularly important role as solvent in "fluorodehydroxylations" (—OH→—F) and "fluorodesulfurizations" (—SH→—F)[235]. In amino acids such as *(61)* the amino groups are protonated by HF and thus made incapable of perturbing side reactions.



$$\underset{\mathrm{OH}}{\mathrm{CH_2}}{-}\underset{\mathrm{NH_2}}{\mathrm{CH}}{-}\mathrm{COOH} \xrightarrow[-78^\circ\mathrm{C}]{\mathrm{SF_4/(HF)_x}} \underset{\mathrm{F}}{\mathrm{CH_2}}{-}\underset{\mathrm{NH_2}}{\mathrm{CH}}{-}\mathrm{COOH}\ [207]$$

*(61)* 51%



49%

The extremely mild reaction conditions are particularly worthy of note. A variety of compounds can be made to react in this way, *e.g.* 2-amino-3-hydroxybutyric esters[236], quinine, hydroxyphenylalanine, thiamine chloride, ephedrine, and pseudoephedrine[237].

*Amino derivatives:* Formal substitution of one or more fluorine atoms in $SF_4$ by secondary amino group or groups leaves the character of the fluorinating agent unchanged[238]. "DAST" *(62)* boils at 46—47 °C/10 torr.

$$\mathrm{SF_4 + Et_2N{-}SiMe_3 \xrightarrow{CCl_3F} Et_2N{-}SF_3 + Me_3SiF}$$

"DAST" *(62)*, 84%

$$\text{“DAST”} + \mathrm{Et_2N{-}SiMe_3 \xrightarrow{CCl_3F} (Et_2N)_2SF_2 + Me_3SiF}$$

*(63)*

The advantages of modified compounds such as *(62)*—*(64)* over $SF_4$ are as follows:

| | |
|---|---|
| chemically: | less reactive; more selective reactions; fewer rearrangements or eliminations |
| technically: | less volatile, reactions under pressure or elaborate cooling are not necessary |

$$\mathrm{CH_3CH{=}CHCH_2OH \xrightarrow[(64)]{Me_2N{-}SF_2{-}NEt_2} CH_3CH{=}CHCH_2F + CH_3CHFCH{=}CH_2}$$

57% 15%

$$\mathrm{(CH_3)_3C{-}CHO \xrightarrow[CCl_3F/25^\circ C]{\text{“DAST”}} (CH_3)_3C{-}CHF_2}$$

78%

The selective fluorination of acid-sensitive substrates such as crotyl alcohol and pivalaldehyde, achieved with these reagents with clear suppression of the otherwise common dehydration, rearrangement, and oligomerization reactions, indicates a shorter lifetime of the ionic intermediates and illustrates the importance of this development. Other preparation processes have been given for the two aminosulfur fluorides *(62)* and *(63)*[239], and analogous compounds with other substituents on the sulfur (*e.g.* piperidine[238], morpholine[240], or those of the type $(R_2N)_3S^+(CH_3)_3SiF_2^-$[241]) have been synthesized, but in preparative fluorination chemistry diethylaminosulfur trifluoride "DAST" *(62)* has been used almost exclusively, among other reasons probably because it is available commercially. Apart from special applications such as the fluorination of the keto groups in spirocyclic four-membered rings[242], substitution in optically active compounds[243], or the skeleton-fluorination of carcinogenic hydrocarbons such as benzanthracene[244] and benzpyrene[245], "DAST" is used primarily in the chemistry of natural products. Pregnadiene derivatives[246] have been fluorinated as also have androstanes[247,248], cholesterol[249], gibberellins[250,251], vitamin $D_3$[252,253], and sugars[254-256]. However, in the face of all these successes it should not be forgotten that even with "DAST" dehydration reactions may occasionally predominate[257]. The reaction with halogenated compounds with halogen fluorine exchange, which is sometimes used for preparative purposes[258], can in other cases prove to be a perturbing influence[259]. Lastly, explosions with the use of "DAST" have been reported[260,261].

*Organo-derivatives:* Phenylsulfur trifluoride[262] has already been in use for some considerable time. Diphenylsulfur difluoride *(68)* is a new development[263] which according to the preliminary data exhibits fluorinating properties. Since the compound is solid, it has become known as "solid $SF_4$". The reactions with *(65)*, *(37)*, and *(67)* are

$$\mathrm{Ph{-}S{-}S{-}Ph + 6\,AgF_2 \xrightarrow{CClF_2{-}CFCl_2} 2\,Ph{-}SF_3 + 6\,AgF}$$

*(65)* *(66)*, 60%

$$\mathrm{Ph{-}CHO \xrightarrow[20^\circ C]{Ph{-}SF_3} Ph{-}CF_2H}$$

*(37)* 71—80%

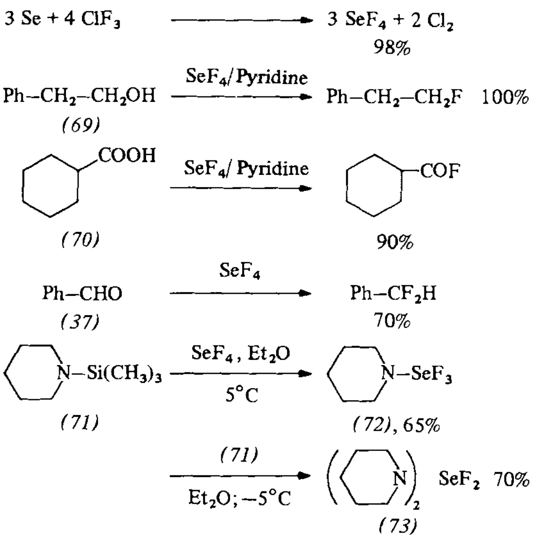
$$\underset{(67)}{\mathrm{Ph{-}S{-}Ph}} \xrightarrow{\mathrm{F_2/Ar}} \underset{(68)}{\mathrm{Ph_2SF_2}}$$

$$\underset{(37)}{\mathrm{Ph{-}CHO}} \xrightarrow{\mathrm{Ph_2SF_2}} \mathrm{Ph{-}CF_2H}$$

examples. The main advantage of *(68)* ("solid sulfur tetrafluoride") over $SF_4$ is the higher boiling point.

### 4.1.6. Selenium Tetrafluoride and Its Amino Derivatives

The fluorination properties of $SeF_4$, b.p. 106 °C, are similar to those of $SF_4$. The compound can be prepared from selenium and $ClF_3$ in very good yield. Pyridine is recommended as a solvent for the reactions to moderate the activity[264]. The reactions with *(69)—(71)* have been selected as examples.

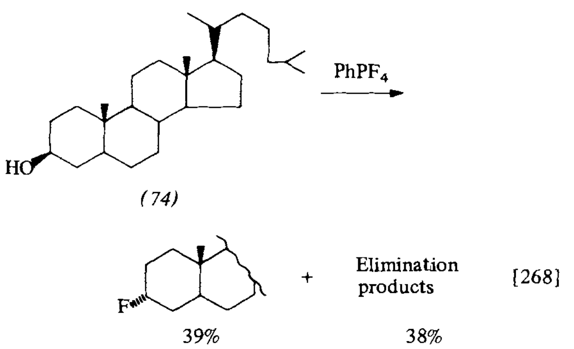


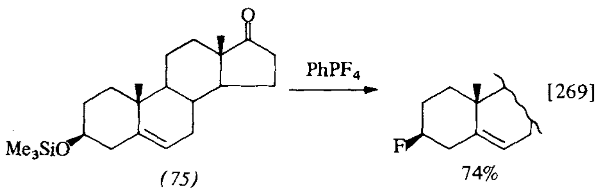
The amino derivatives *(72)* and *(73)* of $SeF_4$[265] (morpholine compounds are also accessible in this way) have not yet been tried out as fluorinating agents.

### 4.1.7. Fluoro(phenyl)phosphoranes

The compounds $Ph_nPF_{5-n}$, $n = 1-3$, can replace OH-groups with fluorine. The fluoro(phenyl)phosphoranes are prepared by reacting their chlorine analogs with $AsF_3$ or $SbF_3$[266] or by reacting chlorophosphanes with $XeF_2$[267]; $Ph_2PF_3$ is available commercially. In general, the reactivity decreases with increasing number of organic groups, a feature also observed with other fluorinating agents. The reaction mechanism, demonstrated here on the steroids *(74)* and *(75)*, probably resembles that of $SF_4$.

In nonesterified alcohols such as *(74)* the elimination process is significant. The use of silylated compounds such as *(75)* suppresses the competing reaction. This method has also become established in the presence of ester groups and arene-bound halogens[270].





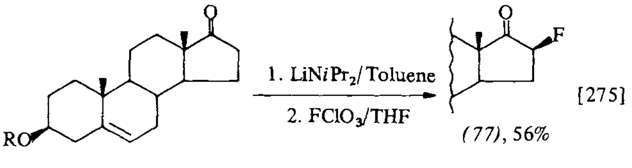
## 4.2. Electrophilic F-Transfer: Perchloryl Fluoride

4.2.1. *Classical applications:* Fluorinations with $FClO_3$ proceed only in the presence of anionic substrates; the primary production of a carbanion with a sufficiently strong base is thus a necessary precondition. The fluorine atom in the $FClO_3$ can be regarded as carrying a partial positive charge, probably in consequence of the high electronegativity of $Cl^{VII}$. However, the problems associated with this method of fluorination are manifested in the reaction with malonic ester *(76)*[271].

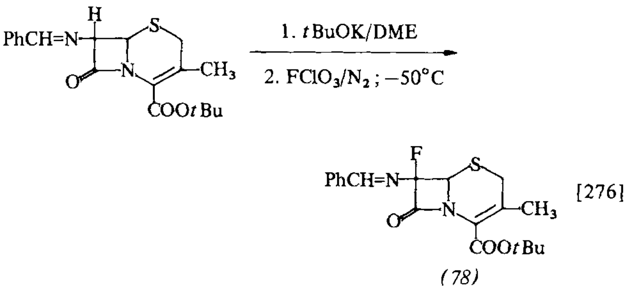
$$\underset{(76)}{\mathrm{CH_2(COOEt)_2}} \xrightarrow{\mathrm{Na/EtOH/FClO_3}} \begin{array}{ll} \mathrm{FCH(COOEt)_2} & 8.7\% \\ \mathrm{F_2C(COOEt)_2} & 36.1\% \\ \mathrm{EtCH(COOEt)_2} & 25.2\% \\ \mathrm{EtCF(COOEt)_2} & 15.3\% \\ (76) & 14.4\% \end{array}$$

The range of products characterizes $FClO_3$ as a nonselective reagent; some of the substances obtained make it necessary to postulate $EtOClO_3$ as an intermediate. The method has nevertheless proved useful with substrates offering a narrow choice of reaction possibilities, as in the fluorination of 4,4-dimethyl-2-cyclopentenone[272] and in the synthesis of tricyanofluoromethane[273] and 2-fluorothiophene[274].

*New variants:* The decisive development is based on the knowledge of how to separate the production of the car-



*(77)*, 56%



*(78)*

banion and the fluorination process and to obtain the carbanion irreversibly[275]. Possibilities are thus opened up for the fluorination of multifunctional compounds, *e.g.* of natural products, frequently in the position α to a keto group (fluorination of an enolate; DME = dimethoxyethane, R = tetrahydropyranyl).

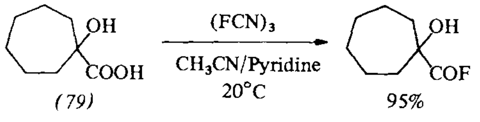
Similar examples are the fluorination of a pregnenone[277] and of a norbornane derivative (86% yield; prostaglandin precursor)[278]. Care must always be exercised when using $FClO_3$, for at higher temperatures this very reactive compound tends towards explosive decomposition on contact with organic substances[279].

## 4.3. Nucleophilic and Electrophilic F-Transfer

The fluorine-containing nitrogen compounds to be discussed here represent a very heterogeneous group of substances with various modes of reaction. The F-atom to be transferred need not be bound to the nitrogen. Since all the reagents are comparatively recent, the classification into classical and modern reactions is superfluous.

### 4.3.1. Cyanuric Fluoride

This compound, easily prepared by chlorine-fluorine metathesis (see Section 4.1.1), converts carboxylic acids such as *(79)* and *(80)* mildly and selectively into the acid fluorides[280].



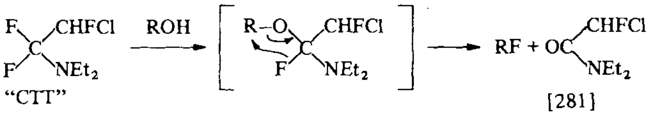
$$\underset{(80)}{\text{PhCH=CHCOOH}} \xrightarrow[\text{CH}_3\text{CN/Pyridine}]{(\text{FCN})_3} \underset{95\%}{\text{PhCH=CHCOF}}$$

As the examples show, CC- and CO-double bonds, alcohol groups, and aryl groups remain unaffected.

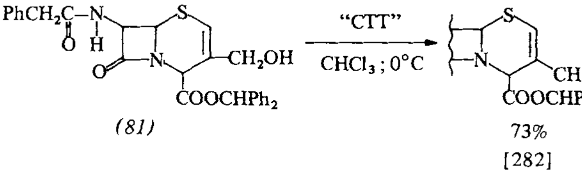
### 4.3.2. 2-Chloro-1,1,2-trifluorotriethylamine, "CTT"

This partly halogenated amine has gained the widest application of the fluorine-containing nitrogen compounds. It is particularly suitable for the fluorination of natural products, since even under mild conditions it replaces alcoholic OH-groups, *e.g.* in the cephalosporin derivative *(81)*.

$$\text{CFCl=CF}_2 + \text{Et}_2\text{NH} \longrightarrow \underset{\text{"CTT", 61\%}}{\text{HClFC–CF}_2\text{–N(C}_2\text{H}_5)_2}$$



[281]

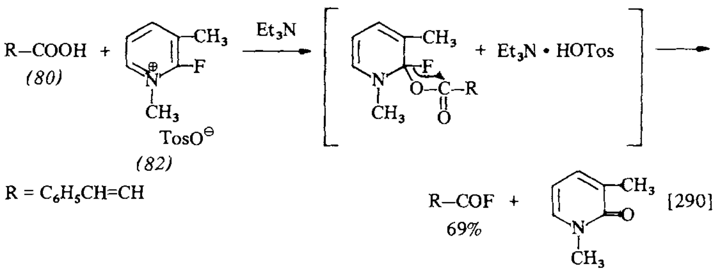


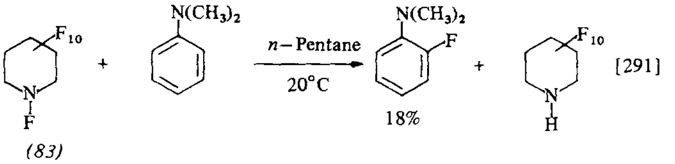
*(81)* 73% [282]

"CTT" fluorinates OH-groups at the bridge-head positions of bicyclic compounds[283] and selectively in the 7-position of norbornadiene[284]. The reagent has proved suitable for the fluorination of complicated substances such as brefeldin A[285] and gibberellin[286], and for the fluorination of kaurenoids[287]. "Bromofluorination" (addition of formal BrF to a double bond in steroids[288]) with "CTT" and *N*-bromoacetamide represents an exception. A "CTT"-analog has recently been obtained from perfluoropropene and diethylamine[289]. This reagent fluorinates cholesterol in a yield of 83%.

### 4.3.3. 2-Fluoro-1,3-dimethylpyridinium Tosylate *(82)* and Perfluoropiperidine *(83)*

The action mechanism of these rather exotic reagents may be demonstrated on one example of each.

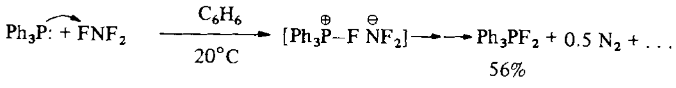




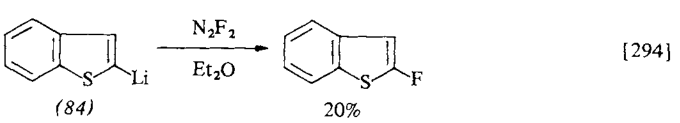
With the piperidine derivative *(83)* the ESR spectra indicate a free radical mechanism. It was already known in 1964 that *(83)* can transfer *N*-bound fluorine to a carbanion[292].

### 4.3.4. Nitrogen Trifluoride and Dinitrogen Difluoride

In conclusion, reference may be made to two remarkable curiosities: even such an inert compound as $NF_3$ can fluorinate suitable substrates, and the same is true of $N_2F_2$.



$$(\text{Me}_2\text{N})_3\text{P} + \text{NF}_3 \xrightarrow[20\text{–}45^\circ\text{C}]{} \underset{80\%}{(\text{Me}_2\text{N})_3\text{PF}_2 + 0.5\ \text{N}_2 + \ldots} \quad [293]$$

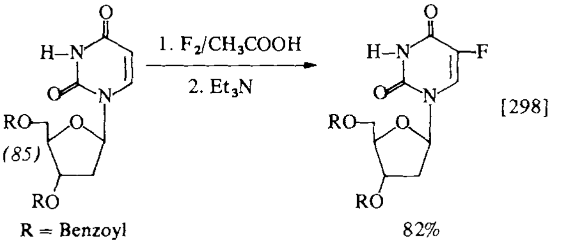


## 4.4. Electrophilic and Radical F-Transfer

### 4.4.1. Elementary Fluorine

*Classical reactions:* The conventional use of $F_2$ has already been discussed in Section 3.1. A characteristic feature of all these reactions is their radical mechanism, with the typically wide range of products. For this reason elementary fluorine has long been considered unsuitable for selective fluorinations.

*Modern techniques:* At the beginning of the 'seventies *Meinert et al.*[295] reported selective fluorination of (partially protected) uracil, uridine, and 2'-deoxyuridine *(85)* in the reactive 5-position of the pyrimidine ring, using an $F_2$-pyridine adduct. The adduct is obtained in the form of a colorless solid which is stable up to $-2\,^\circ C$ by passing fluorine diluted with $N_2$ into a solution of pyridine in a chlorofluorohydrocarbon at $-78\,^\circ C$[296]. The adduct is believed to have an ionic structure, the fluorination being apparently ionic (electrophilic). In the case of uracil the reaction is quantitative. Extension of the investigations to other solvents[297] revealed that glacial acetic is most advantageous, although only if it is saturated with $F_2$ before the addition of the substrate (nucleobase or nucleoside) ("fluorinated acetic acid"). In contrast, complex reactions occur if the $F_2$ is introduced into the reactant-solvent mixture. It has not yet been clarified whether this means that the actual fluorinating species is not $F_2$ itself but a reactive intermediate of a reaction between fluorine and acetic acid (*e.g.* "$CH_3COOF$"). "F" and "$CH_3COO$" probably first add to the CC-double bond of the nucleobase. In the case of nucleosides the corresponding adducts could be detected at an early stage[297], and they have since also been isolated from uracil[299]. The second step of the reaction consists in the elimination of acetic acid which often has to be induced by a base, resulting over-all in an apparently direct replacement of a vinyl hydrogen by fluorine. Other nucleosides have also been fluorinated by the described process[300,301].

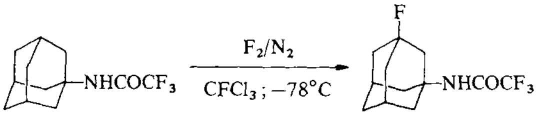


*(85)*

R = Benzoyl

82%

Another method of selective fluorination with elementary fluorine was discovered by *Barton et al.*[302]. In the presence of radical receptors, in suitable solvents, and at low temperatures fluorine diluted with $N_2$ selectively substitutes tertiary hydrogen in steroids[303] and adamantane derivatives such as *(186)*[304].



*(86)*

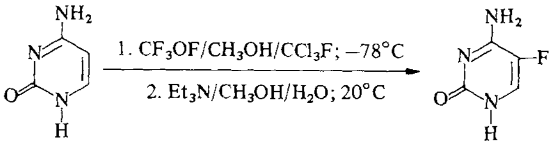
83%

Fluorinations with elementary fluorine have also been successfully tried out in carbohydrate chemistry[305]; the method is suitable for the selective oxidative halogenation of heteroatoms in organic compounds without affecting the C—H, C—halogen, or C=C bonds[306,307]. The fluorination of arenes with elementary fluorine (H→F substitution) has already also been the subject of careful mechanistic studies[308]. Moreover, the reaction of $F_2$ with carbanionic centers has established conclusively the transfer of positively polarized fluorine[309].

### 4.4.2. Trifluorofluoroxymethane and other Fluoroxy Compounds

A classification into classical and modern techniques is again superfluous for $CF_3OF$, since all the results discussed here have been published in the last decade. Trifluorofluoroxymethane ("trifluoromethyl hypofluorite") has two fundamentally different possible reactions: electrophilic and radical F-transfer. In turn, among the ionic reactions a distinction must be drawn between electrophilic addition to double-bond systems and electrophilic substitution of a hydrogen atom at an $sp^3$-hybridized carbon.

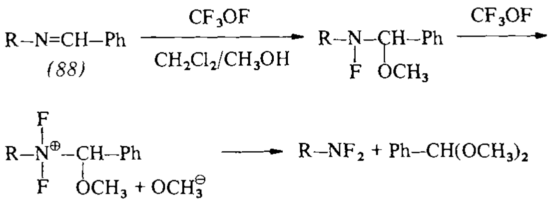
*Addition to double-bond systems (ionic mechanism):* When mixed with $CF_3OF$ in a suitable solvent mixture at low temperature, and after working-up under alkaline conditions, cytosine *(87)* gives a high yield of 5-fluorocytosine[310].



*(87)*

85%

This process had already been used earlier in the synthesis of 5-fluorouracil *(6)*[311,312], pharmacologically a highly interesting substance, and the corresponding complete uracil nucleotide[313]. Though the replacement of a vinyl hydrogen by fluorine is apparently direct, in truth—similarly to the situation with the analogous examples with $F_2$ described above—this is an addition-elimination reaction. Positively polarized fluorine first opens the CC double bond and the carbenium ion formed can then react with the nucleophiles present ($CF_3O^-$, $F^-$, or $CH_3O^-$) to give a saturated compound. Elimination of the same nucleophile in combination with the H-atom geminal to the fluorine (*e.g.* as $CH_3OH$) yields the final product. This reaction pathway is confirmed by results from arene chemistry. $CF_3OF$ can introduce fluorine into aromatic systems[235] and thus simulate direct H-substitution. Careful investigations into the fluorination of specially carcinogenic arenes (reaction in the K region)[314,315] show that here too the primary reaction is an addition with loss of aromaticity of the ring in question. A similar situation applies in the reaction of benzofuran and indole with $CF_3OF$[316]. The fluorination of griseofulvin[317] is also a clearly understandable process, whereas in steroid chemistry limits are revealed: nonactivated double bonds add $CF_3OF$ to give complex product mixtures[319]. Unsaturated sugars can likewise be fluorinated with $CF_3OF$[320-324]. Not only the CC- but also the CN-double bond, *e.g.* in *(88)*, reacts with $CF_3OF$ in the manner described but with subsequent cleavage[324a].



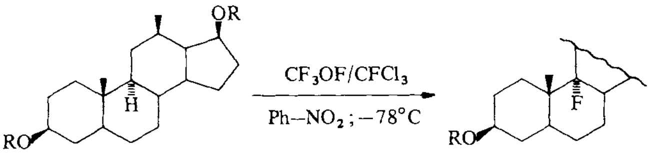
$$R{-}N{=}CH{-}Ph \xrightarrow[CH_2Cl_2/CH_3OH]{CF_3OF} R{-}N(F){-}CH(OCH_3){-}Ph \xrightarrow{CF_3OF} R{-}N^{\oplus}F_2{-}CH(OCH_3){-}Ph + OCH_3^{\ominus} \longrightarrow R{-}NF_2 + Ph{-}CH(OCH_3)_2$$

(88)

R = Adamantyl

The fluorination of α-diazoketones, which can lead to α,α-difluoroketones or to α-fluoro-α-trifluoromethoxyketones[325,326] represents an exceptional case of electrophilic addition to CN double bonds.

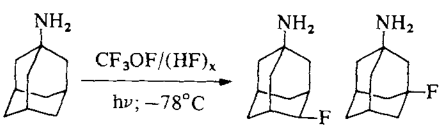
*Substitution at an $sp^3$-hybridized carbon (ionic mechanism):* $CF_3OF$ reacts with adamantane in $CFCl_3$ or $CH_2Cl_2$ at −25 °C to give mainly 1-fluoroadamantane[304]. On the basis of the influence of polar substituents on the reaction rate, of the high selectivity, and the pronounced tendency toward monosubstitution on tertiary carbons, an electrophilic reaction mechanism must be assumed. The reaction starts with an electrophilic attack of positively polarized fluorine on the C—H-σ bond. An analogous reaction occurs with complicated substrates, *e.g.* the steroid *(89)*[303]. Once again a tertiary H-Atom is here substituted.



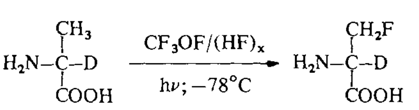
*(89)* 34%

R = $CF_3CO$

*Photofluorination with $CF_3OF$ (radical mechanism):* With 1-aminoadamantane *(14)*[327], as a substrate, radical fluorination with $CF_3OF$ in the liquid phase [$(HF)_x$] yields only two monofluorinated products *(90)* and *(91)* in more or less comparable quantities; the pharmacologically interesting 2-deuterio-3-fluoro-D-alanine *(7)* ("DFA") is formed directly from the nonfluorinated compound in an acceptable yield[21].



*(14)* *(90)*, 27% *(91)*, 25%



$$H_2N{-}C(CH_3)(D){-}COOH \xrightarrow[h\nu;\,-78^\circ C]{CF_3OF/(HF)_x} H_2N{-}C(CH_2F)(D){-}COOH$$

"DFA" *(7)*, 59%

The remarkable fact is that neither the unprotected amino group nor the carboxylic acid group is attacked, which at least in part explains the importance of hydrogen fluoride as a solvent. In place of H-atoms SH-groups are also replaced by F in mercaptoamino acids during photofluorination[328], a reaction pathway known as "fluorodesulfurization". The reaction can be carried out with $CF_3OF$, but only when readily oxidizable secondary and tertiary SH-groups are present; $F_2$ must be used in the case of primary thiols[235].

### 4.4.3. Other Fluoroxy Compounds

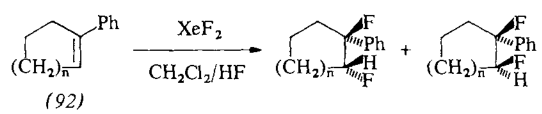
The next higher homolog of $CF_3OF$, $C_2F_5OF$, is formed in addition to $CF_3CF(OF)_2$ in the reaction of $F_2$ with $CF_3COONa$ at low temperatures. The compound can be used to prepare α-fluoroketones from enol acetates *in situ*[329]. The process is also useful in steroid chemistry[330,331]. $CF_2(OF)_2$ fluorinates steroids in the tertiary position[331a] and exchanges N-bound hydrogen for fluorine similarly to $CF_3OF$[331b]. The inorganic parent compound of the fluoroxy compounds described here, oxygen difluoride $OF_2$, itself has fluorinating properties and acts quite selectively under mild conditions (substrate: barbituric acid)[299].

### 4.4.4. Noble-Gas Fluorides[332]

$XeF_2$ and its homologs are also a recent class of fluorinating agents. The first systematic investigations reach back less than 9 years, and only very recently has a dramatic increase in relevant publications taken place. The fact that fluorinations with $XeF_2$ proceed *via* radical cations can be taken as certain, which explains the significance of acid catalysts (HF, $CF_3COOH$). Xenon difluoride, which is available commercially, enters into essentially three types of reaction: it can fluorinate CC-double bonds oxidatively and it can replace aliphatic or aromatic H-atoms with F.

The oxidizing fluorinations on heteroatoms in organic compounds deserve a brief mention because new fluorinating agents are often thus obtained. From experimental findings it can be concluded that when an arene and alkene are present at the same time, the alkene is the more reactive. The comparison of aliphatic and aromatic hydrogen, on the other hand, is less clear.

*Reactions of alkenes and alkynes with $XeF_2$:* The reaction of $XeF_2$ with a cyclic alkene of the type of *(92)* in the presence of traces of HF[333] gives a mixture of products whose composition varies with the ring size of the alkene. The proportion of *cis*-isomers increases with increasing *n*. The cationic reaction mechanism is based on investigations on

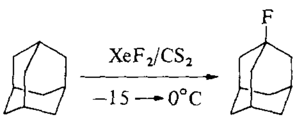


*(92)*

phenyl-substituted ethylenes[334-337] and norbornenes[338,339]. From the preparative standpoint, the rearrangements observed constitute a restriction. Halogen-substituted alkenes react in a similar fashion[340,341]. Lewis acids such as $BF_3$ can also catalyze the reaction[342]. Finally, mention should be made of the bromofluorination of alkenes with $XeF_2/Br_2$[343] and the addition to an alkyne to give a tetrafluorinated product[344].

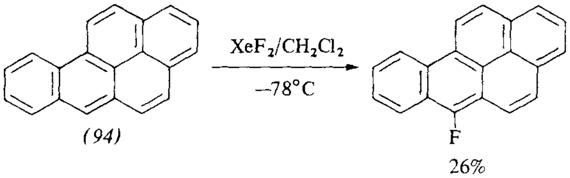
*Reactions of saturated compounds with $XeF_2$:* One noteworthy example is the fluorination of adamantane *(93)*[345].

Further uses of this method relate to linear and cyclic sulfanes[346] and to hexamethylbenzene[347].



(93)

*Reactions of arenes with $XeF_2$:* The fluorination of benzene with $XeF_2$ has been studied in detail[348]: the products formed are mono- and difluorinated benzenes and fluorinated biphenyls. Single and multiple substitution has also been observed with naphthalene[349]. Oxidative fluorination also occurs with anthracene and phenanthrene[350-352]. Besides the monofluorination of pyrene[353], the reaction with carcinogenic arenes such as *(94)* is of primary interest[354].

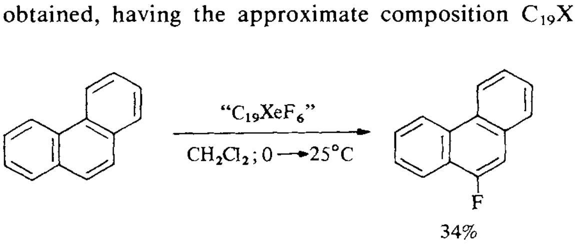


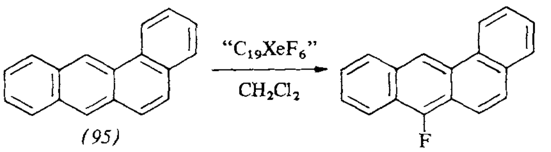
(94)

$OCH_3$- and OH-substituted benzene and naphthalene can even be reacted without catalysis by HF[355]; acenaphthylene reacts at the 1,2-double bond[356]; indane only in the aromatic part of the molecule[357]. It is worth noting that $XeF_2$ fluorinates bromopentafluorobenzene oxidatively with $BF_3$ catalysis[358] and oxidizes hydroquinone to the quinone[359]. Heterocycles such as pyridine and quinoline react smoothly at low temperatures[360], amino groups also remaining intact.

*Fluorination on heteroatoms with $XeF_2$:* A simple reaction leads to the production of $Ph_2SF_2$ *(68)*[361,362] ("solid $SF_4$"; cf. Section 4.1.5, reaction of $Ph_2S$ with $XeF_2$). Arene-bound $CF_3S$- and $CF_3Se$-groups are converted by $XeF_2$ quantitatively into the corresponding $CF_3XF_2$ groups (X = S, Se)[363]. With $XeF_2$, inorganic halides and carbonyl compounds give fluorides of elements in higher states of oxidation[364,365].

*Other noble-gas fluorides:* the aggressive xenon hexafluoride can be "tamed" by its addition to graphite to such an extent that a compound with a limited stability in air is obtained, having the approximate composition $C_{19}XeF_6$.





(95)

The adduct exerts a fluorinating action and can fluorinate phenanthrene[366] and the carcinogen benzanthracene *(95)*[367].

$XeOF_4$ in combination with graphite ("$C_{8.7}XeOF_4$") behaves in a similar fashion[368]. Interestingly enough, "$C_{19}XeF_6$" fluorinates uracil in 90% yield to 5-fluorouracil *(6)*[369]. Mention should also be made of the difficultly accessible krypton difluoride[370], though this has not yet been used in organic chemistry. $KrF_2$ converts a number of elements into fluorides of the highest oxidation state, *e.g.* $I_2$ into $IF_7$ and Au into $AuF_6^-$.

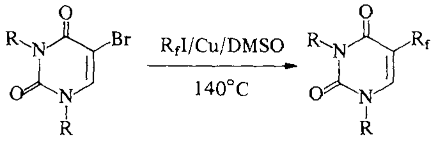
## 5. Preparation of Compounds with Highly Fluorinated Functional Groups

A distinction should be drawn between the methods for the monofluorination of complicated molecules discussed in Section 4 and methods in which fluorine-containing—usually highly fluorinated—groups are introduced into organic compounds. In particular, one should distinguish the preparations of $CF_3$- (and $R_f$-), —$CF_2$-, $CF_3O$- (and $R_fO$-), $CF_3S$- (and $R_fS$-) and $CF_3Se$-substituted species (here $R_f$ denotes a highly fluorinated group).

### 5.1. $CF_3$-(and $R_f$-)Substitution

#### 5.1.1. Nucleophilic Substitution and Related Reactions

Halouracils such as *(96)* react with $R_fI$ in the presence of copper in the sense of a Wurtz reaction[371] (DMSO = dimethyl sulfoxide). Analogous reactions take place with 2-bromobenzofuran[213] and with alkyl halides[372]. Vinyl hydrogens can also be replaced by $R_f$-groups. Similarly, 5-$R_f$-uracil can be produced from uracil [in place of the bromine compound *(96)*] and $R_fCu$ (prepared from $R_fI$ and a specially activated Cu bronze)[373].



(96)

$R = CH_3, C_6H_5CH_2; R_f = C_3F_7$

This reaction is also possible with the complete deoxyribonucleoside[374]; its mechanism has still not been clarified. Some of the products are cytostatic. With $CF_3I$ in the presence of $Ph_3P$, nickelocene gives $CF_3$-substituted cyclopentadiene in 55—60% yield[375].

#### 5.1.2. Radical Reactions

The homolytic cleavage of $CF_3I$ by ultraviolet light with subsequent addition of the radicals to olefinic double bonds[376] is, so to speak, mentioned here only to be dismissed, because of the triviality of the method. The processes with electrolytic production of $CF_3$ radicals are more interesting. These radicals are produced by anodic discharge and decarboxylation of $CF_3CO_2^-$ and add readily to ethylene and 1,1-difluoroethylene to give $CF_3$-substituted oligomers[377]. A variety of other alkenes react in a similar fashion[378]. $CF_3$ radicals can also enter into substitution reactions. Electrolytically produced, they substitute vinyl hydrogen atoms, *e.g.* in the 5-position of uracil[379].

$CF_3$ radicals produced in plasma substitute halogens in aliphatic and aromatic systems[380]. Finally, the following reaction is worth mentioning[381]:

$$R{-}NH_2 \xrightarrow{CF_3{-}NO} \underset{(97)}{R{-}N{=}N{-}CF_3} \xrightarrow{h\nu} R{-}CF_3$$

This reaction is possible with a great number of linear and polycyclic alkylamines. The diazo compound *(97)* can be isolated and in highly viscous solvents reacted by photolysis in the sense of a "cage recombination".

### 5.1.3. Other Reactions

The reaction between arenecarboxylic acid chlorides *(98)* and perfluoropropene is initiated by fluoride ions[382]:

$$\underset{(98)}{Aryl{-}CO{-}Cl} + CF_3CF{=}CF_2 \xrightarrow{F^{\ominus}} Aryl{-}CO{-}CF(CF_3)_2$$

The yields vary between 3 and 66%, depending on the nature and the substituents of the arene. Polyfluorinated acetone derivatives react with the Wittig compounds of steroids to give fluorinated desmosterols[383].

## 5.2. Introduction of the $CF_2$ Group

The $CF_2$ group (or CFX, X = halogen) is produced as a carbene and adds preferentially to double bonds. Ring opening of the cyclopropane produced then allows access to alkenes, which are often biologically important[87]. The carbenes are obtainable from chlorofluoromethanes (*e.g.* $CCl_2F_2$) with bases (*e.g.* $LiCH_3$)[384,385]. Phosphonium salts yield $:CF_2$ in a simple manner[386,387]

$$Ph_3P^{\oplus}CF_2\,Br\;Br^{\ominus} + KF \rightarrow Ph_3PFBr + KBr + :CF_2$$

The carbene can be generated *in situ* from $Ph_3P$ and $CF_2X_2$ (X = Cl, Br).

## 5.3. Introduction of the $CF_3O$ Group

The direct path of introducing the $CF_3O$ group into arenes, reaction with $CF_3OF$, yields no more than about 10% of the desired products[235]. The "single-vessel reaction" of hydroxyarenes + $CCl_4$ + HF, already mentioned in Section 4.1.2, is an elegant method that remains applicable in the presence of many substituents[172]. Partly fluorinated methoxy groups are obtained by condensation of a phenolic OH, *e.g.* with $CH_2F_2$ (performed on pyrimidine derivatives)[388].

## 5.4. Introduction of the $CF_3S$ Group and its Analogues

### 5.4.1. Electrophilic Substitution

The starting compound is a sulfenic acid chloride, for example $CF_3SCl$. This reacts in the sense of a Friedel-Crafts acylation in the presence of acid catalysts, *e.g.* with substituted benzenes[389]. The electrophilic route is by far the most frequently used[390], because of the reactivity and the easy accessibility of the sulfenyl chlorides.

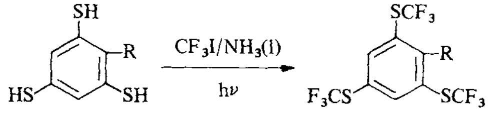
Heterocycles such as furan[13,391], pyrrole[14], imidazole[13,392], and (as an organometallic compound) pyridine[393] can be reacted. Partly halogenated sulfenyl chlorides[393a] and $C_6F_5SCl$[394] react similarly.

### 5.4.2. Nucleophilic Substitution

Suitable aromatic systems such as pyridine[395], quinoline[396], and appropriately activated benzene derivatives[397] can be reacted in the form of their halogen compounds with $CF_3S$-metal compounds (usually $CuSCF_3$).

### 5.4.3. Radical Substitution

This unusual reaction route will be illustrated using the example of photochemical reaction of the trithiol *(99)*[398] with illumination by a mercury vapor lamp. The reaction, which is carried out in liquid ammonia, apparently proceeds *via* a radical-ionic mechanism[399]. Similar reactions are possible with pyrimidines[400] and mercaptoacetic acid[401].



*(99)*

R = OH, $NH_2$, $CH_3$, Cl

37–90%

## 5.5. Introduction of the $CF_3Se$ Group

The processes resemble those for the introduction of the $CF_3S$ group, but much less work has been done on $CF_3Se$ than on $CF_3S$.

### 5.5.1. Electrophilic Substitution

$CF_3SeCl$ reacts with arenes similarly to $CF_3SCl$[402]. $CF_3SeBr$ reacts analogously to $CF_3SCl$ with furan and thiophene[13].

### 5.5.2. Radical Substitution

Like the homologous sulfur compounds, the aromatic selenols react with $CF_3I$ in liquid $NH_3$ under ultraviolet light to give the corresponding $CF_3Se$-compounds[403].

## 6. Summary and Outlook

The significance that fluorinated compounds have now gained in clinical medicine, in phytomedicine and in technology in general was already indicated at the beginning of this review, and there is little doubt that this significance will increase further in the future. In parallel with this, the search for selective, efficient, and "simple" fluorinating agents must inevitably gather momentum.

New methods and techniques will certainly be developed by trying various modifications of the known reagents, as shown by "organo-substitution" (*e.g.* in $SbF_5$ and $SF_4$) and "homologization" ($SF_4 \rightarrow SeF_4$). On the other hand, it pays to explore completely "new" and unusual compounds or substance classes, as has been demonstrated in the cases of $UF_6$, the fluoroxy compounds, and the noble-gas fluorides.

It must be admitted that not all the reactions presented in this review can automatically be generalized, for it is precisely biologically important substrates that are often multifunctional. The group to be fluorinated cannot, therefore, be considered in isolation, and—*e.g.* in the case of cholesterol—one cannot talk simply of "fluorination of an alcohol". At present there are virtually no universal recipes; every new compound is a new challenge that must be faced with a sound experimental attitude. "Instant successes" are rare. Thus, the present review should be regarded only as an aid to orientation, hopefully helping one to formulate the initial strategy for the solution of a particular problem.

The application of known fluorinating agents to untried substrates and thorough documentation of the results may appear to be dull work but it makes an immensely important contribution to opening up this interesting borderland between classical inorganic and organic chemistry.

Received: June 18, 1980 [A 376 IE]
German version: Angew. Chem. *93*, 659 (1981)
Translated by AD-EX Translations Ltd. (London)

---

[1] See also *A. K. Barbour, L. J. Belf, M. W. Buxton*, Adv. Fluorine Chem. *3*, 181 (1963).
[2] *R. J. Plunkett*, US-Pat. 2230654 (1941), Kinetic Chemicals, Inc.
[3] *R. D. Fowler, W. B. Burford III, J. M. Hamilton, Jr., R. G. Sweet, C. E. Weber, J. S. Kasper, I. Litant*, Ind. Eng. Chem. *39*, 292 (1947).
[4] *H. G. Bryce* in *J. H. Simons:* Fluorine Chemistry, Vol. 5, Academic Press, New York 1964, p. 440.
[5] *J. H. Simons*, US-Pat. 2519983 (1948), Minnesota Mining & Manufacturing Co.; Chem. Abstr. *45*, 51h (1951).
[6] *I. N. Rozhkov*, Russ. Chem. Rev. *45*, 615 (1976).
[7] *R. A. Peters*, Proc. R. Soc. Ser. *B 139*, 143 (1957).
[8] *C. Heidelberger*, Annu. Rev. Pharmacol. *7*, 101 (1967).
[9] *R. E. Banks:* Organofluorine Chemicals and Their Industrial Applications, Ellis Horwood, Chichester 1979.
[10] *J. G. Riess, M. Le Blanc*, Angew. Chem. *90*, 654 (1978); Angew. Chem. Int. Ed. Engl. *17*, 621 (1978).
[11] *R. H. Davies, R. D. Bagnall, W. G. M. Jones*, Int. J. Quantum Chem., Quantum Biol. Symp. No. 1, 201 (1974).
[12] *C. Hansch, A. Vittoria, C. Silipo, P. Y. C. Jow*, J. Med. Chem. *18*, 546 (1975).
[13] *M. R. C. Gerstenberger, A. Haas*, unpublished results.
[14] *S. Dorn, P. Eggenberg, M. R. C. Gerstenberger, A. Haas, U. Niemann, P. Zobrist*, Helv. Chim. Acta *62*, 1442 (1979).
[15] *K. H. Büchel, F. Korte, R. B. Beechey*, Angew. Chem. *77*, 814 (1965); Angew. Chem. Int. Ed. Engl. *4*, 788 (1965).
[16] *P. Goldman*, Science *164*, 1123 (1969).
[17] *L. Pauling*, The Nature of the Chemical Bond, 3rd edit., Cornell University Press, Ithaca 1960, p. 82.
[18] *R. A. Peters*, Adv. Enzymol. *18*, 113 (1957).
[19] *D. W. Fanshier, L. K. Gottwald, E. Kun*, J. Biol. Chem. *239*, 425 (1964).
[20] *R. Duschinsky, E. Pleven, C. Heidelberger*, J. Am. Chem. Soc. *79*, 4559 (1957).
[21] *J. Kollonitsch, L. Barash*, J. Am. Chem. Soc. *98*, 5591 (1976).
[22] Chem. Eng. News *53*, No. 40, p. 6 (1975).
[23] *S. Bernstein, R. H. Lenhard, W. S. Allen, M. Heller, R. Littell, S. M. Stolar, L. J. Feldman, R. H. Blank*, J. Am. Chem. Soc. *78*, 5693 (1956).
[24] *H. Günther:* NMR-Spektroskopie, Thieme, Stuttgart 1973, p. 341ff.
[25] *C. H. Dungan, J. van Wazer:* Compilation of Reported $F^{19}$ NMR Chemical Shifts, Wiley-Interscience, New York 1970.
[26] *B. C. Nicholson, T. M. Spotswood*, Aust. J. Chem. *31*, 2167 (1978).
[27] *D. M. Kurtz, Jr., G. B. Wong, R. H. Holm*, J. Am. Chem. Soc. *100*, 6777 (1978).
[28] *R. A. Byrd, W. H. Dawson, P. D. Ellis, R. B. Dunlap*, J. Am. Chem. Soc. *100*, 7478 (1978).
[29] *E. Klauke, E. Kühle, F. Grewe, H. Kaspers, R. Wegler*, Belg. Pat. 609868 (1962), Farbenfabriken Bayer AG; Chem. Abstr. *58*, 9093 (1963).
[30] *P. R. Driscoll*, Br. Pat. 1195672 (1968), Mobil Oil Corp.
[31] Cassella, Fr. Pat. 1193706 (1956).
[32] *A. H. Barrie, G. Booth, I. Durham*, Br. Pat. 882001 (1959), ICI; Chem. Abstr. *56*, 8962h (1962).
[33] *W. Harms* in [9], p. 190.
[34] *R. Lagow, J. L. Margrave*, Prog. Inorg. Chem. *26*, 161 (1979).
[35] *N. J. Maraschin, B. D. Catsikis, L. H. Davis, G. Jarvinen, R. J. Lagow*, J. Am. Chem. Soc. *97*, 513 (1975).
[36] *G. Robertson, E. K. S. Liu, R. J. Lagow*, J. Org. Chem. *43*, 4981 (1978).
[37] *L. A. Harmon, R. J. Lagow*, J. Chem. Soc. Perkin Trans. 1 *1979*, 2675.
[38] *E. K. S. Liu, R. J. Lagow*, J. Chem. Soc. Chem. Commun. *1977*, 450.
[39] *E. K. S. Liu, R. J. Lagow*, J. Am. Chem. Soc. *98*, 8270 (1976).
[40] *E. K. S. Liu, R. J. Lagow*, J. Organomet. Chem. *145*, 167 (1978).
[41] *L. A. Shimp, R. J. Lagow*, Inorg. Chem. *16*, 2974 (1977).
[42] *D. Naumann, L. Deneken*, J. Fluorine Chem. *5*, 443 (1975).
[43] *J. L. Adcock, R. A. Beh, R. J. Lagow*, J. Org. Chem. *40*, 3271 (1975).
[44] *G. E. Gerhardt, R. L. Lagow*, J. Org. Chem. *43*, 4505 (1978).
[45] *I. J. Hotchkiss, R. Stephens, J. C. Tatlow*, J. Fluorine Chem. *10*, 541 (1977).
[46] *I. J. Hotchkiss, R. Stephens, J. C. Tatlow*, J. Fluorine Chem. *6*, 135 (1975).
[47] *I. J. Hotchkiss, R. Stephens, J. C. Tatlow*, J. Fluorine Chem. *8*, 379 (1976).
[48] *R. H. Hauge, S. Gransden, J. L.-F. Wang, J. L. Margrave*, J. Am. Chem. Soc. *101*, 6950 (1979).
[49] *J. L. Adcock, S. Inoue, R. J. Lagow*, J. Am. Chem. Soc. *100*, 1948 (1978).
[50] *L. J. Hayes, D. D. Dixon*, J. Fluorine Chem. *10*, 1, 17 (1977).
[51] *W. B. Burford III, R. D. Fowler, J. M. Hamilton, Jr., H. C. Anderson, C. E. Weber, R. G. Sweet*, Ind. Eng. Chem. *39*, 319 (1947).
[52] *J. Burdon, J. R. Knights, I. W. Parsons, J. C. Tatlow*, Tetrahedron *32*, 1041 (1976).
[53] *J. Burdon, T. N. Huckerby, R. Stephens*, J. Fluorine Chem. *10*, 523 (1977).
[54] *A. Bergomi, J. Burdon*, J. Chem. Soc. Perkin Trans. 1 *1975*, 2237.
[55] *R. G. Plevey, I. J. Sallomi, D. F. Thomas, J. C. Tatlow*, J. Chem. Soc. Perkin Trans. 1 *1976*, 2270.
[56] *J. Burdon, I. W. Parsons*, Tetrahedron *31*, 2401 (1975).
[57] *I. W. Parsons, P. M. Smith, J. C. Tatlow*, J. Fluorine Chem. *5*, 269 (1975).
[58] *M. Brandwood, P. L. Coe, C. S. Ely, J. C. Tatlow*, J. Fluorine Chem. *5*, 521 (1975).
[59] *R. D. Bagnall, W. Bell, K. Pearson*, J. Fluorine Chem. *9*, 359 (1977).
[60] *P. Dodman, J. C. Tatlow*, J. Fluorine Chem. *8*, 263 (1976).
[61] *R. W. Rendell, B. Wright*, Tetrahedron *34*, 197 (1978).
[62] *R. W. Rendell, B. Wright*, Tetrahedron *35*, 2405 (1979).
[63] *J. Burdon, J. R. Knights, I. W. Parsons, J. C. Tatlow*, J. Chem. Soc. Perkin Trans. 1 *1976*, 1930.
[64] *I. N. Rozhkov, N. P. Gambaryan, E. G. Galpern*, Tetrahedron Lett. *1976*, 4819.
[65] *V. S. Plashkin, Yu. P. Dolnakov*, Zh. Prikl. Khim. *48*, 702 (1975).
[66] *V. S. Plashkin*, Zh. Prikl. Khim. *48*, 706 (1975).
[67] *M. Haruta, N. Watanabe*, J. Fluorine Chem. *7*, 159 (1976).
[68] *M. Yonekura, S. Nagase, H. Baba, K. Kodaira, T. Abe*, Bull. Chem. Soc. Jpn. *49*, 1113 (1976).
[69] *V. J. Davis, R. N. Haszeldine, A. E. Tipping*, J. Chem. Soc. Perkin Trans. 1 *1975*, 1263.
[70] *T. Abe, S. Nagase*, J. Fluorine Chem. *13*, 519 (1979).
[71] *H. Bürger, F. Heyder, G. Pawelke, H. Niederprüm*, J. Fluorine Chem. *13*, 251 (1979).
[72] *V. V. Berenblit, B. A. Byzov, V. I. Grachev, I. M. Dolgopol'skii, Yu. P. Dolnakov*, Zh. Prikl. Khim. *48*, 709 (1975).
[73] *V. V. Berenblit, V. P. Sass, L. N. Senyushov, Yu. K. Starobin*, Zh. Org. Khim. *12*, 767 (1976).

[74] *T. Abe, K. Kodaira, H. Baba, S. Nagase,* J. Fluorine Chem. *12,* 1 (1978).

[75] *V. A. Shreider, I. N. Rozhkov,* Bull. Acad. Sci. USSR *28,* 627 (1979).

[76] *V. A. Shreider, I. N. Rozhkov,* Dokl. Phys. Chem. *245,* 246 (1979).

[77] *V. V. Berenblit, Yu. P. Dolnakov, G. A. Dvydov, V. I. Grachev, S. V. Sokolov,* Zh. Prikl. Khim. *48,* 2206 (1975).

[78] *T. Abe, S. Nagase, H. Baba,* Bull. Chem. Soc. Jpn. *49,* 1888 (1976).

[79] *H. Baba, K. Kodaira, S. Nagase, T. Abe,* Bull. Chem. Soc. Jpn. *50,* 2809 (1977).

[80] *H. Baba, K. Kodaira, S. Nagase, T. Abe,* Bull. Chem. Soc. Jpn. *51,* 1891 (1978).

[81] *K. Onori, S. Nagase, H. Baba, K. Kodaira, T. Abe,* J. Fluorine Chem. *9,* 279 (1977).

[82] *I. N. Rozhkov, V. A. Shreider,* Bull. Acad. Sci. USSR *26,* 1528 (1977).

[83] *I. N. Rozhkov, I. Y. Alyev,* Tetrahedron *31,* 977 (1975).

[84] *V. A. Shreider, I. N. Rozhkov,* Bull. Acad. Sci. USSR *28,* 630 (1979).

[85] *I. N. Rozhkov, I. Ya. Aliev, I. L. Knunyants,* Bull. Acad. Sci. USSR *25,* 1361 (1976).

[86] *A. Bensadat, G. Bodennec, E. Laurent, R. Tardivel,* Tetrahedron Lett. *1977,* 3799.

[87] *M. Schlosser,* Tetrahedron *34,* 3 (1978).

[88] *F. W. Hoffmann,* J. Am. Chem. Soc. *70,* 2596 (1948).

[89] *A. F. Maxwell, J. S. Fry, L. A. Bigelow,* J. Am. Chem. Soc. *80,* 548 (1958).

[90] *A. Ya. Zapevalov, I. P. Kolenko, V. S. Plashkin, P. G. Neifeld,* J. Org. Chem. USSR *14,* 239 (1978).

[91] *G. G. Yakobson, V. M. Vlasov,* Synthesis *1976,* 652.

[92] *D. E. Pearson, V. Mitchell, T. J. Sullivan, J. T. Watson,* Synthesis *1978,* 127.

[93] *F. Mutterer, C. D. Weis,* Helv. Chim. Acta *59,* 229 (1976).

[94] *K. Tamao, T. Kakui, M. Kumada,* Tetrahedron Lett. *1979,* 619.

[95] *F. Franke, P. R. Wells,* J. Org. Chem. *44,* 4055 (1979).

[96] *J. E. Drake, B. M. Glavinčevski, K. G. Rutherford,* Inorg. Nucl. Chem. Lett. *15,* 303 (1979).

[97] *N. L. Paddock, D. J. Patmore,* J. Chem. Soc. Dalton Trans. *1976,* 1029.

[98] *D. K. Padma, V. S. Bhat, A. R. Vasudevamurthy,* J. Fluorine Chem. *11,* 187 (1978).

[99] *G.-V. Röschenthaler, R. Starke,* Z. Naturforsch. *B 32,* 721 (1977).

[100] *H. Meinert, A. Dimitrov,* Z. Chem. *16,* 29 (1976).

[101] *A. K. Shukla, W. Preetz,* J. Inorg. Nucl. Chem. *41,* 1295 (1979).

[102] *P. A. Grieco, T. Sugahara, Y. Yokoyama, E. Williams,* J. Osg. Chem. *44,* 2189 (1979).

[103] *P. A. Grieco, E. Williams, T. Sugahara,* J. Org. Chem. *44,* 2194 (1979).

[104] *I. D. Blackburne, P. M. Fredericks, R. D. Guthrie,* Aust. J. Chem. *29,* 381 (1976).

[105] *G. Etzold, M. von Janta-Lipinski, P. Langen,* J. Prakt. Chem. *318,* 79 (1976).

[106] *A. Ya. Ilchenko, R. E. Koval'chuk, L. M. Yagupol'skii,* J. Org. Chem. USSR *13,* 1850 (1977).

[107] *N. Ishikawa, T. Tanabe, D. Hayashi,* Bull. Chem. Soc. Jpn. *48,* 359 (1975).

[108] *Y. Kobayashi, T. Taguchi,* Tetrahedron Lett. *1979,* 2023.

[109] *Y. Kobayashi, I. Kumadaki, A. Ohsawa, S.-I. Murakami,* J. Chem. Soc. Chem. Commun. *1976,* 430.

[110] *C. L. Liotta, H. P. Harris,* J. Am. Chem. Soc. *96,* 2250 (1974).

[111] *N. E. Akhmetova, V. M. Vlasov, G. G. Yakobson,* Bull. Acad. Sci. USSR *27,* 823 (1978).

[112] *R. E. Banks, R. N. Haszeldine, J. V. Latham, I. M. Young,* J. Chem. Soc. *1965,* 594.

[113] *M. Gross, F. Peter,* Bull. Soc. Chim. Fr. *1975,* 871.

[114] *M. Cinquini, F. Montanari,* J. Chem. Soc. Chem. Commun. *1975,* 393.

[115] *S. G. Baram, O. P. Shkurko, V. P. Mamaev,* Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk *1977,* 106.

[116] *B. Fuchs, A. Ellenczweig,* J. Org. Chem. *44,* 2274 (1979).

[117] *J. Cuomo, R. A. Olofson,* J. Org. Chem. *44,* 1016 (1979).

[118] *P. Ykman, H. K. Hall, Jr.,* Tetrahedron Lett. *1975,* 2429.

[119] *Y. M. Saunier, R. Danion-Bougot, D. Danion, R. Carrié,* Bull. Soc. Chim. Fr. *1976,* 1963.

[120] *L. Fitjer,* Synthesis *1977,* 189.

[121] *B. Unterhalt, F. Leiblein,* Synthesis *1978,* 700.

[122] *B. Unterhalt, F. Leiblein,* Arch. Pharm. (Weinheim) *312,* 159 (1979).

[123] *G. Märkl, H. Baier, P. Hofmeister, F. Kees, C. Soper,* J. Organomet. Chem. *173,* 125 (1979).

[124] *T. A. Bianchi, L. A. Cate,* J. Org. Chem. *42,* 2031 (1977).

[125] *J. San Filippo, Jr., L. J. Romano,* J. Org. Chem. *40,* 782 (1975).

[126] *K. M. More, J. Wemple,* Synthesis *1977,* 791.

[127] *D. Landini, F. Montanari, F. Rolla,* Synthesis *1974,* 428.

[128] *D. Bethell, K. McDonald, K. S. Rao,* Tetrahedron Lett. *1977,* 1447.

[129] *G. Cainelli, F. Manescalchi,* Synthesis *1976,* 472.

[130] *S. Colonna, A. Re, G. Gelbard, E. Cesarotti,* J. Chem. Soc. Perkin Trans. 1 *1979,* 2248.

[131] *F. Mathey, J. Bensoam,* C. R. Acad. Sci. Ser. *C 274,* 1095 (1972).

[132] *F. Mathey, J. Bensoam,* Tetrahedron Lett. *1973,* 2253.

[133] *F. Mathey, G. Muller,* C. R. Acad. Sci. Ser. *C 277,* 45 (1973).

[134] *F. Mathey, J. Bensoam,* Tetrahedron *31,* 391 (1975).

[135] *F. Mathey, J. Bensoam,* Tetrahedron *27,* 3965 (1971).

[136] *M. Van der Puy,* J. Fluorine Chem. *13,* 375 (1979).

[137] *G. A. Olah, J. Welch, T.-L. Ho,* J. Am. Chem. Soc. *98,* 6717 (1976).

[138] *L. M. Yagupol'skii, N. V. Kondratenko, V. I. Popov,* J. Org. Chem. USSR *13,* 561 (1977).

[139] *L. M. Yagupol'skii, V. I. Popov, N. V. Kondratenko, B. L. Korsunskii, N. N. Aleinikov,* J. Org. Chem. USSR *11,* 454 (1975).

[140] *L. M. Yagupol'skii, N. V. Kondratenko, V. I. Popov,* J. Gen. Chem. USSR *46,* 618 (1976).

[141] *S. P. Bone, D. B. Sowerby,* J. Chem. Soc. Dalton Trans. *1979,* 1430.

[142] *V. I. Popov, N. V. Kondratenko, S. V. Pazenok,* Ukr. Khim. Zh. *44,* 1078 (1978).

[143] *E. C. Taylor, E. C. Bigham, D. K. Johnson, A. McKillop,* J. Org. Chem. *42,* 362 (1977).

[144] *M. Ephritikhine, J. Levisalles,* J. Chem. Soc. Chem. Commun. *1974,* 429.

[145] *M. Ephritikhine, J. Levisalles,* Bull. Soc. Chim. Fr. *1975,* 339.

[146] *S. M. McElvain, J. W. Langston,* J. Am. Chem. Soc. *66,* 1759 (1944).

[147] *J. H. Simons, C. J. Lewis,* J. Am. Chem. Soc. *60,* 492 (1938).

[148] *K. Bock, C. Pedersen,* Acta Chem. Scand. *B 30,* 727 (1976).

[149] *K. Bock, C. Pedersen,* Acta Chem. Scand. *B 30,* 777 (1976).

[150] *C. Pedersen, S. Refn,* Acta Chem. Scand. *B 32,* 687 (1978).

[151] *A. E. Feiring,* J. Org. Chem. *41,* 148 (1976).

[152] *M. Sheves, B. Sialom, Y. Mazur,* J. Chem. Soc. Chem. Commun. *1978,* 554.

[153] *G. A. Olah, M. Nojima, I. Kerekes,* Synthesis *1973,* 779.

[154] *G. A. Olah, M. Nojima, I. Kerekes,* Synthesis *1973,* 780.

[155] *M. Zupan,* J. Fluorine Chem. *9,* 177 (1977).

[156] *S. Stavber, M. Zupan,* Bull. Chem. Soc. Jpn. *52,* 925 (1979).

[157] *H. Gershon, L. Shanks,* J. Med. Chem. *20,* 606 (1977).

[158] *L. Eckes, M. Hanack,* Synthesis *1978,* 217.

[159] *A. Ambles, R. Jacquesy,* Tetrahedron Lett. *1976,* 1083.

[160] *P. Mazerolles, A. Faucher, J.-P. Beteille,* J. Organomet. Chem. *177,* 163 (1979).

[161] *C. G. Beguin, C. Charlon, C. Coulombeau, G. Luu-Duc,* J. Fluorine Chem. *8,* 531 (1976).

[162] *G. A. Olah, J. T. Welch,* Synthesis *1974,* 896.

[163] *G. A. Olah, J. T. Welch, Y. D. Vankar, M. Nojima, I. Kerekes, J. A. Olah,* J. Org. Chem. *44,* 3872 (1979).

[164] *G. A. Olah, D. Meidar,* Isr. J. Chem. *17,* 148 (1978).

[165] *T. N. Wade, F. Gaymard, R. Guedj,* Tetrahedron Lett. *1979,* 2681.

[166] *H. Brachwitz, P. Langen, A. Otto, J. Schildt,* J. Prakt. Chem. *321,* 775 (1979).

[167] *G. Kowollik, P. Langen,* Z. Chem. *15,* 148 (1975).

[168] *A. Baklouti, R. El Gharbi,* J. Fluorine Chem. *13,* 297 (1979).

[169] *T. N. Wade, R. Guedj,* Tetrahedron Lett. *1978,* 3247.

[170] *G. Alvernhe, E. Kozlowska-Gramsz, S. Lacombe-Bar, A. Laurent,* Tetrahedron *Lett. 1978,* 5203.

[171] *G. Alvernhe, S. Lacombe, A. Laurent,* Tetrahedron Lett. *1980,* 289.

[172] *A. E. Feiring,* J. Org. Chem. *44,* 2907 (1979).

[173] *A. E. Feiring,* J. Fluorine Chem. *10,* 375 (1977).

[174] *A. E. Feiring,* J. Org. Chem. *44,* 1252 (1979).

[175] *D. M. Mulvey, A. M. DeMarco, L. M. Weinstock,* Tetrahedron Lett. *1978,* 1419.

[176] *M. N. Rosenfeld, D. A. Widdowson,* J. Chem. Soc. Chem. Commun. *1979,* 914.

[177] *K. Matsumoto, Y. Ozaki, T. Iwasaki, H. Horikawa, M. Miyoshi,* Experientia *35,* 850 (1979).

[178] *J. P. Ferraris, G. Saito,* J. Chem. Soc. Chem. Commun. *1978,* 992.

[179] *J. A. Montgomery, S. D. Clayton, A. T. Shortnacy,* J. Heterocycl. Chem. *16,* 157 (1979).

[180] *M. S. Newman, K. C. Lilje,* J. Org. Chem. *44,* 1347 (1979).

[181] *D. C. Suster, G. Botez, L. V. Feyns, V. Dobre, I. Niculescu-Duvaz,* Rev. Roum. Chim. *22,* 257 (1977).

[182] *G. D. Hartmann, S. E. Biffar,* J. Org. Chem. *42,* 1468 (1977).

[183] *A. Sweeny, Jr., R. D. Blair, A. Chang, L. Clark,* J. Fluorine Chem. *6,* 389 (1975).

[184] *T. Honoré, H. Hjeds,* Eur. J. Med. Chem. - Chim. Ther. *14,* 285 (1979).

[185] *M. P. Doyle, J. L. Whitefleet, M. A. Zaleta,* Tetrahedron Lett. *1975,* 4201.

[186] *A. J. Fry, Y. Migron,* Tetrahedron Lett. *1979,* 3357.

[187] *F. Fabra, J. Vilarrasa, J. Coll,* J. Heterocycl. Chem. *15,* 1447 (1978).

[188] *F. Fabra, E. Fos, J. Vilarrasa,* Tetrahedron Lett. *1979,* 3179.

[189] *J. C. Reepmeyer, K. L. Kirk, L. A. Cohen,* Tetrahedron Lett. *1975,* 4107.

[190] *A. Murai, H. Sasamori, T. Masamune,* Chem. Lett. *1976,* 975.

[191] *A. Murai, H. Sasamori, T. Masamune,* Bull. Chem. Soc. Jpn. *50,* 437 (1977).

[192] *F. R. Fronczek*, J. Chem. Soc. Perkin Trans. 2 *1979*, 195.
[193] *J. Muray*, J. Chem. Soc. *1959*, 1884.
[194] *A. A. Banks, H. J. Emeléus, R. N. Haszeldine, V. Kerrigan*, J. Chem. Soc. *1948*, 2188.
[195] *J. C. Tatlow*, J. Fluorine Chem. *7*, 397 (1976).
[196] *T. W. Bastock, M. E. Harley, A. E. Pedler, J. C. Tatlow*, J. Fluorine Chem. *6*, 331 (1975).
[197] *C. Lau, J. Passmore*, J. Fluorine Chem. *6*, 77 (1976).
[198] *G. R. Owen, J. P. H. Verheyden, J. G. Moffatt*, J. Org. Chem. *41*, 3010 (1976).
[199] *A. Gregorčič, M. Zupan*, Bull. Chem. Soc. Jpn. *50*, 517 (1976).
[200] *I. I. Maletina, V. V. Orda, N. N. Aleinikov, B. L. Korsunskii, L. M. Yagupol'skii*, J. Org. Chem. USSR *12*, 1364 (1976).
[201] *M. Zupan, A. Pollak*, Tetrahedron Lett. *1975*, 3525.
[202] *M. Zupan, A. Pollak*, J. Chem. Soc. Perkin Trans. 1 *1976*, 1745.
[203] *A. Gregorčič, M. Zupan*, J. Chem. Soc. Perkin Trans. 1 *1977*, 1446.
[204] *R. L. Amey, J. C. Martin*, J. Am. Chem. Soc. *101*, 5294 (1979).
[205] *M. Zupan, A. Pollak*, J. Chem. Soc. Chem. Commun. *1975*, 715.
[206] *W. C. Smith*, Angew. Chem. *74*, 742 (1962); Angew. Chem. Int. Ed. Engl. *1*, 467 (1962).
[207] *J. Kollonitsch, S. Marburg, L. M. Perkins*, J. Org. Chem. *40*, 3808 (1975).
[208] *F. E. Herkes, H. E. Simmons*, J. Org. Chem. *40*, 420 (1975).
[209] *L. M. Yagupol'skii, A. N. Alekseenko, A. Ya. Ilchenko*, Ukr. Khim. Zh. *44*, 1057 (1978).
[210] *V. G. Lukmanov, L. A. Alekseeva, L. M. Yagupol'skii*, J. Org. Chem. USSR *13*, 1979 (1977).
[211] *F. E. Herkes, T. A. Blazer*, J. Heterocycl. Chem. *13*, 1297 (1976).
[212] *V. V. Lyalin, R. V. Grigorash, L. A. Alekseeva, L. M. Yagupol'skii*, Zh. Org. Khim. *11*, 1086 (1975).
[213] *Y. Kobayashi, I. Kumadaki, Y. Hanzawa, N. Fujii*, Heterocycles *3*, 61 (1975).
[214] *R. V. Grigorash, V. V. Lyalin, L. A. Alekseeva, L. M. Yagupol'skii*, J. Org. Chem. USSR *14*, 2414 (1978).
[215] *R. E. Moore, G. L. Driscoll*, J. Org. Chem. *43*, 4978 (1978).
[216] *B. G. Oksenenko, M. M. Shakirov, V. D. Shteingarts*, J. Org. Chem. USSR *12*, 1307 (1976).
[217] *A. P. Khardin, A. D. Popov, P. A. Protopopov*, Zh. Vses. Khim. Ora. *21*, 593 (1976).
[218] *A. M. Aleksandrov, V. P. Kukhar, G. I. Danilenko, A. P. Krasnoshchek*, J. Org. Chem. USSR *13*, 1505 (1977).
[219] *F. N. Shirota, H. T. Nagasawa, J. A. Elberling*, J. Med. Chem. *20*, 1623 (1977).
[220] *R. J. De Pasquale*, J. Org. Chem. *43*, 1727 (1978).
[221] *E. M. Bellott, Jr.*, Tetrahedron *33*, 1707 (1977).
[222] *F. N. Shirota, H. T. Nagasawa, J. A. Elberling*, J. Med. Chem. *20*, 1623 (1977).
[223] *A. P. Khardin, A. D. Popov, P. A. Protopopov*, Zh. Org. Khim. *11*, 1982 (1975).
[224] *V. I. Golikov, A. M. Aleksandrov, L. P. Glushko, V. G. Dryuk, L. A. Alekseeva, L. M. Yagupol'skii, M. S. Malinovskii*, Ukr. Khim. Zh. *41*, 495 (1975).
[225] *A. P. Khardin, A. D. Popov, P. A. Protopopov*, Zh. Vses. Khim. Ora. *22*, 116 (1977).
[226] *Z. V. Pushkareva, N. A. Plashkina, V. I. Troitskaya, L. M. Yagupol'skii*, Khim. Geterotsikl. Soedin. *1976*, 1686.
[227] *A. N. Blakitnyi, I. M. Zalesskaya, B. V. Kunshenko, Yu. A. Fialkov, L. M. Yagupol'skii*, J. Org. Chem. USSR *13*, 2000 (1977).
[228] *V. V. Lyalin, A. V. Grigorash, L. A. Alekseeva, L. M. Yagupol'skii*, Zh. Org. Khim. *11*, 460 (1975).
[229] *R. V. Grigorash, V. V. Lyalin, L. A. Alekseeva, L. M. Yagupol'skii*, J. Org. Chem. USSR *14*, 782 (1978).
[230] *R. V. Grigorash, V. V. Lyalin, L. A. Alekseeva, L. M. Yagupol'skii*, Zh. Org. Khim. *14*, 2623 (1978).
[231] *A. M. Aleksandrov, A. E. Sorochinskii, A. P. Krasnoshchek*, Zh. Org. Khim. *15*, 336 (1979).
[232] *V. M. Belous, L. A. Alekseeva, L. M. Yagupol'skii*, Zh. Org. Khim. *11*, 1672 (1975).
[233] *L. M. Yagupol'skii, V. M. Belous, L. A. Alekseeva*, J. Org. Chem. USSR *12*, 1284 (1976).
[234] *V. M. Belous, K. D. Litvinova, L. A. Alekseeva, L. M. Yagupol'skii*, Zh. Org. Khim. *12*, 1798 (1976).
[235] *J. Kollonitsch*, Isr. J. Chem. *17*, 53 (1978).
[236] *R. S. Loy, M. Hudlicky*, J. Fluorine Chem. *7*, 421 (1976).
[237] *J. Kollonitsch, S. Marburg, L. M. Perkins*, J. Org. Chem. *44*, 771 (1979).
[238] *W. J. Middleton*, J. Org. Chem. *40*, 574 (1975).
[239] *L. N. Markovskii, V. E. Pashinnik, N. A. Kirsanova*, Zh. Org. Khim. *11*, 74 (1975).
[240] *L. N. Markovskii, V. E. Pashinnik, N. A. Kirsanova*, Zh. Org. Khim. *12*, 965 (1976).
[241] *W. J. Middleton*, US-Pat. 3940402 (1976).
[242] *C. M. Sharts, M. E. McKee, R. F. Steed, D. F. Shellhamer, A. C. Greeley, R. C. Green, L. G. Sprague*, J. Fluorine Chem. *14*, 351 (1979).
[243] *J. Leroy, E. Hebert, C. Wakselman*, J. Org. Chem. *44*, 3406 (1979).
[244] *M. S. Newman, J. M. Khanna*, J. Org. Chem. *44*, 866 (1979).
[245] *M. S. Newman, V. K. Khanna, K. Kanakarajan*, J. Am. Chem. Soc. *101*, 6788 (1979).
[246] *M. Biollaz, J. Kalvoda*, Helv. Chim. Acta *60*, 2703 (1977).
[247] *T. G. C. Bird, G. Felsky, P. M. Fredericks, E. R. H. Jones, G. D. Meakins*, J. Chem. Res. (S) *1979*, 388.
[248] *T. G. C. Bird, P. M. Fredericks, E. R. H. Jones, G. D. Meakins*, J. Chem. Soc. Chem. Commun. *1979*, 65.
[249] *S. Rozen, Y. Faust, H. Ben-Yakov*, Tetrahedron Lett. *1979*, 1823.
[250] *B. E. Cross, A. Erasmuson*, J. Chem. Soc. Chem. Commun. *1978*, 1013.
[251] *K. Boulton, B. E. Cross*, J. Chem. Soc. Perkin Trans. 1 *1979*, 1354.
[252] *S. S. Yang, C. P. Dorn, H. Jones*, Tetrahedron Lett. *1977*, 2315.
[253] *S. Yamada, M. Ohmori, H. Takayama*, Tetrahedron Lett. *1979*, 1859.
[254] *M. Sharma, W. Korytnik*, Tetrahedron Lett. *1977*, 573.
[255] *R. A. Sharma, I. Kavai, Y. L. Fu, M. Bobek*, Tetrahedron Lett. *1977*, 3433.
[256] *T. J. Tewson, M. J. Welch*, J. Org. Chem. *43*, 1090 (1978).
[257] *M. J. Green, H. J. Shue, M. Tanabe, D. M. Yasuda, A. T. McPhail, K. D. Onan*, J. Chem. Soc. Chem. Commun. *1977*, 611.
[258] *L. N. Markovski, V. E. Pashinnik*, Synthesis *1975*, 801.
[259] *G. Siegemund*, Liebigs Ann. Chem. *1979*, 1280.
[260] *W. J. Middleton*, Chem. Eng. News *57*, Nr. 21, S. 43 (1979).
[261] *J. Cochran*, Chem. Eng. News *57*, Nr. 12, S. 4, 74 (1979).
[262] *W. A. Sheppard*, J. Am. Chem. Soc. *84*, 3058 (1962).
[263] *I. Ruppert*, Chem. Ber. *112*, 3023 (1979).
[264] *G. A. Olah, M. Nojima, I. Kerekes*, J. Am. Chem. Soc. *96*, 925 (1974).
[265] *N. Ya. Derkach, G. G. Barashenkov*, Zh. Org. Khim. *10*, 2619 (1974).
[266] *R. Schmutzler*, Inorg. Chem. *3*, 410 (1964).
[267] *J. A. Gibson, R. K. Marat, A. F. Janzen*, Can. J. Chem. *53*, 3044 (1975).
[268] *Y. Kobayashi, I. Kumadaki, A. Ohsawa, M. Honda, Y. Hanzawa*, Chem. Pharm. Bull. *23*, 196 (1975).
[269] *N. E. Boutin, D. U. Robert, A. R. Cambon*, Bull. Soc. Chim. Fr. *1974*, 2861.
[270] *A. I. Ayi, R. Condom, P. C. Maria, T. N. Wade, R. Guedj*, Tetrahedron Lett. *1978*, 4507.
[271] *H. Gershon, J. A. A. Renwick, W. K. Wynn, R. D'Ascoli*, J. Org. Chem. *31*, 916 (1966).
[272] *G. V. Thi, P. Margaretha*, Helv. Chim. Acta *59*, 2236 (1976).
[273] *D. Britton, S. Farooq, R. Keese*, Helv. Chim. Acta *60*, 1393 (1976).
[274] *R. D. Schuetz, D. D. Taft, J. P. O'Brien, J. L. Shea, H. M. Mork*, J. Org. Chem. *28*, 1420 (1963).
[275] *M. Schlosser, G. Heinz*, Chem. Ber. *102*, 1944 (1969).
[276] *W. A. Slusarchyk, H. E. Applegate, P. Funke, W. Koster, M. S. Puar, M. Young, J. E. Dolfini*, J. Org. Chem. *38*, 943 (1973).
[277] *P. Wieland*, Helv. Chim. Acta *59*, 1027 (1976).
[278] *C.-L. J. Wang, P. A. Grieco, F. J. Okuniewicz*, J. Chem. Soc. Chem. Commun. *1976*, 468.
[279] *W. Adcock, T. C. Khor*, J. Organomet. Chem. *91*, C20 (1975).
[280] *G. A. Olah, M. Nojima, I. Kerekes*, Synthesis *1973*, 487.
[281] *N. N. Yarovenko, M. A. Raksha*, J. Gen. Chem. USSR *19*, 2125 (1959).
[282] *B. Müller, H. Peter, P. Schneider, H. Bickel*, Helv. Chim. Acta *58*, 2469 (1975).
[283] *J. Kopecký, J. Šmejkal, M. Hudlický*, Chem. Ind. (London) *1969*, 271.
[284] *M. Franck-Neumann, M. Sedrati*, Bull. Soc. Chim. Fr. *1976*, 1476.
[285] *B. E. Cross, P. Hendley*, J. Chem. Soc. Perkin Trans. 1 *1975*, 2523.
[286] *R. E. Banks, B. E. Cross*, J. Chem. Soc. Perkin Trans. 1 *1977*, 512.
[287] *R. E. Banks, J. H. Bateson, B. E. Cross, A. Erasmuson*, J. Chem. Res. (S) *1980*, 46.
[288] *R. Mičková, J. Moural, V. Schwarz*, Tetrahedron Lett. *1978*, 1315.
[289] *A. Takaoka, H. Iwakiri, N. Ishikawa*, Bull. Chem. Soc. Jpn. *52*, 3377 (1979).
[290] *T. Mukaiyama, T. Tanaka*, Chem. Lett. *1976*, 303.
[291] *V. R. Polishchuk, B. Ya. Medvedev, N. N. Bubnov, L. S. German, I. L. Knunyants*, Bull. Acad. Sci. USSR *21*, 2736 (1973).
[292] *R. E. Banks, G. E. Williamson*, Chem. Ind. (London) *1964*, 1864.
[293] *R. E. Banks, R. N. Haszeldine, R. Hatton*, Tetrahedron Lett. *1967*, 3993.
[294] *J. Bensoam, F. Mathey*, Tetrahedron Lett. *1977*, 2797.
[295] *H. Meinert, D. Cech*, Z. Chem. *12*, 292 (1972).
[296] *H. Meinert*, Z. Chem. *5*, 64 (1965).
[297] *D. Cech, H. Meinert, G. Etzold, P. Langen*, J. Prakt. Chem. *315*, 149 (1973).
[298] *D. Cech, A. Holy*, Collect. Czech. Chem. Commun. *41*, 3335 (1976).
[299] *A. Haas, D. Kortmann*, Chem. Ber. *114*, 1176 (1981).
[300] *D. Cech, H. Beerbaum, A. Holy*, Collect. Czech. Chem. Commun. *42*, 2694 (1977).
[301] *D. Cech, G. Hermann, A. Holy*, Nucleic Acid Res. *4*, 3259 (1977).

[302] *R. Hesse, D. H. R. Barton,* Chem. Eng. News *54*, No. 18, p. 23 (1976).

[303] *D. H. R. Barton, R. H. Hesse, R. E. Markwell, M. M. Pechet, S. Rozen,* J. Am. Chem. Soc. *98*, 3036 (1976).

[304] *D. H. R. Barton, R. H. Hesse, R. E. Markwell, M. M. Pechet, H. T. Toh,* J. Am. Chem. Soc. *98*, 3034 (1976).

[305] *T. Ido, C.-N. Wan, J. S. Fowler, A. P. Wolf,* J. Org. Chem. *42*, 2341 (1977).

[306] *I. Ruppert,* Z. Naturforsch. *B 34*, 662 (1979).

[307] *A. V. Fokin, V. P. Stolyarov, V. A. Komarov, A. T. Uzun,* Bull. Acad. Sci. USSR *26*, 1981 (1977).

[308] *F. Cacace, A. P. Wolf,* J. Am. Chem. Soc. *100*, 3639 (1978).

[309] *V. Grakauskas, A. M. Guest,* J. Org. Chem. *43*, 3485 (1978).

[310] *M. J. Robins, M. MacCoss, S. R. Naik, G. Ramani,* J. Am. Chem. Soc. *98*, 7381 (1976).

[311] *M. J. Robins, S. R. Naik,* J. Am. Chem. Soc. *93*, 5277 (1971).

[312] *D. H. R. Barton, R. H. Hesse, H. T. Toh, M. M. Pechet,* J. Org. Chem. *37*, 329 (1972).

[313] *M. J. Robins, G. Ramani, M. MacCoss,* Can. J. Chem. *53*, 1302 (1975).

[314] *T. B. Patrick, M. H. Le Faivre, T. E. Koertge,* J. Org. Chem. *41*, 3413 (1976).

[315] *T. B. Patrick, G. L. Cantrell, C.-Y. Chang,* J. Am. Chem. Soc. *101*, 7434 (1979).

[316] *D. H. R. Barton, R. H. Hesse, G. P. Jackman, M. M. Pechet,* J. Chem. Soc. Perkin Trans. 1 *1977*, 2604.

[317] *D. H. R. Barton, R. H. Hesse, L. Ogunkoya, N. D. Westcott, M. M. Pechet,* J. Chem. Soc. Perkin Trans. 1 *1972*, 2889.

[318] *D. H. R. Barton, L. J. Danks, R. H. Hesse, M. M. Pechet, C. Wilshire,* Nouv. J. Chim. *1*, 315 (1977).

[319] *D. H. R. Barton, L. J. Danks, A. K. Ganguly, R. H. Hesse, G. Tarzia, M. M. Pechet,* J. Chem. Soc. Perkin Trans. 1 *1976*, 101.

[320] *C. G. Butchard, P. W. Kent,* Tetrahedron *27*, 3457 (1971).

[321] *K. Bischofberger, A. J. Brink, A. Jordaan,* J. Chem. Soc. Perkin Trans. 1 *1975*, 2457.

[322] *P. W. Kent, S. D. Dimitrijevich,* J. Fluorine Chem. *10*, 455 (1977).

[323] *C. G. Butchard, P. W. Kent,* Tetrahedron *35*, 2439 (1979).

[324] *C. G. Butchard, P. W. Kent,* Tetrahedron *35*, 2551 (1979).

[324a] *D. H. R. Barton, R. H. Hesse, T. R. Klose, M. M. Pechet,* J. Chem. Soc. Chem. Commun. *1975*, 97.

[325] *C. Wakselman, J. Leroy,* J. Chem. Soc. Chem. Commun. *1976*, 611.

[326] *J. Leroy, C. Wakselman,* J. Chem. Soc. Perkin Trans. 1 *1978*, 1224.

[327] *J. Kollonitsch, L. Barash, G. A. Doldouras,* J. Am. Chem. Soc. *92*, 7494 (1970).

[328] *J. Kollonitsch, S. Marburg, L. S. Perkins,* J. Org. Chem. *41*, 3107 (1976).

[329] *S. Rozen, Y. Menachem,* Tetrahedron Lett. *1979*, 725.

[330] *S. Rozen, Y. Menachem,* J. Chem. Soc. Chem. Commun. *1979*, 479.

[331] *S. Rozen, O. Lerman,* J. Am. Chem. Soc. *101*, 2782 (1979).

[331] a) *D. H. R. Barton, R. H. Hesse, M. M. Pechet, G. Tarzia, H. T. Toh, N. D. Westcott,* J. Chem. Soc. Chem. Commun. *1972*, 122; b) *D. H. R. Barton, R. H. Hesse, M. M. Pechet, H. T. Toh,* J. Chem. Soc. Perkin Trans. 1 *1974*, 732.

[332] *R. Filler,* Isr. J. Chem. *17*, 71 (1978).

[333] *M. Zupan, B. Šket,* J. Org. Chem. *43*, 696 (1978).

[334] *M. Zupan, A. Pollak,* J. Chem. Soc. Chem. Commun. *1973*, 845.

[335] *M. Zupan, A. Pollak,* Tetrahedron *33*, 1017 (1977).

[336] *M. Zupan, A. Pollak,* J. Org. Chem. *42*, 1559 (1977).

[337] *A. Gregorčič, M. Zupan,* J. Org. Chem. *44*, 4120 (1979).

[338] *M. Zupan, A. Gregorčič, A. Pollak,* J. Org. Chem. *42*, 1562 (1977).

[339] *S. A. Shackelford,* Tetrahedron Lett. *1977*, 4265.

[340] *S. A. Shackelford, R. R. McGuire, J. L. Pflug,* Tetrahedron Lett. *1977*, 363.

[341] *A. Gregorčič, M. Zupan,* J. Org. Chem. *44*, 1255 (1979).

[342] *S. A. Shackelford,* J. Org. Chem. *44*, 3485 (1979).

[343] *S. Stavber, M. Zupan,* J. Fluorine Chem. *10*, 271 (1977).

[344] *M. Zupan, A. Pollak,* J. Org. Chem. *39*, 2646 (1974).

[345] *A. T. Podkhalyuzin, M. P. Nazarova,* J. Org. Chem. USSR *11*, 1547 (1975).

[346] *M. Zupan,* J. Fluorine Chem. *8*, 305 (1976).

[347] *M. Zupan,* Chimia *30*, 305 (1976).

[348] *M. Ya. Turkina, I. P. Gragerov,* J. Org. Chem. USSR *11*, 333 (1975).

[349] *M. Rabinovitz, I. Agranat, H. Selig, C.-H. Lin,* J. Fluorine Chem. *10*, 159 (1977).

[350] *S. P. Anand, L. A. Quarterman, P. A. Christian, H. H. Hyman, R. Filler,* J. Org. Chem. *40*, 3796 (1975).

[351] *I. Agranat, M. Rabinovitz, H. Selig, C.-H. Lin,* Chem. Lett. *1975*, 1271.

[352] *M. Zupan, A. Pollak,* J. Org. Chem. *40*, 3794 (1975).

[353] *E. D. Bergmann, H. Selig, C.-H. Lin, M. Rabinovitz, I. Agranat,* J. Org. Chem. *40*, 3793 (1975).

[354] *I. Agranat, M. Rabinovitz, H. Selig, C.-H. Lin,* Experientia *32*, 417 (1976).

[355] *S. P. Anand, L. A. Quarterman, H. H. Hyman, K. G. Migliorese, R. Filler,* J. Org. Chem. *40*, 807 (1975).

[356] *B. Šket, M. Zupan,* J. Chem. Soc. Perkin Trans. 1 *1977*, 2169.

[357] *B. Šket, M. Zupan,* J. Org. Chem. *43*, 835 (1978).

[358] *S. Stavber, M. Zupan,* J. Chem. Soc. Chem. Commun. *1978*, 969.

[359] *M. Zupan, A. Pollak,* J. Fluorine Chem. *7*, 443 (1976).

[360] *S. P. Anand, R. Filler,* J. Fluorine Chem. *7*, 179 (1976).

[361] *R. K. Marat, A. F. Janzen,* Can. J. Chem. *55*, 3031 (1975).

[362] *M. Zupan, B. Zajc,* J. Chem. Soc. Perkin Trans. 1 *1978*, 965.

[363] *Yu. L. Yagupol'skii, T. I. Savina,* Zh. Org. Khim. *15*, 438 (1979).

[364] *D. M. Bruce, A. J. Hewitt, J. H. Holloway, R. D. Peacock, I. L. Wilson,* J. Chem. Soc. Dalton Trans. *1976*, 2230.

[365] *R. C. Burns, I. D. MacLeod, T. A. O'Donnell, T. E. Peel, K. A. Phillips, A. B. Waugh,* J. Inorg. Nucl. Chem. *39*, 1737 (1977).

[366] *H. Selig, M. Rabinovitz, I. Agranat, C.-H. Lin, L. Ebert,* J. Am. Chem. Soc. *98*, 1601 (1976).

[367] *I. Agranat, M. Rabinovitz, H. Selig, C.-H. Lin,* Synthesis *1977*, 267.

[368] *M. Rabinovitz, I. Agranat, H. Selig, C.-H. Lin, L. Ebert,* J. Chem. Res. (S) *1977*, 216.

[369] *S. S. Yemul, H. B. Kagan, R. Setton,* Tetrahedron Lett. *1980*, 277.

[370] *J. H. Holloway, G. J. Schrobilgen,* J. Chem. Soc. Chem. Commun. *1975*, 623.

[371] *V. R. Polishchuk, G. Ya. Bekker, E. A. Avetisyan, L. S. German,* Zh. Vses. Khim. Ora. *21*, 222 (1976).

[372] *Y. Kobayashi, K. Yamamoto, I. Kumadaki,* Tetrahedron Lett. *1979*, 4071.

[373] *D. Cech, R. Wohlfeil, G. Etzold,* Nucleic Acid Res. *2*, 2183 (1975).

[374] *D. Cech, G. Herrmann, R. Staske, P. Langen, B. Preussel,* J. Prakt. Chem. *321*, 488 (1979).

[375] *T. Olsson, O. Wennerström,* Acta Chem. Scand. *B 32*, 293 (1978).

[376] *Y. Maki, K. Inukai,* Yuki Gosei Kagaku Kyokai Shi *34*, 722 (1976).

[377] *V. A. Grinberg, V. R. Polishchuk, E. I. Mysov, L. S. German, L. S. Kanevskii, V. V. Tsodikov, Yu. B. Vasil'ev,* Bull. Acad. Sci. USSR *26*, 2615 (1977).

[378] *C. J. Brookes, P. L. Coe, A. E. Pedler, J. C. Tatlow,* J. Chem. Soc. Perkin Trans. 1 *1978*, 202.

[379] *L. Hein, D. Cech,* Z. Chem. *17*, 415 (1977).

[380] *R. A. Jacob, L. L. Gerchman, T. J. Juhlke, R. J. Lagow,* J. Chem. Soc. Chem. Commun. *1979*, 128.

[381] *P. Gölitz, A. de Meijere,* Angew. Chem. *89*, 892 (1977); Angew. Chem. Int. Ed. Engl. *16*, 854 (1977).

[382] *N. Ishikawa, S. Shin-Ya,* Bull. Chem. Soc. Jpn. *48*, 1339 (1975).

[383] *J. E. Herz, E. Vazquez, S. Cruz, E. Zietz,* J. Fluorine Chem. *8*, 209 (1976).

[384] *M. Schlosser, Le Van Chau, B. Spahič,* Helv. Chim. Acta *58*, 2575, 2586 (1975).

[385] *M. Schlosser, Le Van Chau,* Helv. Chim. Acta *58*, 2595 (1975).

[386] *D. J. Burton, D. G. Naae,* J. Am. Chem. Soc. *95*, 8467 (1973).

[387] *H. S. Kesling, D. J. Burton,* Tetrahedron Lett. *1975*, 3355.

[388] *T. A. Dashevskaya, Yu. A. Fialkov, V. M. Cherkasov, L. M. Yagupol'skii,* Ukr. Khim. Zh. *41*, 498 (1975).

[389] *S. Andreades, J. F. Harris, Jr., W. A. Sheppard,* J. Org. Chem. *29*, 898 (1964).

[390] *A. Haas, U. Niemann,* Adv. Inorg. Chem. Radiochem. *18*, 143 (1976).

[391] *T. S. Croft, J. J. McBrady,* J. Heterocycl. Chem. *12*, 845 (1975).

[392] *D. M. Mulvey, H. Jones,* J. Heterocycl. Chem. *12*, 597 (1975).

[393] *A. Haas, U. Niemann,* J. Fluorine Chem. *11*, 509 (1975).

[393a] *A. Haas, D. Kortmann,* J. Fluorine Chem. *11*, 337 (1978).

[394] *T. S. Leong, M. E. Peach,* J. Fluorine Chem. *5*, 545 (1975).

[395] *D. C. Remy, K. E. Rittle, C. A. Hunt, M. B. Freedman,* J. Org. Chem. *41*, 1644 (1976).

[396] *L. M. Yagupol'skii, N. V. Kondratenko, V. P. Sambur,* Synthesis *1975*, 721.

[397] *I. G. Oksengendler, N. V. Kondratenko, E. A. Luk'yanets, L. M. Yagupol'skii,* J. Org. Chem. USSR *14*, 976 (1978).

[398] *V. N. Boiko, G. M. Shchupak, N. V. Ignat'ev, L. M. Yagupol'skii,* Zh. Org. Khim. *15*, 1245 (1979).

[399] *V. I. Popov, V. N. Boiko, N. V. Kondratenko, V. P. Sambur, L. M. Yagupol'skii,* J. Org. Chem. USSR *13*, 1985 (1977).

[400] *V. N. Boiko, T. A. Dashevskaya, G. M. Shchupak, L. M. Yagupol'skii,* Zh. Org. Khim. *15*, 396 (1979).

[401] *V. N. Boiko, G. M. Shchupak, L. M. Yagupol'skii,* Zh. Org. Khim. *13*, 1057 (1977).

[402] *A. Haas* in Gmelins Handbuch der Anorganischen Chemie, Supplement to the eight edition, Springer, Berlin 1973, Vol. 12, p. 207.

[403] *V. G. Voloshchuk, V. N. Boiko, L. M. Yagupol'skii,* Zh. Org. Khim. *13*, 2008 (1977).

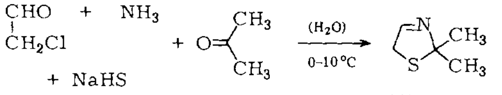
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

## Facile Synthesis of Racemic Cysteine

By *Jürgen Martens*, *Heribert Offermanns*, and
*Paul Scherberich*[*]

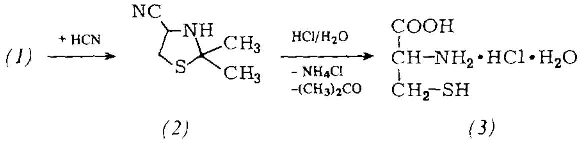
Until now racemic cysteine has only been synthetically accessible *via* expensive multi-step syntheses[1].

In the course of our investigations on the synthesis of natural and unnatural amino acids[2] and amino acid derivatives[3] we have now found a facile and efficient synthesis for DL-cysteine hydrochloride · $H_2O$ *(3)*. The key intermediate, 2,2-dimethyl-3-thiazoline *(1)*, can be obtained in 92% yield in a one-pot reaction from chloroacetaldehyde, sodium hydrogen sulfide, ammonia and acetone. This reaction is based on the fundamental studies of *Asinger et al.*[4].



*(1)*

Anhydrous hydrocyanic acid adds to the azomethine group of *(1)* to give the 2,2-dimethylthiazolidine-4-carbonitrile *(2)* in almost quantitative yield.



*(2)* *(3)*

The crude thiazolidine *(2)* can be directly further reacted. Using aqueous hydrochloric acid, the desired *(3)* is obtained in 70% yield (relative to *(1)*) in a one-pot reaction[5].

*Procedure*

*(1)*: 350 mg of a 45% aqueous solution of chloroacetaldehyde (2.0 mol) is added between 0 and 10 °C, over 45 min, to a suspension of sodium hydrogen sulfide (135 g, 2.4 mol) in acetone (450 mL, 6.1 mol), 235 g water, and ammonia (93 g, 5.5 mol). After 25 min at 5—10 °C, the organic and aqueous phases are separated. Fractional distillation of the organic phase (88—89 °C/100 mbar) gives 106 g *(1)* (92%) as a colorless liquid.

*(2)*: Hydrocyanic acid (50 mL, 1.3 mol) is added over 60 min to a stirred solution of *(1)* (115 g, 1 mol) in 100 mL methanol at 5—10 °C. After 30 min at 15—20 °C, the solution of *(2)* obtained is directly further reacted.

*(3)*: A solution of *(2)*, as prepared above, is dropped over 60 min into 1000 mL (*ca.* 11 mol) conc. hydrochloric acid at 20—30 °C. After 3 h stirring at 40—50 °C the mixture is diluted with 600 mL water, the methanol and acetone distilled off, the resulting solution refluxed for 4—5 h, clarified with activated charcoal and the solvent removed. Ammonium chloride, which does not dissolve upon digestion of the residue in 400 mL methanol, is filtered off. The methanolic filtrate is evaporated to dryness and the residue recrystallized from 20% hydrochloric acid; *(3)* forms thick colorless crystals. The latter are suction-filtered, washed with cold 20% hydrochloric acid, and dried in a fluidized bed dryer at 20—40 °C. 122.9 g (70%) of *(3)* is obtained from two crystallization fractions; the product is found to be pure by thin layer chromatography.

Received: December 5, 1980 [Z 797 IE]
German version: Angew. Chem. *93*, 680 (1981)

CAS Registry numbers: *(1)*, 66692-88-4; (±)-*(2)*, 78249-03-3; (DL)-*(3)* · HCl, 10318-18-0; acetone, 67-64-1; chloraldehyde, 107-20-0; sodium hydrogen sulfide, 16721-80-5

---

[1] *J. P. Greenstein, M. Winitz:* Chemistry of the Amino Acids, Vol. 3, Wiley, New York 1961, p. 1892.

[2] *W. M. Weigert, H. Offermanns, P. Scherberich,* Angew. Chem. *87*, 372 (1975); Angew. Chem. Int. Ed. Engl. *14*, 330 (1975).

[3] *A. Kleemann, B. Lehmann, J. Martens,* Angew. Chem. *91*, 858 (1979); Angew. Chem. Int. Ed. Engl. *18*, 797 (1979); *A. Kleemann, W. Leuchtenberger, J. Martens, H. Weigel, ibid. 92*, 640 (1980); *19*, 627 (1980).

[4] *F. Asinger, H. Offermanns,* Angew. Chem. *79*, 953 (1967); Angew. Chem. Int. Ed. Engl. *6*, 907 (1967); *M. Thiel, F. Asinger, K. Schmiedel,* Justus Liebigs Ann. Chem. *611*, 121 (1958).

[5] The isolated intermediates and *(3)* gave correct elemental analysis and spectroscopic data.

---

[*] Dr. J. Martens, Dr. H. Offermanns, Dr. P. Scherberich
Degussa AG
Postfach 2644, D-6000 Frankfurt/Main (Germany)

---

## New Tungsten-Iridium Dinuclear Complexes Containing Cyclopentadienyl and Hydrido Bridges

By *Paul S. Pregosin*, *Antonio Togni*, and
*Luigi M. Venanzi*[*]

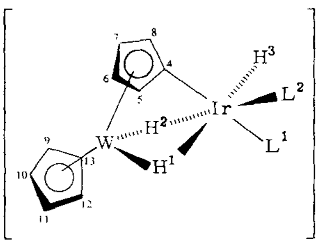
We have previously shown that neutral monomeric hydrido complexes of platinum(II)[1a] and iridium(III)[1b] react with cationic species to form dimeric complexes containing one or more bridging hydrido ligands.

As an extension of this work we report here the new dinuclear complex *(1a)* obtained by reacting *(2)* with *(3a)*.

---

[*] Prof. Dr. L. M. Venanzi, Dr. P. S. Pregosin, A. Togni (Ciba-Geigy-Fellow)
Laboratorium für Anorganische Chemie
ETH-Zentrum, Universitätstrasse 6, CH-8092 Zürich (Switzerland)

Cation (3a) is produced *in situ* as previously described for the formation of (3b) and (3c)[2].



$PF_6$ (1a), L = $PEt_3$

$[WH_2(\eta^5\text{-}C_5H_5)_2]$ (2)

$[IrH_2L_2(EtOH)_2]PF_6$
(3a), L = $PEt_3$; (3b), L = $PMePh_2$;
(3c), L = $PPh_3$

Compound (1a) is a green solid and is stable in air for several days. It is moderately soluble only in polar organic solvents and the solutions obtained decompose rapidly in the presence of oxygen.

Support for the proposed structure for (1a) stems from its $^1H$-, $^{13}C$- and $^{31}P$-NMR spectra (in $CD_2Cl_2$):

$^1H$-NMR: $\delta = -17.57$ [H1, $^2J(H1,H2) = 3.7$ Hz, $^1J(W,H1) = 95.2$ Hz]; $-18.86$ [H2, $^2J(H1,H2) = {}^2J(H2,H3) = {}^2J(H2,P1) = 3.7$ Hz, $^2J(H2,P2) = 47.6$ Hz, $^1J(W,H2) = 92.4$ Hz]; $-23.78$ [H3, $^2J(H3,P1)$, $^2J(H3,P2) = 16.8$, 28.4 Hz]; 6.42 [(1H), 6.36 (1H), 5.09 (2H), H5—H8, 5.34 (5H), H9—H13; $^{13}C$-NMR: $\delta = 85.5$ [C9—C13]; 110.3 [C4, $^2J(P1,C4) = 84.2$ Hz, $^2J(P2,C4) = 8.3$ Hz]; 95.1 [C5 or C8, $^3J(P1,C) = 7.4$ Hz]; 93.6 [C8 or C5, $^3J(P1,C) = 5.5$ Hz]; 91.2 [C6 or C7]; 89.9 [C7 or C6]; 20.3, 19.8, [$PCH_2$, $^1J(P,C) = 25$ Hz]; 8.0, 7.8 [$PCH_2CH_3$]. $^{31}P$-NMR: $\delta = 6.2$ [P1, $^2J(P1,P2) = 11.8$ Hz]; 4.7 [P2].

The $^{31}P\{^1H\}$-NMR spectrum of the two non-equivalent tertiary phosphorus atoms appears as an AB pattern. The magnitude of $^2J(P1,P2)$ is consistent with a *pseudo-cis*-orientation of the phosphorus atoms. The $^1H$-NMR spectrum between $\delta = -17$ and $-24$ ppm comprises three groups of resonances, which may be assigned to H1, H2 and H3. The two lower field signals are assigned to H1 and H2 since they show $^{183}W$-satellites (natural abundance of $^{183}W = 14.3\%$) with $J(W,H) \approx 90$ Hz, consistent with one-bond interactions. Reported $^1J(W,H)$ values in related complexes are 107 Hz for (4)[3] and 60.3 and 59.7 Hz for (5a) and (5b)[4] respectively. A further relatively large splitting of the H2 signal stems from P2, and hence it can be concluded that these two atoms occupy a *pseudo-trans* arrangement. H3 couples to two *cis*-phosphorus atoms and H1 but, interestingly, the *trans*-coupling $^2J(H1,H3)$ is quite small (< 1.5 Hz).

$[(\eta^5\text{-}C_5H_5)_2W(\mu\text{-}H)_2Rh(PPh_3)_2]PF_6$ (4)
$[(\eta^5\text{-}C_5H_5)_2W(\mu\text{-}H)_2PtR(PEt_3)_2]BF_4$ (5a), R = H
(5b), R = $C_6H_5$

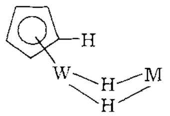
The assignment of C5 and C8 in the $^{13}C\{^1H\}$-NMR spectrum follows from the suggestions of *Davison* and *Wreford*[5], while the signal at $\delta = 110.3$ may be assigned on the basis of its position[6], spin-lattice relaxation time and $^{31}P$ coupling pattern.

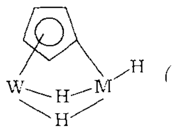
Complex (1a) appears to be a member of a general class of compounds of type (1); (1b) and (1c) can be prepared in a similar way to (1a) (L = $PMe_2Ph$ or $PMePh_2$).

To our knowledge, the complexes of type (1) are the first examples of compounds containing both "$C_5H_4^{2-}$" and "$H^-$" bridging ligands. Although ($\eta^5:\eta^1$-$C_5H_4$) bridges have been observed in complexes of zirconium[6], molybdenum and tungsten[7,8], when bridging hydrides are present[5,8], the cyclopentadienyl moiety is present as a bridging $\eta^5:\eta^5$-fulvalene.

The mechanistic pathway leading to (1) is likely to involve the initial formation of $[(\eta^5\text{-}C_5H_5)_2W(\mu\text{-}H)_2\text{-}Ir(PEt_3)_2]^+$, which is analogous to (4) and contains the structural unit (A), followed by the oxidative addition of a cyclopentadienyl C—H bond, resulting in the formation of structural unit (B). (Hydrogen-abstraction reactions occur easily and often irreversibly in $Ir^I$ complexes[9].) A species of type (B) (M = Rh) has been postulated to explain the H/D-exchange observed in compound (4)[3].

(A)





(B)

## *Experimental*

A vigorously stirred deep-red suspension of $[Ir(cod)(PEt_3)_2]PF_6$ (0.539 g, 0.79 mmol) (cod = 1,5-cyclooctadiene) in 25 mL EtOH at 0 °C was treated with $H_2$ for 15 min. A solution of (2) (0.250 g, 0.79 mmol) in 15 mL EtOH was added to the resulting clear pale-yellow solution and stirring continued for an additional 0.5 h. Solvent was evaporated (with cooling) until precipitation began and this was followed by rewarming to room temperature and subsequent recrystallization at −22°. The green microcrystalline (1a) formed was recrystallized again from EtOH to afford the product: yield 0.218 g (31%).

Received: December 19, 1980 [Z 800 IE]
German version: 93, 684 (1981)

---

[1] a) *G. Bracher, D. M. Grove, L. M. Venanzi, F. Bachechi, P. Mura, L. Zambonelli*, Angew. Chem. *90*, 826 (1978); Angew. Chem. Int. Ed. Engl. *17*, 778 (1978); *G. Bracher, D. M. Grove, P. S. Pregosin, L. M. Venanzi, ibid. 91*, 169 (1979); *18*, 155 (1979); b) *A. Immirzi, A. Musco, P. S. Pregosin, L. M. Venanzi, ibid. 92*, 744 (1980); *19*, 721 (1980).

[2] *R. H. Crabtree, H. Felkin, T. Fillebeen-Khan, G. E. Morris*, J. Organomet. Chem. *168*, 183 (1979).

[3] *N. W. Alcock, O. W. Howarth, P. Moore, G. E. Morris*, J. Chem. Soc. Chem. Commun. *1979*, 1160.

[4] *A. Togni*, Diplomarbeit, Eidgenössische Technische Hochschule, Zürich 1979.

[5] *A. Davison, S. S. Wreford*, J. Am. Chem. Soc. *96*, 3017 (1974).

[6] *K. I. Gell, J. Schwartz*, J. Chem. Soc. Chem. Commun. *1979*, 244.

[7] *R. J. Hoxmeier, J. R. Blickensderfer, H. D. Kaesz*, Inorg. Chem. *18*, 3453 (1979).

[8] *M. Berry, N. J. Cooper, M. L. H. Green, S. J. Simpson*, J. Chem. Soc. Dalton Trans. *1980*, 29.

[9] *A. D. English, T. Herskovitz*, J. Am. Chem. Soc. *99*, 1648 (1977) and references therein.

# Double Ring-Opening of Bicyclic Oxaziridines to *N*-(3-Oxopropyl)amides by Iron(II) Sulfate

By *David St. C. Black* and *Lynn M. Johnstone*[*]

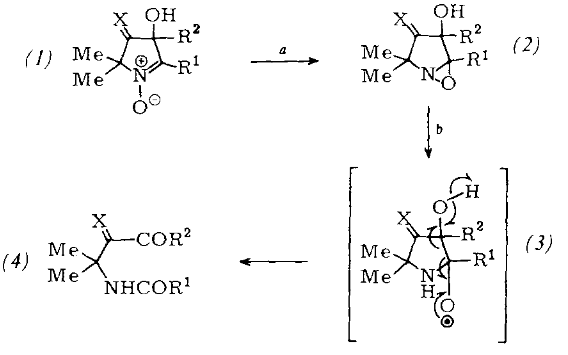
*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

Iron(II) sulfate has been shown to cleave *C*-alkyl-, *C*-aryl-[1, 2] and *C*-cyano-[3] substituted oxaziridines, the nature of the products depending on the particular substitution pattern. We now report that oxaziridines of type (2),

---

[*] Dr. D. St. C. Black, L. M. Johnstone
Department of Chemistry, Monash University
Clayton, Vic. 3168 (Australia)

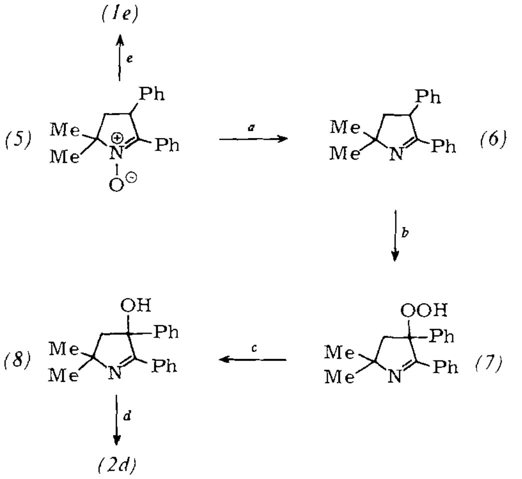
whose *C*-hydroxymethylene substituents form part of a pyrrolidine ring, undergo a reaction with iron(II) sulfate which results in opening of both rings to afford the oxoamides *(4)* (Scheme 1). An isolated example of a similar reaction which has, however a different outcome, has been previously reported by *Bischoff*[4].



| (1)—(4) | X | R¹ | R² |
|---|---|---|---|
| *a* | H, H | *t*Bu | Me |
| *b* | H, H | Ph | Me |
| *c* | H, H | Ph | Et |
| *d* | H, H | Ph | Ph |
| *e* | O | Ph | Ph |

Scheme 1. *a)*: hν, benzene, 1—12 h. *b)*: $FeSO_4$, aqueous EtOH, 2 h.

The oxaziridines *(2a—e)* are formed as isomeric mixtures by photorearrangement ($\lambda_{max}$ = 254 or 300 nm, benzene) of the related cyclic nitrones *(1a—e)*. The known nitrones *(1a—d)*[5] can be prepared by Grignard reactions from the corresponding 3-oxo-derivatives. However, oxaziridine *(2d)* is more readily available from the method shown in Scheme 2. It is noteworthy that, on attempted recrystallization from hexane in air, the 1-pyrroline *(6)* was rapidly transformed into the stable hydroperoxide *(7)*. Unlike the 3*H*-indolyl hydroperoxides[6], *(7)* did not undergo thermal CC-bond cleavage, but afforded the alcohol *(8)* in low yield. Yields were improved by addition of triethyl phosphite. Peracid oxidation of *(8)* yielded isomerically pure *(2d)* (with *cis*-phenyl groups).—The 4-oxonitrone *(1e)* ($\nu_{max}$ = 1776 $cm^{-1}$ (CO)) can be prepared in 36% yield as shown in Scheme 2.



Scheme 2. *a:* $Fe(CO)_5$/*n*$Bu_2O$, reflux, 24 h. *b:* $O_2$, hexane, reflux, 2 h. *c:* $(EtO)_3P$, tetrahydrofuran, room temperature, 1 h. *d:* 2% $CH_3CO_3H$ in $CH_3CO_2H$, room temperature, 16 h. *e:* $HNO_3$, $CH_3CN$, reflux, 1 h.

The oxoamides *(4)* show infrared absorptions characteristic of the ketone and amide groups. Some other physical data are presented in Table 1.

Table 1. Selected physical data of compounds *(4)*, *(7)* and *(8)*.

| Cpd. | Yield [%] | M.p. [°C] | ¹H-NMR ($CDCl_3$), δ-values *gem*-$Me_2$ | —$CH_2$— |
|---|---|---|---|---|
| *(4a)* | 92 [a] | 54—55 | 1.40 | 2.92 |
| *(4b)* [7] | 88 [a] | 98—100 | 1.53 | 3.00 |
| *(4c)* | 83 [a] | [e] | 1.53 | 2.95 |
| *(4d)* | 50 [b] | 82—84 | 1.63 | 3.51 |
| *(4e)* | 55 [a] | 135—136 | 1.77 | — |
| *(7)* | 74 [c] | 139—142 | 1.28, 1.41 [f] | 2.10, 2.90 ($J_{AB}$ = 14 Hz) |
| *(8)* | 74 [d] | 147—148 | 1.40, 1.47 | 2.33 |

[a] From nitrones *(1)*. [b] From oxaziridine *(2d)*. [c] From the 1-pyrroline *(6)*. [d] From the hydroperoxide *(7)*. [e] B.p. = 70—82 °C/1 torr (air bath temp.). [f] In [$D_6$]DMSO.

It is proposed that the conversion *(2)*→*(4)* involves the intermediate formation of oxyl radicals *(3)* (cf. [1]). The reactions proceed to completion only when stoichiometric amounts of iron(II) sulfate are used. The reaction proceeds much more slowly when iron(II) sulfate is replaced by iron(III) chloride; furthermore, it is not catalyzed by trifluoroacetic acid. These observations support the proposed radical mechanism.

### *General Procedure*

A solution of $FeSO_4 \cdot 7H_2O$ in water is added to a solution of *(2)* in ethanol (1 : 1 molar ratio) and the resulting mixture stirred and heated under reflux for 2 h. The mixture is concentrated, the aqueous residue extracted with chloroform, and the extracts dried and concentrated to give *(4)*, which is purified by recrystallization or distillation.

Received: January 8, 1981 [Z 802a IE]
German version: Angew. Chem. *93*, 703 (1981)

---

[1] *W. D. Emmons*, J. Am. Chem. Soc. *79*, 5739 (1957); *E. Schmitz*, Adv. Heterocycl. Chem. *24*, 63 (1979).
[2] *D. St. C. Black, K. G. Watson*, Aust. J. Chem. *26*, 2515 (1973); *D. St. C. Black, N. A. Blackman, L. M. Johnstone, ibid. 32*, 2041 (1979).
[3] *D. St. C. Black, N. A. Blackman*, Aust. J. Chem. *32*, 2035 (1979).
[4] *C. Bischoff*, J. Prakt. Chem. *318*, 848 (1976).
[5] *D. St. C. Black, N. A. Blackman, L. M. Johnstone*, Aust. J. Chem. *32*, 2025 (1979).
[6] *E. Leete*, J. Am. Chem. Soc. *83*, 3645 (1961).
[7] *P. J. Scheuer, H. C. Botelho, C. Pauling*, J. Org. Chem. *22*, 674 (1950).

## Three-Atom Ring Expansion of Cyclic Ketones *via* Nitrones and Oxaziridines

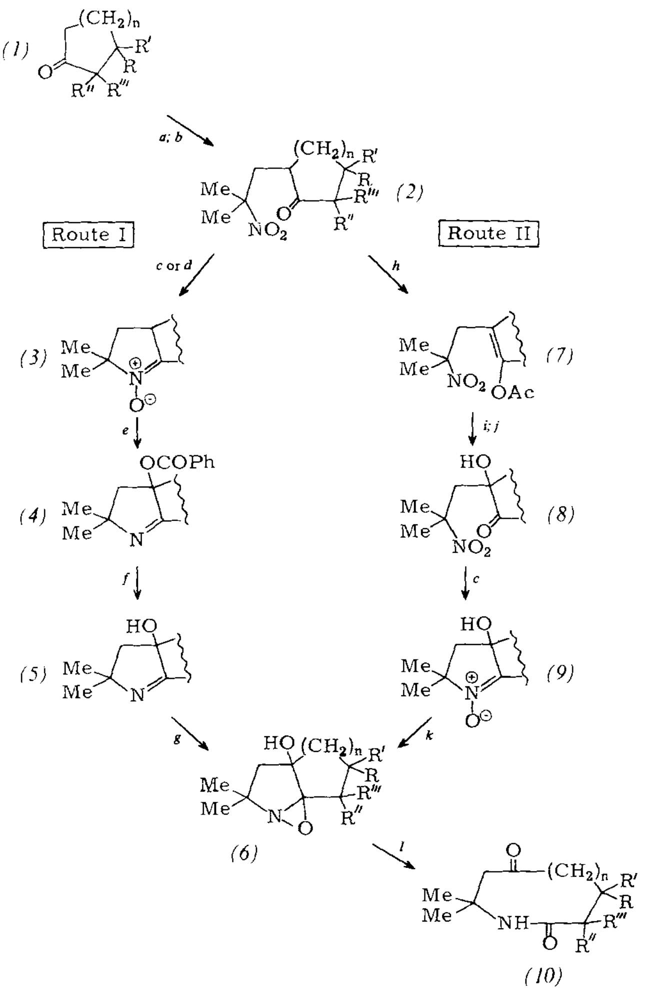
By *David St. C. Black* and *Lynn M. Johnstone*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

Ring-opening of bicyclic *C*-hydroxymethylene-substituted oxaziridines on treatment with iron(II) sulfate leads to *N*-(3-oxopropyl)amides[1]. This reaction can also be applied to tricyclic oxaziridines *(6)* and thus opens up a good route to a variety of eight- and nine-membered oxolactams

---

[*] Dr. D. St. C. Black, L. M. Johnstone
Department of Chemistry, Monash University
Clayton, Vic. 3168 (Australia)



| (1)—(10) | n | R | R' | R'' | R''' | Route |
|---|---|---|---|---|---|---|
| *a* | 1 | =CH—CH=CH—CH= | | | | I, II |
| *b* | 2 | =CH—CH=CH—CH= | | | | I, II |
| *c* | 2 | H | H | H | H | II |
| *d* | 2 | H | H | =CHPh | | I |

Scheme 1. *a:* $H_2CO$, $Me_2NH\cdot HCl$, EtOH, reflux, 0.5—4 h. *b:* NaOH or KF, *i*$PrNO_2$, reflux, 4 h. *c:* Zn, $NH_4Cl$, aqueous THF, 0°, 3 h. *d:* freshly reduced Fe, HCl, aqueous EtOH, reflux, 3 h. *e:* PhCOCl, ether, room temp., 1 h. *f:* 2 N NaOH, aqueous EtOH, reflux, 2 h. *g:* 2% $CH_3CO_3H$ in $CH_3CO_2H$, room temp., 4 h. *h:* $Ac_2O$, $CCl_4$, $HClO_4$, room temp., 16—48 h. *i:* *m*-$ClC_6H_4CO_3H$, $CH_2Cl_2$, room temp., 24 h. *j:* 2 N HCl, EtOH, reflux, 2H. *k:* hv, EtOh, 4—20 h. *l:* $FeSO_4$, aqueous EtOH, 2 h.

Table 1. Selected physical data of compounds *(2)*, *(5)*, *(9)* and *(10)*.

| Cpd. | Yield [%] | M.p. [°C] | IR (Paraffin) [$cm^{-1}$] |
|---|---|---|---|
| *(2a)* | 29 [a] | 80—83 | 1710 bs, 1544 s |
| *(5a)* | 30 [b] | 189—191 | 3180 bs, 1684 s |
| *(9a)* | 38 [b] | 189—191 | 3270 bm, 1630 s |
| *(10a)* | 29 [c]<br>52 [d] | 198—201 | 3280 w, 3200 m, 3060 w, 1702 s, 1644 s |
| *(2b)* | 40 [a] | 42—43 | 1670 s, 1532 s |
| *(5b)* | 17 [b] | 182—183 | 3200 bm, 1626 m |
| *(9b)* | 35 [b] | 177—179 | 3210 bm, 1578 m |
| *(10b)* | 33 [c]<br>41 [d] | 131—132 | 3280 m, 1698 s, 1630 bs |
| *(2c)* [3] | 48 [a] | [e] | 1702 bs, 1534 bs |
| *(9c)* | 16 [b] | 131—134 | 3120 bs, 1626 s |
| *(10c)* [f] | 40 [d] | 141—143 | 3280 s, 3200 m, 3080 m, 1700 s, 1650 s |
| *(2d)* | 35 [a] | 66—68 | 1680 bs, 1538 bs |
| *(5d)* | 27 [b] | 169—170 | 3240 bm, 1628 w |
| *(10d)* | 32 [c] | 123—124 | 3430 m, 1700 s, 1666 s |

[a] From *(1)* [b] From *(2)*. [c] From *(5)*. [d] From *(9)*. [e] B.p.=92—96 °C/0.05 torr. [f] $^1$H-NMR (242 K): $\delta$=1.33 (s, 3 H), 1.66 (s, 3 H), 1.33—3.03 (br. m, 9 H), 3.76 (d, $J$=3 Hz, 1 H), 5.67 (br. s, 1 H).

*(10)* (Scheme 1). Two distinct routes from the γ-nitroketones *(2)* to the oxaziridines *(6)* have been developed. In route I the nitroketones *(2)* are converted by reductive cyclization into the bicyclic nitrones *(3)*, which on treatment with benzoyl chloride undergo *O*-benzoylation and allylic rearrangement[2] to the benzoyloxy-1-pyrrolines *(4)*, and can readily be saponified to the alcohols *(5)*. Treatment of *(5)* with peracetic acid affords isomerically pure oxaziridines *(6)* having *cis*-coupled rings (assignment of the structures was confirmed by $^1$H-NMR spectroscopy). In route II, the γ-nitroketones *(2)* are converted *via* the enol acetates *(7)* and their epoxides into the α-hydroxy-γ-nitroketones *(8)*, which undergo reductive cyclization to the bicyclic nitrones *(9)*. Photorearrangement of *(9)* affords *cis*- and *trans*-*(6)*.

Both routes are suitable for the synthesis of lactams *(10a)* and *(10b)* (see Table 1). *(10c)* is only accessible *via* route II since *(3c)* rapidly decomposes. It is significant that the stability of the hydroxynitrones *(9)* is, in general, much greater than that of the nitrones *(3)*; route II is generally preferable to route I, where both are applicable. Route I, however, was chosen for the synthesis of the benzylidene-substituted lactam *(10d)* because of the expected lack of selectivity in the peracid oxidation of the benzylidene-enol acetate *(7d)*. The C=N-double bond in *(5d)* can be oxidized, without concomitant epoxidation of the C=C-double bond, to form *(6d)* in high yield.

Isolation of *(6)* is not required in either route I or II. Indeed, nitrones *(9)* can be irradiated in ethanol and the concentrated reaction solution treated directly with iron(II) sulfate to afford the lactams *(10)*. The $^1$H-NMR spectra of the latter compounds at room temperature generally consist of broad signals, which indicates that the systems are considerably flexible. The low temperature spectra are, however, much sharper.

The overall reaction *(1)*→*(10)* permits a three-atom condensative ring-expansion of cyclic ketones.

Received: January 8, 1981 [Z 802b IE]
German version: Angew. Chem. 93, 704 (1981)

---

[1] *D. St. C. Black, L. M. Johnstone,* Angew. Chem. *93*, 703 (1981); Angew. Chem. Int. Ed. Engl. *20*, 669 (1981).

[2] *N. J. A. Gutteridge, J. R. M. Dales,* J. Chem. Soc. C *1971*, 122.

[3] *N. S. Gill, K. B. James, F. Lions, K. T. Potts,* J. Am. Chem. Soc. *74*, 4923 (1952).

## Formation of Oxiranes from Methyl(phenyl)selenoniomethanide and Aldehydes or Ketones

By *Ken Takaki, Masateru Yasumura,* and
*Kenji Negoro*[*]

Organoselenium compounds have been widely investigated in the last decade[1]. Selenium ylides, in which carbanions are stabilized by a carbonyl group, react with α,β-unsaturated ketones to give cyclopropanes[2]. However, their reactivities, especially those of non-stabilized ylides,

---

[*] Prof. Dr. K. Negoro, Dr. K. Takaki, Dipl.-Chem. M. Yasumura
Department of Applied Chemistry, Faculty of Engineering
Hiroshima University, Sendamachi-3, Hiroshima 730 (Japan)

have not been as completely investigated as sulfonium and phosphonium ylides.

We report here on reactions of methyl(phenyl)selenoniomethanide *(1)* with carbonyl compounds *(2)*, which afford oxiranes *(3)* in good yields (Table 1).

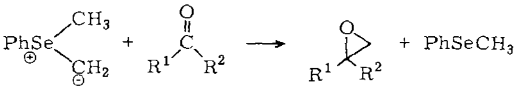

*(1)* *(2)* *(3)* *(4)*

Table 1. Selected data of the oxiranes *(3)* obtained from methyl(phenyl)selenoniomethanide *(1)* and carbonyl compounds *(2)*. *(3a)*, *(3b)*, *(3e)* and *(3f)* show molecular ions in the mass spectrum.

| Cpd. [a] | $R^1$ | $R^2$ | Yield [%] [b] | B.p. [°C/torr] |
|---|---|---|---|---|
| *(3a)* | Ph | H | 94 | 83—85/15 |
| *(3b)* | $p$-$NO_2C_6H_4$ | H | 82 | [c] |
| *(3c)* | $n$-$C_6H_{13}$ | H | — | |
| *(3d)* | $n$-$C_4H_9$ | $CH_3$ | 76 | 55—57/75 |
| *(3e)* | $n$-$C_4H_9$ | $C_2H_5$ | 88 | 62—65/25 |
| *(3f)* | —$(CH_2)_5$— | | 83 | 46—48/23 |

| Cpd. | $^1$H-NMR ($\delta$, TMS int., in $CDCl_3$) |
|---|---|
| *(3a)* | 2.70 (dd, $J$ = 5.5 and 2.7 Hz, 1 H), 3.05 (dd, $J$ = 5.5 and 4.0 Hz, 1 H), 3.73 (dd, $J$ = 4.0 and 2.7 Hz, 1 H), 7.03—7.40 (m, 5 H) |
| *(3b)* | 2.73 (dd, $J$ = 5.8 and 2.8 Hz, 1 H), 3.20 (dd, $J$ = 5.8 and 4.0 Hz, 1 H), 3.93 (dd, $J$ = 4.0 and 2.8 Hz, 1 H), 7.40 (d, $J$ = 8.4 Hz, 2 H), 8.15 (d, $J$ = 8.4 Hz, 2 H) |
| *(3d)* | 0.73—1.63 (t and m, $J$ = 7.0 Hz, 12 H), 2.30—2.60 (m, 2 H) |
| *(3e)* | 0.77—1.87 (t and m, $J$ = 7.0 Hz, 14 H), 2.20—2.67 (m, 2 H) |
| *(3f)* | 0.83—2.06 (m, 10 H), 2.33—2.60 (m, 2 H) |

[a] The products *(3)* were identified by comparison with authentic samples prepared from dimethylsulfoniomethanide and the corresponding carbonyl compounds [3]. [b] Yields were determined by NMR. [c] M.p. = 83—85 °C.

The ylide *(1)* was generated *in situ* from dimethylphenylselenonium methyl sulfate and sodium hydride in the presence of carbonyl compounds *(2)*, since selenium ylides are relatively unstable and undergo fission of the ylide bonds[4]. Generally, these reactions are mild and result in good yields of ketones and aromatic aldehydes. In the reaction with heptanal *(2c)* GC analysis of the reaction mixture showed a small peak, in addition to those of the educts, which may be assigned to the expected oxirane *(3c)*, the isolation of which was, however, difficult. These epoxidations are the first examples, to our knowledge, of reactions of non-stabilized selenium ylides with "enolizable" carbonyl compounds.

### *General Procedure*

A solution of dimethyl(phenyl)selenonium methyl sulfate[5] (12 mmol) and the aldehyde or ketone (10 mmol) in dry dimethylformamide (30 mL) is added dropwise over a period of 30 min to a stirred suspension of NaH (12 mmol) in dry tetrahydrofuran (30 mL); all operations were conducted under nitrogen and the mixture was cooled on an ice bath. The mixture was then warmed to room temperature for 4 h and held at 50 °C for 30 min. After cooling, 10% aqueous $NH_4Cl$ (20 mL) was added and the organic layer extracted with ether, washed with NaCl solution, and dried over $Na_2SO_4$. Evaporation of the solvent *in vacuo* gave a residue which contained the oxirane *(3)*, methyl phenyl selenide *(4)*, and a small amount of unreacted *(2)*. Distillation of the residue afforded analytically pure *(3)*.

Received: September 8, 1980 [Z 804 IE]
German version: Angew. Chem. *93*, 707 (1981)

[1] *H. J. Reich*, Acc. Chem. Res. *12*, 22 (1979).
[2] *N. N. Magdesieva, L. N. Ngu, N. M. Koloskova*, J. Org. Chem. USSR *13*, 928 (1977).
[3] *B. M. Trost, L. S. Melvin, Jr.*: Sulfur Ylides, Academic Press, New York 1975.
[4] *D. L. Klayman, W. H. H. Günther*: Organic Selenium Compounds: Their Chemistry and Biology, Wiley-Interscience, New York 1973.
[5] *H. M. Gilow, G. L. Walker*, J. Org. Chem. *32*, 2580 (1967).

---

## Experimental Evidence for the $[H_2SSH_2]^{+\cdot}$ Radical Cation in Solution

By *Shamim A. Chaudhri* and *Klaus-Dieter Asmus*[*]

The $H_2S$ molecule and radical species derived from it have been the subjects of numerous investigations. The ionization and excitation energies, as well as geometrical parameters, for example, have been calculated using various theoretical models[1] and the results compared with experimental values[2]. Recently, *Clark*[3] has used theoretical calculations (HF/4-31G, MP2/4-31G and MNDO) to consider some thermodynamic and optical characteristics of an $[H_2SSH_2]^{+\cdot}$ radical cation.

A significant feature of $[H_2SSH_2]^{+\cdot}$ is assumed to be a three-electron bond; two p-electrons forming a σ-bond and the third, unpaired electron being promoted into an antibonding σ*-orbital. A corresponding three electron bond has been experimentally well established in the analogous $[R_2SSR_2]^{+\cdot}$ radical cations formed as intermediates in the oxidation of thioethers[4,5]. We are now able to present experimental evidence on the formation, stability and optical absorption spectrum of $[H_2SSH_2]^{+\cdot}$ for purpose of comparison with *Clark*'s calculations.

The experiments were carried out using a pulse radiolysis technique. $^\cdot$OH and H$^\cdot$ react with $H_2S$ according to

$$H_2S + {}^\cdot OH/H^\cdot \rightarrow HS^\cdot + H_2O/H_2$$

to yield HS$^\cdot$ radicals ($k_{^\cdot OH} \approx 10^{10}$ and $k_{H^\cdot} \approx 10^9$ mol$^{-1}$ L s$^{-1}$)[6]. The HS$^\cdot$ radicals exhibit no detectable optical absorption in the UV/VIS-region as is apparent from, for example, pulse radiolysis investigations (aqueous solutions, pH = 3, $10^{-4}$ mol/L $H_2S$). At higher $H_2S$ concentrations, (*e.g.* $10^{-2}$ mol/L and lower pH values (*e.g.* with 0.2 mol/L $HClO_4$), however, a well characterized transient optical absorption band can be observed in the UV ($\lambda_{max}$ = 370 nm; Fig. 1a).

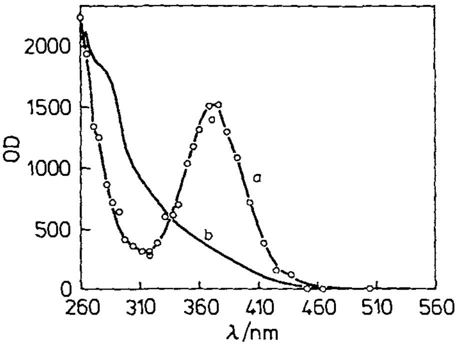


Fig. 1. a) UV/VIS-absorption spectrum of the $[H_2SSH_2]^{+\cdot}$ radical cation, measured immediately after a 4 μs pulse in an aqueous solution of $10^{-2}$ mol/L $H_2S$ and 0.2 mol/L $HClO_4$, b) UV/VIS-absorption spectrum after decay of $[H_2SSH_2]^{+\cdot}$(*ca.* 0.5 ms after pulse).—Optical density (OD) in arbitary units.

---

[*] Prof. Dr. K.-D. Asmus, Dr. S. A. Chaudhri
Hahn-Meitner-Institut für Kernforschung Berlin GmbH,
Bereich Strahlenchemie
Postfach 39 01 28, D-1000 Berlin 39 (Germany)

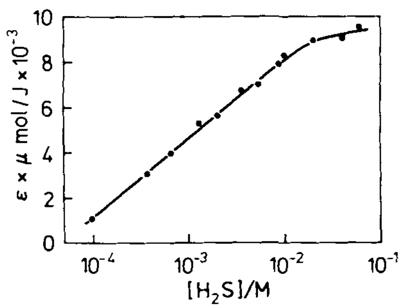
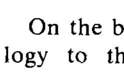


Fig. 2. Yield of $[H_2SSH_2]^{\dot{+}}$ measured from the absorption at 370 nm as a function of $H_2S$ concentration in aqueous solutions containing 0.2 mol/L $HClO_4$.

The absorption is fully developed at the end of the 4 µs pulse. This species decays with a first half-life of *ca.* 60 µs to a non-identified product (Fig. 1b). The decay kinetics follow a second order decay process *i.e.* a radical-radical reaction, with a rate constant of $2k = (3.0 \pm 1.0) \times 10^9$ mol$^{-1}$ L s$^{-1}$, based on the assumption of quantitative conversion of each ˙OH and H˙ into this transient absorbing species.

The yield of the 370 nm transient depends markedly on the $H_2S$ concentration as can be seen from the plot in Figure 2 (all solutions contained 0.2 mol/L $HClO_4$); a saturation value was reached first at *ca.* 0.1 mol/L $H_2S$[7].

The yield of the species absorbing at 370 nm is practically constant at high proton concentrations ($> 10^{-2}$ mol/L $HClO_4$). At lower proton concentrations its yield decreases and the already known $[HSSH]^{\dot{-}}$ radical anion ($\lambda_{max} = 380$ nm)[6b] appears. The latter is formed by complexation of HS˙ by $HS^-$ and thus its yield strongly depends on the actual $HS^-$ concentration and on the pH-value of the solution. At pH = 3, for example, the yield of $[HSSH]^{\dot{-}}$ is low, as indicated by a short-lived "spike" absorption which practically decays already during the 4 µs pulse. To further distinguish between our new 370 nm-species and the $[HSSH]^{\dot{-}}$ absorption we also performed corresponding experiments in methanol as solvent, in which the pK of $H_2S$ is considerably higher. As anticipated, no absorption attributable to $[HSSH]^{\dot{-}}$ was observed. The absorption at 370 nm also appeared in methanolic solutions containing $HClO_4$. (In methanol HS˙ radicals are formed in the reaction of $H_2S$ with $^{\bullet}CH_2OH$ radicals.)[6b]



On the basis of our experimental findings and by analogy to the $[R_2SSR_2]^{\dot{+}}$ radical cations obtained from thioethers, the 370 nm absorption (Fig. 1a) is assigned to the complex radical cation $[H_2SSH_2]^{\dot{+}}$ formed in the overall reaction:

$$HS^{\bullet} + H_2S + H^{+}_{aq} \rightarrow [H_2SSH_2]^{\dot{+}}$$

The stabilization of the three-electron bond structure in $[H_2SSH_2]^{\dot{+}}$ and in $[R_2SSR_2]^{\dot{+}}$ is considered to be facilitated by the symmetrical resonance structures which are provided by charge- and spin-delocalization over both sulfur atoms. A similar situation would also explain the relative stability of the radical anions $[HSSH]^{\dot{-}}$, $[RSSR]^{\dot{-}}$. The radical cation $[H_2SSH_2]^{\dot{+}}$ should result from addition of two protons to $[HSSH]^{\dot{-}}$, and this is indicated by the corresponding pH-dependent decay of the absorption of $[HSSH]^{\dot{-}}$.

We exclude the possibility of an asymmetrical $[H_2SSH]^{\bullet}$ radical, since one of the resonance forms would require charge separation formed by addition of HS˙ addition to $H_2S$. Such a conclusion is also in accordance with the fact that the analogous $[R_2SSR]^{\bullet}$ radicals apparently cannot be stabilized in solution. Evidence for the latter has only been found in some low temperature (77 K) rigid matrices and with electron withdrawing substituents R[8]. The lower stability of the asymmetrical radical can also be understood from a MO picture. Thus, the separation of the energy levels should be smaller in $[H_2SSH]^{\bullet}$ than in $[H_2SSH]^{\dot{+}}$ ESR data on analogous $[R_2SSR]^{\bullet}$ radicals further support this picture by invoking a much weaker sulfur-sulfur bond in such species relative to the symmetrical $[R_2SSR_2]^{\dot{+}}$ radical cations[8b].

The optical absorption of the $[R_2SSR_2]^{\dot{+}}$ radical cation has been attributed to a $\sigma \rightarrow \sigma^*$ transition[5] and this should, in principle, also apply to absorptions of the $[RSSR]^{\dot{-}}$, $[HSSH]^-$, and $[H_2SSH_2]^{\dot{+}}$ species. *Clark* has essentially substantiated this assignment in his theoretical calculations on $[H_2SSH_2]^{\dot{+}}$[3]. He indicated, however, that the newly established $a_g(\sigma)$ level may interact with the $a_g(n^-)$ level of the non-bonding s-electrons of the two sulfur atoms leading to a split into $a_g(\sigma - n^-)$ and $a_g(\sigma + n^-)$ levels. The optically excited electron would then be a σ-electron with more or less non-bonding character. Using the MP2/4-31G-method *Clark* has calculated the $\sigma \rightarrow \sigma^*$ transition ($a_g(\sigma - n^-) \rightarrow b_n(\sigma^*)$) to be 3.25 eV or 380 nm and this is in excellent agreement with our experimental value of 3.35 eV or 370 nm. Finally, the extinction coefficient of $[H_2SSH_2]^{\dot{+}}$ is estimated to be $\varepsilon = 1600 \pm 300$ mol$^{-1}$ L cm$^{-1}$, based on our experimental results.

Received: December 11, 1980 [Z 806 IE]
German version: Angew. Chem. *93*, 690 (1981)

---

[1] *H. Sakai, S. Yamabe, T. Yamabe, K. Fukui, H. Kato,* Chem. Phys. Lett. *25*, 541 (1974); *A. Hinchcliffe,* J. Mol. Struct. *55*, 127 (1979); *J. B. Collins, P. v. R. Schleyer, J. S. Binkley, J. A. Pople,* J. Chem. Phys. *64*, 5142 (1976).

[2] *H. C. Allen, E. Plyler,* J. Chem. Phys. *25*, 1132 (1956); *G. Duxbury, M. Horani, J. Rostas,* Proc. R. Soc. *A 331*, 109 (1972); *D. D. Wagman, W. H. Evans, V. B. Barker, I. Halow, S. M. Bailey, R. H. Schumm,* Natl. Bur. Stand. Techn. Note, No. 270—3 (1968). *H. Bock, G. Wagner,* Angew. Chem. *84*, 119 (1972); Angew. Chem. Int. Ed. Engl. *11*, 150 (1972).

[3] *T. Clark,* J. Comput. Chem., in press.

[4] *G. Meissner, A. Henglein, G. Beck,* Z. Naturforsch. *B 22*, 13 (1967). *B. C. Gilbert, D. K. C. Hodgeman, R. O. C. Norman,* J. Chem. Soc. Perkin Trans. 2 *1973*, 1748; *M. C. R. Symons, ibid. 1974*, 1618; *M. Bonifačić, H. Möckel, D. Bahnemann, K.-D. Asmus, ibid. 1975*, 657.

[5] *K.-D. Asmus,* Acc. Chem. Res. *12*, 436 (1979).

[6] a) *G. Meissner, A. Henglein,* Ber. Bunsenges. Phys. Chem. *69*, 3 (1965); b) *W. Karmann, G. Meissner, A. Henglein,* Z. Naturforsch. *B 22*, 273 (1967).

[7] Acidic solutions containing more than $10^{-2}$ mol/L $H_2S$ became somewhat turbid, presumably due to formation of colloidal sulfur. It was found, however, that this did not significantly influence the results of pulse experiments.

[8] a) *D. J. Nelson, R. L. Peterson, M. C. R. Symons,* J. Chem. Soc. Perkin Trans. 2 *1977*, 2005; b) *J. R. M. Giles, B. P. Roberts, ibid. 1980*, 1497.

---

## An *ab initio* Investigation of the Mechanism of Ester Reduction[**]

By *Pietro Cremaschi, Gabriele Morosi,* and
*Massimo Simonetta*[*]

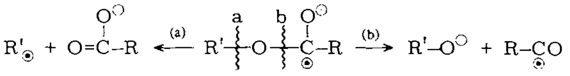
The dissolving metal reduction of alkyl carboxylic esters affords, predominantly, the corresponding alkanes rather

---

[*] Prof. Dr. M. Simonetta, P. Cremaschi, G. Morosi
Centro del CNR e Istituto di Chimica Fisica
Via Golgi 19, I-20133 Milano (Italy)

[**] We are indebted to Prof. *D. H. R. Barton* for communicating his results prior to their publication.

than the parent alcohols[1]; in this connection it has been established that the main products are formed *via* scission of the $C_{Alkyl}$—O bond in the ester radical anion. The experimental data have been rationalized by a mechanism in which cleavage of the $C_{Alkyl}$—O bond [pathway (a)] is favored with respect to $C_{Carbonyl}$—O fragmentation [pathway (b)].



We present here *ab initio* calculations on the ester radical anion and the products in which only the relative stability of reagent and different products are compared.

Methyl formate was used as a model system ($R'=CH_3$, $R=H$) for the *ab initio* calculations (restricted HF-SCF calculations) using a STO-3G[2a] and a 4—31 G basis set[2b]. All the geometrical parameters of the four products were optimized, while the CH bond lengths and the HCH bond angles of the methyl group of the methyl formate anion were assumed to be equal to the corresponding optimized values of $CH_3O^{\ominus}$, and the remaining CH bond length corresponds to the value of optimized $HCOO^{\ominus}$.

Table 1. Geometrical parameters and energies of the methyl formate radical anion and its products [a].

| | STO-3G | 4—31 G | | |
|---|---|---|---|---|
| | Energy | Geometrical parameters | | Energy |
| $H\overset{\odot}{C}O$ | −111.72947 | C—O | = 1.176 | −113.06497 |
| | | C—H | = 1.088 | |
| | | H—C—O | = 128.5 | |
| $CH_3O^{\ominus}$ | −112.70359 | C—O | = 1.364 | −114.21840 |
| | | C—H | = 1.122 | |
| | | H—C—O | = 115.7 | |
| $HCOO^{\ominus}$ | −185.45627 | C—O | = 1.252 | −187.90198 |
| | | C—H | = 1.112 | |
| | | O—C—O | = 130.4 | |
| ${}^{\odot}CH_3$ | − 39.07701 | C—H | = 1.067 | − 39.50179 |
| | | H—C—H | = 120.0 | |
| $HCOOCH_3^{\ominus}$ | | C═O | = 1.303 | −227.34175 |
| | | C—O | = 1.473 | |
| | | O—$CH_3$ | = 1.427 | |
| | | H—C═O | = 126.2 | |
| | | H—C—O | = 110.6 | |
| | | C—O—$CH_3$ | = 113.1 | |

[a] Bond lengths in Å, bond angles in °, and energies in Hartree. (1 Hartree = 27.21 eV = 627.71 kcal/mol.)

The results are shown in Table 1. Using the STO-3G basis set, $HCOO^{\ominus} + \overset{\odot}{C}H_3$ ($E = -224.53328$ Hartree) is more stable than $H\overset{\odot}{C}O + CH_3O^{\ominus}$ ($E = -224.43306$ Hartree) by 0.10022 Hartree (62.9 kcal/mol). With the 4—31 G basis set the corresponding values are −227.40377, −227.28337, 0.12040 Hartree (75.6 kcal/mol) and $HCOO^{\ominus} + \overset{\odot}{C}H_3$ is, hence, more stable than $HCOOCH_3^{\ominus}$ by 0.06202 Hartree (38.9 kcal/mol). Preliminary calculations on pathway (a) indicate a barrier to stretching of the $H_3C$—O bond $(HCOO...CH_3)^{\ominus}$, the height of which has not yet been determined.

In conclusion, $HCOO^{\ominus} + {}^{\odot}CH_3$ is the most favored system energetically. The relative amount of products cannot, however, be predicted theoretically since the barrier heights for the pathways have not been determined. Furthermore, entropy and solvation effects could be of paramount importance, and other reaction mechanisms, *e.g.* those involving nucleophiles could occur under the majority of experimental conditions[1c].

Received: January 8, 1981 [Z 810 IE]
German version: Angew. Chem. 93, 712 (1981)

---

[1] a) *A. G. M. Barrett, P. A. Prokopiou, D. H. R. Barton, R. B. Boar, J. F. McGhie*, J. Chem. Soc. Chem. Comm. *1979*, 1173; b) *A. G. M. Barrett, P. A. Prokopiou, D. H. R. Barton*, J. Chem. Soc. Chem. Comm. *1979*, 1175; c) *A. G. M. Barrett, C. R. A. Godfrey, D. M. Hollinshead, P. A. Prokopiou, D. H. R. Barton, R. B. Boar, L. Joukhadar, J. F. McGhie, S. C. Misra*, unpublished results.

[2] a) *W. J. Hehre, R. F. Stewart, J. A. Pople*, J. Chem. Phys. *51*, 2657 (1969); b) *R. Ditchfield, W. J. Hehre, J. A. Pople, ibid. 54*, 724 (1971).

[3] *W. A. Lathan, L. A. Curtiss, W. J. Hehre, J. B. Lisle, J. A. Pople*, Prog. Phys. Org. Chem. *11*, 175 (1974).

[4] *L. Radom*, Aust. J. Chem. *29*, 1635 (1976).

## Addition of Olefins to 2,5-Diphenyl-1,3,4-oxadiazin-6-one[**]

By *Manfred Christl, Ulrike Lanzendörfer*, and *Silke Freund*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

*Steglich et al.*[1] recently prepared 2,5-diphenyl-1,3,4-oxadiazin-6-one *(1)* for the first time, and examined its reac-

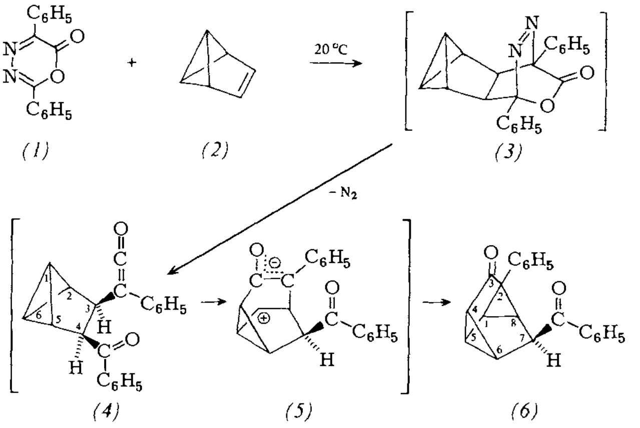


Table 1. Some physical data of the new compounds [NMR spectra in $CDCl_3$, in the case of *(9)* $(CF_3)_2CO \cdot 1.5\,D_2O$, δ values; IR spectra in KBr].

*(6)*, m.p. 140—142 °C; IR: 1700 (3-C═O), 1670 $cm^{-1}$ (benzoyl-C═O); $^1$H-NMR: 1.93 (dd, 4-H, $J_{4,5} = 5.7$ Hz, $J_{4,6} = 9.0$ Hz), 2.1—2.4 (m, 6-H, 8-H), 2.61 (dt, 5-H, $J_{5,6} = J_{1,5} = 5.1$ Hz), 2.88 (dd, 1-H, $J_{1,8} = 5.7$ Hz), 4.58 (t, 7-H, $J_{6,7} = J_{7,8} = 4.1$ Hz), 7.30 (s, 2-$C_6H_5$), 7.3—7.7 and 7.9—8.2 (each m, 3 H and 2 H, benzoyl-$C_6H_5$); $^{13}$C-NMR: 25.9, 30.2, 32.6, 34.1, 40.6 (each d, 185, 179, 183, 176, 173 Hz, C-1, C-4, C-5, C-6, C-8), 43.7 (s, C-2), 46.7 (d, 131 Hz, C-7), 198.1, 204.9 (each s, C-3, benzoyl-CO), $C_6H_5$: 127.2, 133.3 (each d, C-4, C-4′), 128.3 (double band), 128.8, 129.7 (each d, C-2, C-3, C-2′, C-3′), 135.3, 136.9 (each s, C-1, C-1′)

*(9)*, m.p. 201—203 °C; IR: 1755 $cm^{-1}$ (C═O); $^1$H-NMR: 0.39 (br. d, 7-$H_{syn}$, $J_{7,7} \approx 10$ Hz), 1.00 (br. d, 7-$H_{anti}$), 1.5—2.0 (m, 2 × 5-H, 2 × 6-H), 2.44 (br. s, 4-H), 2.97 (br. d, 3-H, $J_{3,8} = 7.0$ Hz), 3.00 (br. s, 1-H), 4.28 (d, 8-H), 7.0—7.8 (m, 2 $C_6H_5$)

*(10)*, m.p. 210 °C; IR: 1750 $cm^{-1}$ (C═O)

*(11)*, m.p. 153—155 °C; IR: 1740 (ester-C═O), 1674 $cm^{-1}$ (benzoyl-C═O); $^1$H-NMR: 1.58 (dq, 7-$H_{anti}$, $J_{7,7} = 8.7$ Hz, $J_{1,7anti} \approx J_{3,7anti} \approx J_{4,7anti} \approx 1.8$ Hz), 1.78 (br. d, 7-$H_{syn}$), 2.77 (m, 4-H), 3.07 (m, 1-H), 3.10 (ddd, 3-H, $J_{3,8} = 11.4$ Hz, $J_{2,3} = 4.5$ Hz), 3.33 (dd, 2-H, $J_{1,2} = 3.3$ Hz), 3.50 (d, 8-H), 3.67 (s, $OCH_3$), 5.72 (dd, 5-H, $J_{5,6} = 5.4$ Hz, $J_{4,5} = 3.0$), 6.45 (dd, 6-H, $J_{1,6} = 3.0$), 6.9—7.6 (m, 2 $C_6H_5$)

*(12)*, m.p. 195—196 °C; IR: 1754 $cm^{-1}$ (C═O)

---

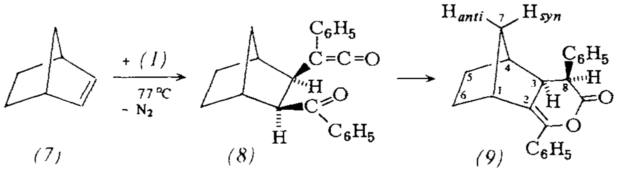
[*] Prof. Dr. M. Christl, Dipl.-Chem. U. Lanzendörfer, Dipl.-Chem. S. Freund
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

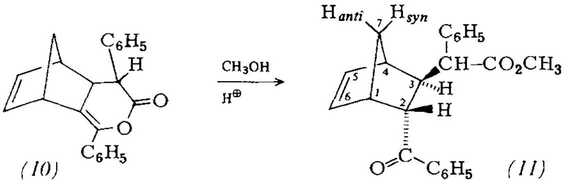
tions with 1-diethylaminopropyne and with dehydrobenzene. The initial Diels-Alder addition is followed by a cycloreversion with elimination of nitrogen and formation of an α-pyrone. We report here on reactions of olefins with *(1)*, which enable simultaneous addition of a benzoyl- and a phenylketenyl group to a CC double bond.

In an ether solution of benzvalene *(2)*, an olefin of high activity in Diels-Alder additions with inverse electron demand[2], *(1)* is converted within 24 h at 20 °C into the tetracyclic diketone *(6)*, which can be isolated in 75% yield. Probably in a $[_{\sigma}2+_{\sigma}2+_{\sigma}2]$-cycloreversion with elimination of nitrogen and cleavage of the lactone bond the primary adduct *(3)* forms (4-benzoyltricyclo[3.1.0.0$^{2,6}$]hex-3-yl)phenylketene *(4)*. The electrophilic ketene function then adds intramolecularly in a novel cycloaddition to the nucleophilic bicyclo[1.1.0]butane system, finally resulting in the formation of the tetracycle *(6)*, possibly *via* the zwitterion *(5)*. For assignment of the structure of *(6)* the $^{13}$C-NMR spectrum is decisive: The direct $^{13}$C-H coupling constants show that five of the six CH groups belong to cyclopropane moieties, but the sixth to a cyclopentane.

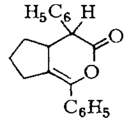
Norbornene *(7)* reacts with *(1)* only in boiling tetrachloromethane. Here, in contrast to the addition of *(2)*, the ketene intermediate containing a benzoyl function *(8)* is detected in solution by IR bands at 2100 and 1680 cm$^{-1}$, but after 10 hours reaction time it has completely disappeared again. The enol lactone *(9)*, which is presumably formed by enolization and intramolecular addition of the enol hydroxy group to the ketene function of *(8)*, is then isolated in 35% yield. This slow process takes place because the bridged cyclopentane in *(8)* is far less nucleophilic than the bicyclo[1.1.0]butane system in *(4)*.



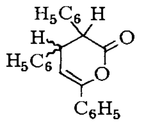
The $^{1}$H-NMR spectrum of *(9)* (Table 1) provides arguments for the configuration at C-3 and C-8. Since $J_{3,4}$ is not resolved, 3-H should be in the *endo* position, indicating the expected *exo* attack of *(1)* on *(7)*. The large difference between the chemical shifts of the two 7-H atoms shows that 7-H$_{syn}$ protrudes into the shielding region of the 8-phenyl group, thus suggesting the *exo* arrangement of the latter.



A 43% yield of *(10)* is obtained from *(1)* and norbornadiene in tetrachloromethane after 4 d at 45—50 °C. The reaction of *(10)* with methanol in the presence of sulfuric acid as catalyst leads to the opening of the lactone ring. In the $^{1}$H-NMR spectrum of *(11)* (73% yield) the coupling constants of 2-H and 3-H show that the benzoyl function occupies the *endo* position and the phenylacetate group the *exo* position. The stereochemistry at C-3 proves the *exo* addition of *(1)* to norbornadiene.



(12)



(13)

Reaction of cyclopentene with *(1)* in tetrachloromethane at 100 °C in an autoclave affords only 4% of the enol lactone *(12)* after 10 d. Nonetheless, the two diastereomeric dihydrotriphenyl-α-pyrones *(13)* are formed in 24% yield when *(1)* and styrene are heated in tetrachloroethane for 24 h at 121 °C. Proof of the structure in this case was provided by comparison with the authentic[3] substances *(13)*. Thus, the addition of *(1)* to styrene proceeds regioselectively, just as that to 1-diethylaminopropyne[1].

Received: November 25, 1980 [Z 812 IE]
German version: Angew. Chem. 93, 686 (1981)

---

[1] *W. Steglich, E. Buschmann, G. Gansen, L. Wilschowitz*, Synthesis *1977*, 252.

[2] *M. Christl, H.-J. Lüddeke, A. Nagyrevi-Neppel, G. Freitag*, Chem. Ber. *110*, 3745 (1977); *M. Christl*, Angew. Chem. *93*, 515 (1981); Angew. Chem. Int. Ed. Engl. *20*, 529 (1981).

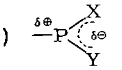
[3] *S. Avery, G. C. Jorgensen*, J. Am. Chem. Soc. *52*, 3628 (1930); *R. B. Meyer, C. R. Hauser*, J. Org. Chem. *27*, 1067 (1962).

## Valence Isomerization of an Imino(methylene)phosphorane to a 1,2λ$^{3}$-Azaphosphiridine: A Novel Rearrangement in the Phosphorus System[**]

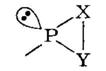
By *Edgar Niecke, Anette Seyer*, and
*Dirk-Andreas Wildbredt*[*]

*Dedicated to Professor Marianne Baudler on the occasion of her 60th birthday*

Phosphorus compounds of the ylide- *(A)*[1] and of the tricyclic-type *(B)*[2] have found great interest recently because of their unusual bonding properties and their suitability as valuable synthetic building blocks.



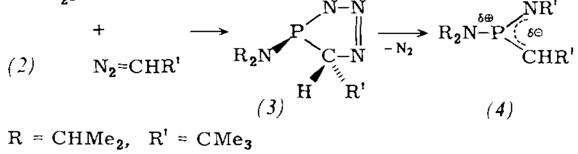
(A)



(B)

Having recently shown that both these classes of compounds could be generated from the same isoelectronic precursor[3], we attempted the preparation of both isomers *(A)* and *(B)* in one system. We report here on a valence isomerization of an imino(methylene)phosphorane *(A)* to a 1,2λ$^{3}$-Azaphosphiridine *(B)* (X = N—, Y = C<)[8].

Diisopropylamino(*tert*-butylimino)phosphane *(1)* reacts with 1-diazo-2,2-dimethylpropane *(2)* to give the crystalline [2+3]-cycloadduct *(3)*. The elimination of N$_2$ from the λ$^{3}$-Triazaphospholine *(3)*, which commences at 40 °C, leads to the corresponding imino(methylene)phosphorane *(4)*; this can be isolated in pure form by rapid distillation.



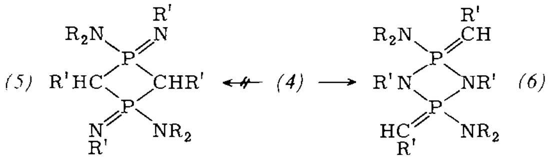
R = CHMe$_2$, R' = CMe$_3$

---

[*] Prof. Dr. E. Niecke, A. Seyer, Dipl.-Chem. D.-A. Wildbredt
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld (Germany)

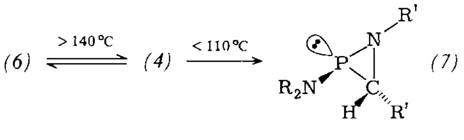
[**] Phosphazenes of Coordination Number 2 and 3, Part 20. This work was supported by the Fonds der Chemischen Industrie.—Part 19: *E. Niecke, M. Engelmann, H. Zorn, B. Krebs, G. Henkel*, Angew. Chem. *92*, 738 (1980); Angew. Chem. Int. Ed. Engl. *19*, 709 (1980).

By-product of this reaction is the cycloadduct *(6)*, which can also be isolated from aged samples of *(4)*. The previously observed formation of a diphosphetane *(5)*[4] in the case of the kinetically labile imino(methylene)phosphoranes, does not take place here; due to steric effects, the [2+2]-cycloaddition leading to the diazaphosphetidine system *(6)* is favored.



Surprisingly, the thermally induced ring-opening of *(6)* leads not to the expected product of a cycloreversion *(4)*, but to a thermostable compound, which could be identified as the unknown $\lambda^3$-azaphosphiridine *(7)*, an isomer of *(4)*.

Proof of the valence isomerization *(4)*→*(7)* was obtained experimentally by $^{31}$P-NMR controlled temperature-studies on toluene solutions of imino(methylene)phosphorane, where we observed the formation of the tricyclic phosphorus compound already below the decomposition temperature of *(6)*.



Compounds *(3)*, *(4)*, *(6)* and *(7)* were characterized by elemental analysis, mass spectra, and by IR and NMR data (Table 1).

Table 1. $^{31}$P-, $^{1}$H- and $^{13}$C-NMR-data of the compounds *(3)*, *(4)*, *(6)* and *(7)* [a].

| | *(3)* | *(4)* | *(6)* | *(7)* |
|---|---|---|---|---|
| $\delta(^{31}P)$ | 17.8 | 77.2 | 21.5 | −73.3 |
| $\delta(^{1}H)$ ($J_{HP}$ [Hz] | | | | |
| PNC$<^{Me}_{Me}$ | 0.92 (2.6) [b]<br>1.00 (2.8) [b] | 1.08 (<0.2) | 1.38 [c] | 1.05 (<0.2) [b]<br>1.09 (<0.2) [b] |
| PNCH | 2.63 (10.1) [c] | 3.33 (14.8) [c] | 4.70 (12.5) | 3.10 (8.0) [c] |
| PNCMe$_3$ | 1.51 (<0.4) | 1.32 (1.2) | 1.61 (<0.2) | 1.19 (<0.2) |
| PCCMe$_3$ | 1.08 (<0.3) | 1.28 (1.5) | 1.39 (0.7) [d] | 0.92 (0.7) |
| PCH | 4.39 (2.8) | 2.71 (18.2) | 1.84 (15.0) | 2.30 (3.4) |
| $\delta(^{13}C)$ ($J_{CP}$ [Hz]) | | | | |
| PNC$<^{C}_{C}$ | 21.3 (14.8) [b]<br>24.3 (18.5) [b] | 23.0 (2.1) | 26.0 (1.8) [d] | 23.6 (6.2) [b]<br>24.3 (10.3) [b] |
| PNC$<$ | 49.0 (6.5) | 48.5 (1.8) | 48.7 (3.7) [d] | 47.4 (8.3) |
| PNCC$_3$ | 30.6 (2.3) | 34.6 (12.6) | 35.5 (4.3) [d] | 30.6 (3.7) |
| PNC$\leqslant$ | 56.1 (6.2) | 53.5 (12.4) | 54.2 (<0.2) | 52.4 (5.4) |
| PCCC$_3$ | 26.6 (2.3) | 33.1 (13.0) | 32.2 (4.1) [d] | 28.8 (5.0) |
| PCC$\leqslant$ | 35.3 (31.2) | 43.1 (11.8) | 32.6 (2.9) [d] | 45.9 (5.1) |
| PC | 91.8 (24.9) | 79.2 (199.5) | 38.2 (208.7) [d] | 49.4 (9.8) |

[a] 30% solution in $C_6D_6$ or $C_7D_8$; $H_3PO_4$ as external ($^{31}$P) and TMS ($^{1}$H, $^{13}$C) as internal standard. [b] Anisochronous methyl groups in a prochiral unit. [c] $^{3}J_{HH}=6.9$ Hz. [d] $|J_{HP}+J_{HP'}|$ and $|J_{CP}+J_{CP'}|$, resp.

The constitution of *(7)* as the cyclic valence isomer of *(4)* was proved beyond doubt by comparing their NMR-data. The $^{31}$P-NMR-spectrum of *(4)* shows a downfield shift, typical of sp$^2$-hybridized $\lambda^5$-phosphorus, while in the $^{13}$C{$^1$H}-NMR-spectrum the position of the resonance signal of the methylene carbon atom corresponds to the values observed for the imino(methylene)phosphoranes. The change in hybridization of the phosphorus and methylene-carbon atoms and also the development of the strained $\lambda^3$-azaphosphiridine-system *(7)* leads to the expected strong shielding of the phosphorus and methylene-carbon atoms, and is connected with a drastic reduction in the P—C-coupling constant [199.5 Hz in *(4)*, 9.8 Hz in *(7)*]. In accordance with this valence isomerization at the phosphorus atom, we found a doubling of the methyl resonances of the isopropyl group in the now prochiral unit. The phosphorus ylide structure of the [2+2]-cycloadduct *(6)* manifests itself in the similar absolute value of the P—C-coupling constants of *(4)* and *(6)*. An examination of molecular models indicates the sterically favored *trans*-form with a *Z*-configuration in the $R_2N—P{=}CHR'$-fragment.

The low absolute value of $^2J_{PCH}$ in *(3)* and *(7)* indicates a *trans* relation of the lone pair at the phosphorus atom to the hydrogen atom, because of the significant dependence of this interaction on the interplanar angle[5].

This investigations show that in the C—P—C-system as well as in the C—P—N-system, the formation of the cyclic is energetically favored over the acyclic dipolar form. While the previously described amine-silylated amino(imino)methylenephosphorane derivatives avoid the formation of a $\lambda^3$-azaphosphiridine by thermally induced 1,3-silyl group rearrangement to a diiminophosphorane[6], in the alkylated system the reaction is directed to a valence isomerization[7].

### *Procedure:*

*(3)*: To a stirred solution of about 50 mmol of *(2)* in 20 ml of tetrahydrofuran (THF) is added dropwise 8 g (40 mmol) of *(1)* at a temperature of −30 °C. After 2 h stirring at −30 °C, half of the solvent is removed at −30 °C, giving a crystalline solid, which is isolated at −30 °C and washed with a little cold THF. Yield: 7.3 g (63%) *(3)*; decomp. above *ca.* 45 °C.

*(4)*: *(3)* (6 g, 20 mmol) is pyrolized at 50 °C, until no more N$_2$-formation is observed. The resulting bright-yellow, crude liquid product (about 85%) is at once purified by short-path distillation and the distillate is frozen out at −30 °C in the collector. Yield: 3.8 g (70%) *(4)*; b.p. 52—53 °C/0.01 torr.

*(6)*: After 6 h at 0 °C *(4)* (1.5 g, 5 mmol) affords the corresponding [2+2]-cycloaddition product *(6)* as a colorless crystalline solid in almost quantitative yield. M.p. 147—149 °C (dec.).

*(7)*: *(4)* (3 g, 10 mmol) is heated at 140 °C for a short time (about 5 min). Subsequent distillation yields 1.7 g (57%) of *(7)* as a colorless liquid. B.p. 53—55 °C/0.01 torr.

Received: March 4, 1981 [Z 814 IE]
German version: Angew. Chem. *93*, 687 (1981)

CAS Registry numbers:
*(1)*, 63950-84-5; *(2)*, 762-64-1; *(3)*, 78342-52-6; *(4)*, 78342-53-7; *(5)*, 78354-70-8; *(6)*, 78342-54-8; *(7)*, 78342-55-9

---

[1] Review: *E. Fluck*, Top. Phosphorus Chem. *10*, 194 (1980); *E. Niecke, D.-A. Wildbredt*, J. Chem. Soc. Chem. Commun. *1981*, 72.

[2] Review: *M. Baudler*, Pure Appl. Chem. *52*, 755 (1980, and references cited therein); *E. Niecke, A. Nickloweit-Lüke, R. Rüger*, Angew. Chem. *93*, 406 (1981); Angew. Chem. Int. Ed. Engl. *20*, 385 (1981).

[3] *E. Niecke, W. W. Schoeller, D.-A. Wildbredt*, Angew. Chem. *93*, 119 (1981); Angew. Chem. Int. Ed. Engl. *20*, 131 (1981).

[4] *E. Niecke, D.-A. Wildbredt*, Chem. Ber. *113*, 1549 (1980).

[5] *W. Mc. Fairlane*, Proc. R. Soc. London, Ser. *A 306*, 185 (1968); *J. P. Albrand, D. Gagnaire, J. Martin, J. B. Robert*, Bull. Soc. Chim. Fr. *1969*, 40.

[6] *E. Niecke, D.-A. Wildbredt*, unpublished results.

[7] Valence isomerization of this type in other systems, cf. *F. D. Greene, S. S. Hecht*, J. Org. Chem. *35*, 2482 (1970). *R. Huisgen*, Angew. Chem. *89*, 589 (1977); Angew. Chem. Int. Ed. Engl. *16*, 572 (1977); *R. M. Kellog*, Tetrahedron *32*, 2165 (1976). Regarding this problem in the phosphorus system cf. *H. Quast, M. Heuschmann*, Liebigs Ann. Chem. *1981*, 967.

[8] *Note added in proof:* We have in the meantime succeeded in carrying out the electrocyclic ring-opening to the ylide, *(B)*→*(A)*, in the 1,2,3$\lambda^3$-diazaphosphiridine system. *E. Niecke, K. Schwichtenhövel, H. G. Schäfer, B. Krebs*, Angew. Chem., in press.

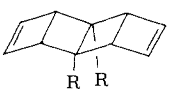
---

## Pterodactyladiene (Tetracyclo[4.4.0.0$^{2,5}$.0$^{7,10}$]deca-3,8-diene)[**]

By *Hans-Dieter Martin, Bernhard Mayer, Marianne Pütter*, and *Hans Höchstetter*[*]

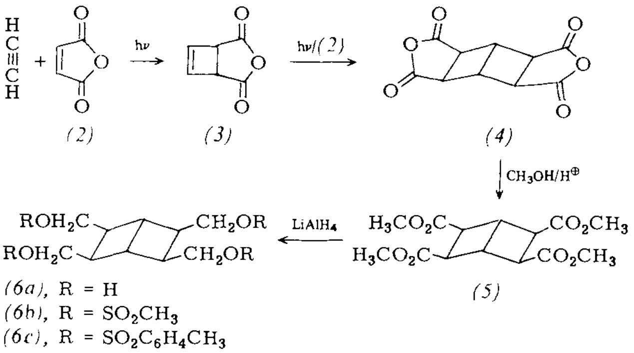
*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

Pterodactyladiene derivatives *(1)*, highly strained members (strain energy about 110 kcal/mol) of the (CH)$_{10}$-family, have hitherto been accessible by two different routes: Diels-Alder reaction of electrophilic alkynes with two equivalents of cyclobutadiene[1] or by reaction of 3,6-disubstituted 1,2,4,5-tetrazines with cyclobutadiene, followed by photoelimination of nitrogen[2], respectively, allowed the preparation of the 1,6-disubstituted tetracyclics *(1b)*–*(1d)*. Pterodactyladiene *(1a)* cannot be synthesized in this way. We now report on a third synthetic route, by means of which *(1a)* can also be obtained.



*(1a)*, R = H
*(1b)*, R = COOCH$_3$
*(1c)*, R = CH$_3$
*(1d)*, R = C$_6$H$_5$

Maleic anhydride *(2)* adds photochemically to acetylene yielding *(4)*[3] (conditions of photolysis: acetone, benzophenone, 700 W high-pressure Hg lamp, Solidex filter, *(3)*: −30 °C, *(4)*: room temperature).



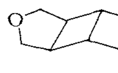
*(2)* *(3)* *(4)*

*(6a)*, R = H
*(6b)*, R = SO$_2$CH$_3$
*(6c)*, R = SO$_2$C$_6$H$_4$CH$_3$

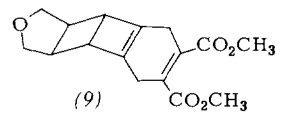
*(5)*

Treatment with CH$_3$OH/H$^{\oplus}$ gives the all-*exo*-ester *(5)* [$^{13}$C-NMR (CDCl$_3$): $\delta$ = 37.4 (C-1, C-4), 45.8 (C-2, C-3, C-5, C-6)] which can be reduced by LiAlH$_4$/tetrahydrofuran (THF) to *(6a)*, m.p. = 134 °C. In the preparation of the sulfonate *(6c)*, m.p. = 147 °C, from alcohol *(6a)*, the bisether *(7)*, m.p. = 62 °C, could be isolated as a by-product. On treatment with potassium *tert*-butoxide in dimethyl sulfoxide (DMSO) the sulfonate *(6b)*, m.p. = 134 °C, was converted into the diene *(8)* [$^1$H-NMR (CDCl$_3$, 60 MHz): $\delta$ = 2.75 (cm; 2 H, C*H*—CH$_2$), 2.85 (s; 2 H, C*H*—C=), 3.19—4.00 (m; 4 H, C*H*$_2$—O—), 4.68 (s; 2 H, =C*H*$_2$), 5.10 (s; 2 H, =C*H*$_2$)] which reacted with dimethyl acetylenedicarboxylate to afford the Diels-Alder adduct *(9)*, m.p. = 152 °C. On treatment with anhydrous sodium sulfide in DMSO, *(6c)* cyclized to the bisthioether *(10)*, m.p. = 126 °C, which was easily oxidized by H$_2$O$_2$/sodium tungstate to the sulfone *(11)*, m.p. = 288 °C. Since direct chlorination of sulfone *(11)* proved to be problematic, bisthioether *(10)* was chlorinated using *N*-chlorosuccinimide (NCS). The doubly chlorinated bisthioether is moisture-sensitive and was not isolated but directly oxidized with *m*-chloroperbenzoic acid (MCPBA) to the chlorinated sulfone *(12)*, m.p. = 214 °C (dec.). The double Ramberg-Bäcklund ring contraction to *(1a)* could be successfully achieved by treatment with potassium *tert*-butoxide in THF. *(1a)*, which is present in a mixture with four non-identified other products could be purified by preparative gas chromatography (OV 17, 105 °C), affording a colorless liquid with characteristic odor [$^1$H-NMR (CDCl$_3$, 90 MHz): $\delta$ = 2.40 (m; 2 H, 1-H, 6-H), 3.10 (m; 4 H, allylic), 6.35 (m; 4 H, olefinic). — $^{13}$C-NMR (CDCl$_3$): $\delta$ = 45.3 (C-1, C-6), 48.6 (C-2, C-5, C-7, C-10), 141.2 (C-3, C-4, C-8, C-9). — $^1J_{\text{C-1,H}}$ = 153 Hz, $^1J_{\text{C-2,H}}$ = 156 Hz, $^1J_{\text{C-3,H}}$ = 171 Hz. — MS (70 eV): m/e = 130 (5%, M$^{\oplus}$), 129 (39%, M − H), 128 (68%, M − H$_2$), 52 (100%, M − C$_6$H$_6$)].

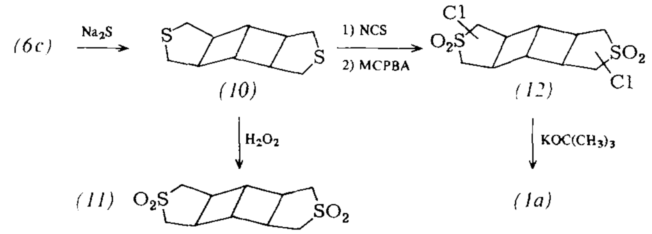
*(7)*



*(8)*



*(9)*



*(6c)* *(10)* *(12)* *(11)* *(1a)*

$^{13}$CH-coupling constants yield information on the hybridization state of the corresponding C—H bonds. The values for C-1 (30% s-character) and C-2 (31% s-character) are considerably different from the coupling constant of cyclobutane ($^1J_{^{13}\text{CH}}$ = 134 Hz, 26% s-character) and are in better accord with that of cubane ($^1J_{^{13}\text{CH}}$ = 153 Hz, 30% s-character[4]). Force-field calculations[5] predict a heat of formation of 141 kcal/mol and a strain energy of 113 kcal/mol for *(1a)*. The thermal lability of *(1a)* is apparent even at 130 °C, the most stable thermolysis product being naphthalene[6].

Received: February 26, 1981 [Z 816 IE]
German version: Angew. Chem. *90*, 695 (1981)

CAS Registry numbers:
*(1a)*, 78418-52-7; *(2)*, 108-31-6; *(3)*, 10374-07-9; *(4)*, 78418-53-8; *(5)*, 78418-54-9; *(6a)*, 78354-61-7; *(6b)*, 78354-62-8; *(6c)*, 78354-63-9; *(7)*, 78354-64-0; *(8)*, 78354-65-1; *(9)*, 78354-66-2; *(10)*, 78354-67-3; *(11)*, 78354-68-4; *(12)*, 78370-95-3; acetylene, 74-86-2.

---

[*] Prof. Dr. H. D. Martin, Dipl.-Chem. B. Mayer, M. Pütter, Dipl.-Chem. H. Höchstetter
Institut für Organische Chemie I der Universität
Universitätstrasse 1, D-4000 Düsseldorf 1 (Germany)

[**] "Small and Medium Rings", Part 39. This work was by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Part 38: *B. Albert, W. Berning, C. Burschka, S. Hünig, H.-D. Martin, F. Prokschy*, Chem. Ber. *114*, 423 (1981).

[1] *H.-D. Martin, M. Hekman*, Angew. Chem. *85*, 615 (1973); Angew. Chem. Int. Ed. Engl. *12*, 572 (1973); *J. Meinwald, J. Mioduski*, Tetrahedron Lett. *1974*, 3839.

[2] *H.-D. Martin, M. Hekman*, Tetrahedron Lett. *1978*, 1183.

[3] *G. Koltzenburg, P. G. Fuss, J. Leitich*, Tetrahedron Lett. *1966*, 3409; *W. Hartmann*, Chem. Ber. *102*, 3974 (1969).

[4] *E. W. Della, P. T. Hine*, J. Org. Chem. *42*, 2940 (1977).

[5] *N. L. Allinger, M. T. Tribble, M. A. Miller, D. H. Wertz*, J. Am. Chem. Soc. *93*, 1637 (1971).

[6] An intermediary thermolysis product shows $^1$H-chemical shifts pointing to *trans*-9,10-dihydronaphthalene [7] (*S. Masamune*, J. Am. Chem. Soc. *89*, 4804 (1967)).

---

## Periodated Cyclosilanes

By *Edwin Hengge* and *Dieter Kovar*[*]

Hitherto, periodated silanes were little known and mostly inadequately described; iodated cyclosilanes were completely unknown. We have now been able to prepare and characterize for the first time the periodated cyclosilanes $Si_4I_8$, $Si_5I_{10}$, and $Si_6I_{12}$[1]. As starting material we used the perphenylated cyclosilanes $(SiPh_2)_n$, $n=4$, 5, and 6, which are obtainable by reaction of dichlorodiphenylsilane with Na/K alloy or Li *via* a kind of Wurtz synthesis. The separation of the individual components of the reaction mixture was possible owing to the differences in solubility: $(SiPh_2)_5$ is readily soluble, $(SiPh_2)_4$ sparingly soluble and $(SiPh_2)_6$ very sparingly soluble in benzene.

Treatment of a benzene solution or suspension of $(SiPh_2)_n$ with anhydrous and iodine-free aluminum iodide and passage of hydrogen iodide into the mixture leads to quantitative replacement of the phenyl groups by iodine and formation of the corresponding iodosilanes.

$$(SiPh_2)_n + 2n\,HI \xrightleftharpoons{AlI_3} (SiI_2)_n + 2n\,PhH$$

Presence of free iodine leads to cleavage of the ring and formation of chain-like products—as is evident from the $^{29}$Si-NMR data.

The catalyst $AlI_3$ is absolutely necessary. In the case of the readily soluble $(SiPh_2)_5$ only half of the phenyl groups are cleaved in the absence of $AlI_3$ (in a bomb-tube with liquid HI); $Si_5Ph_5I_5$ and its derivatives $Si_5Ph_5X_5$ (X = H, OMe) have been synthesized in this way[2]. The sparingly soluble educts $Si_4Ph_8$ and $Si_6Ph_{10}$ react to an even a lesser extent with HI in the absence of $AlI_3$. The cleavage of phenyl moieties, which can be regarded as an electrophilic reaction[3], is consequently very much favored by aluminium halides.

The products $(SiI_2)_n$, $n=4$, 5, 6, are yellow and extraordinarily sensitive to moisture. The color becomes distinctly more intense and slightly shifted bathochromically on going from $Si_6I_{12}$ to the smaller rings. The solubilities correspond to those of the cyclosilanes. The five-membered ring is the most readily soluble, while $Si_4I_8$ and, in particular, $Si_6I_{12}$ are sparingly soluble.

Only the $^{29}$Si-NMR spectrum of $Si_5I_{10}$ could be recorded. The measured value fits very well in the series of values of the remaining cyclopentasilanes $Si_5X_{10}$ [X = Cl ($\delta=-1.67$), Br ($-28.08$), Ph ($-34.41$), Me ($-42.12$), I ($-98.55$), H ($-105.53$)].

Molecular weight determinations were not possible, even mass spectroscopically. However, vibration spectroscopic findings (number and frequency of the vibrations, see Table 1) would indicate the cyclic structure. On using the force constants $f_{SiSi}=1.5\times10^2$ N m$^{-1}$, $f_{SiI}=1.4\times10^{-2}$ N m$^{-1}$ and the expected symmetries, normal coordinate analysis[4] enables very good reproducibility of the measured frequencies.

Table 1. Raman and IR vibrations of $(SiI_2)_n$, $n=4$, 5, 6.

| $Si_4I_8$ | | $Si_5I_{10}$ | | $Si_6I_{12}$ | |
|---|---|---|---|---|---|
| Raman | IR | Raman | IR | Raman | IR |
| 56 m | 55 sh | 50 sh | 64 m | 46 m | 110 w |
| 71 s | 88 s | 60 m | 93 s | 54 s | 235 vs |
| 83 w | 229 sh | 83 mw | 111 s | 62 s | 330 m |
| 100 vw | 242 vs | 100 m | 242 vs | 98 m | 340 sh |
| 115 s | 264 w | 104 m | 304 s | 134 vs | 395 m |
| 122 w | 333 vw | 134 vs | 390 vs | 293 vw | 405 s |
| 136 vs | 380 w | 304 w | 400 vs | 386 w | 468 w |
| 163 vw | 400 s | 335 w | 463 m | 407 w | |
| 174 vw | 480 m | 389 w | 475 s | 453 w | |
| 208 vw | | 406 w | 488 s | 500 w | |
| 327 m | | 464 w | | | |
| 344 w, sh | | 495 w | | | |
| 388 w | | | | | |
| 398 w | | | | | |
| 503 w | | | | | |

### *Procedure*

$Si_4Ph_8$ (4 g, 5.4 mmol) is treated with benzene (150 mL) and a spatula tip of $AlI_3$. HI (free of $H_2O$ and iodine) is then passed through the solution until it is no longer warm due to heat of reaction. Yellow $Si_4I_8$ already precipitates out during the passage of HI. It is filtered off and dried in a vacuum; yield 5.4 g (87%). $Si_4I_8$ starts to decompose on melting at 184 °C (uncorrected)—$Si_5I_{10}$ and $Si_6I_{12}$ are synthesized analogously; yields (from 4 and 3 g of educt, respectively), 4.7 g (83%) and 4.1 g (89%), m.p. (uncorr.) 205 °C (dec.) and 258 °C (dec.), respectively.

Received: November 26, 1980 [Z 818 IE]
German version: Angew. Chem. *93*, 698 (1981)

---

[1] Perchlorinated and perbrominated cyclosilanes, see: *E. Hengge, D. Kovar*, J. Organomet. Chem. *125*, C29 (1977); Z. Anorg. Allg. Chem. *458*, 163 (1979).

[2] *E. Hengge, H. Marketz*, Monatsh. Chem. *100*, 890 (1969); *101*, 528 (1970).

[3] *E. Hengge, H. Eberhardt*, Monatsh. Chem. *110*, 39 (1979).

[4] *E. Hengge et al.*, unpublished; normal coordinate analysis for perchlorinated and perbrominated cyclosilanes: *K. Hassler, E. Hengge, D. Kovar*, J. Mol. Struct. *66*, 25 (1980); Spectrochim. Acta *A 34*, 1199 (1978).

[*] Prof. Dr. E. Hengge, Dr. D. Kovar
Institut für Anorganische Chemie der Technischen Universität
Stremayrgasse 16, A-8010 Graz (Austria)

---

## The First Lithium Fluorosilanolate—A Building Block for Directed Siloxane Synthesis[**]

By *Uwe Klingebiel*[*]

A route currently used for the synthesis of acyclic and cyclic polysiloxanes is the condensation of silanols $R_3SiOH$ and silanediols $R_2Si(OH)_2$[1]. The thermal stability of the silanols increases with increasing size of the substituents. Thus, *e.g.* di-*tert*-butylsilanediol condenses only under drastic conditions[2,3]. Cyclic condensation products have so far not been obtained[3].

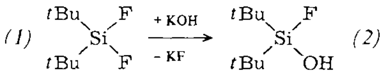
A favorable method for the synthesis of di-*tert*-butylsilanediol is the reaction of di-*tert*-butyldifluorosilane *(1)* with

---

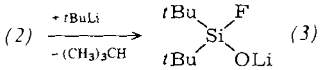
[*] Priv.-Doz. Dr. U. Klingebiel
Institut für Anorganische Chemie der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the State of Niedersachsen and by the Fonds der Chemischen Industrie.

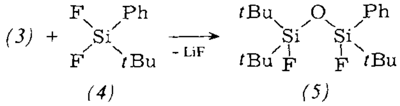
KOH in the molar ratio 1:2. If a molar ratio of 1:1 is used, then the stable fluorosilanol *(2)* is formed in high yields[4]. At room temperature it forms colorless, readily sublimable crystals.



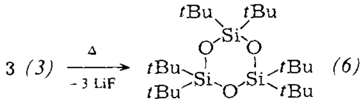
*(2)* reacts quantitatively with *tert*-butyllithium with cleavage of isobutane to give the unexpected stable lithium di-*tert*-butylfluorosilanolate *(3)*[5], which melts at 238 °C with partial decomposition.



As the reaction of *(3)* with *tert*-butyl(difluoro)phenylsilane *(4)* to give unsymmetrically substituted *(5)* demonstrates[6], lithium fluorosilanolates are valuable building blocks for the synthesis of siloxanes.



The hitherto sterically most overcrowded silicon-oxygen ring *(6)*[7] is preparable from *(3)* by thermal cleavage of LiF.



*Procedure*

*(2)*[4]: KOH (0.1 mol) in pellet form is gradually added to a stirred solution of *(1)* (0.1 mol) in 100 mL of petroleum ether (PE) at room temperature. After dissolution of the KOH pellets (*ca.* 8 h) the petroleum ether is removed by evaporation *in vacuo* and *(2)* is sublimed at room temperature and 0.01 torr. *(2)* also slowly sublimes under normal pressure in a glass flask; yield *ca.* 80% [by-product: $(tBu)_2Si(OH)_2$]; m.p. 40 °C.

*(3)*[5]: *tert*-$C_4H_9Li$ (0.1 mol, 15% solution in pentane) is added dropwise with stirring to a solution of *(2)* (0.1 mol) in PE (50 mL) at room temperature. The liberated isobutane is condensed in a cold trap. *(3)* can be purified by recrystallization from hexane or by vacuum sublimation; yield 95%, m.p. 238 °C (dec.).

*(5)*[6]: A stirred solution of *(4)* (0.1 mol) in PE (50 mL) is treated with a suspension of *(3)* (0.1 mol) in hexane (100 mL). *(5)* is purified by distillation; yield 95%; b.p. 115 °C/0.5 torr.

*(6)*[7]: *(3)* (0.1 mol) is heated at 230—240 °C for 1 h. Sublimation from the melt is then carried out at 0.1 torr. *(6)* sublimes, together with unreacted *(3)*, and is purified by recrystallization from PE (80—100 °C); yield 30%, m.p. 297 °C.

Received: December 5, 1980 [Z 819 IE]
German version: Angew. Chem. 93, 696 (1981)

---

[1] *I. Haiduc*: The Chemistry of Inorganic Ring Systems I, Wiley-Interscience, London 1970.

[2] *C. Eaborn*, J. Chem. Soc. *1952*, 2840; *M. Weidenbruch, H. Pesel, D. V. Hieu*, Z. Naturforsch. *B 35*, 31 (1980).

[3] *L. H. Sommer, L. J. Tyler*, J. Am. Chem. Soc. *76*, 1030 (1954).

[4] *(2)*, MS (70 eV): $m/z = 178$ (31%, $M^+$); $^1H$-NMR (in $CH_2Cl_2$, TMS int.): $\delta = 1.07$ ($t$Bu, $J_{HF} = 1.07$ Hz), 3.32 (OH); $^{19}F$-NMR ($C_6F_6$ int.): $\delta = 5.73$; $^{29}Si$-NMR (in $CH_2Cl_2/C_6F_6$, TMS int.): $\delta = -6.38$ ($J_{SiF} = 312.61$ Hz).

[5] *(3)*, MS (70 eV): $m/z = 178$ (13%, $[M-Li, +H]^+$); $^1H$-NMR (in $C_6H_6$, TMS int.): $\delta = 1.15$ ($t$Bu); $^{29}Si$-NMR (TMS int.): $\delta = -18.36$ ($J_{SiF} = 294.5$ Hz).

[6] *(5)*, MS (70 eV): $m/z = 358$ (17%, $M^+$); $^1H$-NMR (in $CH_2Cl_2$, TMS int.): $\delta = 0.10$ (Si$t$Bu, $J_{HF} = 0.5$ Hz), 0.11 ($Si(tBu)_2$, $J_{HF} = 1$ Hz), 7.5 ($C_6H_5$); $^{19}F$-NMR ($C_6F_6$ int.): $\delta = 7.9$, 12.5.

[7] *(6)*, MS (70 eV): $m/z = 417$ (100%, $[M-tBu]^+$); $^1H$-NMR (in $C_6H_6$, TMS int.): $\delta = 1.98$.

---

## $RuCo_2(CO)_{11}$ and $Ru_2Co_2(CO)_{13}$, Two New "Pure" Carbonylmetal Clusters[**]

By *Eckehart Roland* and *Heinrich Vahrenkamp*[*]

About 50 "pure" carbonylmetal compounds have so far been documented; the last time that the synthesis of such a complex was described in Germany was some 38 years ago[1]. Interest in this sector has recently reawakened, but important developments are taking place mainly in the case of carbonylmetal derivatives. There are only a few heterometal complexes which hold out promise as new parent compounds, two of which are presented here.

We found an entry to the chemistry of the carbonylruthenium-cobalt compounds *via* the trinuclear cluster *(1)*, which is accessible *via* several routes, the most favorable having proven to be the reaction of $[Ru(CO)_3Cl_2]_2$ with $KCo(CO)_4$. *(1)* shows a high reactivity towards inorganic and organic donor reagents[2]. In solution, *(1)* also reacts with itself in the sense of a disproportionation to give the two tetranuclear clusters *(2)* and $Co_4(CO)_{12}$. *(2)* is markedly less reactive than *(1)* and is air-stable in the solid state.

| $RuCo_2(CO)_{11}$ | $Ru_2Co_2(CO)_{13}$ |
|---|---|
| *(1)* | *(2)* |

*(1)* and *(2)* were identified by EI mass spectra, which show the molecular ions and stepwise loss of all CO groups. The CO stretching vibrations prove *(1)* (in $C_6H_{12}$ [cm$^{-1}$]: 2126 vw, 2069 s, 2056 sh, 2050 vs, 2018 w, 2005 w, 1820 w) to be a homologue of $OsCo_2(CO)_{11}$ with a bridging carbonyl ligand[3]. In the case of *(2)* (in $C_6H_{12}$ [cm$^{-1}$]: 2103 vw, 2068 vs, 2059 vs, 2050 vs, 2035 m, 2025 s, 1922 sh, 1895 w, 1843 w) they likewise indicate CO bridges, but do not provide any further structural information. Therefore, the structure of *(2)* was determined crystallographically[4]. Figure 1 shows the observed distorted $Ru_2Co_2$-tetrahedral arrangement with unsymmetrical distribution of terminal and bridging ligands, which can only roughly be related to those in $Co_4(CO)_{12}$[5] or $Ru_3Co(CO)_{13}^-$[6]. The polyhedron formed by the O atoms of the CO groups is however the [13]-polyhedron of lowest energy[7]. The structure of *(2)* thus complies with the previous finding, that the spatial distribution of the ligands rather than the localization of bonding relationships determines the structure of many polynuclear carbonyl complexes[7,8].

---

[*] Prof. Dr. H. Vahrenkamp, Dipl.-Chem. E. Roland
Institut für Anorganische Chemie der Universität
Albertstr. 21, D-7800 Freiburg (Germany)

[**] We thank Dr. *K. Steinbach* (Marburg) and Dr. *P. Merbach* (Erlangen) for recording the mass spectra, Heraeus GmbH (Hanau) for a gift of ruthenium chloride and the Rechenzentrum der Universität Freiburg for computer time.

Both ruthenium and cobalt are catalytic elements. The bimetallic character of the two new clusters and the proven reactivity of *(1)* open up numerous possibilities here. With the parent compounds *(1)* and *(2)* as starting materials, ligand substitution, metal exchange and electron transfer provide access to a wide field of derivative chemistry.

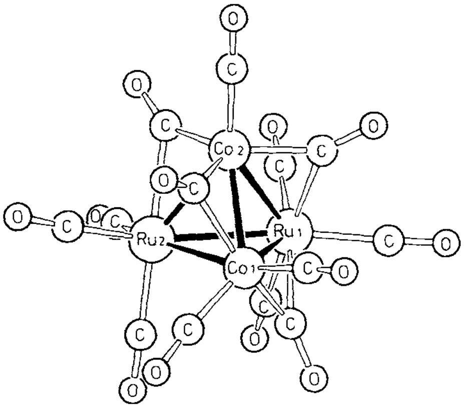


Fig. 1. Molecular structure of *(2)* in the crystal. Bond lengths [pm]: Ru1—Ru2 278.3(3), Ru1—Co1 273.1(2), Ru1—Co2 266.0(2), Ru2—Co1 270.3(3), Ru2—Co2 261.4(3), Co1—Co2 248.7(3).

### *Procedure*

A suspension of $[Ru(CO)_3Cl_2]_2$ (300 mg, 0.59 mmol) in 50 mL of an aqueous solution of $KCo(CO)_4$ (500 mg, 2.38 mmol) is stirred for 1 h at room temperature. The black precipitate which is formed is filtered off, dried in vacuum, taken up in hexane, filtered, and cooled to −35 °C. *(1)* separates out as black crystals; 470 mg (76%), m.p. 208 °C (dec.).

A solution of *(1)* (200 mg, 0.38 mmol) in hexane (30 mL) is stirred for 3 d at 35 °C and then chromatographed on a silica gel column (65 × 2.5 cm). Hexane elutes $Co_4(CO)_{12}$ and some $Ru_3(CO)_{12}$. Elution with benzene/hexane (1 : 7) affords 60 mg (46%) of balck *(2)*, m.p. 182 °C (dec.).

Received: October 27, 1980 [Z 821a IE]
supplemented: November 17, 1980
German version: Angew. Chem. 93, 714 (1981)

---

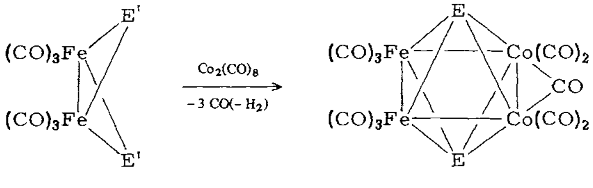
[1] *W. Hieber, H. Lagally,* Z. Anorg. Allg. Chem. *251,* 96 (1943).
[2] *E. Roland, H. Vahrenkamp,* unpublished.
[3] *J. R. Moss, W. A. G. Graham,* J. Organomet. Chem. *23,* C23 (1970).
[4] Monoclinic, $P2_1/c$, $Z=4$, $a=928.0(2)$, $b=2364.1(4)$, $c=1191.8(3)$ pm, $\beta=133.39(1)°$; 3011 reflections, $R=0.065$.
[5] *C. H. Wei,* Inorg. Chem. *8,* 2384 (1969).
[6] *P. C. Steinhardt, W. L. Gladfelter, A. D. Harley, J. R. Fox, G. L. Geoffroy,* Inorg. Chem. *19,* 332 (1980).
[7] *R. E. Benfield, B. F. G. Johnson,* J. Chem. Soc. Dalton Trans. *1980,* 1743.
[8] *E. Keller, H. Vahrenkamp,* Z. Naturforsch. *B33,* 537 (1978).

## Cluster-Construction: Synthesis and Structure of $Fe_2Co_2(CO)_{11}(PC_6H_5)_2$ and $Fe_2Co_2(CO)_{11}S_2$[**]

By *Heinrich Vahrenkamp* and *Edward J. Wucherer*[*]

The principle of ligand bridging for the stabilization of organometal-clusters has been realized on numerous occasions[1,2]. Its application as a synthetic concept calls for cluster precursors containing appropriate functional ligands. For the synthesis of RP- or S-bridged clusters, suitable precursors are, *e.g.*, those with P—H or S—S bonds, which can react directly with carbonylmetal complexes[2,3].

We have been able to use this concept for the first time for the directed synthesis of tetranuclear clusters from two dinuclear precursors. The reactive educts were the dinuclear complexes *(1a)* and *(1b)*, which are predestined by their functionality and folded structure[4] for the addition of further carbonylmetal units. As expected, their reactions with carbonylcobalt led smoothly to the new clusters *(2a)* and *(2b)*, respectively.



*(1a)*, E' = PPhH
*(1b)*, E' = S (with S–S bonding)
*(2a)*, E = PPh
*(2b)*, E = S

The relationship between the two complexes *(2)* manifests itself in the needle-like shape and black color of their crystals and in their IR spectra in the νCO region (in $CH_2Cl_2$ [cm⁻¹], *(2a)*: 2080 vw, 2041 vs, 2020 s, 1950 m, 1862 m; *(2b)*: 2090 vw, 2050 vs, 2039 sh, 2021 sh, 1953 m, 1875 m). They were characterized by crystal structure analyses[5]. The molecular structures and most important bond lengths are shown in Figure 1 and Table 1, respectively.

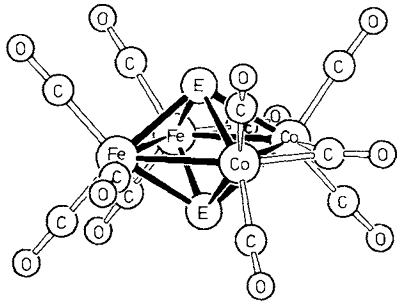


Fig. 1. Molecular structures of *(2a)* (E = phosphorus atom of the $PC_6H_5$ group) and *(2b)* (E = S) in the crystal.

Table 1. Values (average) of the most important atomic distances [pm] in the clusters *(2)*.

| Bond | *(2a)* | *(2b)* |
|---|---|---|
| Fe—Fe | 272.4(3) | 260.4(2) |
| Fe—Co | 262 ± 2 | 258 ± 0.03 |
| Co—Co | 251.5(3) | 249.5(2) |
| Fe—E | 223 ± 0.5 | 227 ± 0.5 |
| Co—E | 227 ± 2 | 231 ± 2 |

*(2a)* and *(2b)* belong to the relatively small group of tetranuclear clusters containing planar metal frameworks[6]. Their metal-metal and metal-bridge atom bond lengths lie in the normal range for such compounds. For both complexes, there exist "pure" cobalt analogues, the clusters $Co_4(CO)_{10}E_2$ (E = PPh, S), which were formed by non-specific syntheses and whose structures are known[7]. These clusters also contain rectangular planar arrays of metal atoms; their $Co_2(CO)_5E_{2/2}$-halves are very similar to those

---

[*] Prof. Dr. H. Vahrenkamp, E. J. Wucherer
Institut für Anorganische Chemie der Universität
Albertstr. 21, D-7800 Freiburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and by Rechenzentrum der Universität Freiburg. We thank Frl. *D. Steiert* for her valuable help with the preparative work.

of the complexes *(2)*, and their M—M and M—E bond lengths show the same trend as in *(2a)* and *(2b)*.

The intrinsic novelty of the clusters *(2)* is, therefore, their systematic preparation. Since numerous functional dinuclear complexes having the butterfly structure shown in *(1a)* and *(1b)* and suitable simple carbonylmetals for reaction exist, the route described here to planar tetranuclear clusters should not be merely limited to *(2a)* and *(2b)*.

### *Procedure*

Equimolar amounts (1—2 mmol) of *(1a)* or *(1b)* and $Co_2(CO)_8$ are added to 50 ml of hexane. For the formation of *(2a)* the mixture is stored in the dark for 20 d at room temperature, then chromatographed on silica gel, and finally the product obtained from the third fraction is crystallized from hexane at −30 °C. The complex *(2b)* precipitates from the reaction mixture in analytically pure form after 12 h at 0 °C. The yields of *(2a)* (m.p. 134 °C, dec.) and *(2b)* (dec. at 100—200 °C without recognizable m.p.) are 20—25%.

Received: October 27, 1980 [Z 821b IE]
German version: Angew. Chem. *93*, 715 (1981)

---

[1] *D. Seyferth*, Adv. Organomet. Chem. *14*, 97 (1976).

[2] *H. Vahrenkamp*, Angew. Chem. *87*, 363 (1975); Angew. Chem. Int. Ed. Engl. *14*, 322 (1975).

[3] *F. Richter, H. Beurich, H. Vahrenkamp*, J. Organomet. Chem. *166*, C5 (1979).

[4] *B. K. Teo, M. B. Hall, R. F. Fenske, L. F. Dahl*, Inorg. Chem. *14*, 3103 (1975).

[5] *(2a)*: triclinic, $P\bar{1}$, $Z=2$, $a=962.7(1)$, $b=1567.8(2)$, $c=960.2(2)$ pm, $\alpha=91.04(1)$, $\beta=109.05(1)$, $\gamma=84.83(1)°$; 3190 reflections, $R=0.059$.—*(2b)*: monoclinic, $P2_1/c$, $Z=4$, $a=1615.4(5)$, $b=655.6(2)$, $c=1872.2(5)$ pm, $\beta=115.06(2)°$; 2946 reflections, $R=0.051$.

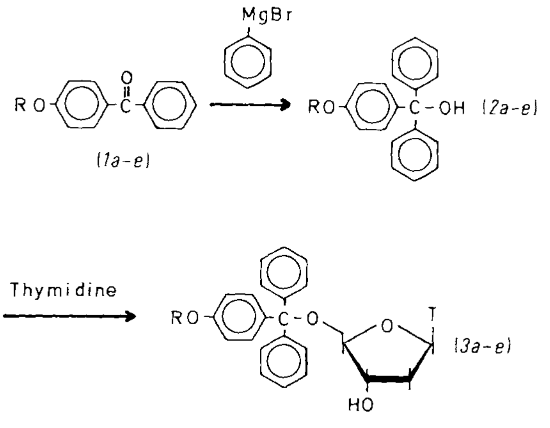
[6] *P. Chini, B. T. Heaton*, Top. Curr. Chem. *71*, 1 (1977).

[7] *R. C. Ryan, L. F. Dahl*, J. Am. Chem. Soc. *97*, 6904 (1975).

## New Hydrophobic Protecting Groups for the Chemical Synthesis of Oligonucleotides[**]

By *Hans-Helmut Görtz* and *Hartmut Seliger*[*]

In the chemical synthesis of polynucleotide fragments by the triester procedure[1,2], chromatographic methods are important for the purification of protected intermediates and for the isolation of the unprotected final product[2,3]. The chromatographic behavior of the oligomers can be varied within certain limits by protecting groups, generally producing an unspecific change in the total polarity of the molecule. We have introduced 4-alkoxytrityl groups as a novel type of hydrophobic protection for the 5′-end of oligonucleotides[4]. For this purpose, the 4-alkoxytritanols *(2a—e)* were prepared by Grignard reaction from *(1a—e)* and the trityl chlorides reacted with thymidine to produce *(3a—e)*.



| (1)-(3) | a | b | c | d | e |
|---|---|---|---|---|---|
| R = | $C_8H_{17}$ | $C_{10}H_{21}$ | $C_{12}H_{25}$ | $C_{14}H_{29}$ | $C_{16}H_{33}$ |

As expected, the $R_f$-values of the 5′-*O*-(4-alkoxytrityl)thymidines *(3a—e)* on silica gel are somewhat higher and on RP-2 somewhat lower than the $R_f$-values of 5′-O-(4,4′-dimethoxytrityl)thymidine. These changes reflect the reduction in total polarity. The behavior of *(3a—e)* upon RP (reversed phase) chromatography on a $C_{18}$-phase is, however, different: here, an apparently specific interaction between the alkyl chains of the sorbent and sorbate leads to a dramatic reduction of the $R_f$-values with increasing chain length upon thin layer chromatography (Fig. 1) and increasing retention times in HPLC (Fig. 2).

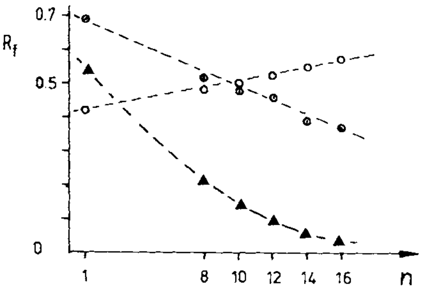


Fig. 1. Dependence of the $R_f$-values on the alkyl chain length n of compounds *(3)* [n = 8, 10, 12, 14, 16 ≡ *(3a, b, c, d, e)*]. ○: silica gel 60 (Merck), chloroform/methanol 9:1; ●: silica gel RP-2 (Merck), acetone/water 75:25; ▲: silica gel $KC_{18}$ (Whatman), acetone/water 75:25.

The 4-hexadecyloxytrityl ($C_{16}$Tr-) derivatives [*(6), (8), (11), (13)* and *(16)*] among the oligonucleotide phosphotriesters *(4)—(16)* (Table 1) exhibit the same characteristic behavior as the monomers *(3)* upon RP-18 chromatography. Of prime interest for preparative application is the magnitude of the $R_f$-difference between the $C_{16}$Tr-derivatives and the corresponding compounds having free 5′-OH groups, which indicates an easy and complete HPLC separation of both types of components irrespective of the chain length and sequence. This is in contrast to separations of the 4-methoxy- or 4,4′-dimethoxytrityl (DMTr) derivatives used so far, in which the starting components with 3′-terminal phosphate charge can readily be separated from the reaction mixture arising from nucleotide condensations, however, good separation of the oligonucleotides

---

[*] Prof. Dr. H. Seliger, Dr. H.-H. Görtz
Sektion Polymere der Universität
Oberer Eselsberg, D-7900 Ulm (Germany)

[**] Syntheses with Nucleic Acid Constituents, Part 9.—Part 8: *H. Seliger, B. Haas, M. Holupirek, T. Knäble, G. Tödling, M. Philipp*, Nucleic Acids Res. Symp. Ser. *7*, 191 (1980).

with free 5'-OH groups requires a complicated after-treatment[5]. For purposes of clarification, the $R_f$-values of the nucleotide sequences having a terminal $C_{16}$Tr-[*(8)*, *(13)*, *(16)*] or DMTr-group [*(7)*, *(12)*, *(15)*] shown in Table 1, should be compared with their precursors *(4)*, *(9)* and *(14)*.

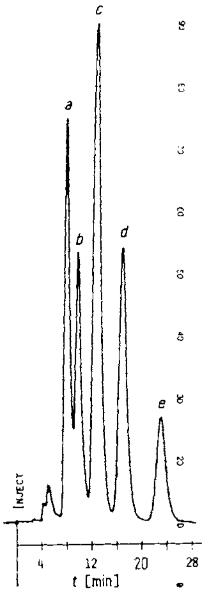


Fig. 2. HPLC separation of compounds *(3a–e)*. Column: μ-Bondapak $C_{18}$ (Waters), eluent: 2-propanol/methanol/water 6:2:2, flow rate: 1 mL/min, pressure: 130 bar, detection: $UV_{254}$.

Table 1. $R_f$-values of compounds *(4)–(16)* [a] in systems A, B and C [b].

| | Cpd. | A | B | C |
|---|---|---|---|---|
| *(4)* | $\mathrm{dTpTpT_{Bz}}$ | 0.31 | 0.81 | 0.68 |
| *(5)* | DMTrdTpTpTp(CE) | 0.41 | 0.72 | 0.50 |
| *(6)* | $\mathrm{C_{16}TrdTpTpTp(CE)}$ | 0.48 | 0.52 | 0.19 |
| *(7)* | $\mathrm{DMTrdTpTpTpTpTpT_{Bz}}$ | 0.35 | 0.69 | 0.44 |
| *(8)* | $\mathrm{C_{16}TrdTpTpTpTpTpT_{Bz}}$ | 0.45 | 0.52 | 0.18 |
| *(9)* | $\mathrm{dG^{ibu}pA^{bz}p(CE)}$ | 0.19/0.30 [c] | 0.92 | 0.97 |
| *(10)* | $\mathrm{DMTrdG^{ibu}pA^{bz}p(CE)}$ | 0.57/0.65 [c] | 0.81/0.83 [c] | 0.89/0.91 [c] |
| *(11)* | $\mathrm{C_{16}TrdG^{ibu}pA^{bz}p(CE)}$ | 0.63/0.69 [c] | 0.36/0.39 [c] | 0.24/0.29 [c] |
| *(12)* | $\mathrm{DMTrdG^{ibu}pA^{bz}pG^{ibu}pA^{bz}p(CE)}$ | 0.40 | 0.76 | 0.81 |
| *(13)* | $\mathrm{C_{16}TrdG^{ibu}pA^{bz}pG^{ibu}pA^{bz}p(CE)}$ | 0.48 | 0.40 | 0.28 |
| *(14)* | $\mathrm{dTpC^{bz}pTpC^{bz}_{Bz}}$ | 0.73 | 0.89 | 0.96 |
| *(15)* | $\mathrm{DMTrdG^{ibu}pA^{bz}pG^{ibu}pA^{bz}pTpC^{bz}pTpC^{bz}_{Bz}}$ | 0.56 | 0.86 | 0.87 |
| *(16)* | $\mathrm{C_{16}TrdG^{ibu}pA^{bz}pG^{ibu}pA^{bz}pTpC^{bz}pTpC^{bz}_{Bz}}$ | 0.72 | 0.33 | 0.21 |

[a] p = *p*-chlorophenylphosphoryl; CE = β-cyanoethyl; DMTr = 4,4'-dimethoxytrityl, $C_{16}$Tr = 4-hexadecyloxytrityl. [b] A: silica gel 60 (Merck); chloroform/methanol 9:1; B: silica gel RP-8 (Merck); acetone/water 85:15; C: silica gel RP-18 (Merck); acetone/water 85:15. [c] Diastereomeric pairs.

Bearing in mind that the advantage of the triester method rests mainly upon the rapid and simple removal of the reaction precursors, the possibility of also separating the hydroxy component in a selective way should substantially increase the efficiency of the process. In this context the analogy of the $C_{16}$Tr- to the 4-methoxy-group with respect to the introduction and cleavage conditions requires no change in the synthetic strategy.

## *Procedure*

*(1e)*: 4-Hydroxybenzophenone (39.6 g, 0.2 mol), 1-bromohexadecane (61.1 g, 0.2 mol) and a trace of KI are added to a solution of 0.2 mol sodium ethoxide in 200 mL ethanol. After refluxing the mixture for 5 h, the ethanol is removed *in vacuo* and the residue is taken up in 100 mL $CH_2Cl_2$/1 N NaOH. The aqueous phase is separated, extracted twice with $CH_2Cl_2$, the combined organic phases washed with a little water, dried over sodium sulfate and the solvent removed. Vacuum distillation of the residue (air condenser!) gives 45.6 g (54%) of a light beige liquid, b.p. = 255 °C/1 torr, which solidify on cooling (m.p. = 73 °C)[6].

*(2e)*: A solution of *(1e)* (42.2 g, 0.1 mol) in 50 mL tetrahydrofuran (THF) is dropped into a solution of 0.125 mol phenylmagnesium bromide in 50 mL ether over 30 min. After the addition, the mixture is boiled for 1 h and upon cooling poured onto an ice/hydrochloric acid slush. The organic phase is separated and the aqueous phase extracted with THF (2 x 50 mL). After being washed with water, $NaHCO_3$ solution and water again, the combined organic phases are dried over sodium sulfate and the solvent removed. The oily residue is taken up in pentane and recrystallized at −20 °C; yield 37.6 g (75%), m.p. = 56–58 °C[6].

*(3e)*: A solution of *(2e)* (750 mg, 1.5 mmol) in 10 mL benzene and 3 mL acetyl chloride are heated for 1 h under reflux, concentrated and evaporated to dryness three times with benzene (3 x 10 mL). The residual oil is taken up in 3 mL anhydrous pyridine, and thymidine (242 mg, 1 mmol) and 2 mg 4-dimethylaminopyridine are added. At the end of the reaction (*ca.* 2 h, monitored by thin layer chromatography) and after addition of 10 mL 5% $NH_4HCO_3$ solution, the mixture is extracted twice (2 x 10 mL) with chloroform. The dried organic phase is concentrated, successively twice evaporated to dryness with toluene, ethanol and chloroform, dissolved in a little chloroform and chromatographed on silica gel (Merck 7733, 1.5 x 7 cm column, chloroform eluent). The product fractions are concentrated and solid *(3c)* obtained by concentrating twice with pentane; yield 545 mg (75%)[6].

Received: December 17, 1980 [Z 807a IE]
German version: Angew. Chem. *93*, 708 (1981)

---

[1] *H. Seliger, T. C. Bach, E. Happ, M. Holupirek, E. H. Teufel,* Hoppe-Seylers Z. Physiol. Chem. *360*, 1044 (1979).

[2] *S. A. Narang, R. Brousseau, H. M. Hsiung, J. J. Michniewicz,* Methods Enzymol. *65*, 610 (1980); *S. A. Narang, H. M. Hsiung, R. Brousseau, ibid. 68*, 90 (1979).

[3] *H. Seliger, M. Holupirek, T. C. Bach, E. Happ,* Proceedings, Königsteiner Chromatographie-Tage, Bad Homburg, *1979*, 132.

[4] *H. Seliger, H.-H. Görtz,* Proceedings, Königsteiner Chromatographie-Tage, Bad Homburg, *1979*, 304.

[5] *J. Stawinski, T. Hozumi, S. A. Narang, C. P. Bahl, R. Wu,* Nucleic Acids Res. *4*, 353 (1977).

[6] *(1e),* IR: 2960, 2850, 1640, 1600, 1575, 1500, 1250 cm$^{-1}$; $^1$H-NMR ($CDCl_3$/TMS): $\delta$=0.88 (t, 3H), 1.28 (s, 26H), 1.79 (t, 2H), 4.00 (t, 2H), 6.85–7.85 (m, 9H); *(2e):* IR: 3580, 3480, 3060, 2920, 2850, 1610, 1580, 1510, 1245 cm$^{-1}$; *(3e):* IR: 3400, 3050, 2920, 2850, 1700, 1600, 1500, 1250 cm$^{-1}$.

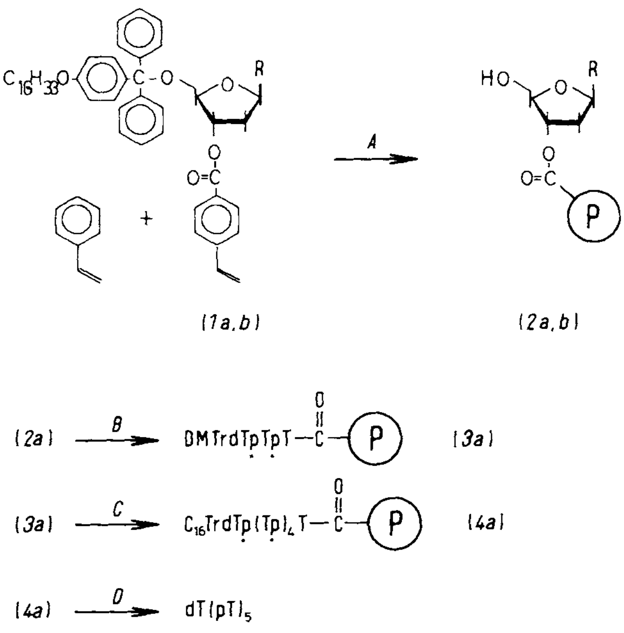
## Specific Separation of Products in Supported Oligonucleotide Syntheses Using the Triester Method[**]

By *Hartmut Seliger* and *Hans-Helmut Görtz*[*]

In the search for simplified syntheses of oligonucleotides having a specific sequence, methods involving polymeric supports are of considerable interest. However, incomplete lengthening of the chains immobilized on the carrier leads to formation of a mixture of homologous sequence fragments from which the desired product can only be obtained in sufficient purity with considerable expenditure of effort. Earlier we described procedures to separate the product chain, *i. e.* generally the longest sequence, from all by-products by selective affinity labelling[1]. We have now applied this scheme to supported oligonucleotide syntheses using the triester method[2]. This aspect has not been considered in other triester carrier syntheses[3].

As new support materials we prepared "popcorn" copolymers[4] from styrene and the 5′-tritylated deoxynucleoside-3′-*p*-vinyl benzoates *(1)* [styrene :*(1)* ≅ nucleoside loading of support material = 0.09 mmol/g *(2a)* and 0.02 mmol/g *(2b)*] (Scheme 1).

With this support a chain-lengthening step was performed in which, *1)* the 5′-OH protecting group was removed by treatment with acid, *2)* the product was condensed with *ca.* a threefold excess of 5′-O-(4,4′-dimethoxytrityl)thymidine-3′-*p*-chlorophenyl phosphate and *3)* the unreacted chain-ends were blocked by reaction with acetic anhydride in pyridine. This chain-lengthening step was repeated. Subsequently, the chains were further lengthened by block condensation with a trithymidylate moiety, which was protected at the 5′-end by a hexadecyloxytrityl group[5]. Following ammoniacal cleavage from the support, the product mixture was separated by HPLC. By this means the hexanucleotide $C_{16}TrdT(pT)_5$ was specifically separated (Fig. 1, fraction P); after cleavage of the $C_{16}Tr$-group it proved to be chromatographically homogeneous and identical with authentic material synthesized by a support-free method[5]. The yields, relative to the immediate precursor, were determined to be 51, 57 and 58% respectively, following VIS spectroscopic investigation of the acid-treated carrier samples. By means of the support-method described here, the advantages of the triester method—generally increased yields at shortened reaction times and with only a slight excess of one reactant—can be used in solid phase synthetic procedures.



| (1)–(4) | a | b |
|---|---|---|
| R = | Thymin-1-yl | N$^4$-Benzoyl-cytosin-1-yl |

Scheme 1. Synthesis of $dT(pT)_5$ on support. *A:* 1) "Popcorn" copolymerization, 2) H$^+$; *B:* 1) DMTrTp$^-$, mesitylenesulfonyl tetrazolide, 2) acetic anhydride, pyridine, 3) H$^+$, 4) Repeat of 1)–3); *C:* $C_{16}Trd(Tp)_3^-$, mesitylenesulfonyl tetrazolide; *D:* 1) aqueous $NH_3$/pyridine, 2) HPLC on $C_{18}$-phase, 3) H$^+$. p=*p*-chlorophenylphosphoryl, DMTr=4,4′-dimethoxytrityl, $C_{16}Tr$=4-hexadecyloxytrityl.

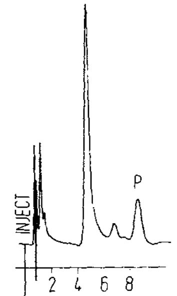


Fig. 1. Separation of the sequence $C_{16}TrdT(pT)_5$ (P) from the by-products of the supported synthesis by HPLC. Column: μ-Bondapak $C_{18}$ (Waters), eluent: 2-propanol/methanol/water 50 : 15 : 35, flow rate: 2 ML/min, pressure: 110 bar, detection: UV$_{254}$.

### *Procedure*

*(1a):* 5′-*O*-(4-Hexadecyloxytrityl)thymidine[5] (725 mg, 1 mmol) is dissolved in 5 mL anhydrous pyridine and the solution mixed with 4-vinylbenzoyl chloride[6] (500 mg, 3 mmol). After stirring for 30 min, 10 mL of a 5% $NH_4HCO_3$ solution is added to the mixture which is then extracted with chloroform (2 x 15 mL). After drying over sodium sulfate, the organic phase is separated, the pyridine removed by azeotropic distillation with toluene, and the residue chromatographed (Merck 7734, column 1.5 x 7 cm, eluent chloroform). Approximately 700 mg (80%) of a light yellow oil, $R_f$ = 0.73 (educt: 0.43; silica gel, chloroform/methanol 9 : 1); UV: $\lambda_{max}$ = 265 nm.—*(1b)* is synthesized analogously.

---

[*] Prof. Dr. H. Seliger, Dr. H.-H. Görtz
Sektion Polymere der Universität
Oberer Eselsberg, D-7900 Ulm (Germany)

[**] Polymer supported synthesis, Part 9.—Part 8: see [1].

*(2):* Nucleoside *(1)* is lyophilized from benzene and then dissolved in the stoichiometric amount of freshly distilled styrene. After addition of 0.2% divinyl benzene and some popcorn-polystyrene-seeds, the mixture is maintained at 50 °C until the reaction had ceased (*ca.* 4 to 8 h). The polymer is thoroughly washed with benzene and ether and dried *in vacuo* (yield almost quantitative). Cleavage of the 5′-*O*-protecting group follows by treatment with a 2% solution of benzenesulfonic acid in chloroform/methanol (7 : 3; 1 h, 0 °C). After washing with methanol, chloroform and ether and repeated drying, the support is ready for use.

Received: December 17, 1980 [Z 807b IE]
German version: Angew. Chem. *93*, 709 (1981)

*(1a)*, 78421-05-3; *(1b)*, 78421-06-4; *(2a)*, 78421-11-1; *(2b)*, 78421-09-7; styrene, 100-42-5; 5′-*O*-(4-hexadecyloxytrityl)thymidine, 78421-07-5; 4-vinylbenzoyl chloride, 1565-41-9.

---

[1] *H. Seliger, M. Holupirek, H.-H. Görtz*, Tetrahedron Lett. *1978*, 2115.

[2] *S. A. Narang, R. Brousseau, H. M. Hsiung, J. J. Michniewicz*, Methods Enzymol. *65*, 610 (1980); *S. A. Narang, H. M. Hsiung, R. Brousseau, ibid. 68*, 90 (1980); *H. Seliger, T. C. Bach, E. Happ, M. Holupirek, E. H. Teufel*, Hoppe-Seylers Z. Physiol. Chem. *360*, 1044 (1979).

[3] *K. Miyoshi, K. Itakura*, Tetrahedron Lett. *1979*, 3635; *M. J. Gait, M. Singh, R. C. Sheppard, M. D. Edge, A. R. Greene, G. R. Heathcliffe, T. C. Atkinson, C. R. Newton, A. F. Markham*, Nucleic Acids Res. *8*, 1081 (1980); *R. Crea, T. Horn, ibid. 8*, 2331 (1980).

[4] *J. W. Breitenbach, B. Herrmann*, Angew. Makromol. Chem. *10*, 197 (1970); *R. L. Letsinger, H. Seliger*, Macromolecular Preprints, XXIII$^{rd}$ International Congress of Pure and Applied Chemistry, Boston *1971*, 1261.

[5] *H.-H. Görtz, H. Seliger*, Angew. Chem. *93*, 708 (1981); Angew. Chem. Int. Ed. Engl. *20*, 681 (1981).

[6] *Y. Iwakura, K. Uno, N. Nakabayashi, T. Kozima*, Bull. Chem. Soc. Jpn. *41*, 186 (1968).

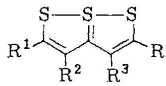
## Catalytic Lithiation of 1-Olefins

By *Borislav Bogdanović* and *Bernd Wermeckes*[*]

In 1967 *D. L. Skinner et al.*[1] described the reaction of 1-olefins with lithium to give 1-lithio-1-alkynes and lithium hydride, whereby (*E*)-1-lithio-1-alkenes are formed as by-products. In 1975, *V. Rautenstrauch*[2] reported that small amounts of 1-lithioethylene and 1,4-dilithiobutane are formed in the reaction of lithium with ethylene in dimethoxymethane or tetrahydrofuran (THF) in the presence of biphenyl and naphthalene. Direct lithiation, however, has so far been limited to "acidic" hydrocarbons such as 1-alkynes[3a], triphenylmethane[3b] or cyclopentadiene[3c,d].

In our studies on the catalytic properties of the poly(alkali metal) complexes[4a] obtainable from 1,6,6a$\lambda^4$-trithiapentalenes *(1)* or related compounds and alkali metals, we found catalysts for a direct reaction of 1-olefins with lithium to give organolithium compounds of the vinyl- and allyl-type, respectively, and lithium hydride[4b].

For the catalytic lithiation, the 1-olefins were allowed to react with lithium sand in THF at 0 °C in the presence of a catalytic amount of a 1,6,6a$\lambda^4$-trithiapentalene *(1)* (or a related compound) and a metal salt[5]. Combinations of 2,5-[6] or 2,4-diphenyl-1,6,6a$\lambda^4$-trithiapentalene[6b] [*(1a)* and *(1b)*, respectively], anhydrous zinc- or iron(III) chloride, and lithium have proven to be particularly effective catalysts for the lithiation of olefins.



*(1a)*, $R^1 = R^4 = C_6H_5$, $R^2 = R^3 = H$
*(1b)*, $R^1 = R^3 = C_6H_5$, $R^2 = R^4 = H$

Lithiation of ethylene with the catalysts prepared from *(1a)*, $ZnCl_2$ and lithium affords vinyllithium in 70—75% yield, together with lithium hydride and small amounts (2—3%) of 1,ω-dilithioalkanes[2]. The course of the reaction with time is illustrated in Figure 1.

$$H_2C{=}CH_2 + 2\ Li \xrightarrow[THF]{cat.} H_2C{=}CHLi + LiH$$

After completion of reaction $H_2C{=}CHLi$ can be separated from the precipitated LiH and isolated in crystalline form as $C_2H_3Li \cdot THF$.

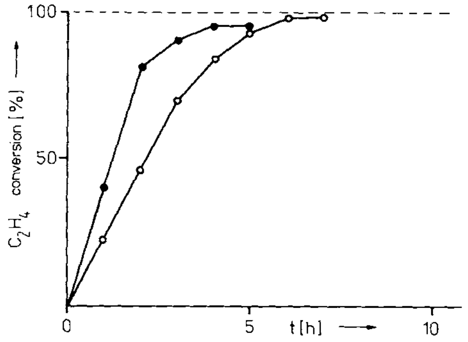
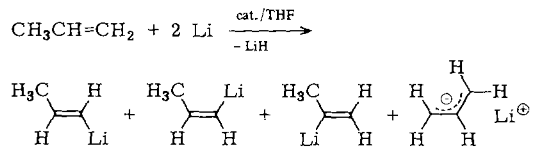


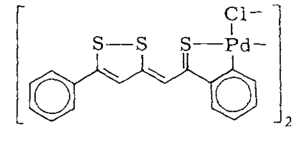
Fig. 1. Plot of the lithiation of ethylene at 0 °C/1 bar in THF with time; (—●—) Li : *(1a)* : $ZnCl_2$ = 100 : 1 : 2, [*(1a)*] = 0.04 mol/L; (—○—) Li : *(1a)* : $ZnCl_2$ = 200 : 1 : 2, [*(1a)*] = 0.02 mol/L.

In the catalytic lithiation of propene the four isomeric $C_3H_5Li$ compounds *(2)*—*(5)* are formed along with LiH. On using the catalyst of combined *(1a)*, $ZnCl_2$ and Li, the $C_3H_5Li$ compounds are obtained in a total yield of 75—85%. The (*E*)-propenyllithium *(2)* is present up to 85—90% in the mixture; it can be enriched to 98.5% by double recrystallization from THF/pentane (1 : 1).



*(2)* *(3)* *(4)* *(5)*

When combinations of *(1a)* or *(1b)*, palladium(II)- or platinum(II) chloride and lithium are used as catalysts the main product is *(5)*. The highest selectivity for the formation of *(5)* (80—90%) has so far been achieved with the complex *(6)*[7], preparable from *(1a)* and $PdCl_2$, as catalyst.



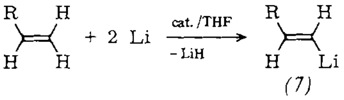
*(6)*

Analogously to propene, higher 1-olefins also react with the catalyst from *(1a)*, $ZnCl_2$ and lithium to give (*E*)-1-lithio-1-alkenes. Moreover, the selectivity is higher than in

---

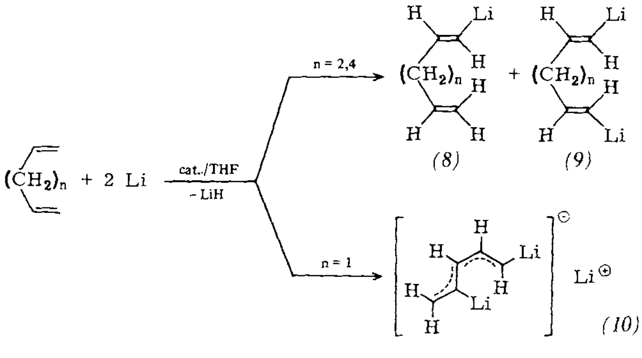
[*] Prof. Dr. B. Bogdanović, Dr. B. Wermeckes
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr 1 (Germany)

the case of propene; thus, 1-butene, 1-hexene and 1-octene can be catalytically lithiated to the products *(7)* with selectivities of 90—95, 95, and 94—97%, respectively.



R = $(CH_2)_nCH_3$; n = 1,3,5

1,ω-Dienes (1,5-hexadiene and 1,7-octadiene) react with lithium and the same catalysts to give a mixture of (*E*)-1-lithio-1,ω-alkadienes *(8)* and (*E,E*)-1,ω-dilithio-1,ω-alkadienes *(9)*. The catalytic lithiation of 1,4-pentadiene, on the other hand, leads to a crystalline trilithium compound $C_5H_5Li_3$, which according to $^1$H- and $^{13}$C-NMR data and the results of silylation experiments has the constitution



*(10)*[8]; the compounds *(8)—(10)* are new. Isobutene and (*Z*)-2-butene cannot be lithiated under analogous conditions (0 °C, THF) and with the catalysts employed so far.

Organolithium compounds of the vinyl- and allyl-type are finding ever increasing use as reagents in organic syntheses[9]. The (*E*)-1-lithio-1-olefins *(2)* and *(7)* were previously synthesized[11] from (*E*)-1-halo-1-alkenes by reaction with lithium[10a–f], *n*-butyllithium[10g] or *tert*-butyllithium[10h–k]. (*E*)-1-Halo-1-alkenes, on their part, are obtainable by hydroalumination or hydroboration of 1-alkynes or of their 1-trimethylsilyl derivatives, followed by reaction with halogens[10e, 10k, 12], or by other methods[10h, k].

Catalytic lithiation opens up a first direct entry to (*E*)-1-lithio-1-olefins and hence also to (*E*)-1,2-disubstituted olefins and derivatives thereof[10k].

### *Procedure*[13]

All reactions must be carried out under argon.—

$C_2H_3Li$: A solution of *(1a)* (0.34 g, 1.1 mmol) and $ZnCl_2$ (anhydrous; 0.30 g, 2.2 mmol) in anhydrous THF (50 mL) is saturated with ethylene (1 bar) at 0 °C; lithium sand (1.45 g, 0.21 mol) is then added to the stirred solution under an atmosphere of ethylene. The uptake of ethylene, which commences after 10—15 min, is measured by means of a gas burette. Until completion of reaction at 0 °C a total of 2.28 L of ethylene (1 bar, 20 °C) is taken up within 6 h (Fig. 1). The suspension is filtered and the separated LiH washed with THF. Hydrolysis of an aliquot of the filtrate and mass spectroscopic analysis (MS) of the ethylene thus liberated reveals a $C_2H_3Li$-yield of 75% (referred to Li). The THF solution is evaporated down under reduced pressure, the residue taken up in ether/pentane (1 : 1), and the catalyst (violet precipitate) removed by filtration. The filtrate is evaporated down again and the residue recrystallized 2—3 times (each recrystallization at −78 °C) from THF/pentane (1 : 1). After drying (0.2 torr), $C_2H_3Li$ THF is obtained as colorless crystals[14].

$C_3H_5Li$: The lithiation of propene is carried out analogously to that of ethylene. The reaction mixture [*(1a)* (2.20 g, 7.0 mmol), $ZnCl_2$ (1.93 g, 14.2 mmol), $C_3H_6$ (1 bar) and lithium sand (4.89 g, 0.70 mol) in THF (150 mL)] takes up a total of 6.7 L of $C_3H_6$ (1 bar, 20 °C) within 14 h. The reaction mixture is filtered. The overall yield of $C_3H_5Li$ compounds (corresponding to their hydrolysis to propene) is 75% (referred to Li). Reaction of a part of the solution with trimethylchlorosilane and gas-chromatographic analysis of the silylation products formed[10c, 15] gives the following composition of $C_3H_5Li$ compounds (in %): 89.8 *(2)*, 0.5 *(3)*, 1.9 *(4)*, 7.8 *(5)*. $C_3H_5Li \cdot THF$ is isolated in crystalline form in the same way as described for $C_2H_3Li \cdot THF$. After two recrystallizations from THF/pentane (1 : 1) $C_3H_5Li \cdot THF$ is obtained with 98.5% content of *(2)* (rest: 0.1% *(3)*, 1.4% *(4)*)[16].

$C_8H_{15}Li$: Lithium sand (1.73 g, 249 mmol) is added with stirring to a solution of 1-octene (11.55 g, 103 mmol), *(1a)* (0.32 g, 1.0 mmol) and anhydrous $ZnCl_2$ (0.28 g, 2.0 mmol) in THF (100 mL) at 0 °C. The reaction mixture is stirred for 24 h at 0 °C. The dark-violet suspension is removed by filtration and the filtrate is evaporated to dryness at 0.2 torr; the distillate is found by gas chromatography to contain THF and 3.56 g of 1-octene (30.8% of that employed). The residue is dissolved in ether and the resulting solution, after treatment with trimethylchlorosilane (in excess) is stirred for 12 h. It is then extracted with water, washed neutral, dried with $CaCl_2$, and the ether is distilled off at normal pressure. Subsequent distillation under reduced pressure affords, *inter alia*, 13.97 g of a fraction (b.p. 35—43 °C/0.2 torr), which according to GC or GC-MS analysis consists of 74.8, 1.9, 0.8, 0.4 and 0.4% of the isomeric trimethylsilyloctenes (MW = 184.4) (rest hexamethyldisiloxane). The main component is (*E*)-1-trimethylsilyl-1-octene. The overall yield of $C_8H_{15}Li$ compounds is 83.2% (based on reacted 1-octene), with a selectivity of lithiation in the (*E*)-1-position of 95.5%.

Received: December 23, 1980 [Z 794 IE]
German version: Angew. Chem. *93*, 691 (1981)

CAS Registry numbers:
*(1a)*, 1033-90-5; *(1b)*, 14905-03-4; *(2)*, 6386-72-7; *(3)*, 6524-17-0; *(4)*, 6386-71-6; *(5)*, 3052-45-7; *(6)*, 71328-64-8; *(7)* ($R = CH_2CH_3$), 67140-05-0; *(7)* ($R = (CH_2)_3CH_3$), 62839-68-3; *(7)* ($R = (CH_2)_5CH_3$), 37730-25-9; *(8)*, (n = 2), 78371-49-0; *(8)* (n = 4), 76814-25-0; *(9)* (n = 2), 78371-50-3; *(9)* (n = 4), 76814-26-1; *(10)*, 76814-27-2; vinyllithium, 917-57-7; ethylene, 74-85-1; propene, 115-07-1; 1-butene, 106-98-9; 1-hexene, 592-41-6; 1-octene, 111-66-0; 1,5-hexadiene, 592-42-7; 1,7-octadien, 3710-30-3.

---

[1] *D. L. Skinner, d. J. Peterson, T. J. Logan*, J. Org. Chem. *32*, 105 (1967).

[2] a) *V. Rautenstrauch*, Angew. Chem. *87*, 254 (1975); Angew. Chem. Int. Ed. Engl. *14*, 259 (1975); b) Schweiz. Pat. 585760 (20. 5. 1974); Chem. Abstr. *87*, 135878 (1977).

[3] a) *H. Ogura, H. Takahashi*, Synth. Commun. *3*, 135 (1973); b) *H. Gilman, B. J. Gaj*, J. Org. Chem. *28*, 1725 (1963); c) *K. Hafner, H. Kaiser*, Justus Liebigs Ann. Chem. *618*, 140 (1958); d) *H. Gilman, R. D. Gorsich*, J. Org. Chem. *23*, 550 (1958).

[4] a) *B. Bogdanović*, DOS 2722221 (1978), Studiengesellschaft Kohle; Chem. Abstr. *91*, 39135 (1979); b) *B. Bogdanović*, DOS 2908928 (1980), Studiengesellschaft Kohle.

[5] Reaction of 1,6,6aλ$^4$-trithiapentalenes and 1,2-dithiol-3-thione derivatives with some heavy metal salts ($FeCl_3$, $CuCl_2$, CuCl) affords 1 : 2 adducts which can be used instead of the mixtures of the two components for the preparation of the catalysts.

[6] a) *G. Traverso*, Ann. Chim. (Rome) *44*, 1018 (1954); b) *E. Klingsberg*, J. Am. Chem. Soc. *85*, 3244 (1963).

[7] *B. Bogdanović, C. Krüger, P. Locatelli,* Angew. Chem. *91*, 745 (1979); Angew. Chem. Int. Ed. Engl. *18*, 684 (1979).

[8] *B. Wermeckes,* Dissertation, Universität Bochum 1979.

[9] Nachr. Chem. Tech. Lab. *28*, 78 (1980), and references cited therein.

[10] a) *D. Y. Curtin, J. W. Crump,* J. Am. Chem. Soc. *80*, 1022 (1958); b) *N. L. Allinger, R. B. Hermann,* J. Org. Chem. *26*, 1040 (1961); c) *D. Seyferth, L. G. Vaughan,* J. Am. Chem. Soc. *86*, 883 (1964); d) *G. M. Whitesides, C. P. Casey, J. K. Krieger, ibid. 93*, 1379 (1971); e) *J. W. Patterson Jr., J. H. Fried,* J. Org. Chem. *39*, 2506 (1974); f) *C. J. Sih, R. G. Salomon, P. Price, R. Sood, G. Peruzzotti,* J. Am. Chem. Soc. *97*, 857 (1975); g) *A. F. Kluge, K. G. Untch, J. H. Fried, ibid. 94*, 7827 (1972); h) *E. J. Corey, D. J. Beames, ibid. 94*, 7210 (1972); i) *E. J. Corey, H. S. Sachdev, ibid. 95*, 8483 (1973); j) *C. J. Sih, J. B. Heather, R. Sood, P. Price, G. Peruzzotti, L. F. Hsu Lee, S. S. Lee, ibid. 97*, 865 (1975); k) *H. Neumann, D. Seebach,* Chem. Ber. *111*, 2785 (1978), and references cited therein.

[11] One route to (*E*)-1-lithio-1-alkenes which circumvents the (*E*)-1-halo-1-alkenes is the reaction of (*E*)-1-tri-*n*-butylstannyl-1-alkenes with *n*-butyllithium described by *E. J. Corey* and *R. H. Wollenberg* (J. Org. Chem. *40*, 2265 (1975)).

[12] a) *G. Zweifel, C. C. Whitney,* J. Am. Chem. Soc. *89*, 2753 (1967); b) *H. C. Brown, D. H. Bowman, S. Misumi, M. K. Unni, ibid. 89*, 4531 (1967); c) *H. C. Brown, T. Hamaoka, N. Ravindran, ibid. 95*, 5786 (1973); d) *R. B. Miller, T. Reichenbach,* Tetrahedron Lett. *1974*, 543.

[13] We wish to thank Frau Chem.-Tech. *A. Marjanović* for valuable assistance in organizing the experimental procedures.

[14] 3/4 of the vinyllithium present in solution could be isolated in this way; $C_2H_3Li\cdot C_4H_8O$ (106.0); calc. 6.55% Li, obs. 6.56% Li; hydrolysis afforded 94% of the calculated amount of ethylene.

[15] *D. Seyferth, L. G. Vaughan,* J. Organomet. Chem. *1*, 138 (1963).

[16] *Ca.* 70% of *(2)* present in the solution could be isolated; $C_3H_5Li\cdot C_4H_8O$ (120.1); calc. 5.76% Li; obs. 5.75% Li.

---

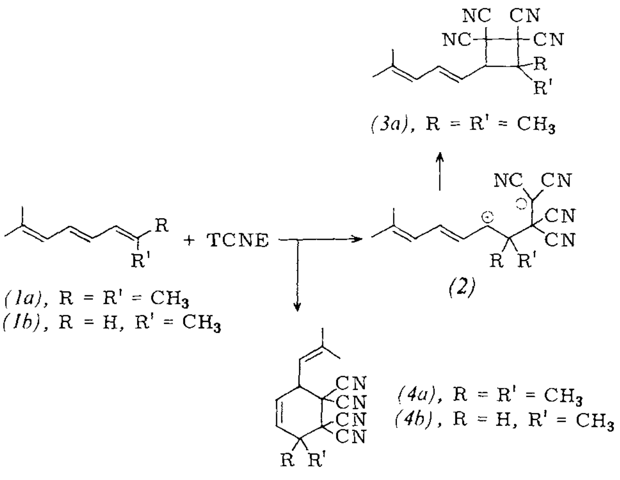
## Isomer Formation in the Cycloaddition Reaction of 2,7-Dimethyl-2,4,6-octatriene with Tetracyanoethylene

By *Alden D. Josey*[*]

Dimerization of isoprene in the presence of maleic anhydride bis(triphenylphosphane)palladium(0) occurs in a linear, tail-to-tail fashion to give 2,7-dimethyl-1,3,7-octatriene, which under conditions of base-catalysis rearranges to 2,7-dimethyl-2,*trans*-4,6-octatriene *(1a)*[1]. Isoprene is dimerized directly to *(1a)* by dad-modified chromium catalysts (dad = 1,4-diaza-1,3-diene)[2]. Reaction of *(1a)* with tetracyanoethylene (TCNE) resulted in formation of the "expected" Diels-Alder adduct 3,3-dimethyl-6-(2-methyl-1-propenyl)-4-cyclohexene-1,1,2,2-tetracarbonitrile *(4a)*[2]. The behavior of the triene in cycloaddition reactions proved, however, to be somewhat different: *(1a)* reacts with TCNE to form two cycloadducts in amounts dependent on the polarity of the solvent.

In anhydrous solvents, equimolar amounts of *(1a)* and TCNE produce an intense blue charge-transfer complex whose color is discharged slowly, increases in intensity as solvent is evaporated, and disappears completely on removal of the solvent *in vacuo*[3]. The crystalline residue could be separated by extraction with hot hexane into two isomeric compounds—the less-soluble *(3a)*, m.p. = 140—141.5 °C (from ethanol), and *(4a)*, m.p. = 90—92 °C. Conversion was quantitative.

The isomers were identified by NMR and UV spectroscopy[4]. As indicated by the relative intensities of the $^1$H-NMR signals at $\delta = 3.55$ (d, $J = 10$ Hz) and 4.15 (d, $J = 10$ Hz) of the non-olefinic ring H atoms of the [2+2]-cycloadduct *(3a)* or of the normal [2+4]-cycloadduct *(4a)* in the product mixture, formation of *(3a)* is favored by more polar solvents [*(3a)*:*(4a)* ≈ 33:67 in tetrahydrofuran (THF), 50:50 in acetonitrile], implicating *(2)* as a key intermediate.



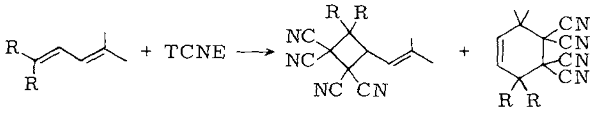
*(3a)*, R = R' = $CH_3$

*(2)*

*(1a)*, R = R' = $CH_3$
*(1b)*, R = H, R' = $CH_3$

*(4a)*, R = R' = $CH_3$
*(4b)*, R = H, R' = $CH_3$

That the cycloaddition of TCNE and substituted 1,3-butadienes leads to competing [2+2]-/[2+4]-cycloadditions is well known *e.g.* the reaction of *(5a)* to *(6a)*—in which the cyclobutane ring is closed at the less-hindered diene terminus—and to *(7a)* [0% in nitromethane, 30% in cyclohexane]. Our own work shows that full methyl-substitution of both diene termini in *(5b)* does not hinder the reaction but directs its course in $CH_3CN$ exclusively to the [2+2]-adduct *(6b)* in quantitative yield[6].



*(5a)*, R = H
*(5b)*, R = $CH_3$

*(6a)*, R = H
*(6b)*, R = $CH_3$

*(7a)*, R = H

In the formation of *(3a)* electronic factors (hexadienyl cation in *(2)*) alone cannot account for the regiospecificity of the [2+2]-cycloaddition toward the more hindered terminal double bond since the reaction of the less substituted triene *(1b)* with TCNE results in exclusive formation of the [2+4]-adduct *(4b)*[7].

It appears that the ability of the diene portion of the polyene to assume a planar, or very nearly planar, cisoid configuration in the transition state for cycloaddition (good in *(1b)*, poor in *(5b)*, intermediate in *(1a)*) must share with electronic stabilization of intermediate ions the role of determining how cycloaddition products are partitioned into the two observed modes. The unusual triene *(1a)* represents a case in which these effects are sufficiently balanced to permit both reaction modes.

Received: February 25, 1980 [Z 795 IE]
German version: Angew. Chem. *93*, 702 (1981)

---

[*] Dr. A. D. Josey
Experimental Station, E. I. du Pont de Nemours and Co.
Wilmington, Delaware 19898 (USA)

[1] *A. D. Josey,* J. Org. Chem. *39*, 139 (1974).

[2] *H. tom Dieck, A. Kinzel,* Angew. Chem. *91*, 344 (1979); Angew. Chem. Int. Ed. Engl. *18*, 324 (1979).

[3] 6.8 g *(1a)* and 6.4 g TCNE (0.05 mol of each) in 75 mL THF or $CH_3CN$; the initially intense blue solution becomes pale green after 4 d at 25 °C under $N_2$.

[4] $^1$H-NMR ($CDCl_3$, TMS int.): *(3a)* $\delta = 1.48$ (s, 3 H), 1.53 (s, 3 H), 1.82 (s, 6 H), 3.55 (d, 10 Hz, 1 H), 5.3—6.9 (m, 3 H); *(4a)* $\delta = 1.67$ (s, 3 H), 1.78 (s, 3 H), 2.0 (m, 6 H), 4.15 (d, 10 Hz, 1 H), 5.35 (d, 10 Hz, 1 H), 5.4—5.95 (m, 2 H, AB-system, 10 Hz; low- and high-field components exist as doublets with $J = 2.0$ or 1.5 Hz splittings). UV ($CH_2Cl_2$): *(3a)* $\lambda = 263$ nm ($\varepsilon = 25400$).

[5] *C. A. Stewart*, J. Org. Chem. *28*, 3320 (1963); J. Am. Chem. Soc. *84*, 117 (1962).
[6] *(6b)*, m.p. = 128.5—129.5 °C (from ethanol); $^1$H-NMR ($CDCl_3$, TMS int.): $\delta = 5.33$ (d, 9.5 Hz, 1 H), 3.83 (d, 9.5 Hz, 1 H), 1.88 (d, 1 Hz, 3 H), 1.78 (d, 1 Hz, 3 H), 1.51 (s, 3 H), 1.49 (s, 3 H).
[7] Reaction in THF; *(4b)*, m.p. = 104—104.5 °C (from hexane/$CH_2Cl_2$); $^1$H-NMR ($CDCl_3$, TMS int.): $\delta = 5.75$ (s, 2 H), 5.33 (d, 10 Hz, 1 H), 3.99 (d, 10 Hz, 1 H), 3.24 (q, 7 Hz, 1 H), 1.88 (s, 6 H), 1.61 (d, 7 Hz, 3 H).

---

## Synthesis of a Novel Amphoteric Polyelectrolyte by Polymerization of 6-Amino-2,4-hexadienoic Acid in Layer Perovskites[**]

By *Bernd Tieke* and *Gerhard Wegner*[*]

Alkylammonium compounds can be incorporated into inorganic matrices *via* hydrogen bridges. Well known examples of this phenomenon are intercalations in sheet silicates[1] and formation of complex crystals with transition metal halides $MX_2$, the so-called layer perovskites of formula $(C_nH_{2n+1}—NH_3)_2MX_4$[2]. Numerous investigations of the magnetic properties and phase changes in these layer perovskites have appeared[3]. However, their suitability as matrices for organic solid state reactions has not yet been studied.

The starting point for our investigations was the observation that ω-amino acids, as well as *n*-alkylamines, are able to crystallize in "layer perovskites". 6-Amino-2,4-hexadienoic acid *(1)* forms complex crystals with several transition metal halides $MX_2$ ($CdCl_2$, $CdBr_2$, $MnCl_2$, $FeCl_2$, and $CuCl_2$). Only the complexes with $CdCl_2$, $MnCl_2$ and $FeCl_2$ undergo a solid state reaction, upon UV- ($\lambda = 254$ nm) and $^{60}$Co-γ-irradiation, to form a 1,4-disubstituted *trans*-polybutadiene of structure *(2)*.

$$\underset{(1)}{n\,CHR^1{=}CH{-}CH{=}CHR^2} \rightarrow \underset{(2)}{\left(CHR^1{-}CH{=}CH{-}CHR^2\right)_n}$$

$$R^1 = CH_2NH_2,\ R^2 = COOH$$

The degree of conversion amounts to over 90% after a γ-dose of 30 Mrad. In the other complexes no polymerization reaction occurs. The possibility of a 1,4-addition polymerization of 1,4-disubstituted *trans,trans*-dienes has not previously been demonstrated, either for reactions occurring in the solid state or within canal complexes[4]. Apart from signals from the unreacted monomer, the 22.6 MHz $^{13}$C-NMR spectrum of a 1 N KOD solution of the dissolved crystals only showed signals from the 1,4-adduct after 30 Mrad irradiation: $COO^-$ ($\delta = 184.2$), isolated *trans*-C=C ($\delta = 135.4/134.2$) and three signals in the aliphatic C atom region ($\delta = 59.2/49.8/45.2$), which are assigned to the two asymmetric C atoms formed and the $CH_2NH_2$ group.

Assuming for present that the signals from the asymmetric C atoms can be assigned only to one chiral center and considering the mode of formation of the polymer in the crystalline state, an *erythro*-diisotactic arrangement of the substituents is proposed. The polymer occurs as a racemate.

X-ray structure investigations indicate that only slight structural changes occur during the reaction. In the $CdCl_2$ complex the distance between the two metal ion sheets only increases by 0.9 to 17.9 Å. The tacticity of the product, small structural changes, as well as the control of the reactivity by the ionic nature of the matrix, make a topochemical control of the reaction probable. From Figure 1 it is evident that the polymer chains, formed by 1,4-addition of the diene groups, lie extended in a plane parallel to the inorganic matrix.

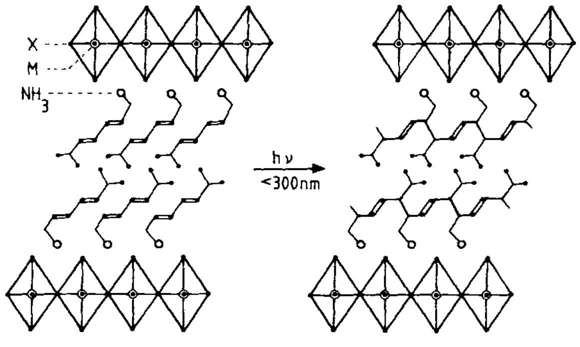


Fig. 1. Schematic representation of the reaction.

The polymerized amino acid can be separated from the matrix by solvation in strong bases and finally by reprecipitation as an amphoteric polyelectrolyte. It has an average molecular weight of *ca.* 35000 (determined by GPC in 2.5% aqueous $N(CH_3)_4OH$ solution), dissolves in strong acids ($pH \leq 2.0$) and bases ($pH \geq 10.2$) and is crystalline after reprecipitation. At present, we are investigating its suitability as a polymeric complexing agent.

### *Procedure*

2 mL of a 0.5 M aqueous solution of $MX_2$ is added to *(1)*[5] (2 mmol) dissolved in *ca.* 20 mL 0.1 N HCl. Crystallization follows by evaporation of the solvent over $P_2O_5$ in a desiccator. It is recommended that operations with $Mn^{2+}$ and $Fe^{2+}$ are carried out under a nitrogen atmosphere.

Received: January 14, 1981 [Z 796 IE]
German version: Angew. Chem. *93*, 693 (1981)

CAS Registry numbers:
*(1)*, 78249-26-0; *(1)* homopolymer, 78249-42-0

[1] *G. Lagaly, A. Weiss*, Kolloid-Z. Z. Polym. *243*, 48 (1971).
[2] a) *U. Walther, D. Brinkmann, G. Chapuis, H. Arend*, Solid State Commun. *27*, 901 (1978); b) *H. Arend, W. Huber, F. H. Mischgofsky, G. H. Richter-van Leeuwen*, J. Cryst. Growth *43*, 213 (1978).
[3] a) *H. Arend, J. Schoenes, P. Wachter*, Phys. Status Solidi *B69*, 105 (1975); b) *W. Depmeier, J. Felsche, G. Wildermuth*, J. Solid State Chem. *21*, 57 (1977); c) *C. Bellitto, P. Day*, J. Chem. Soc. Dalton Trans. *1978*, 1207.
[4] a) *G. M. J. Schmidt et al.*: Solid State Photochemistry, Verlag Chemie, Weinheim 1976, p. 93pp.; b) *K. Takemoto, M. Miyata*, J. Macromol. Sci. *C18*, 83 (1980).
[5] *P. Karrer, R. Schwyzer*, Helv. Chim. Acta *29*, 1191 (1946).

---

[*] Prof. Dr. G. Wegner [+], Dr. B. Tieke
Institut für Makromolekulare Chemie der Universität
Stefan-Meier-Strasse 31, D-7800 Freiburg (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Stiftung Volkswagenwerk (Project: „Physik und Chemie unkonventioneller Materialien"). We thank Dr. *H. Arend*, ETH Zürich, for stimulating discussions.

---

## A General Procedure for Intramolecular α-*tert*-Alkylation of Carbonyl Compounds[**]

By *Manfred T. Reetz*, *Ioannis Chatziiosifidis*, and *Konrad Schwellnus*[*]

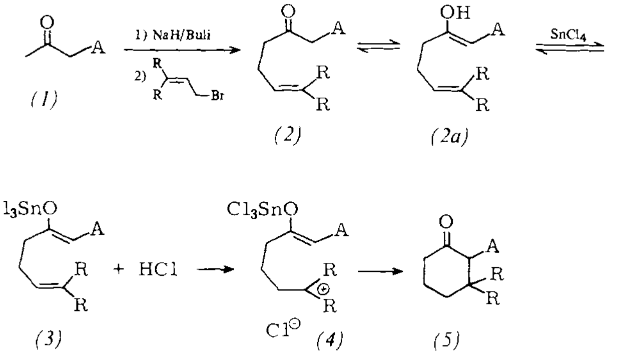
The problem of α-*tert*-alkylation of carbonyl compounds can be solved in a general way by reacting the cor-

---

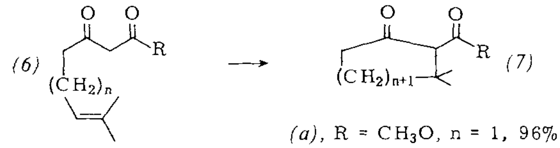
[*] Prof. Dr. M. T. Reetz, Dr. I. Chatziiosifidis and Dipl.-Chem. K. Schwellnus
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, 3550 Marburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

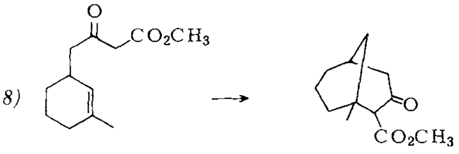
responding silyl enol ethers with *tert*-alkyl halides in the presence of Lewis acids[1]. We now report the results of systematic studies of *intramolecular* α-*tert*-alkylations[2]. Compounds having silyl enol ether and *tert*-alkyl halide functions are difficult to prepare[3]. In contrast, an alternative strategy involving Lewis acid-mediated cyclization of olefins of the type *(2)* derived from active methylene compounds *(1)*[4] to afford *(5)* is simple (A = activating group). In case of $SnCl_4$, the assumption of *O*-stannylation of the enolized form *(2a)* to generate *(3)* and HCl is plausible. Protonation of the olefin results in cyclization of the cation *(4)*[5].

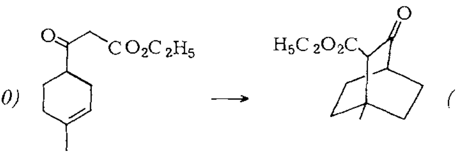


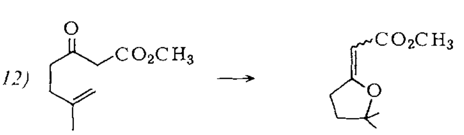
Besides catalytic amounts of $SnCl_4$, such Lewis acids as $TiCl_4$ or $(CH_3)_3SiCl$ in the presence of $ZnCl_2$ are also effective but the yields are lower by 20—30%. The intramolecular α-*tert*-alkylations leading to *(7)*, *(9)*, and *(11)* represent favored 6- and 7-*endo* trigonal cyclizations[6]. *(12)* does not undergo disfavored 5-*endo* trigonal CC bond formation, but rather *O*-alkylation yielding *(13)*.



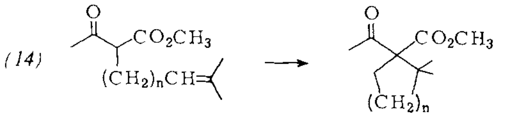
*(a)*, R = $CH_3O$, n = 1, 96%
*(b)*, R = $CH_3O$, n = 2, 62%
*(c)*, R = $CH_3$, n = 1, 80%


*(8)* → *(9)*, 61%


*(10)* → *(11)*, 63%

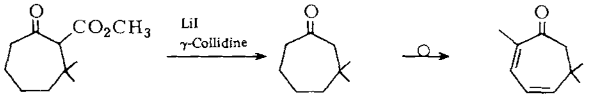

*(12)* → *(13)*, 65%

Rings with exocyclic carbonyl functions are also accessible. Whereas *(14a)* undergoes a favored 5-*exo* trigonal cyclization to yield *(15a)*, the ring forming reaction *(14b)*→*(15b)* is surprisingly slow. After a reaction time of 4 d, only *ca.* 20% of the product is present, in addition to some starting material *(14b)*. Although 6-*exo* and 6-*endo* trigonal cyclizations are both supposed to be favored[6], comparative kinetic data are seldom available: either the Baldwin-Rules do not apply to cationic systems, or other (perhaps thermodynamic) factors are involved.

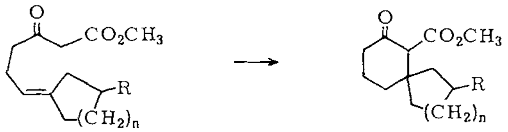

*(14)* → *(15)*

*(a)*, n = 2, 66%
*(b)*, n = 3, ≈ 20%

The method is likely to have application in terpene or steroid chemistry. For example, *(7b)* is easily decarboxylated to form the otherwise not readily accessible *(16)*, a compound which has been used previously as a precursor of eucarvone *(17)*[7]. The methodology described herein is also useful in the synthesis of spiro compounds of type *(19)*. Since the starting materials *(18)*[8] are rather easily prepared, the procedure is of synthetic interest.



*(7b)* → *(16)*, 97% → *(17)*


*(18)* → *(19)*

*(a)*, R = H, n = 1, 73%
*(b)*, R = H, n = 2, 72%
*(c)*, R = $CH_3$, n = 2, 71%

### Procedure

*(7a)*: $SnCl_4$ (0.73 g, 20 mol%) is slowly added to a stirred solution of methyl 7-methyl-3-oxo-6-octenoate *(6a)* (2.58 g, 14 mmol) in 40 mL dry methylene chloride at 0°C. The mixture is allowed to warm up to room temperature, stirred for about 14 h and poured into 50 mL ice-water. After washing twice with water and drying over $Na_2SO_4$, the solvent is stripped off and the residue distilled (kugelrohr, 80°C/0.4 torr): 2.48 g (96%) methyl-2,2-dimethyl-6-oxocyclohexanecarboxylate *(7a)*; $^1$H-NMR ($CDCl_3$): $\delta = 1.00$ (s, 3 H), 1.06 (s, 3 H), 1.33—2.33 (m, 6 H), 3.16 (s, 1 H), 3.66 (s, 3 H).

Received: May 7, 1980 [Z 798 IE]
Supplemented: June 9, 1981
German version: Angew. Chem. *93*, 716 (1981)

CAS Registry numbers:
*(6a)*: 53067-23-5 / *(6b)*: 78249-27-1 / *(6c)*: 51297-46-2 / *(7a)*: 71135-95-1 / *(7b)*: 78249-28-2 / *(7c)*: 54200-63-4 / *(8)*: 78249-29-3 / *(9)*: 78249-30-6 / *(10)*: 6090-11-5 / *(11)*: 78249-31-7 / *(12)*: 59529-68-9 / *(13)*: 78249-32-8 / *(14a)*: 24115-69-3 / *(14b)*: 78249-33-9 / *(15a)*: 78249-34-0 / *(15b)*: 78249-35-1 / *(16)*: 23438-70-2 / *(18a)*: 78249-36-2 / *(18b)*: 78249-37-3 / *(18c)*: 78249-38-4 / *(19a)*: 78249-39-5 / *(19b)*: 78249-40-8 / *(19c)*: 78249-41-9.

---

[1] *M. T. Reetz, W. F. Maier, I. Chatziiosifidis, A. Giannis, H. Heimbach, U. Löwe*, Chem. Ber. *113*, 3741 (1980); and lit. cited therein.
[2] Only a few isolated examples of such processes are known: The cyclization of *(6a)* has been described independently: *F. W. Sum, L. Weiler*, J. Am. Chem. Soc. *101*, 4401 (1979); see also other strategies: *E. J. Corey, N. N. Girota, C. T. Mathew, ibid. 91*, 1557 (1969); *G. Ohloff, F. Näf, R. De-*

*corzant, W. Thommen, E. Sundt*, Helv. Chim. Acta *56*, 1414 (1973); *J. C. Fairlie, G. L. Hodgson, T. Money*, J. Chem. Soc. Perkin Trans. 1 *1973*, 2109.

[3] *G. Anastassiou*, Diplomarbeit, Universität Bonn 1980.

[4] *S. N. Huckin, L. Weiler*, J. Am. Chem. Soc. *96*, 1082 (1974).

[5] This process is related to the *tert*-butylation of dicarbonyl compounds under Friedel-Crafts conditions: *P. Boldt, H. Militzer, W. Thielecke, L. Schulz*, Justus Liebigs Ann. Chem. *718*, 101 (1969).

[6] *J. E. Baldwin*, J. Chem. Soc. Chem. Comm. *1976*, 734.

[7] *R. A. Barnes, W. J. Houlihan*, J. Org. Chem. *26*, 1609 (1961).

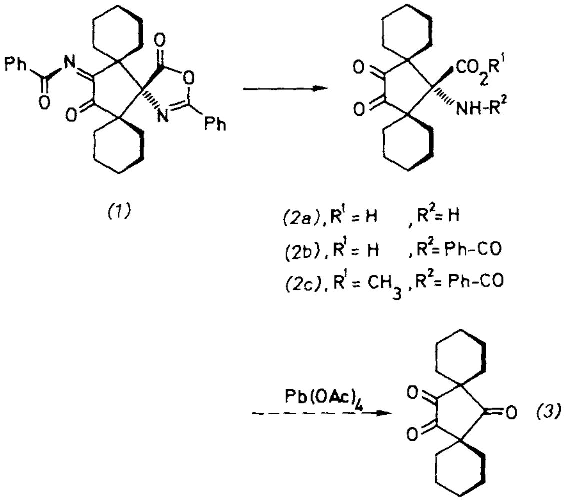
[8] *(18a–c)* were prepared analogously to *(1)→(2)*. The corresponding allyl bromides can be made classically by addition of vinylmagnesium bromide to cyclic ketones and subsequent treatment with HBr.

---

## Preparation of a Stable Diacyl Orthoester by O-Insertion on Reaction of a 1,2-Diketone with Lead Tetraacetate[**]

By *Siegfried Mohr*[*]

The readily accessible solid-state photodimer *(1)*[1a,b] should be suitable as an educt for the preparation of the previously unknown dispirotriketone *(3)*[1c]. The dioxoamino acids *(2a)* and *(2b)*, each of which are obtainable in high yield in one step from *(1)* by hydrolysis[1a,c], can be used as precursors for *(3)*. Lead tetraacetate has been used for the oxidative degradation of the amino acid function to the carbonyl group[2], but complications through the diketone group could not be ruled out, since non-enolizable 1,2-diketones can react with lead tetraacetate with O-insertion and formation of cyclic anhydrides or the corresponding esters[3].



*(1)*

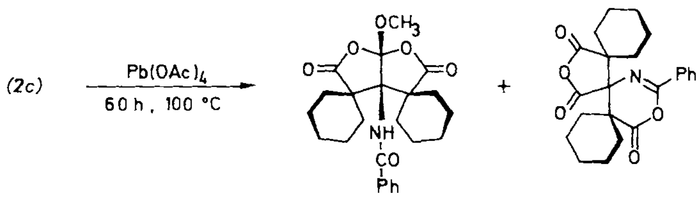
*(2a)*, $R^1 = H$, $R^2 = H$

*(2b)*, $R^1 = H$, $R^2 = Ph\text{-}CO$

*(2c)*, $R^1 = CH_3$, $R^2 = Ph\text{-}CO$

*(3)*

We first examined the reaction of the ester *(2c)*. It was found that the diketone group is seemingly stable towards an O-insertion on using lead tetraacetate; the yellow color of *(2c)* disappeared only on heating for 60 h at 100 °C in acetic acid, and the colorless oxidation products *(4)*[4] and *(5)*[5] were formed.



*(4)*, 71 %   *(5)*, 7 %

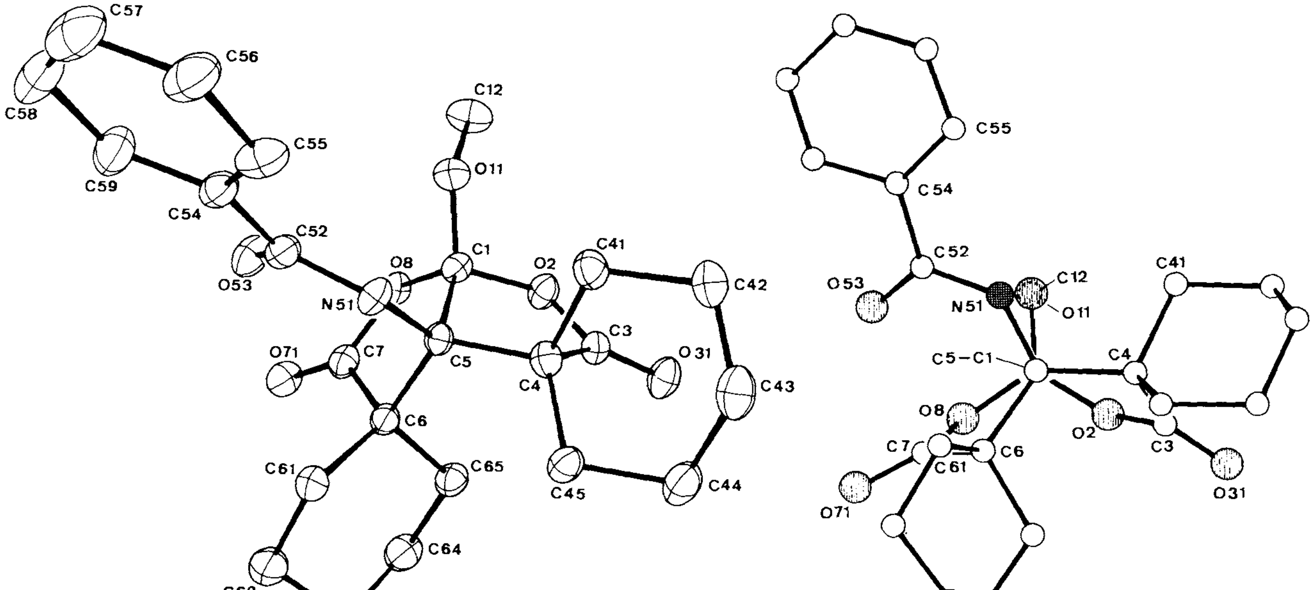


Fig. 1. a) ORTEP diagram (30%) of the diacyl orthoester *(4)*; b) parallel projection of *(4)* along the C5—C1 bond. Torsional angles: C4—C5—C1—O2 = 29.8, C6—C5—C1—O8 = 20.9, N51—C5—C1—O11 = 25.5°.—*(4)* forms colorless prisms; $a = 12.751(2)$, $b = 13.685(2)$, $c = 13.401(2)$ Å, $\beta = 108.46(1)°$, $P2_1/c$, $Z = 4$; 4541 independent reflections (4936 measured), of which 2419 with $I > 2\sigma(I)$, Enraf-Nonius CAD-4; direct methods, SHELX; $R = 0.054$.—The X-ray structure analysis was carried out in collaboration with Priv.-Doz. Dr. *C. Krüger* at the Max-Planck-Institut für Kohlenforschung, Mülheim/Ruhr.

The main product *(4)*[6] has a molecular weight of about 16 mass units higher than that of *(2c)* and the diketone group is no longer present (IR, UV)[4]. The spectroscopic data of *(4)*, however, are not completely reconcilable with

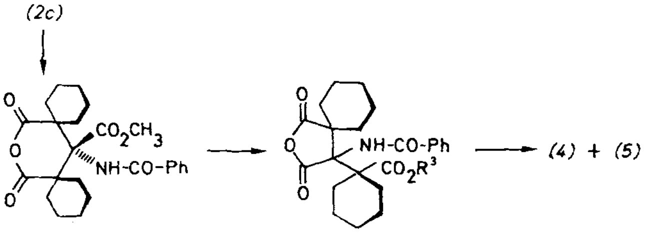
---

[*] Dr. S. Mohr
Institut für Organische Chemie der Universität
Olshausenstr. 40–60, D-2300 Kiel (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

the expected six-membered ring anhydride structure *(6)*; an unproblematical assignment of the IR and $^{13}$C-NMR spectra[4] was only possible after an X-ray structure analysis, which gave the very unusual structure of a tetracyclic dispirodiacyl orthoester (Fig. 1a) for this oxidation product. According to the $^{13}$C-NMR spectrum *(4)* has m-symmetry in solution. This is not so in the crystalline state; the central bicyclic dilactone system is twisted (Fig. 1b). The crystal structure analysis thus also confirms the similar conformation of the perhydrofuro[2,3-*b*]furans recently derived from LIS and force field calculations[7].

Acyl orthoesters are sensitive to hydrolysis; nevertheless, some monoacyl orthoesters have been isolated[8]. The diacyl orthoesters ought to be more sensitive. The unusual stability of *(4)* is possibly due to the bulkiness of the tetracyclic spiro structure.



*(6)*

*(7a)*, $R^3 = H$
*(7b)*, $R^3 = CH_3$

The colorless by-product *(5)* is formed from *(2c)* by formal O-insertion and subsequent cleavage of methanol. The given structure was confirmed by independent synthesis (cleavage of water with $Ac_2O$)[9a] from the five-membered cyclic anhydride-carboxylic acid *(7a)*[9b]. The last named reaction demonstrates that *(4)* and *(5)* could be formed *via* the anhydride esters *(6)* and *(7b)*, which have so far not been isolated.

Received: October 7, 1980 [Z 799 IE]
German version: Angew. Chem. *93*, 694 (1981)

---

[1] a) *S. Mohr*, Tetrahedron Lett. *1979*, 2461; b) *1980*, 593; c) Habilitationsschrift, Universität Kiel 1980.

[2] *R. Lohmar, W. Steglich*, Angew. Chem. *90*, 493 (1978); Angew. Chem. Int. Ed. Engl. *17*, 450 (1978).

[3] *L. Canonica, B. Danieli, P. Manitto, G. Russo*, Gazz. Chim. Ital. *100*, 1026 (1970).

[4] *(4)*, m.p. 199—201 °C (chloroform/ether), yield 71%; IR (KBr): 3380 (NH), 1790, 1770 (furanone C=O), 1672 (amide I), 1515 cm$^{-1}$ (amide II); $^{13}$C-NMR ($CDCl_3$): $\delta = 52.5$ (q, $CH_3O$), 52.5 (s, spiro-C), 73.0 (s, C—NH), 117.8 (s, $C(—O)_3$), 168.0 (s, amide C=O), 172.9 (s, furanone C=O).—A further modification is obtainable from chloroform/ether: colorless prisms of the composition $C_{24}H_{29}NO_6 \cdot 1/2(C_2H_5)_2O$, m.p. 145—148 °C, IR (KBr): 3450, 1795—1775, 1672, 1520 cm$^{-1}$.

[5] *(5)*, m.p. 180—181 °C (chloroform/methanol), yield 7%; IR (KBr): 1850, 1780 (anhydride and oxazinone C=O), 1665 cm$^{-1}$ (C=N); $^{13}$C-NMR ($CDCl_3$): $\delta = 45.4$, 54.9 (s, spirocyclohexane-C), 77.3 (s, spiro-C—N), 154.3 (s, O—C=N), 167.0, 168.6 (s, anhydride C=O), 171.3 (s, oxazinone C=O).

[6] *(4)* and *(5)* were separated by fractional crystallization from chloroform/ether and chromatography of the mother liquor with benzene/3% methanol on silica gel 60 (Merck).

[7] *Y. Kojima, N. Kato, Y. Terada*, Tetrahedron Lett. *1979*, 4667.

[8] *H. W. Post, E. R. Erickson*, J. Org. Chem. *2*, 260 (1937); *R. P. Narain, R. C. Mehrotra*, Indian J. Chem. *4*, 538 (1966); *R. C. Blume*, Tetrahedron Lett. *1969*, 1047; *J. F. W. McOmie, J. M. Blatchly*, Org. React. *19*, p. 199, 210 (1972); *R. H. DeWolfe*, Synthesis *1974*, 153; *G. Wulff, U. Schröder, W. Schmidt*, Angew. Chem. *91*, 337 (1979); Angew. Chem. Int. Ed. Engl. *18*, 309 (1979).

[9] a) *C. C. Barker*, J. Chem. Soc. *1954*, 317; b) *W. Dasch*, Diplomarbeit, Universität Kiel 1977.

---

# Trichloro(methyl)silane/Sodium Iodide, A New Regioselective Reagent for the Cleavage of Ethers[**]

By *George A. Olah, Altaf Husain, B. G. Balaram Gupta*, and *Subhash C. Narang*[*]

Since our first report in 1976[1a] and the independent studies of *Jung et al.*[1b] as well as *Voronkov et al.*[1c] numerous synthetic transformations have been carried out using iodotrimethylsilane. However, due to its hydrolytic susceptibity, its handling and storage pose difficulties. In view of this, several alternative *in situ* iodotrimethylsilane reagents or their equivalents have recently been reported. These methods include use of trimethyl(phenyl)silane/iodine[1a,2], hexamethyldisilane/iodine[3a,b,4], allyltrimethylsilane/iodine[5], 3,6-bis(trimethylsilyl)-1,4-cyclohexadiene[5] and chlorotrimethylsilane/sodium iodide[3b,c,6] reagents.

For the cleavage of ethers *(1)* in the presence of alcohols, however, all these reagents are unsuitable since the alcohols react to give the corresponding iodides. We now wish to report, however, the use of trichloromethylsilane/sodium iodide for the selective cleavage of ethers. The reagent reacts extremely readily with ethers at ambient temperatures resulting in highly regioselective cleavage (dealkylation) (Table 1). Trichloro(methyl)silane/sodium iodide was found to be more selective than chlorotrimethylsilane/sodium iodide.

Table 1. Dealkylation of ethers *(1)* by the methyltrichlorosilane/sodium iodide reagent:

$$\underset{(1)}{ROR'} + \underset{(2)}{MeSiCl_3} + \underset{(3)}{NaI} \xrightarrow[CH_3CN]{25\,^\circ C} \underset{(4)}{ROH} + \underset{(5)}{R'OH} + \underset{(6)}{RI} + \underset{(7)}{R'I}$$

| | Ether *(1)* | | *t*[h] | Products and Yields [%] [a] | | | |
|---|---|---|---|---|---|---|---|
| | R | R' | | *(4)* | *(5)* | *(6)* | *(7)* |
| *a* | $c$-$C_6H_{11}$ | $CH_3$ | 7 | 81 | 0 | 0 | — [b] |
| *b* | $c$-$C_6H_{11}$ | $C_2H_5$ | 8 | 85 | 0 | 0 | — [b] |
| *c* | $c$-$C_6H_{11}$ | $PhCH_2$ | 4 | 90 | 0 | 0 | 85 |
| *d* | $c$-$C_6H_{11}$ | $CPh_3$ | 4 | 75 | 0 | 0 | 100 [c] |
| *e* | $c$-$C_6H_{11}$ | THP [d] | 3 | 88 | 0 | 0 | — [b] |
| *f* | $n$-$C_3H_7$—CH—$n$-$C_4H_9$ | $CH_3$ | 10 | 85 | 0 | 0 | — [b] |
| *g* | $n$-$C_3H_7$—CH—$n$-$C_4H_9$ | $C_2H_5$ | 8 | 75 | 0 | 0 | — [b] |
| *h* | $n$-$C_9H_{19}$ | $CH_3$ | 9 | 100 | 0 | 0 | — [b] |
| *i* | $n$-$C_9H_{19}$ | $C_2H_5$ | 36 | 57 | — [b] | 43 | — [b] |
| *j* | $n$-$C_{11}H_{23}$ | $C_2H_5$ | 36 | 55 | — [b] | 45 | — [b] |
| *k* | $n$-$C_{11}H_{23}$ | $CPh_3$ | 3 | 87 | 0 | 0 | 100 [c] |
| *l* | $c$-$C_7H_{13}CH_2$ | $C_6H_5CH_2$ | 4 | 100 | 0 | 0 | 95 |
| *m* | $c$-$C_7H_{13}CH_2$ | THP [d] | 16 | 98 | 0 | 0 | — [b] |
| *n* | $(CH_3)_2C$—$n$-$C_7H_{15}$ | $CH_3$ | 6 | 0 | — [b] | 100 | 0 |
| *o* | 3-stigmastanyl | $CH_3$ | 16 | 97 | 0 | 0 | — [b] |
| *p* | 3-stigmastanyl | $C_2H_5$ | 36 | 86 | 0 | 0 | — [b] |

[a] Isolated yield of the product. [b] Not isolated. [c] Isolated as a mixture of triphenylmethanol and triphenylmethane [8]. [d] THP = tetrahydropyranyl.

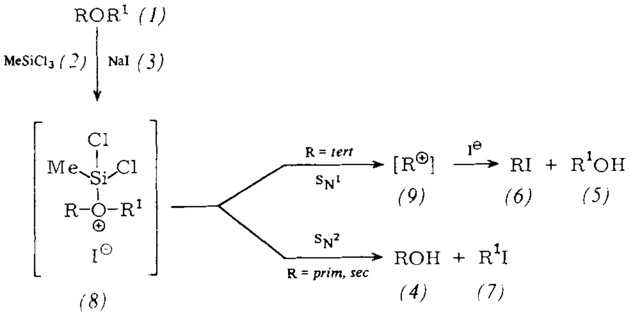
From Table 1, it is clear that for methyl ethers *(1a, f, h, o)* demethylation was the major reaction, affording alcohols as the sole products, provided the alkyl groups are either primary or secondary. In contrast, when as in *(1n)* alkyl group is tertiary the resulting cleavage product was

---

[*] Prof. Dr. G. A. Olah, A. Husain, Dr. B. G. B. Gupta, Dr. S. C. Narang
Hydrocarbon Research Institute
Department of Chemistry, University of Southern California
University Park, Los Angeles, California, 90007 (USA)

[**] Part 96 in the series: Synthetic Methods and Reactions. This work was supported by the National Institutes of Health and National Science Foundation.—Part 95, see *G. A. Olah, B. G. B. Gupta, A. P. Fung*, Synthesis, in press.

solely iodide. This can be rationalized on the basis of the increased Lewis acidity of trichloro(methyl)silane compared to that of chlorotrimethylsilane. Thus, in the case of *tert*-alkyl methyl ethers, the reaction predominantly takes place *via* an $S_N1$-pathway through a carbocation intermediate *(9)* producing iodides *(6)* as the major products. The *prim-* and *sec*-alkyl methyl ethers, however, prefer an $S_N2$-pathway resulting in alcohols *(4)* as the major products (Scheme 1).



Scheme 1. *(6)* or *(4)* are the major products.

Benzyl ethers *(1c, l)*, trityl ethers *(1d, k)* as well as tetrahydropyranyl ethers *(1e, m)* also undergo regioselective cleavage at ambient temperature to give quantitative yields of alcohols (Table 1). Ethyl ethers are, however, depending on the nature of the alkyl group cleaved with varying yields of alcohols *(4)* and iodides *(6)*. Thus, *sec*-alkyl ethyl ethers *(1b, g, p)* were cleaved regioselectively to the corresponding alcohols. But *prim*-alkyl ethyl ethers *(1i, j)* gave approximately 1 : 1-mixtures of alcohols and iodides (Table 1).

We have also found that the trichloro(methyl)silane/sodium iodide reagent can be used for the selective cleavage of ethers in the presence of alcohol or ester functions. Since this versatile highly regio- and stereoselective, mild and inexpensive reagent is easy to handle and is free of some of the difficulties connected with iodotrimethylsilane[7] reagents, it should find substantial synthetic use.

### *Experimental: General Procedure*

Trichloro(methyl)silane (1.8 g, 12 mmol) and *(1)* (10 mmol) are added, successively, with continuous stirring under a nitrogen atmosphere to a solution of NaI (1.8 g, 12 mmol) in dry acetonitrile (20 mL). The reaction mixture is monitored by thin layer chromatography (hexane) and $^1H$-NMR, and is then quenched with water, extracted with ether and the ethereal extract washed with aqueous solutions of $Na_2S_2O_3$ and NaCl. The ethereal extract is dried over anhydrous $Na_2SO_4$ and the solvent evaporated to yield the crude product, which is further purified by crystallization or distillation.

Received: August 11, 1980 [Z 801 IE]
German version: Angew. Chem. *93*, 705 (1981)

CAS Registry numbers:
*(1a)*, 931-56-6; *(1b)*, 932-92-3; *(1c)*, 16224-09-2; *(1d)*, 20705-40-2; *(1e)*, 709-83-1; *(1f)*, 77067-56-2; *(1g)*, 77067-57-3; *(1h)*, 7289-51-2; *(1i)*, 16979-32-1; *(1j)*, 78371-01-4; *(1k)*, 78371-02-5; *(1l)*, 78371-03-6; *(1m)*, 78371-04-7; *(1n)*, 78371-05-8; *(1o)*, 78371-06-9; *(1p)*, 78371-07-0; *(2)*, 75-79-6; *(3)*, 768-82-5; *(4a)*, 108-93-0; *(4f)*, 589-62-8; *(4h)*, 143-08-8; *(4j)*, 112-42-5; *(4l)*, 4448-75-3; *(4o)*, 78419-36-0; *(6i)*, 4282-42-2; *(6j)*, 4282-44-4; *(6n)*, 78371-08-1; *(7c)*, 620-05-3; *(7d)*, 2206-53-3.

---

[1] a) *T. L. Ho, G. A. Olah*, Angew. Chem. *88*, 847 (1976); Angew. Chem. Int. Ed. Engl. *15*, 774 (1976); b) *M. E. Jung, M. A. Lyster*, J. Am. Chem. Soc. *99*, 968 (1977).

[2] *T. L. Ho, G. A. Olah*, Proc. Natl. Acad. Sci. USA *75*, 4 (1978).

[3] a) *G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra*, Angew. Chem. *91*, 648 (1979); Angew. Chem. Int. Ed. Engl. *18*, 612 (1979); b) J. Org. Chem. *44*, 1247 (1979); c) Synthesis *1979*, 61.

[4] *D. E. Seitz, L. Ferreira*, Synth. Commun. *9*, 931 (1979).

[5] *M. E. Jung, T. A. Blumenkopf*, Tetrahedron Lett. *1978*, 3657.

[6] *T. Morita, Y. Okamoto, H. Sakurai*, J. Chem. Soc. Chem. Commun. *1978*, 874.

[7] *M. E. Jung, M. A. Lyster*, J. Org. Chem. *42*, 3761 (1977).

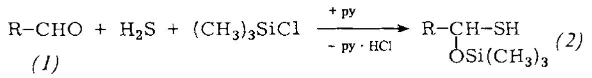
[8] A mixture of triphenylmethanol and triphenylmethane was obtained in these cases, presumably due to the facile hydrolysis and reduction of trityl iodide formed during the reaction. For deoxygenation of triphenylmethanol using diiododimethylsilane, see *W. Ando, M. Ikeno*, Tetrahedron Lett. *1979*, 4941.

---

## Synthesis of α-Trimethylsiloxythiolene and α,α'-Bis(trimethylsiloxy) Disulfides[**]

By *T. Aida, T.-H. Chan*, and *David N. Harpp*[*]

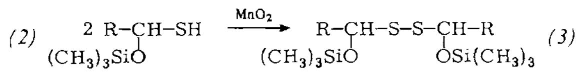
Recently, we reported that α-trimethylsiloxy sulfides provided high-yield access to α-iodosulfides and vinyl sulfides under mild conditions[1]. This success, and the possibility of developing novel α-functionalized sulfur compounds prompted us to examine the preparation and chemistry of α-trimethylsiloxythiols *(2)*. We wish to report that the title compounds can be prepared in good yield by an analogous method from the aldehyde (1), hydrogen sulfide and chlorotrimethylsilane in the presence of pyridine.



$$\underset{(1)}{R-CHO} + H_2S + (CH_3)_3SiCl \xrightarrow[-\,py\cdot HCl]{+\,py} R-\underset{OSi(CH_3)_3}{CH}-SH \quad (2)$$

A number of α-trimethylsiloxythiols *(2)* have been prepared by this method and are shown in Table 1. These compounds have a powerful stench, similar to that of an ordinary thiol and are reasonable stable. No decomposition is observed at periods up to 2—3 months storage under dry nitrogen in the refrigerator.

These siloxythiols *(2)* can be oxidized in high yield by $MnO_2$ at room temperature to the corresponding disulfides *(3)* (Table 1). These compounds are isolated as a 1 : 1 mixture of *meso-* and DL-forms and do not decompose after several months in the refrigerator. To our knowledge there are no examples of pure stable, α-functionalized disulfides in the literature.



$$(2) \quad 2\,R-\underset{(CH_3)_3SiO}{CH}-SH \xrightarrow{MnO_2} R-\underset{(CH_3)_3SiO}{CH}-S-S-\underset{OSi(CH_3)_3}{CH}-R \quad (3)$$

The compounds *(2)*, like other thiols, add photochemically to olefinic compounds affording the corresponding α-trimethylsiloxy sulfides thus providing an alternative route to vinyl sulfides[1,3]. *(4a)* and *(4b)* are typical examples.

It should be noted that *(4a)* is formed regiospecifically with an isolated yield of 88%.

---

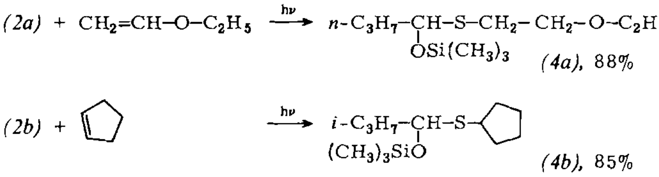
[*] Prof. T.-H. Chan, Prof. D. N. Harpp, T. Aida
Department of Chemistry, McGill University
Montreal, Quebec, Canada H3A 2K6

[**] This work was supported by the Natural Science and Engineering Research Council of Canada and the Ministry of Education, Government of Quebec.

Table 1. Preparation of α-trimethylsiloxythiols *(2)* and α,α'-bis(trimethylsiloxy) disulfides *(3)*.

| R | Comp. | Yield [%] [a] | B.p. [°C/Torr] | $^1$H-NMR ($\delta$, TMS, in CDCl$_3$) | Compd. | Yield [%] [b] | $^1$H-NMR ($\delta$, TMS, in CDCl$_3$) |
|---|---|---|---|---|---|---|---|
| $n$-C$_3$H$_7$ | *(2a)* | 73 | 46/8 | 5.03 (dt, $J=8$ Hz; $J=5$ Hz, 1 H), 2.06 (d, $J=7$ Hz, 1 H), 2.0—1.1 (m, 4 H), 0.92 (br. t, 3 H), 0.18 (s, 9 H) | *(3a)* | 84 | 4.82, 4.76 (each t, $J=6$ Hz, 2 H), 2.05—1.15 (m, 8 H), 0.90 (t with fine structure, 6 H), 0.20 (s, 18 H) |
| $i$-C$_3$H$_7$ | *(2b)* | 80 | 42/8 | 4.83 (dd, $J=8$ Hz; $J=5$ Hz, 1 H), 2.2—1.6 (m, 1 H), 1.90 (d, $J=8$ Hz, 1 H) 0.98 (d, $J=6$ Hz, 6 H), 0.18 (s, 9 H) | *(3b)* | 82 | 4.74, 4.65 (each d, $J=5$ Hz, 2 H), 2.42—1.87 (m, 2 H), 1.00 (dd, $J=7$ Hz, 12 H), 0.20 (s, 18 H) |
| $t$-C$_4$H$_9$ | *(2c)* | 75 | 61/15 | 4.72 (d, $J=7$ Hz, 1 H), 1.75 (d, $J=7$ Hz, 1 H), 0.95 (s, 9 H), 0.16 (s, 9 H) | | | |
| $c$-C$_6$H$_{11}$ | *(2d)* | 83 | 64/0.1 | 4.80 (dd, $J=7$ Hz; $J=5$ Hz, 1 H), 1.90 (d, $J=7$ Hz, 1 H), 2.2—0.9 (m, 11 H), 0.17 (s, 9 H) | *(3d)* | 80 | 4.70, 4.58 (each d, $J=5$ Hz, 2 H), 2.15—0.80 (m, 22 H), 0.18 (s, 18 H) |
| C$_6$H$_5$ | *(2e)* | 25, 48 [c] | 63/0.25 | 7.7—7.2 (m, 5 H), 6.14 (d, $J=7$ Hz, 1 H), 2.50 (d, $J=7$ Hz, 1 H), 0.20 (s, 9 H) | *(3e)* | 75 | 7.65—7.10 (m, 10 H), 5.78, 5.52 (each s, 2 H), 0.15 (s, 18 H) |
| CH$_3$CH═CH | *(2f)* | 30 [d] | 50/7 | 5.80—5.20 (m, 3 H), 2.20 (d, $J=7$ Hz, 1 H), 1.8—1.6 (m, 3 H), 0.20 (s, 9 H) | | | |

[a] Isolated yield. *(2)* decompose upon gas chromatography and show no molecular ion in the mass spectrum; the (CH$_3$)$_3$SiO group is cleaved first. [b] Isolated yield. *meso*- and DL-forms could not be separated by gas chromatography. *(3)* shows no molecular ion in the mass spectrum. [c] Determined by $^1$H-NMR spectroscopy. [d] The $^1$H-NMR indicates additional products. *(2f)* was fully polymerized after 13 h at room temperature.



$$(2a) + \mathrm{CH_2{=}CH{-}O{-}C_2H_5} \xrightarrow{h\nu} n\text{-}\mathrm{C_3H_7{-}\underset{OSi(CH_3)_3}{CH}{-}S{-}CH_2{-}CH_2{-}O{-}C_2H_5}$$

*(4a)*, 88%

*(2b)* +

$$\xrightarrow{h\nu} i\text{-}\mathrm{C_3H_7{-}\underset{(CH_3)_3SiO}{CH}{-}S{-}}$$

*(4b)*, 85%

*General Procedure*

H$_2$S is bubbled into a dry dichloromethane solution (150 mL) of *(1)* (0.07 mol), (CH$_3$)$_3$SiCl (0.10 mol) and pyridine (0.10 mol), and the solution vigorously stirred until no further gas is absorbed; the solution temperature is maintained below 15 °C. The solution is then stirred for 2 h at room temperature. After addition of dry pentane (150 mL), the mixture is cooled to −78 °C and the pyridinium chloride collected by filtration. The thiol *(2)* is distilled under reduced pressure.

Received: November 18, 1980 [Z 803 IE]
German version: Angew. Chem. *93*, 706 (1981)

---

[1] *T. Aida, D. N. Harpp, T. H. Chan*, Tetrahedron Lett. *1980*, 3247. *T. H. Chan, B. S. Ong, ibid. 1976*, 319.

[2] A solution of CH$_2$Cl$_2$ (2.0 ml), *(2)* (0.5 mol) and olefin (1.0 mol) was sealed under dry nitrogen into a Pyrex tube. After 12 h irradiation at 5 °C (General Electric Co., Model SHK-2,275 W), *(4)* was isolated by column chromatography (silica gel, hexane) or preparative GC. The yield was determined by GC using an internal standard. $^1$H-NMR (CDCl$_3$): *(4a)*: $\delta=4.90$ (t, $J=6$ Hz, 1 H), 3.50 (q with fine structure, $J=6$ Hz, 4 H), 2.75 (t, $J=6$ Hz, 2 H), 2.0–0.8 (m, 7 H), 1.22 (t, $J=1$ Hz, 3 H), 0.18 (s, 9 H); *(4b)*: $\delta=4{,}70$ (d, $J=6$ Hz, 1 H), 3.45–2.9 (m, 1 H, 2.3–1.0 (m, 9 H), 1.00 (d, $J=7$ Hz, 6 H), 0.17 (s, 9 H).

[3] For alternative routes to α-trimethylsiloxy sulfides, see *D. J. Ager, R. C. Cookson*, Tetrahedron Lett. *1980*, 1677; *P. J. Kocienski, ibid. 1980*, 1559.

---

## Hexameric Molybdenum Tetrachloride

By *Ulrich Müller*[*]

*Dedicated to Professor Josef Goubeau on the occasion of his 80th birthday*

Two modifications of molybdenum tetrachloride have so far been described in the literature: α-MoCl$_4$, which is probably made up of linear chains of octahedra sharing edges[1], and β-MoCl$_4$, which has been described as a layer lattice in which three Mo atoms are assumed to statistically occupy four positions with formation of cationic and anionic regions, [Mo$_2$Cl$_6$]$^{2+}$ and [MoCl$_6$]$^{2-}$, respectively[2]. However, recent theoretical studies on the possible structures of tetrahalides[3] led to a more detailed determination of the β-MoCl$_4$ structure.

Crystals of β-MoCl$_4$, which were prepared under exactly the same conditions as described earlier[2], exhibit an X-ray diffraction pattern of sharp reflections, strong diffuse lines, and weak diffuse lines which indicate the presence of a one-dimensional disorder. If the intensity maxima on the strong diffuse lines are treated as sharp reflections then these, together with the actual sharp reflections indicate the unit cell described earlier (trigonal, $a=605$, $c=1172$ pm)[2]. In disordered crystals the actual structure can only be determined if the intensities in the diffuse lines are fully investigated[4]; the maxima on them cannot be simply treated as sharp reflections. The sharp reflections alone are inadequate for a structure determination, they afford only a statistically averaged structural model[4]. In the case of β-MoCl$_4$ even the weak diffuse lines must also be taken into consideration; they require a doubling up of the lattice constants $a$ and $b$ to $a=b=1209$ pm.

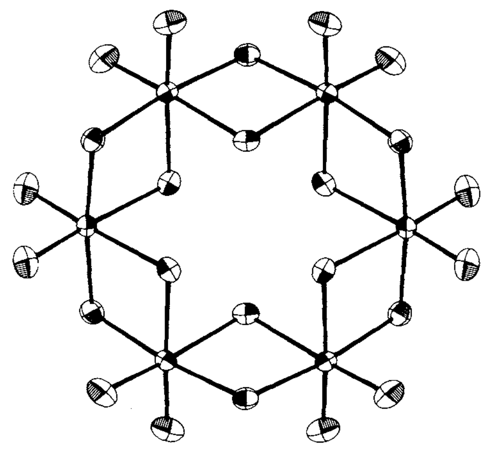


Fig. 1. (MoCl$_4$)$_6$ molecule in β-MoCl$_4$; ellipsoids of thermal vibration for 68% probability at 21 °C.

---

[*] Prof. Dr. U. Müller
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

A comparison of these lattice constants with the values expected for the theoretically predicted structural possibilities[3] suggests the likelihood of a structure type containing cyclic $(MoCl_4)_6$ molecules. An analysis of the intensities on the diffuse lines according to a recently described method[5] confirms this (refinement to $R=7.2\%$ for 226 measured points on diffuse lines and $R=2.8\%$ for 155 sharp reflections).

Our structural model shows that β-$MoCl_4$ is made up of hexameric cyclic molecules $(MoCl_4)_6$ (Fig. 1). The bond lengths are: Mo—$Cl_{terminal}$ 220, Mo—$Cl_{bridge}$ 243 and 251 pm. The molecules are arranged in layers (parallel to the plane of the picture in Figure 1. The stacking of the layers is disordered, but in such a way that the Cl atoms assume an hexagonal closest-packed arrangement. The pairwise closing up of metal atoms between adjacent octahedra, which is often observed in compounds of metals with electron configuration $d^1$ and $d^2$, is not apparent here, the Mo···Mo distances of 367 pm are too large for any notable interactions between the metal atoms; this is consistent with the known magnetic properties[2], which indicate a virtually undistorted $d^2$-configuration.

Although molybdenum tetrachloride has already been known for some time and has been the subject of repeated investigations, nothing has previously been mentioned about its ability to form hexameric molecules. There is as yet no other such example of a structure of this kind.

Received: January 29, 1981 [Z 822 IE]
German version: Angew. Chem. *93*, 697 (1981)

CAS Registry number:
$(MoCl_4)_6$, 78456-38-9.

---

[1] *D. L. Kepert, R. Mandyczewsky*, Inorg. Chem. *7*, 2091 (1968).
[2] *H. Schäfer, H. G. von Schnering, J. Tillack, F. Kuhnen, H. Wöhrle, H. Baumann*, Z. Anorg. Allg. Chem. *353*, 281 (1967).
[3] *U. Müller*, Acta Crystallogr. *B 37*, 532 (1981).
[4] *H. Jagodzinski*, Acta Crystallogr. *2*, 201, 209 (1949).
[5] *U. Müller*, Acta Crystallogr. *A 35*, 957 (1979).

# Gas Chromatographic Separation of Carbohydrate Enantiomers on a New Chiral Stationary Phase

By *Wilfried A. König, Ingrid Benecke*, and *Hagen Bretting*[*]

Micromethods for the configurational analysis of low molecular weight chiral compounds are essential for the structural elucidation of natural products[1,2].

While the problem of the gas chromatographic determination of the configuration of the constituents of peptides and proteins seems to be solved[2], this is not the case with the constituents of polysaccharides. Since in nature sugars occur rather more frequently than amino acids in both configurations[3], a simple gas chromatographic procedure would be of interest for their analysis.

As early as 1968 *Pollock* and *Jermany* suggested a method involving oxidation of aldoses to aldonic acids, esterification with a chiral alcohol to diastereomeric aldonic acid esters and separation of the acetylated derivatives[4]. In a similar procedure the preparation of diastereomeric derivatives was achieved by glycosidation with (−)-2-butanol and separation of the trimethylsilylated derivatives on glass capillary columns[5]. In addition to the difficulties involved with the derivatization, the quantitative determination of enantiomers *via* formation of diastereomeric derivatives suffers from a systematic error arising from the incomplete purity of the chiral reagents.

We have now for the first time prepared a temperature-stable chiral stationary phase which allows the separation of volatile derivatives of carbohydrate enantiomers. This involves the saponification of methyl(cyanoethyl)silicone XE-60[6] with alkali and coupling the carboxylic groups formed to L-valine-(*S*)-α-phenylethylamide by conventional methods. Glass capillaries were coated with this modified polymer and trifluoroacetylated sugars[7] or their methyl glycosides separated. Columns prepared according to this procedure did not exhibit a reduction in their separation efficiency after continuous operation at temperatures up to 180 °C over several weeks.

Trifluoroacetylation of sugars (TFA = trifluoracetyl) resulted in an isomeric mixture of α- and β-furanosides and α- and β-pyranosides, which were identified by GC/MS-investigation[7]. The TFA-methyl glycosides (prepared by reaction of the sugars with methanolic 1.5 N HCl at 100 °C and subsequent trifluroacetylation) formed isomeric mixtures corresponding in composition to literature data[8] and were identified by measurement of their peak areas. The results are presented in Table 1 and in some examples in Figure 1. The TFA-groups appear to be essential for the separation, since trimethylsilyl derivatives of the sugars with comparable volatility are not separated.

Table 1. Gas chromatographic enantiomer separation of carbohydrates on a glass capillary column coated with XE-60-L-valine-(*S*)-α-phenylethylamide (TFA = trifluoroacetyl, P = pyranoside, F = furanoside). For conditions see Figure 1.

| Sugar | Separation Factor α/Column Temperature [°C] | | | |
|---|---|---|---|---|
| | TFA-Derivative | | TFA-Methyl Glycoside | |
| Glucose | α-(P) | 1.071/140 | α-P | 1.032/120 |
| | (F) | 1.044/140 | β-P | 1.035/120 |
| | (F) | 1.031/140 | | |
| | β-(P) | 1.140/140 | | |
| Mannose | α-(P) | 1.036/140 | α-P | 1.053/120 |
| | (F) | 1.045/140 | β-P | 1.084/120 |
| | β-(P) | 1.247/140 | | |
| Galactose | α-(P) | 1.019/140 | β-F | 1.010/120 |
| | (F) | 1.019/140 | α-F | 1.044/120 |
| | β-(P) | 1.045/140 | α-P | 1.049/120 |
| | (F) | 1.029/140 | β-P | 1.089/120 |
| Xylose | β-(P) | 1.030/100 | — | — |
| Arabinose | [a] | 1.028/100 | α-F | 1.019/100 |
| | [a] | 1.017/100 | α-P | 1.023/100 |
| | [a] | 1.048/100 | β-P | 1.046/100 |
| | [a] | 1.026/100 | | |
| Fucose | | — | | — |
| | | — | | — |
| | [a] | 1.035/100 | [a] | 1.014/100 |
| | | | [a] | 1.046/100 |

[a] Designation uncertain.

The order of elution of enantiomers is not identical in all the examples investigated. In the case of TFA-derivatives of glucose and mannose and in that of the TFA-methyl glycosides, the L-enantiomers eluted before the D-enantiomers: the same order was observed for the first three isomeric pairs of TFA-arabinose, however, for the pair

---

[*] Prof. Dr. W. A. König, Dipl.-Chem. I. Benecke
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)
Dr. H. Bretting
Zoologisches Institut und Zoologisches Museum der Universität
Martin-Luther-King-Platz 3, D-2000 Hamburg 13 (Germany)

with the longest retention time the order of elution is reversed (Fig. 1).

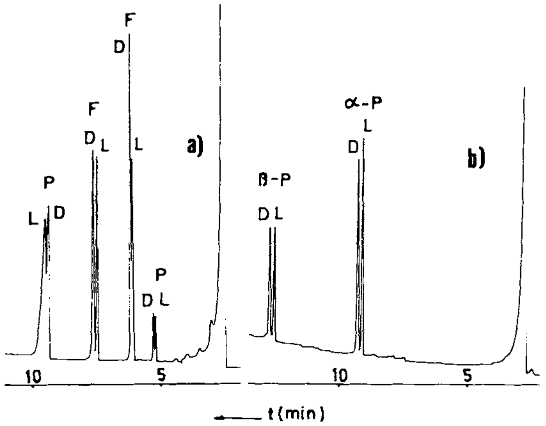


Fig. 1. Separation of carbohydrate enantiomers. a) TFA-derivatives of arabinose isomers, b) TFA-derivatives of α- and β-methylpyranosides of glucose. Glass capillary column (borosilicate glass, 40 m, 0.2 mm inner diameter) with XE-60-L-valine-(*S*)-α-phenylethylamide. $T = 100\,^\circ C$, temperature program 3 °C/min. (Carlo Erba 2101 A gas chromatograph, carrier gas: 0.7 bar $H_2$.) P = pyranoside, F = furanoside.

For galactose and fucose (6-deoxygalactose), in any case, the D-enantiomers are eluted prior to the L-enantiomers. The TFA-methyl glycosides of xylose (α- and β-pyranoses) are not separated. In the TFA-derivatives only one pair of enantiomers is separated (β-pyranoses). As in the case of glucose the L- is eluted before the D-form.

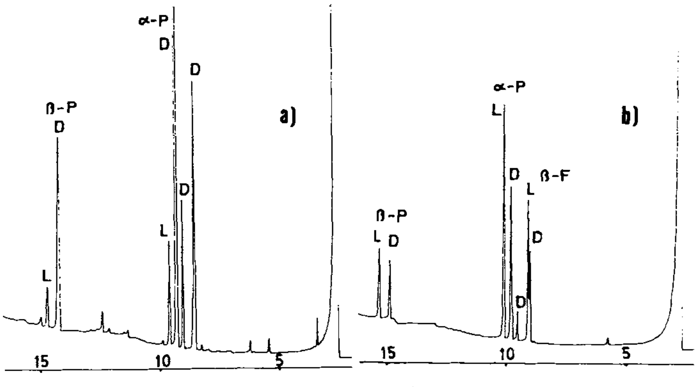


Fig. 2. Separation of TFA-methyl galactoside enantiomers: a) acid hydrolysate of *Helix pomatia* galactan, b) reference mixture of D- and L-galactose derivatives. For conditions, see Figure 1.

The utility of the new method may be demonstrated by the investigation of a hydrolysate of the galactan of the snail *Helix pomatia*. This high molecular, branched polysaccharide consists of D- and L-galactose. The chromatographic separation of the TFA-methyl glycosides and the electronic integration of peak areas of the α- and β-pyranosides, which are well separated (Fig. 2), showed that the galactan contains 14.4% L-galactose. This result is in agreement with measurements of the optical rotation by *Bell* and *Baldwin*[9].

Received: February 24, 1981 [Z 805 IE]
German version: Angew. Chem. *93*, 688 (1981)

---

[1] *W. A. König, S. Sievers, U. Schulze*, Angew. Chem. *92*, 935 (1980); Angew. Chem. Int. Ed. Engl. *19*, 910 (1980); *W. A. König, S. Sievers*, J. Chromatogr. *200*, 189 (1980).

[2] *E. Gil-Av, B. Feibush, R. Charles-Sigler* in *A. B. Littlewood:* Gas Chromatography 1966, Institute of Petroleum, London 1967, p. 227; *W. A. König, G. J. Nicholson*, Anal. Chem. *47*, 951 (1975); *U. Beitler, B. Feibush*, J. Chromatogr. *123*, 149 (1976); *S. Weinstein, B. Feibush, E. Gil-Av, ibid. 126*, 97 (1976); *H. Frank, G. J. Nicholson, E. Bayer*, Angew. Chem. *90*, 396 (1978); Angew. Chem. Int. Ed. Engl. *17*, 363 (1978).

[3] *J. Stanek, M. Cerny, J. Kocourek, J. Pacák:* The Monosaccharides, Academic Press, New York 1963.

[4] *G. E. Pollock, D. A. Jermany*, J. Gas Chromatogr. *6*, 412 (1968); J. Chromatogr. Sci. *8*, 296 (1970).

[5] *G. J. Gerwig, J. P. Kamerling, J. F. G. Vliegenthart*, Carbohydr. Res. *62*, 349 (1978).

[6] Supplier, Macherey, Nagel & Co., D-5160 Düren (Germany).

[7] *W. A. König, H. Bauer, W. Voelter, E. Bayer*, Chem. Ber. *106*, 1905 (1973).

[8] *J. Lehmann:* Chemie der Kohlenhydrate, Thieme, Stuttgart 1976, p. 94.

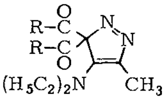
[9] *D. J. Bell, E. Baldwin*, J. Chem. Soc. *143*, 125 (1941).

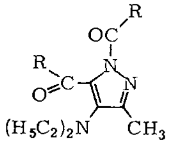
## Reaction of Dibenzoyldiazomethane with 1-Diethylaminopropyne

By *Rolf Huisgen, Maria Pilar Bosch Verderol, Alfred Gieren*, and *Viktor Lamm*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

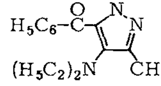
Dimethyl diazomalonate combines with 1-diethylaminopropyne at room temperature to give the 3*H*-pyrazole derivative *(1)*, which is converted into the pyrazole-1,5-dicarboxylic ester *(3)* by a 1,5-sigmatropic shift of an ester group ($t_{1/2} \sim 30$ days at 25 °C in $CDCl_3$)[1]; this aromatization of 3*H*-pyrazoles is known as the van-Alphen-Hüttel rearrangement[2].



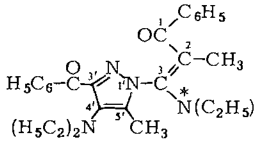


*(1)* R = $OCH_3$ *(3)*
*(2)* R = $C_6H_5$ *(4)*

As expected, the cycloaddition of dibenzoyldiazomethane to the same ynamine is slower, and the ensuing sigmatropic shift faster, than in the preceding example. The reaction of equimolar amounts in benzene (8 days, 20 °C, chromatography on silica gel) yielded 66% *(4)* (orange yellow needles, m.p. 74—75 °C) and 13% of a yellow 1:2 adduct (m.p. 84—85 °C); the primary adduct *(2)* was not detected. *Different* signals for ketone carbonyl ($\delta = 188.1$) and amide carbonyl C-atoms ($\delta = 165.2$) appear in the $^{13}C$-NMR spectrum ($CDCl_3$) of *(4)*, and the chemical shifts of the ring carbon atoms ($\delta = 152.1$, 137.4, 136.6) correspond to those of *(3)* ($\delta = 149.3$, 134.4, 130.9). The carbonyl frequencies of *(4)* absorb at 1670 and 1697 $cm^{-1}$. The aminolysis of *(4)* in refluxing diethylamine produced *(5)* and *N,N*-diethylbenzamide quantitatively.



*(5)*



*(6)*

---

[*] Prof. Dr. R. Huisgen, Dr. M. P. Bosch Verderol
Institut für Organische Chemie der Universität
Karlstr. 23, D-8000 München 2 (Germany)
Dr. habil. A. Gieren, Dipl.-Phys. V. Lamm
Max-Planck-Institut für Biochemie
Abteilung für Strukturforschung I
D-8033 Martinsried (Germany)

The pyrazole *(4)* reacted with 1-diethylaminopropyne to afford the above-mentioned 1 : 2 adduct (20 days, benzene, 20 °C, 70% yield), which was identified by an X-ray structure analysis (Fig. 1) as the vinylog *(6)* of a 1,3-dibenzoylpyrazole.

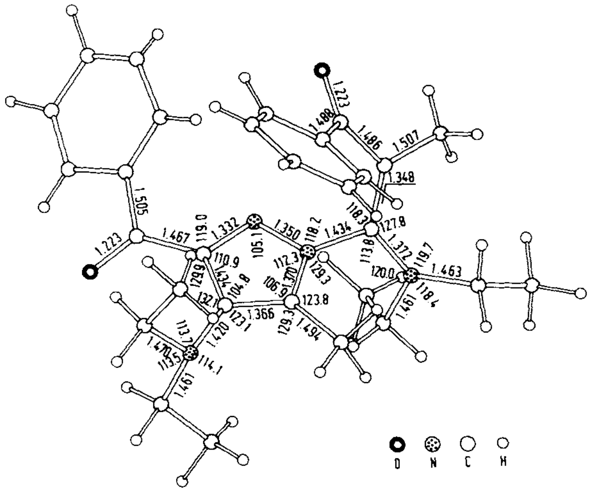
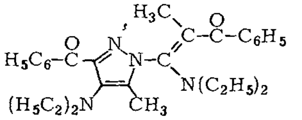
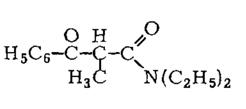


Fig. 1. Structure of 3-(3-benzoyl-4-diethylamino-5-methyl-1-pyrazolyl)-3-diethylamino-2-methyl-1-phenyl-2-propen-1-one *(6)* in the crystal. Bond lengths [Å] and angles [°] averaged between the two molecules of the asymmetric unit (σ of the non-averaged values: 0.002—0.006 Å and 0.2—0.3°) [3].

The $^1$H-NMR spectrum ($CDCl_3$) of this compound [$\delta = 2.09$ (s, $CH_3$), 2.16 (s, $CH_3$), 0.62, 2.78 (t and q, resp., ring-$N(C_2H_5)_2$), 1.18, 3.05 (t and q, resp., $^*N(C_2H_5)_2$] affords evidence of the stronger alkylideneammonium character of the amine function in the side chain due to β-ketoenamine resonance. When the solution of *(6)* in $CDCl_3$ was kept for several days at 20 °C, an equilibrium with 17% of a rotameric form was established in which the methyl singlets ($\delta = 1.72$ and 2.35) show a greater difference than in *(6)*. After slow evaporation, crystalline *(6)* was reisolated completely. A *cis,trans* isomerization, *(6)* $\rightleftharpoons$ *(7)*, is probable. Mild acid hydrolysis of the enamine *(6)* (two phases, ether/2 N HCl) furnished 95% *(5)* and 96% of *N,N*-diethyl α-benzoylpropionamide *(8)*.



*(7)*

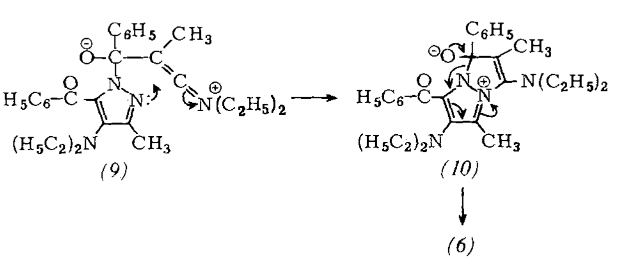


$$H_5C_6-\overset{O}{\overset{\|}{C}}-\underset{H_3C}{\overset{H}{C}}-C\genfrac{}{}{0pt}{}{\nearrow O}{\searrow N(C_2H_5)_2}$$

*(8)*

How does the insertion of the ynamine with concomitant rearrangement proceed in the reaction of *(4)*? Acylazoles are acylating reagents. The addition of the nucleophilic ynamine to give the zwitterion *(9)* is followed by a rearrangement to *(6)* *via* *(10)* as a conceivable further intermediate.

Insertions of ynamines into acylating reagents have been observed, *e.g.*, with phosgene[4] or diketene[5]. The migration of the side chain to the second pyrazole-N-atom in the conversion *(4)*→*(6)* presents a specialty. It was recently reported that the rearrangement of *(1)* into the corresponding 1,3-dicarboxylic ester is catalyzed by phenyl isothiocyanate or carbon disulfide[6]; a "conducted tour" mechanism presents a certain analogy to *(9)*→*(6)*.



The bond lengths of the planar pyrazole ring (Fig. 1) correspond to values between single and double bonds with a predominance of structure *(6)*. Neighboring substituents are twisted up to 6° against each other as a result of intramolecular van der Waals interactions. The conjugation of the π-substituents with the heterocycle is weakened by sterically enforced torsions. Whereas the bond plane of the 3′-carbonyl is only slightly twisted *versus* the pyrazole ring, the conjugation of the 4′-diethylamino group has vanished; the orbital of the lone pair is located in the ring plane and the nitrogen is pyramidal. The β-ketoenamine side chain is twisted by 52° at C3—N1′; its planarity is disturbed at C2—C3 only by 15°, but at C3—N* and C1—C2 by 43° and 45°, respectively. The shortening of the C3—N* bond to 1.372 Å is indicative of the conjugative coupling in the vinylogous carboxamide system, although the 5′-methyl enforces a substantial torsion of the mentioned bond.

Finally, structure *(6)* proves the orientation in the 1,3-dipolar cycloaddition which leads to *(2)* (the analogous structure *(1)* was established by chemical methods[1]); it is connected with the direction of addition, which is accompanied by a maximal energy gain in the HOMO-LUMO interactions (within the framework of the MO perturbation treatment of the concerted cycloaddition). The same orientation has been observed in the addition of α-diazocarbonyl compounds to enamines[7], whereas the addition to olefinic or acetylenic carboxylic esters takes place in the opposite direction[1].

Received: March 2, 1981 [Z 808 IE]
German version: Angew. Chem. *93*, 710 (1981)

CAS Registry numbers:
*(2)*, 78354-85-5; *(4)*, 78354-86-6; *(5)*, 78354-87-7; *(6)*, 78354-88-8; *(7)*, 78354-89-9; *(8)*, 51975-15-6; dibenzoyldiazomethane, 2085-31-6; 1-diethylaminopropyne, 4231-35-0.

---

[1] *R. Huisgen, H.-U. Reissig, H. Huber*, J. Am. Chem. Soc. *101*, 3647 (1979).

[2] *J. van Alphen*, Recl. Trav. Chim. Pays-Bas *62*, 485, 491 (1943); *R. Hüttel, J. Riedl, H. Martin, K. Franke*, Chem. Ber. *93*, 1425 (1960); *R. Hüttel, K. Franke, H. Martin, J. Riedl, ibid. 93*, 1433 (1960).

[3] *(6)* crystallizes from benzene in the monoclinic space group $P2_1$ with $a = 8.978(2)$, $b = 16.522(4)$, $c = 19.307(6)$ Å, $\gamma = 106.07(2)°$, $Z = 4$. Automatic single-crystal diffractometer, $Cu_{K\alpha}$ radiation (Ni filter), 5114 independent reflections ($I > 2\sigma_I$); direct methods and Fourier syntheses, least squares refinement (including the H-atoms), $R = 0.047$.—Detailed communication: *A. Gieren, V. Lamm*, Acta Crystallogr., in press.

[4] *R. Buyle, H. G. Viehe*, Tetrahedron *24*, 3987 (1968); *W. Eberlein, J. Heider, H. Machleidt*, Justus Liebigs Ann. Chem. *738*, 54 (1970).

[5] *J. Ficini, J.-P. Genet*, Bull. Soc. Chim. Fr. *1974*, 2086.

[6] *H.-U. Reissig, R. Huisgen*, J. Am. Chem. Soc. *101*, 3648 (1979).

[7] *R. Huisgen, H.-U. Reissig*, Angew. Chem. *91*, 346 (1979); Angew. Chem. Int. Ed. Engl. *18*, 330 (1979).

## The ($\eta^5$-$CH_3C_5H_4$)$Mn(CO)_2$ Moiety as Protecting Group in the Monohalogenation of Diphenylsilane[**]

By *Ulrich Schubert*, *Barbara Wörle*, and *Peter Jandik*[*]

Most of the methods currently used for the synthesis of silanes of the type $R_2Si(H)X$ (R = alkyl, aryl; X = halogen)

---

[*] Priv.-Doz. Dr. U. Schubert, Dipl.-Chem. B. Wörle, Ing. P. Jandik, M. Sc.
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

*0570-0833/81/0808-0695 $ 02.50/0*

lead to formation of difficultly separable mixtures. We have now developed a method for synthesizing the silanes $Ph_2Si(H)X$ *(5)*, in the first instance, in good yields and free of silicon-containing by-products.

Triorganosilanes $R_3SiH$ react photochemically with $CpMn(CO)_3$ ($Cp = \eta^5$-$C_5H_5$) and with ($\eta^5$-$CH_3C_5H_4$)$Mn(CO)_3$ *(1)* to give $Cp(CO)_2(H)Mn$—$SiR_3$ and the ($\eta^5$-$CH_3C_5H_4$)-complex, respectively[1]. We found in the case of diphenylsilane *(2)* (and other diorganosilanes) that only *one* Si—H bond is cleaved:

$$\underset{(1)}{(MeCp)Mn(CO)_3} + \underset{(2)}{Ph_2SiH_2} \xrightarrow[\text{hexane}]{h\nu,\ -CO} \underset{(3)}{(MeCp)(CO)_2(H)Mn\text{-}SiHPh_2}$$

$$(3) \xrightarrow[\text{reaction}]{\text{halogenation}} (MeCp)(CO)_2(H)Mn\text{-}SiXPh_2 \quad (4)$$

*(a)*, X = F; *(b)*, X = Cl; *(c)*, X = Br; *(d)*, X = I
(MeCp) = $\eta^5$-$CH_3C_5H_4$

In complex *(3)*[2], which is obtained in 75% yield, the remaining H-atom can be replaced by a halogen atom without the Mn—H or the Si—H bond being opened. Thus, *(4a)* can be prepared in 78% yield by reacting *(3)* for 30 min with a stoichiometric amount of $[Ph_3C]BF_4$ in $CH_2Cl_2$ at room temperature. When a solution of *(3)* in $CCl_4$ is treated with a small amount of $PCl_5$, *(3)* is chlorinated to *(4b)* in 72% yield within a few minutes. When dilute solutions of stoichiometric amounts of $Br_2$ or $I_2$ are slowly added dropwise at 0 °C to dilute solutions of *(3)* in pentane, *(4c)* and *(4d)* are obtained in 70 and 69% yield, respectively.

The new complexes *(3)* and *(4a)—(4d)* can be isolated as pale yellow solids by crystallization from pentane or by gel-chromatography[3]. They cannot be kept in the analytically pure state over a longer period, even with cooling. Their stability falls off on going from *(3)*≈*(4a)* to *(4d)* and rapidly decreases in polar solvents.

Reaction of *(4)* with CO under pressure leads to formation of the silanes *(5)* without by-products and with cleavage of the protecting group and regeneration of *(1)*. Beginning thermal decomposition of *(4)* is no problem, since the same silanes *(5)* are formed.

$$(4) \xrightarrow[\text{pentane, 100–120 °C, 3 h}]{\text{50–60 bar CO}} \underset{(1)}{(MeCp)Mn(CO)_3} + \underset{(5)}{Ph_2Si(H)X}$$

The silanes *(5)* can be smoothly separated on a gram scale from complex *(1)*, *i.e.* without major losses, by preparative high pressure liquid chromatography (PHPLC)[4] (overall yields of *(5)* 80—90% depending on the educt).

The reactions described here thus enable one only of the two silicon-bonded hydrogen atoms of diphenylsilane *(2)* to be replaced by halogen.

Received: November 26, 1980 [Z 817 IE]
German version: Angew. Chem. *93*, 683 (1981)

CAS Registry numbers:
*(1)*, 12108-13-3; *(2)*, 775-12-2; *(3)*, 78420-94-7; *(4a)*, 78420-95-8; *(4b)*, 78420-96-9; *(4c)*, 78420-97-0; *(4d)*, 78420-98-1; *(5a)*, 1013-91-8; *(5b)*, 1631-83-0; *(5c)*, 17995-01-6; *(5d)*, 78408-01-2.

---

[1] *A. J. Hart-Davis, W. A. G. Graham*, J. Am. Chem. Soc. *94*, 4388 (1971); *E. Colomer, R. J. P. Corriu, A. Vioux*, Inorg. Chem. *18*, 695 (1979).

[2] IR (pentane): $\nu_{CO}$ = 1994 (vs), 1935 (vs), $\nu_{Si-H}$ = 2032 (w), $\nu_{Mn-H}$ = 1901 (w) cm$^{-1}$; $^1$H-NMR ($CCl_4$, TMS int.): $\delta$ = 8.0, 7.4 (m, 10 H, $C_6H_5$), 6.7 (d, 1 H, Si—H), 3.95 (s, 4 H, $C_5H_4$), 1.5 (s, 3 H, $CH_3$), −11.5 (d, 1 H, Mn—H); $J_{HMnSiH}$ = 4.95 Hz.

[3] All the compounds gave correct elemental analyses. The IR and NMR spectra essentially correspond to those of *(1)* [2].

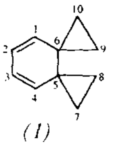
[4] Separator system: Knauer steel column (50 × 1.6 cm) packed with Nucleosil 100—30 silica gel [for *(5a)*] and with Alox 60-D 10 aluminum oxide [for *(5b—c)*]. Pump and detector were units from the Philips-Pye-Unicam LC system. Pump rate 25 mL/mn, detector wavelength 254 nm. Eluent: heptane/ether (5 : 1).

## Dispiro[2.0.2.4]deca-7,9-diene as a Ligand in Carbonyl-Transition Metal Complexes[**]

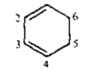
By *Dieter Wormsbächer, Frank Edelmann, Dieter Kaufmann, Ulrich Behrens*, and *Armin de Meijere*[*]

*Dedicated to Professor Edgar Heilbronner on the occasion of his 60th birthday*

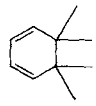
The highest occupied molecular orbital (HOMO) of dispiro[2.0.2.4]deca-7,9-diene *(1)* [formula numbered by analogy to *(2)*] is exceptionally high[1a] owing to conjugation of the diene moiety with the two neighboring spirocyclopropyl groups[1a]. As is well known, cyclopropyl substituents are particularly effective electron donors towards electron-deficient centers, but poor electron acceptors[1b]. Since a diene(tricarbonyl)iron group as a rule also acts as an electron donor[2], we were interested to know whether or not there was a mutual electronic influence between diene(carbonyl)metal unit and spirobicyclopropyl group.

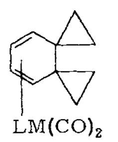


*(1)*

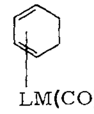


*(2)*

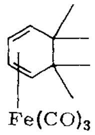

*(3)*



*(4a)*, M = Fe, L = CO
*(4b)*, M = Fe, L = $P(C_6H_5)_3$
*(4c)*, M = Fe, L = $P(OC_6H_5)_3$
*(4d)*, M = Ru, L = CO



*(5a)*, M = Fe, L = CO
*(5b)*, M = Fe, L = $P(C_6H_5)_3$



*(6)*

The tricarbonyliron complex *(4a)* is obtained as an orange-yellow oil in 75% yield by reaction of *(1)* with (benzylideneacetone)tricarbonyliron ((bda)$Fe(CO)_3$)[3a] followed by chromatography on silica gel. In an analogous way reaction with (bda)[$P(C_6H_5)_3$]$Fe(CO)_2$[3b] and (bda)[$P(OC_6H_5)_3$]$Fe(CO)_2$[3b] afforded the corresponding complexes *(4b)* (40%, yellow crystals, m.p. 198—199 °C) and *(4c)* (35%, orange oil), respectively. Surprizingly, the reaction of *(1)* with $Fe_2(CO)_9$ led to formation of *(4a)* as the only product, although many vinylcyclopropane derivatives undergo ring opening under these conditions[4]. $Ru_3(CO)_{12}$ catalyzes the rearrangement of *(1)* to *o*-ethylstyrene[1a], whereas reaction with the more reactive tricarbonyl(1,5-cyclooctadiene)ruthenium[3c] leads, under mild conditions, to the complex *(4d)* (21%, lemon-yellow oil). In

---

[*] Prof. Dr. A. de Meijere, Dipl.-Chem. D. Wormsbächer, Dipl.-Chem. F. Edelmann, Dr. D. Kaufmann, Dr. U. Behrens
Fachbereich Chemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

contrast, *(1)* cannot be converted—even by treatment with tris(acetonitrile)tricarbonylchromium—into a tricarbonylchromium complex, in which the spirobicyclopropyl group also ought to function as a ligand[5].

Reaction of 5,5,6,6-tetramethyl-1,3-cyclohexadiene *(3)*[6], having the same type of substitution as *(1)*, with (bda)Fe(CO)$_3$ similarly afforded the tricarbonyliron complex [*(6)*]. The spectroscopic data of *(6)* and those of the complexes *(5a)*[7] and *(5b)*[8] of 1,3-cyclohexadiene *(2)* have been selected for comparison with those of the new carbonylmetal complexes *(4a)—(4d)* (Table 1).

Table 1. Spectroscopic data of the carbonylmetal complexes *(4)—(7)* and the free ligands *(1)—(3)* [numbering as shown in *(1)* and *(2)*].

| Cpd. | Solvent [a] | Characteristic data $\nu$C≡O [cm$^{-1}$] or $\delta_{TMS}$ (assignment) | | |
|---|---|---|---|---|
| *IR spectrum* | | | | |
| *(4a)* | I | 2048 | 1984 | 1970 |
| *(5a)* | I | 2049 | 1981 | 1975 |
| *(4b)* | I | 1980 | 1922 | |
| *(4b)* | II | 1974 | 1898 | |
| *(4c)* | I | 2001 | 1946 | |
| *(5b)* | II | 1960 | 1894 | |
| *(7b)* | V | 2113 | 2065 | 2059 |
| *$^1$H-NMR spectrum* [b] | | | | |
| *(4a)* | III | 4.67 (H$^{2,3}$), | 2.23 (H$^{1,4}$), | 0.21, 0.15 (H$^{7,8,9,10}$) |
| *(4b)* | III | 4.90 | 2.07 | 0.47, 0.36, 0.16, 0.03 |
| *(4c)* | III | 4.71 | 2.37 | 0.19—0.03 |
| *(4d)* | III | 4.89 | 2.29 | 0.07 |
| *(1)* | IV | 5.92 | 5.03 | 0.31, 0.19 (H$^{7,8,9,10}$) |
| *(5a)* | — [c] | 5.22 | 3.14 | 1.41, 1.14 (H$^{5,6}$) |
| *(5b)* | — [c] | 4.85 | 2.50 | 1.60 |
| *(2)* | III | 5.83 | 5.68 | 1.96 |
| *(6)* | III | 4.51 | 2.52 | 0.91, 0.71 |
| *(3)* | IV | 5.72 | 5.31 | 0.91 |
| *(7b)* | V | 7.41 (t, H$^2$), 6.01 (t, H$^3$), 5.51 (d, H$^1$), 3.95 (d, H$^4$), 1.93 (m, H$^9$), 1.63 (dt, H$^8$), 1.18 (m, H$^8$), 0.99 (t, H$^{10}$), 0.73 (dt, H$^7$), 0.61 (dt, H$^7$) | | |
| *$^{13}$C-NMR spectrum* [b] | | | | |
| *(4a)* | III | 212.6 (C≡O),<br>24.5 (C$^{5,6}$), | 83.8 (C$^{2,3}$),<br>15.4 (C$^{7,9/8,10}$), | 72.9 (C$^{1,4}$),<br>12.6 (C$^{8,10/7,9}$) |
| *(1)* | III | 133.7 (C$^{2,3}$), 123.6 (C$^{1,4}$), 20.8 (C$^{5,6}$), 11.6 (C$^{7,8,9,10}$) | | |
| *(3)* | III | 138.8 (C$^{2,3}$), 121.0 (C$^{1,4}$), 37.3 (C$^{5,6}$), 22.3 (C$^{7,8,9,10}$) | | |
| *(7b)* | V | 200.8 (C≡O), 110.5 (C$^1$), 100.1 (C$^3$), 95.7 (C$^2$), 85.1 (C$^6$), 72.7 (C$^4$), 25.6 (C$^5$), 24.6 (C$^9$), 24.4 (C$^{10}$), 13.1 (C$^7$), 10.7 (C$^8$) | | |

[a] I cyclohexane, II KBr, III $C_6D_6$, IV $CCl_4$, V $CD_2Cl_2$. [b] Detailed analysis of the $^1$H- and $^{13}$C-NMR spectra of *(4a)* and *(6)*: *H. Günther*, unpublished results. [c] *F. M. Chaudhari, P. L. Pauson*, J. Organomet. Chem. *5*, 73 (1966). [d] *R. Burton, L. Pratt, G. Wilkinson*, J. Chem. Soc. *1961*, 594.

From the C≡O stretching vibration frequencies of *(4a)*, which were found to be insignificantly lower than those of *(5a)*, it can only be concluded that there must be very little difference between the π*-MOs of *(4a)* and *(5a)*[2]. The $^1$H- and $^{13}$C-NMR data would also lead to the same conclusion. Thus, the signals of the cyclopropyl protons of *(4a)—(4d)* are shifted only slightly (0.1—0.2 ppm) upfield compared to those of *(1)*, and the $^{13}$C-NMR signals of the cyclopropyl C-atoms C7—C10 in the complex *(4a)* are even shifted downfield. Consequently, the metal-complexed diene moiety cannot exercise its electron-donor action on the spirobicyclopropyl group.

According to an X-ray structure analysis the diene moiety in *(4b)* is completely planar (see Fig. 1), as is usual in such complexes[2]. The angle between this plane and the C$^4$—C$^5$—C$^6$—C$^1$ plane is *ca.* 39°; the bicyclopropyl group, with a dihedral angle of *ca.* 4°, has an almost synplanar conformation.

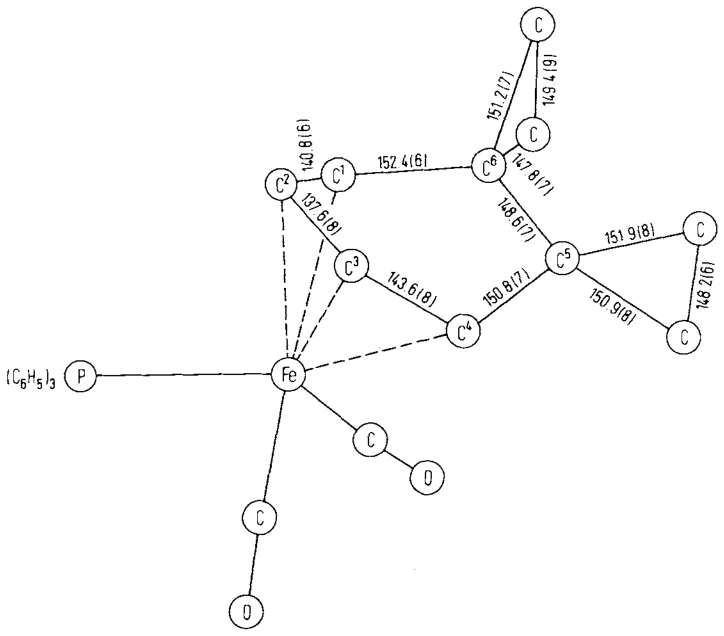
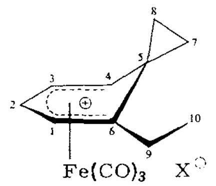


Fig. 1. Structure of *(4b)* in the crystal (monoclinic crystals, space group $P2_1/c$, $a = 871(1)$, $b = 1542(1)$, $c = 1867(2)$ pm, $\beta = 97.3(1)$; 2478 measured reflections, refined to $R = 0.041$).



*(7a)*, X = $BF_4$
*(7b)*, X = $PF_6$

The most remarkable property of *(4a)* is its smooth reaction with ethereal tetrafluoroboric acid at room temperature to give the stable complex *(7a)*, while the free ligand *(1)* spontaneously polymerizes with superacids, even at −80 °C[9]. The orange-yellow crystalline compound *(7b)*, which precipitates from the aqueous solution of oily *(7a)* on addition of ammonium hexafluorophosphate, is to our knowledge the first complex of an ethylenebenzenium ion [formula numbered by analogy to *(2)*]. From its $^1$H- and $^{13}$C-NMR data (see Table 1) it is evident that the positive charge—other than in the case of the uncomplexed ion[10]—is not delocalized into the cyclopropyl group. Consequently, *(7)* should react with nucleophiles like a tricarbonylcyclohexadienyliron cation[11] and not like an ethylenebenzenium ion.

Received: December 12, 1980 [Z 809 IE]
German version: Angew. Chem. *93*, 701 (1981)

---

[1] a) *A. de Meijere*, Chem. Ber. *107*, 1684 (1974); b) cf. recent review: Angew. Chem. *91*, 867 (1979); Angew. Chem. Int. Ed. Engl. *18*, 809 (1979), and references cited therein.

[2] Cf. reviews in: *R. Pettit, G. F. Emerson*, Adv. Organomet. Chem. *1*, 1 (1964).

[3] a) *J. A. S. Howell, B. F. G. Johnson, P. L. Josty, J. Lewis*, J. Organomet. Chem. *39*, 329 (1972); b) *B. F. G. Johnson, J. Lewis, G. R. Stephenson, E. J. S. Vichi*, J. Chem. Soc. Dalton Trans. *1978*, 369; c) *A. J. Deeming, S. S. Ullah, A. J. P. Domingos, B. F. G. Johnson, J. Lewis, ibid. 1974*, 2093.

[4] Cf. a) *R. Aumann, H. Ring*, Angew. Chem. *89*, 47 (1977); Angew. Chem. Int. Ed. Engl. *16*, 50 (1977); b) *S. Sarel*, Acc. Chem. Res. *11*, 204 (1978); c) *P. Eilbracht, U. Mayser*, Chem. Ber. *113*, 2211 (1980), and references cited therein.

[5] Cf. on the other hand: *W. E. Bleck, W. Grimme, H. Günther, E. Vogel*, Angew. Chem. *82*, 292 (1970); Angew. Chem. Int. Ed. Engl. *9*, 303 (1970).

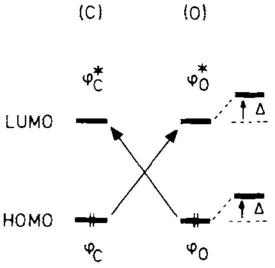
[6] *D. Kaufmann, A. de Meijere*, Tetrahedron Lett. *1979*, 779.
[7] *R. Burton, L. Pratt, G. Wilkinson*, J. Chem. Soc. *1961*, 594.
[8] *F. M. Chaudhari, P. L. Pauson*, J. Organomet. Chem. *5*, 73 (1973).
[9] *A. de Meijere*, Chem. Ber. *107*, 1702 (1974).
[10] *G. A. Olah, R. D. Porter*, J. Am. Chem. Soc. *92*, 7627 (1970).
[11] Cf. *A. J. Birch, I. D. Alpers* in *H. Alper:* Transition Metal Organometallics in Organic Synthesis, Academic Press, New York 1976, p. 1—82.

# Direct and Inverse Reactivity-Selectivity Relationship in the [1.2]-Addition of Singlet Carbenes to Olefins[**]

By *Wolfgang W. Schoeller*[*]

*Dedicated to Professor Josef Goubeau on the occasion of his 80th birthday*

Hitherto it has generally been assumed that the reactivities of carbenes towards olefins decrease with increasing selectivity in the order $CF_2 > CCl_2 > CBr_2$[1]. Contrary to this common understanding, we show that the selectivity of singlet carbenes $CL_2$ (L = halogen, $OCH_3$ *etc.*) can increase with increasing reactivity (inverse reactivity-selectivity relationship[2]).



Scheme 1.

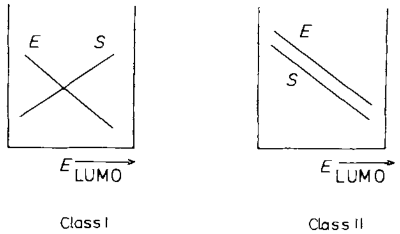
According to frontier orbital theory[3] the interaction between a carbene (C) and an olefin (O) (Scheme 1) is given by the following relation:

$$E = \frac{\beta^2 \varphi_0 \varphi_{C^*}}{E\varphi_C^* - (E\varphi_0 + \Delta)} + \frac{\beta^2 \varphi_C \varphi_{O^*}}{(E\varphi_O^* + \Delta) - E\varphi_C} \qquad \text{(a)}$$

where $E$ is determined in this picture by mutual transfer of electron density between the frontier orbitals HOMO and LUMO and is proportional to the logarithm of the rate constant of the reaction. A variation in O ($O_1, O_2, \ldots O_i$) causes a change in reactivity ($\lg k_1, \lg k_2, \ldots \lg k_i$) and hence corresponds to a change in the interaction energy $E$. If the trapping olefins $O_i$ differ only slightly in their electronic properties (*e.g.* by alkyl substitution at the π-system), the frontier orbitals of $O_i$ will be energetically raised or lowered[4] by the small amount $\Delta$[5]. Hence selectivity [eq. (b)] is related to reactivity [eq. (a)] as derived in the formalism of *differential* frontier orbital theory.

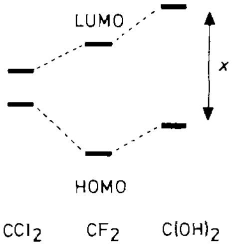
$$S \equiv \frac{\partial E}{\partial \Delta} = \frac{\beta^2 \varphi_O \varphi_{C^*}}{[E\varphi_C^* - (E\varphi_O + \Delta)]^2} - \frac{\beta^2 \varphi_C \varphi_{O^*}}{[(E\varphi_O^* + \Delta) - E\varphi_C]^2} \qquad \text{(b)}$$

For a reactivity-selectivity relationship the following limiting cases ($S > 0$) can be recognized:



Scheme 2.

*Class I:* Increase in selectivity and decrease in reactivity on raising the LUMO energy level of the carbene. This case corresponds to the classical reactivity selection principle (RSP)[2] (direct RSP). In the series of the halocarbenes (L = F, Cl, Br) the energy difference between the innermolecular frontier orbitals ($X = E_{LUMO(C)} - E_{HOMO(C)}$) decreases (less favorable $C_{2p} \cdot L_{np}$ overlap, $n = 2, 3, 4$) *e.g.*, with respect to $CF_2$ the species $CCl_2$ is more reactive, both electrophilically as well as nucleophilically[6].



Scheme 3.

Hence, the reactivity according to eq. (a) increases and simultaneously the selectivity according to eq. (b) decreases. Similar considerations hold for the selectivity region $S<0$ (nucleophilic carbenes).

For the series of halocarbenes we have plotted their selectivities against the corresponding LUMO energies[7] (Fig. 1).

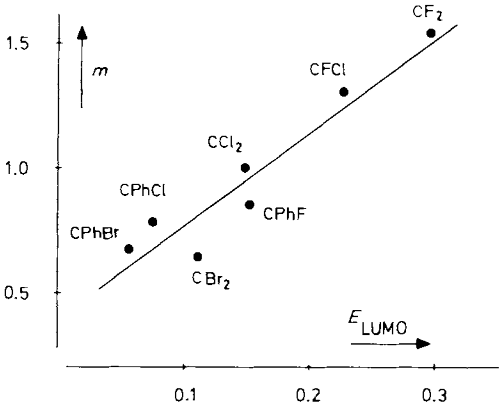


Fig. 1. Relative selectivities (with respect to $CCl_2$ under standard conditions [1]) *m* of the halocarbenes as a function of their LUMO energies (in β).

Accordingly, the selectivity of the carbene increases with increasing LUMO energy. Therefore, the halocarbenes are ruled by the direct RSP, which is in agreement with the view[1] that the selectivity of carbenes increases with increasing resonance stabilization ($CBr_2 < CCl_2 < CF_2$).

*Class II:* Decrease in reactivity and concomitant decrease in selectivity (inverse RSP) with increasing LUMO

---

[*] Priv.-Doz. Dr. W. W. Schoeller
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

0570-0833/81/0808-0698 $ 02.50/0

energy of the carbene. If however the ligands at the carbene site (L = F, $OCH_3$, $NH_2$) stem from the second row of the long periodic system, the intermolecular HOMO-LUMO energy difference X remains constant to a first approximation (constant $C_{2p}-L_{2p}$ overlap). Lifting the LUMO of the carbene[3] therefore decreases its electrophilicity and diminishes its nucleophilicity. Contrary to $CF_2$, $C(OCH_3)_2$ reacts as a nucleophilic species[8a]. In addition, the selectivity of nucleophilic carbenes increases along the ligand sequence $L = OCH_3 < N(CH_3)_2$[8].

To summarize, our investigations reveal two different classes of carbenes on the basis of a differential formulation[9] of the frontier orbital model. These two classes obey a direct or inverse relationship between reactivity and selectivity.

The concept which we have demonstrated here for the series of carbenes is more general and can be equally applied to other frontier orbital controlled reactions, such as cycloadditions and radical reactions[9].

Received: February 17, 1981 [Z 811 IE]
revised: March 23, 1981
German version: Angew. Chem. *93*, 685 (1981)

---

[1] *W. Kirmse:* Carbene Chemistry, Academic Press, New York 1971; *R. A. Moss* in *M. Jones, Jr.:* Carbenes, Vol. I, Wiley, New York 1973.

[2] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977).

[3] *W. W. Schoeller*, Tetrahedron Lett. *1980*, 1505; see also *W. W. Schoeller, U. H. Brinker*, Z. Naturforsch. *B 35*, 475 (1980).

[4] *E. Heilbronner, H. Bock:* The HMO-Model and its Application, Weinheim 1976.

[5] The change in the energies of the frontier orbitals of the olefin is small compared with the absolute HOMO-LUMO energy differences, as can be estimated from experimentally determined orbital energies (see also [6]).

[6] Estimated according to *J. S. Shapiro, F. P. Lossing*, J. Phys. Chem. *72*, 1552 (1968); *D. E. Milligan, M. E. Jacox*, J. Chem. Phys. *47*, 703 (1967), and references cited therein. Compared to $CF_2$, in $CCl_2$ the HOMO is raised to a greater extent than the drop in LUMO.

[7] Calculated according to HMO theory using standard parameters for the heteroatoms. *A. Streitwieser, Jr.:* Molecular Orbital Theory for Organic Chemists, Wiley, New York 1961.

[8] a) *R. W. Hoffmann, B. Hagenbruch, D. M. Smith*, Chem. Ber. *110*, 23 (1977); *K. Steinbach*, Dissertation, Universität Marburg 1974. I wish to thank Professor *R. W. Hoffmann* for informing me of this result; b) MNDO calculations are in agreement with these findings. For the reaction of the carbenes ($\sigma^2$ configuration) $CF_2$, $C(OH)_2$, $C(NH_2)_2$, and $CCl_2$ with the substrates ethylene (1,1-dihydroxyethylene, 1,1-difluoroethylene), we find the following energy barriers (in kcal per mol for the totally resolved energy hypersurfaces of each reaction) towards the substrates: 21.9 (17.4, 21.7); 24.5 (28.6, 21.0); 21.4 (27.2, 14.6); 12.5 (8.2, 15.8).

[9] *E* in eq. (a) can be viewed as total differential, which allows the derivation of a general relationship between reactivity and selectivity within the frontier orbital model concept. *W. W. Schoeller*, unpublished results.

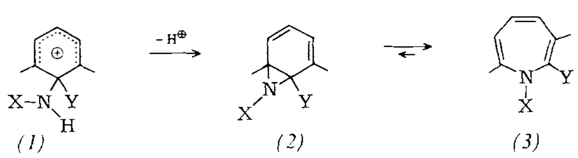
---

## 1*H*-Azepines from Anilides—A Novel Ring Expansion[**]

By *Heinz H. Eckhardt, Dorothea Hege, Werner Massa, Hartwig Perst,* and *Roland Schmidt*[*]

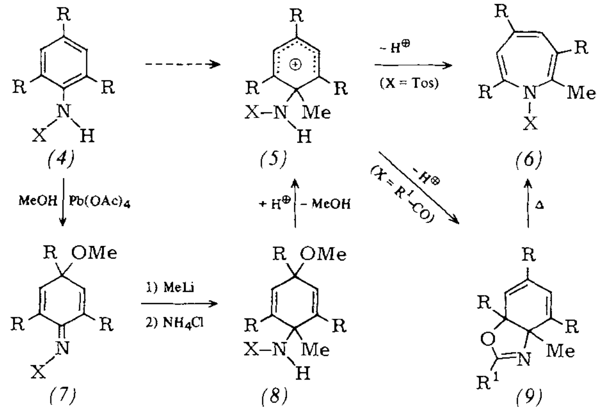
*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

1-Substituted 1*H*-azepines[1] such as *(3)* have not yet been synthesized by ring-closure of an amino-substituted benzenium ion [*(1)*→*(2)*→*(3)*].



Although there are also other reaction routes open to a benzenium ion such as *(1)*[2] we have now been able to realize this mode of entry to 1*H*-azepine derivatives *(6)* in the triaryl series starting from the 2,4,6-triphenylanilides *(4)*. Formally, the requisite cation *(5)* is formed by electrophilic "*ipso*alkylation"[3] at the arene-C atom of *(4)* bearing nitrogen. Since *(5)* is not preparatively accessible in this way we have chosen the alternative route *via* the reactivity-umpolung of *(4)*[4]. Oxidation of the anilides *(4a)*—*(4f)*[5] with lead tetraacetate in the presence of methanol affords the *N*-(4-methoxy-2,5-cyclohexadien-1-ylidene)carboxamides *(7a)*—*(7f)* in 68—86% yield, which readily add nucleophiles at the C=N moiety[6]. Thus, the cyclohexadienylamides *(8a)*—*(8f)* are accessible in yields of up to 80—90% as potential precursors of *(5)* by reaction of *(4)* with methyllithium in diethyl ether[7].

Reaction of *p*-toluenesulfonic acid with *(8)* in toluene leads to elimination of methanol and formation of products which can be derived from a cation *(5)*. Whether the ring closure ensues *via* the nitrogen atom or *via* a center of the X moiety depends on the nucleophilicity of the substituents X in the *N*-position. Only the amide *(8f)* with the slightly nucleophilic tosyl moiety is directly converted (72% yield) into the 1*H*-azepine derivative *(6f)*.



$R = C_6H_5$

| *(4)*-*(8)* | X |
|---|---|
| *(a)* | $C_6H_5$–CO |
| *(b)* | *p*-$CH_3$–$C_6H_4$–CO |
| *(c)* | *p*-$CH_3O$–$C_6H_4$–CO |
| *(d)* | *p*-Br–$C_6H_4$–CO |
| *(e)* | $CH_3$–CO |
| *(f)* | *p*-$CH_3$–$C_6H_4$–$SO_2$ |

| *(9)* | $R^1$ |
|---|---|
| *(a)* | $C_6H_5$ |
| *(b)* | *p*-$CH_3$–$C_6H_4$ |
| *(c)* | *p*-$CH_3O$–$C_6H_4$ |
| *(d)* | *p*-Br–$C_6H_4$ |
| *(e)* | $CH_3$ |

Under the same conditions, in the case of *(8a)*—*(8e)* the *O*-alkylation typical for carboxamides[8] dominates over the desired *N*-alkylation, so that the bicyclic oxazoline derivatives *(9a)*—*(9e)* are obtained in yields of up to 85%. In addition, the anilides *(4a)*—*(4e)* are formed as demethylation products of *(5)* in *ca.* 10% yield. The compounds *(9)* are characterized $^1H$-NMR spectroscopically, *inter alia*, by an AB system for the vinyl protons (in $CDCl_3$; $\delta = 5.86$—

---

[*] Prof. Dr. H. Perst [+], Dr. H. H. Eckhardt, D. Hege, Dr. W. Massa [++], R. Schmidt
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)

[+] Author to whom correspondence should be addressed.

[++] X-ray structure analysis.

[**] This work was supported by the Fonds der Chemischen Industrie.

6.01 and 6.42—6.49, $J=1.3—1.5$ Hz); in the $^{13}C$-NMR spectrum they always show two signals typical for the quaternary bridgehead centers [in $CDCl_3$; $\delta=73.4—73.7$ (C—N) and 91.9—92.5 (C—O)]. The thermally unstable oxazolines *(9)* are suitable precursors for the azepines *(6)*: by heating to 180 °C, the derivatives *(9a)—(9e)* can be smoothly converted (84—93%) into the *N*-acyl-1*H*-azepines *(6a)—(6e)*[9] which, unlike the yellow tosylazepine *(6f)*, are almost colorless. The 1*H*-azepine structure *(6)* is confirmed by an X-ray analysis of a single crystal of *(6d)* (Fig. 1).

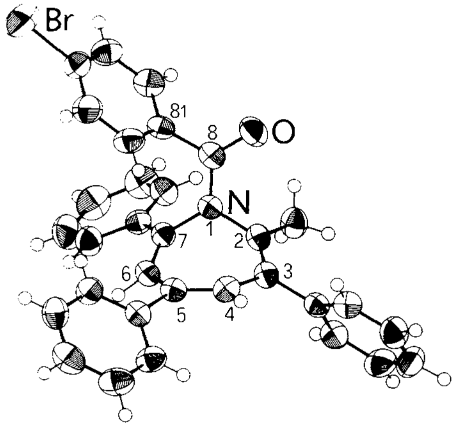


Fig. 1. ORTEP diagram of a molecule of *(6d)* in the crystal (thermal vibration ellipsoids with 50% probability). Space group $P\bar{1}$, $Z=2$, $a=1076.5(4)$, $b=1212.6(2)$, $c=1048.3(6)$ pm, $\alpha=93.62(3)$, $\beta=113.48(3)$, $\gamma=88.66(2)°$, $\rho_c=1.374$ g cm$^{-3}$. With 3089 independent reflections ($F_0>3\sigma$), measured on a four-circle diffractometer (CAD4, Enraf-Nonius, $Mo_{K\alpha}$-radiation) the structure could be refined to $R_w=0.046$ (weight $3/\sigma^2$). Bond lengths in the azepine ring: N—C2 = 144.8(4), C2—C3 = C6—C7 = 134.1(5), C3—C4 = 145.7(5), C4—C5 = 135.1(4), C5—C6 = 144.7(5), C7—N = 143.4(3) pm; amide moiety: N—C8 = 135.5(4), C8—O = 122.3(4) pm.

The azepine ring has, as expected, the boat-shaped conformation[10]; the atoms C2, C3, C6, and C7 lie in a plane which forms an angle of 120.7° with the NC2C7 plane and one of 151.2° with the C3C4C5C6 plane. The NC8OC81 plane is at an angle of only about 9.4° to the NC2C7 plane (in the direction of the equatorial position)[10]. The amide bond N—C8 in the crystal of *(6d)* is exclusively *E*-configurated; on the other hand, equilibrium mixtures are $^1H$- and $^{13}C$-NMR spectroscopically observable in solutions of *(6a)—(6e)*, in which the *E*-rotamer is slightly preferred[11].

Apart from the signals of the methyl-C atoms the $^{13}C$-NMR spectra of *(6)* contain only absorptions for $sp^2$-C atoms, among which C4 ($\delta=130.3—132.3$) and C6 (121.8—123.2) and the amide-carbonyl C-atoms (168.5—170.3) are always unambiguously assignable. In the IR spectrum (KBr) the C=O bands appear in the region typical for tertiary amides at 1638—1666 cm$^{-1}$.

Table 1. Characteristic data of the 1*H*-azepines *(6)* [a].

| *(6)* | Yield [%] | M.p. [°C] | $^1H$-NMR [b] H-4 [c] | C2—CH$_3$ [c] | others |
|---|---|---|---|---|---|
| *(a)* | 93 | 149—150 | (*E*): 7.00 | 2.33 | |
| | | | (*Z*): 6.90 | 1.76 | |
| *(b)* | 91 | 145—146 | (*E*): 7.02 | 2.31 | 2.21 (Aryl—CH$_3$) |
| | | | (*Z*): 6.93 | 1.78 | 2.38 (Aryl—CH$_3$) |
| *(c)* | 85 | 154—155 | (*E*): 6.95 | 2.30 | 3.68 (Aryl—OCH$_3$) |
| | | | (*Z*): 6.83 | 1.80 | 3.82 (Aryl—OCH$_3$) |
| *(d)* | 87 | 138—139 | (*E*): 7.03 | 2.31 | |
| | | | (*Z*): 6.93 | 1.79 | |
| *(e)* | 84 | 134—135 | (*E*): 6.90 | 2.15 | 1.91 (CO—CH$_3$) |
| | | | (*Z*): 6.82 | 2.08 | 2.18 (CO—CH$_3$) |
| *(f)* | 72 | 182—184 | 6.03 | 2.27 | 2.03 (Aryl—CH$_3$) |

[a] In $CDCl_3$ the (*E*):(*Z*) ratio for *(6a)—(6d)* is 4:3 and for *(6e)* 7:3. [b] 100-MHz spectra, $\delta$ values in $CDCl_3$ (int. TMS). [c] Homoallyl coupling between vinyl-H-4 and C2—CH$_3$ (*J ca.* 0.7 Hz) leads to weak signal broadening; the vinyl-H-6 signal is masked by the phenyl-H multiplet ($J_{H\text{-}4/H\text{-}6}<0.5$ Hz).

### *Procedure*

*(7a)*: Lead tetraacetate (8.0 g, 18 mmol) is added to a solution of *(4a)*[5] (6.08 g, 15 mmol) in toluene (50 mL) and methanol (100 mL) and the mixture stirred for 150 min at room temperature then treated with 30 mL of a saturated aqueous NaCl solution. The organic phase recovered after removal of the precipitate by filtration is washed, dried (over $Na_2SO_4$), and evaporated to dryness under reduced pressure. Yield 5.12 g (75%) *(7a)* as colorless crystals of m.p. 169—170 °C (from $CHCl_3$/methanol).

*(9a)*: A suspension of *(7a)* (1.37 g, 3 mmol) in anhydrous diethyl ether (1 mL) is treated at room temperature under $N_2$ with 10 mL of a 2 M ethereal solution of methyllithium. After one hours' stirring the mixture is hydrolyzed with 5 mL of water, then washed with 100 mL of a saturated aqueous $NH_4Cl$ solution and with water. The ethereal phase, after drying over $MgSO_4$ and evaporation to dryness under reduced pressure, yields 1.22 g (88%) of *(8a)* as an oil (mixture of *cis-trans*-isomers in the ratio 3:2). *(8a)* obtained from two such runs (2.30 g, 5 mmol) is dissolved without further purification in toluene (50 mL), treated with 50 mg of *p*-toluenesulfonic acid, and the resulting mixture stirred for 50 min at room temperature. After washing with 20 mL of a 0.2 M aqueous solution of $NaHCO_3$ and with water, the reaction solution is dried (over $Na_2SO_4$) and evaporated to dryness; the residue is taken up in $CHCl_3$ (5 mL) treated with *n*-hexane until cloudy and the anilide *(4a)* (0.19 g, 9.4%) allowed to crystallize out. The filtrate, after evaporation to dryness and recrystallization from $CHCl_3$/*n*-hexane furnishes 1.87 g (85%) of *(9a)* as colorless crystals of m.p. 173—174 °C.

*(6a)*: *(9a)* (0.31 g, 0.7 mmol) is heated under $N_2$ for 30 min at 180 °C in the absence of a solvent. After cooling it is taken up in 3 mL of $CHCl_3$ and *(6a)* is precipitated by addition of methanol; yield: 0.29 g (93%) as colorless crystals (Table 1).

*(6b)—(6e)* are prepared analogously; *(6f)* is formed directly on treatment of *(8f)* with *p*-toluenesulfonic acid.

Received: February 20, 1981 [Z 813 IE]
German version: Angew. Chem. *93*, 713 (1981)

CAS Registry numbers:
*(4a)*, 36771-04-7; *(4b)*, 72470-62-3; *(4c)*, 72470-63-4; *(4d)*, 78354-92-4; *(4e)*, 72470-61-2; *(4f)*, 78354-93-5; *(6a)*, 78354-94-6; *(6b)*, 78354-95-7; *(6c)*, 78354-96-8; *(6d)*, 78354-97-9; *(6c)*, 78354-98-0; *(6f)*, 78354-99-1; *(7a)*, 78355-00-7; *(7b)*, 78355-01-8 *(7c)*, 78355-02-9; *(7d)*, 78355-03-0; *(7e)*, 78355-04-1; *(7f)*, 78355-05-2; *cis-(8a)*, 78355-06-3; *trans-(8a)*, 78355-07-4; *(8b)*, 78355-08-5; *(8a)*, 78355-09-6; *(8d)*, 78355-10-9; *(8e)*, 78355-11-0; *(8f)*, 78355-12-1; *(9a)*, 78355-13-2; *(9b)*, 78355-14-3; *(9c)*, 78355-15-4; *(9d)*, 78355-16-5; *(9e)*, 78355-17-6

---

[1] Reviews: a) *H. Prinzbach, G. Kaupp, R. Fuchs, M. Joyeux, R. Kitzing, J. Markert*, Chem. Ber. *106*, 3824 (1973), and references cited therein; b) *M. R. Acheson:* An Introduction to the Chemistry of Heterocyclic Compounds, 3rd edit., Wiley, New York 1976, p. 442; cf. also *E. Vogel, H. J. Altenbach, J.-M. Drossard, H. Schmickler, H. Stegelmeier*, Angew. Chem. *92*, 1053 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1016 (1980), and references cited therein.

[2] *Inter alia*, migration of Y and *N*-deprotonation to 2,4-cyclohexadienylideneamines or aromatization with cleavage of $Y^{\oplus}$ is to be expected. For a detailed discussion of the reaction paths of other benzenium ions see, *e.g.* a) *S. Hünig, P. Schilling*, Chem. Ber. *108*, 3355 (1975) and refer-

ences cited therein; b) *A. Rieker, G. Henes, S. Berger, ibid. 108,* 3700 (1975); cf. therein, the preparation of oxepin derivatives in analogy to the azepine synthesis.

[3] For more about *ipso*-attack see *e.g. R. B. Moodie, K. Schofield,* Acc. Chem. Res. *9,* 287 (1976); *P. B. D. de la Mare, ibid. 7,* 361 (1974).

[4] Review: *D. Seebach,* Angew. Chem. *91,* 259 (1979); Angew. Chem. Int. Ed. Engl. *18,* 239 (1979).

[5] *H. H. Eckhardt, H. Perst,* Tetrahedron Lett. *1979,* 2125, and references cited therein.

[6] For analogous 1,2-additions to 2,5-cyclohexadienones cf. *J. Bracht, E. L. Dreher, A. Rieker, H. P. Schneider* in *Houben-Weyl-Müller:* Methoden der Organischen Chemie, 4th edit., Vol. VII/3b. Thieme, Stuttgart 1979, p. 746; cf. also [2b].

[7] 3:2 mixtures of *cis-trans* isomers with preference for the components with *cis*-orientation of methoxy and amide groups.

[8] Review, *e.g., H. Perst:* Oxonium Ions in Organic Chemistry, Verlag Chemie, Weinheim—Academic Press, Weinheim and New York 1971, p. 131.

[9] This formal reversal of the acylaziridine-oxazoline rearrangement *via* a benzimine—cf., *e.g., H. C. van der Plaas:* Ring Transformations of Heterocycles, Vol. 1, Academic Press, New York 1973, p. 66—could occur, because *(6)* is favored in an ultimate benzimine-azepine equilibrium, cf. [1].

[10] Cf. the structure of the 1-phenoxycarbonyl-1*H*-azepine: *H. J. Lindner, B. von Gross,* Chem. Ber. *105,* 434 (1972), and references cited therein; the amide-N—C8 bond is at an angle of 15.8° to the plane through NC2C7.

[11] The temperature dependence of the NMR spectra can be interpreted in terms of the diastereomerization by rotation about the amide N—CO bond, cf. [1a].

# BOOK REVIEWS

**NMR of Chemically Exchanging Systems.** By *J. I. Kaplan* and *G. Fraenkel.* Academic Press, New York 1980. xi, 165 pp., $ 19.50.

The concept of a quantum-mechanical density matrix, introduced by *Johann (John) von Neumann* some 50 years ago, is widely regarded as an advanced subject. Apart from the classic works of *Abragam* and of *Slichter,* written by and for physicists, it has rarely made its way into textbooks on NMR spectroscopy; of those addressed to the chemist, many do not condescend to mention it at all. And that in spite of the fact that the density matrix formalism is not only indispensable for a genuine understanding of relaxation and exchange phenomena in NMR, but is also used routinely, by means of "canned" computer programs, in applications especially to exchange problems. A monograph which purports to fill this gap would thus appear to be a highly welcome addition to the NMR textbook literature.

Provided that it succeeds in its stated aim. The overwhelming impression on a first reading is that of an excessively formal treatment. About 70% of a typical page in the main body of the text, which is principally concerned with exchange, with one chapter on relaxation thrown in for good measure, is taken up by mathematical symbols; more precisely, there are no less than 1045 equations all told, squeezed into 162 pages of text. There probably exist readers who take delight in such a wallowing in formalism, but one wonders at their frequency. The typical needs of a nonspecialist would in this reviewer's opinion be better served by a concise presentation designed to exhibit the logical transparency of the theory. Such a compact and modern formulation does in fact exist, but the authors have chosen to follow their own predilections.

As an unavoidable consequence of this heavy emphasis on formalism, the physical content of the theory and its applications get short shrift. The opportunity of counterbalancing the overdose of mathematics by a copious use of well-designed figures has remained largely unexploited. There are preciously few in the first place, and the majority are moreover trivial or uninformative. Lineshapes are frequently displayed as freehand drawings, and drawn with a shaky hand to boot. Quite the worst example of its kind has been selected by the publisher to disgrace the cover of the book. One single page is devoted to experimental problems, which is of course totally inadequate. The authors acknowledge the necessity of using a computer for actual calculations, but no information is provided about where to obtain the relevant programs or how to use them. Readers wishing to learn about how to apply the formalism to the study of permutational mechanisms in the presence of molecular symmetry, which ranks among the chemically most exciting applications of the theory, are left out in the cold. The possibility of using group-theoretical techniques for simplifying the calculations is ignored. The citation policy is strangely selective; references to papers of marginal relevance are sometimes listed at great length, whereas there are gaping omissions otherwise. The carelessness in assembling the references is also reflected in the numerous misspellings and misquotations. As long as this fate only befalls some of the lesser luminaries, a kind of excuse may perhaps be concocted for the authors' sloppiness, but when it comes to names such as *Wangsness, McConnell, Hoffman,* even the patience of an indulgent reviewer begins to wear thin. It is particularly sad to notice that *Erwin Hahn,* one of the early pioneers, is not spared the indignity of seeing his name perverted to *Holm,* in the references as well as in the text.

Users of NMR spectroscopy wishing to educate themselves about density matrix methods are advised to turn to other sources, especially to articles in the modern review literature. Since they are not cited in the book, the authors of four of them, all excellent, are mentioned here: *P. D. Buckley, K. W. Jolly* and *D. N. Pinder* (1975); *R. L. Vold* and *R. R. Vold* (1978); *S. Szymanski, M. Witanowski* and *A. Gryff-Keller* (1978); *A. Steigel* (1978). The attention of specialists is drawn to the SNOB (selective neglect of bilinear terms) technique, which is based on the authors' original research. Although information about that topic can also be extracted from the journal literature, it is convenient to have it between the covers of a book. This is an interesting idea, whose potential for applications has hardly been tapped, but which holds great promise for the future. It is the part of the book which the present reviewer found worthwhile enough to read more than once.

*Gerhard Binsch* [NB 545 IE]

*0570-0833/81/0808-0701 $ 02.50/0*

## Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Atmospheric Pollution.** By *A. R. Meetham, D. W. Bottom, S. Cayton, A. Henderson-Sellers* and *D. Chambers*. Pergamon Press, New York 1981. 5th revised Edit., xi, 232 pp., bound, $ 15.00. — ISBN 0-08-024002-X

**Low Temperature Properties of Polymers.** By *I. Perepechko*. Pergamon Press, New York 1980. ix, 301 pp., bound, $ 40.00. — ISBN 0-08-025301-6

**Grundlagen und Anwendungen der Mössbauer-Spektroskopie.** By *D. Barb*. Akademie-Verlag, Berlin 1980. x, 468 pp., bound, *ca.* DM 73.00

**Chemie des Bauwesens. Band 1. Anorganische Chemie.** By *K. Krenkler*. Springer-Verlag, Berlin 1980. xviii, 494 pp., bound, DM 88.00. — ISBN 3-540-10107-1

**Spectroscopic Properties of Inorganic and Organometallic Compounds. Vol. 13.** Senior Reporters *D. M. Adams* and *E. A. V. Ebsworth*. The Royal Society of Chemistry, London 1980. vx, 413 pp., bound, £ 66.00. — ISBN 0-85186-113-X — A volume in the series "Specialist Periodical Reports"

**Chemistry and Physics of Carbon. Vol. 16.** Edited by *Ph. L. Walker, Jr.* and *P. A. Thrower*. Marcel Dekker, New York 1981. xii, 322 pp., bound, SFr. 95.00. — ISBN 0-8247-6991-0

**Advances in Catalysis. Vol. 29.** Edited by *D. D. Eley, H. Pines* and *P. B. Weisz*. Academic Press, New York 1980. xiv, 367 pp., bound, $ 45.00. — ISBN 0-12-007828-5

**The Carbohydrates.** Edited by *W. Pigman* and *D. Horton*. Academic Press, New York 1981. 2nd Edit., xxiii, 984 pp., bound, $ 69.50. — ISBN 0-12-556351-5

**Analytische Methoden zur Prüfung gesundheitsschädlicher Arbeitsstoffe.** Edited by *D. Henschler*. Verlag Chemie, Weinheim 1980. **Band 1/2. Luftanalysen.** 322 pp., loose-leaf DM 118.00. — ISBN 3-527-25857-4; **Band 2/3. Analysen in biologischem Material.** 145 pp., loose-leaf, DM 106.00. — ISBN 3-527-25858-2

**Standards in Absorption Spectrometry.** Edited by *C. Burgess* and *A. Knowles*. Chapman & Hall, London 1981. xii, 142 pp., bound, £ 9.50. — ISBN 0-412-22470-4

**Gmelin Handbuch der Anorganischen Chemie.** Springer-Verlag, Berlin 1981. 8th Edit. U-Uranium. Ergänzungsband Teil A: Das Element. xxvii, 297 pp., bound, DM 732.00. — ISBN 3-540-93429-4

**Berichte. Band 5/80. Umwelt- und Gesundheitskriterien für Quecksilber.** Issued by the Umweltbundesamt. Erich Schmidt Verlag, Berlin 1980. 140 pp., bound, DM 29.00. — ISBN 3-503-01868-9

**Thermal Electrocyclic Reactions.** By *E. N. Marvell*. Academic Press, New York 1980. ix, 422 pp., bound, $ 51.00. — ISBN 0-12-476250-6

**Line Coincidence Tables for Inductively Coupled Plasma Atomic Emission Spectrometry. Vol. 1 and 2.** By *P. W. J. M. Boumans*. Pergamon Press, New York 1980. Loose-leaf $ 250.00. — ISBN 0-08-026243-0

**Organic Reaction Mechanisms.** Edited by *A. C. Knipe* and *W. E. Watts*. John Wiley & Sons, Chichester 1981. 759 pp., bound, £ 58.00. — ISBN 0-471-27818-1

**Progress in Surface Science. Vol. 9.** Edited by *S. G. Davison*. Pergamon Press, New York 1981. 268 pp., bound, $ 93.00 — ISBN 0-08-026052-7

**Liquid Phase High Pressure Chemistry.** By *N. S. Isaacs*. John Wiley & Sons, Chichester 1981. vii, 414 pp., bound, £ 33.00 — ISBN 0-471-27849-1

**Materialien. Band 6/80. Der Fall Kepone - Wirkungen eines Schadstoffes auf die Umwelt.** Issued by the Bundesumweltamt. Erich Schmidt Verlag, Berlin 1980. 66 pp., bound, DM 24.80. — ISBN 3-503-01896-4

---

## Corrigendum

The following corrections should be made to the short communication entitled "The Unusual Stereochemistry of the Cycloaddition of Vinyl Ethers with Sulfonyl Isothiocyanates" by *Ernst Schaumann, Hans-Günther Bäuch,* and Gunadi Adiwidjaja, Angew. Chem. Int. Ed. Engl. *20*, 613 (1981):

On p. 614, left-hand column, the table caption "Ylides" should read "Yields".

On p. 614, right-hand column, $^2J_{cis}$ and $^2J_{trans}$ in lines eight and nine should read $^3J_{cis}$ and $^3J_{trans}$, respectively.

On p. 614, right-hand column, in the last sentence "... between cumulated π-electron systems ..." should read "... between *non*-cumulated π-electron systems ...".

---

**Editorial office:** Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

**Editor:** *O. Smrekar*, **Translation Editors:** *I. G. Neil* and *A. Stimson*.

**Publishers:** Verlag Chemie GmbH. (Managing Director *Dr. Helmut Grünewald*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany, Telephone Weinheim (06201) 14031 (602-1), Telex 465516 vchwh d.

ANGEWANDTE
CHEMIE

Volume 20 · Number 9
September 1981
Pages 703–818

International Edition in English

# Syntheses of Pyrethroid Acids

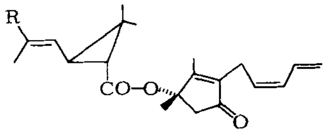
**By Dieter Arlt, Manfred Jautelat, and Reinhard Lantzsch**[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

In the course of the last decade the chemistry of insecticides was expanded with the discovery of new cyclopropanecarboxylic acid esters of specific structure, far superior in action to the hitherto known insecticides of other substance classes or the natural prototypes from the group of pyrethrum constituents. The discovery quickly precipitated a host of wide-ranging studies on the synthesis of these compounds. The development of selective methods of synthesizing complicated small rings called for a comprehensive repertoire: thus, synthesis of the compounds on an industrial scale makes use of sigmatropic rearrangement, radical addition, and nucleophilic ring closure with carbanions. These new industrial syntheses have acquired particular topicality because of their use of stereospecific and enantioselective methods.

## A) Introduction

The constituents of some chrysanthemum species (pyrethrum) have been used as insecticides since the early 19th century. In 1924 *Staudinger* and *Ruzicka*[1] discovered that the active constituents, *e.g.* pyrethrin I *(1)* and II *(2)*, are esters of 2,2-dimethyl-3-(2-methyl-1-propenyl)-1-cyclopropanecarboxylic acid [chrysanthemic or chrysanthemumic acid, cf. *(49)*] and of 3-(2-methoxycarbonyl-1-propenyl)-2,2-dimethyl-1-cyclopropanecarboxylic acid (pyrethric acid).



*(1)*, R = $CH_3$
*(2)*, R = $COOCH_3$

The first synthetic analogues of the natural chrysanthemic acid esters had already been prepared by *Staudinger*[2]. Some subsequently synthesized compounds of this group proved to be superior to the natural substances in their action, but due to their photolability their use remained restricted to the hygiene sector.

The situation changed at the beginning of the 'seventies, when a research team at the National Research and Development Corporation (NRDC)[3], led by *M. Elliott*, reported new analogues of the active constituents of pyrethrum, which stood out against the previously known chrysanthemates due to their quite extraordinary activity and photostability.

Thus began a worldwide development which ended in a new class of insecticides whose technical and economic significance is already comparable with that of the insecticidal esters of phosphorus acids and carbamates. The abnormally fast, almost spectacular development of these new pyrethroids—synthetic descendants of natural pyrethrum insecticides—has been due to their stability to atmospheric influences. In contrast to the natural prototypes,

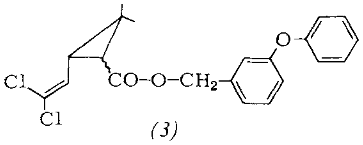
---

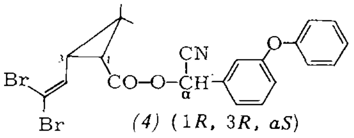
[*] Prof. Dr. D. Arlt, Dr. M. Jautelat
Bayer AG, Zentralbereich Forschung und Entwicklung
D-5090 Leverkusen (Germany)
Dr. R. Lantzsch
Bayer AG, Pflanzenschutz - Chem. Forschung
D-5600 Wuppertal (Germany)

0570-0833/81/0909-0703 $ 02.50/0

they can thus be used in agriculture. At the same time, this new class of substances includes the most effective insecticides known to date, the increase in activity making it possible to reduce the amount applied per unit area to a hundreth of that of conventional phosphorus acid esters.

*Farkas et al.* reported as early as 1958[4] that certain esters of 3-(2,2-dichlorovinyl)-2,2-dimethyl-1-cyclopropanecarboxylic acid [permethrinic acid, cf. *(147)*] act similarly to analogous chrysanthemic acid esters. Making use of this observation the above British group[3] combined this acid with *m*-phenoxybenzyl alcohol to obtain the ester permethrin *(3)*. A few years previously the chrysanthemic acid ester of this alcohol had already come to the attention of researchers at Sumitomo Chemical Co. Ltd. owing to its special insecticidal action. Minor structural alterations led to the enantiomerically pure active substance decamethrin *(4)*, characterized by still greater activity.


*(3)*
Permethrin


*(4)* (1*R*, 3*R*, α*S*)
Decamethrin

It is clear that the outstanding properties of the new pyrethroids have precipitated worldwide research activity in this sphere. The activity and imagination of industrial researchers have been particularly stimulated, leading to an abundance of new synthetic results in the pyrethroid sector. The development of rational and diverse routes for the preparation of the acid components of the new active constituents, termed the pyrethroid acids, was also of particular importance for their industrial preparation.

The hitherto most active insecticides are derived from cyclopropanecarboxylic acids in which the three-membered ring contains two geminal methyl groups and a β-substituted vinyl group. The advances in the synthesis of these important active substances are described synoptically in Section B of this review.

The cyclopropanecarboxylic acids on which the most important insecticides are based are listed in Scheme 1.

Analogous esters of 2,2,3,3-tetramethyl-1-cyclopropanecarboxylic acid *(222)* and of 2-(4-chlorophenyl)-3-methylbutyric acid, which in their action are comparable with the described cyclopropanecarboxylic acid derivatives, have also found practical application as insecticides. The synthesis of these compounds are more conveniently presented separately (see Section D).

R = $CH_3$:
Chrysanthemic acid
R = $COOCH_3$:
Pyrethric acid

X = Y = Cl: Permethrinic acid
X = Y = Br, (1*R*, 3*R*):
Decamethrinic acid
X or Y = $CF_3$ or Cl, X≠Y
X or Y = Cl or *p*-$ClC_6H_4$

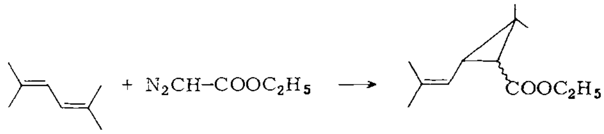
Scheme 1. Important pyrethroid acids.

## B) Methods of Synthesizing Substituted 2,2-Dimethyl-3-vinyl-1-cyclopropanecarboxylic Acids

### 1. [2+1]-Addition

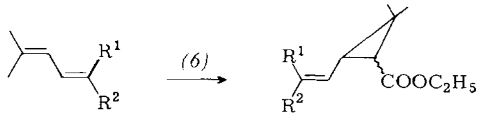
### 1.1. Diazoacetic Ester Synthesis

Following the structural elucidation[1] of the natural pyrethroids, *Staudinger* and *Ruzicka et al.* succeeded in synthesizing ethyl chrysanthemate *(7)*[5] by the reaction of 2,5-dimethyl-2,4-hexadiene *(5)* with the diazoacetic ester *(6)*, but the yield only amounted to 14% since only impure diene was available and no catalyst had been used.



*(5)* *(6)* *(7)*

*Campbell* and *Harper*[6] used very pure diene *(5)*[7] and worked at high temperatures with copper bronze as catalyst. They thus obtained a yield of 64% (*cis*:*trans* ratio = 1:3). When the synthesis is performed in a continuous fashion, the yield can be raised to 80%[8]. A further enhancement of the yield was achieved by catalyzing the reaction with rhodium(II) acetate[9].

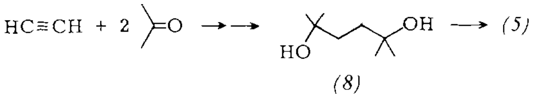


$R^1$, $R^2$ = $CH_3$, $CH_3$[5]; $CH_3$, $COOC_2H_5$[15];
Cl, Cl[4]; Cl, $CF_3$[37]; Cl, *p*-$ClC_6H_4$[31]

The diazoacetic ester synthesis is very generally applicable and relatively simple to perform in the laboratory; it has thus been used for practically all pyrethroid acid components. It is also carried out on the industrial scale. The main problem with these syntheses is preparation of the dienes.

1.1.1. 2,5-Dimethyl-2,4-hexadiene *(5)*

*Staudinger et al.*[5] only obtained *(5)* in an impure form by the dehydrochlorination of 2,5-dichloro-2,5-dimethylhexane. One very elegant synthetic method starts from acetylene and acetone[10] and proceeds *via* *(8)*.



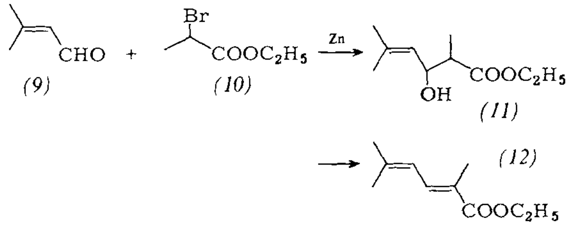
*(8)*

In other syntheses of *(5)*, methallyl chloride is dimerized with magnesium[7], sodium[11], or carbonylnickel compounds[12]. Above 500 °C addition of methallyl chloride to isobutene also takes place in low yield[13]. The primary product, 2,5-dimethyl-1,5-hexadiene, must then be isomerized to *(5)* at *ca.* 450 °C in the presence of an acid catalyst[7].

The diene *(5)* has also been obtained by Wittig reaction[14].

### 1.1.2. Ethyl 2,5-Dimethyl-2,4-hexadienoate *(12)*

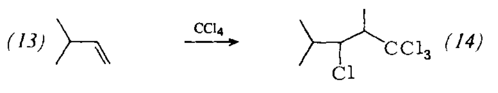
The diene *(12)* is obtained by a Reformatsky reaction of 3-methylcrotonaldehyde *(9)* with ethyl 2-bromopropionate *(10)* and subsequent dehydration with $POCl_3$[15].

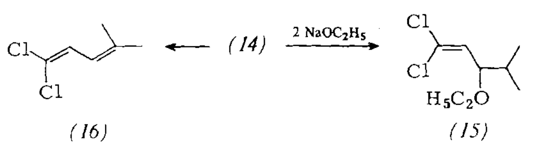


### 1.1.3. 1,1-Dichloro-4-methyl-1,3-pentadiene *(16)*

In the preparation of 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid (permethrinic acid)[4] the main difficulty was also the synthesis of the educt *(16)*.

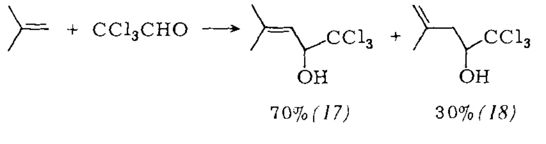
*(16) from 3-methyl-1-butene (13):* To arrive at *(16)*, *Farkas et al.*[4] added carbon tetrachloride to 3-methyl-1-butene *(13)*, but did not succeed in cleaving off two molecules of hydrogen chloride from the adduct *(14)* to give *(16)*; action of heat only resulted in formation of tar, while the allyl chloride produced by the action of sodium ethoxide immediately reacts further in a nucleophilic manner to give *(15)*.

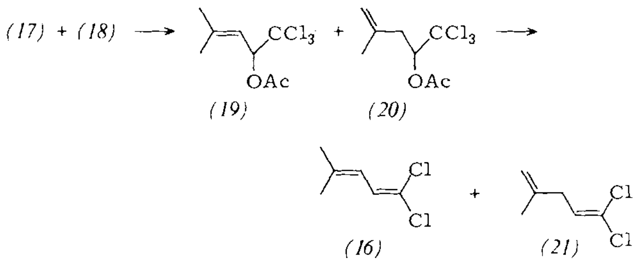




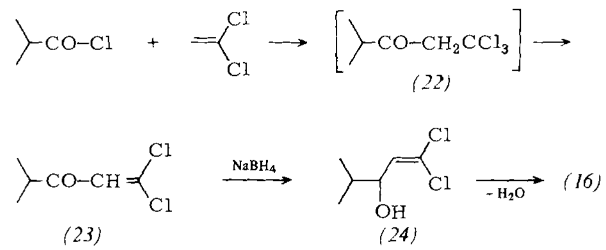
However, twofold dehydrochlorination by means of amines[16], with tin(IV) chloride[17], and with potassium hydroxide in anhydrous solvents[18] is described in the later patent literature.

*(16) from isobutene and chloral:* Because of the reactions described, *Farkas* did not introduce the chlorine atoms with carbon tetrachloride but with chloral. The addition of chloral to isobutene was already known[19]. The isomeric alcohols *(17)* and *(18)* were acetylated to *(19)* and *(20)* respectively and then converted into the isomeric dienes *(16)* and *(21)* with zinc in glacial acetic acid. Once the significance of permethrinic acid (cf. Scheme 1) as the basis for outdoor insecticides had been recognized, many industrial researchers[20] started examining ways of improving the diene synthesis of *Farkas et al.*[4]. Independently of this trend, the four completely new syntheses outlined below were also discovered.



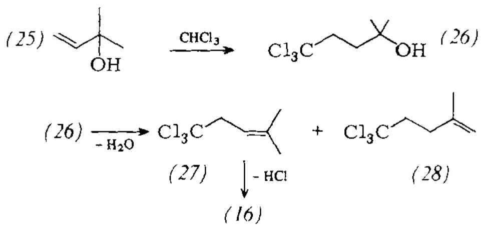


*(16) from isobutanoyl chloride:* The reaction of isobutanoyl chloride with 1,1-dichloroethene in the presence of aluminum chloride gives excellent yields of 1,1-dichloro-4-methyl-1-penten-3-one *(23)*[21]. The hydrogen chloride can be thermally cleaved from the initially obtained trichloroketone *(22)* by distillation[21], or better, especially in the preparation of larger quantities, with the aid of aqueous sodium hydroxide in the presence of phase-transfer catalysts[22]. After reduction with $NaBH_4$ and subsequent dehydration, the desired diene *(16)* is obtained in a high state of purity[23].



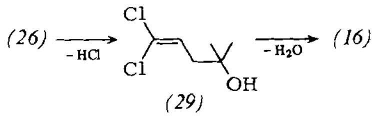
A patent application was later filed for the same synthetic route by other workers[24], the only difference being the reducing agent: Al(O*i*Pr)$_3$ was used instead of $NaBH_4$.

*(16) from isoprenol:* The second new synthetic route starts out from the known[25] addition product *(26)* of chloroform and 2-methyl-3-buten-2-ol *(25)*. The desired diene *(16)* is obtained by dehydration and dehydrochlorination.

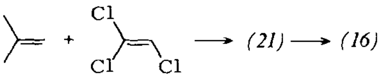


A mixture of 5,5,5-trichloro-2-methyl-2-pentene *(27)* and 5,5,5-trichloro-2-methyl-1-pentene *(28)* is obtained from *(26)*[25-27]. The latter must be isomerized or purified by distillation before the hydrogen chloride can be cleaved off[26].

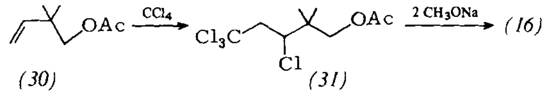
It is more advantageous—since it avoids the need for the non-quantitative isomerization of *(28)*—to cleave the hydrogen chloride from *(26)* first and then to dehydrate the product *(29)*[27]. In this case the newly formed double bond enters into conjugation with the one already present, and hence practically no *(21)* is produced.



*(16) from isobutene and trichloroethene:* At 500—540 °C 1,1-dichloro-4-methyl-1,4-pentadiene *(21)* is obtained in 65% yield by radical addition of isobutene and trichloroethene at 500—540 °C, with a conversion of about 20%. The compound must then be isomerized to the desired diene *(16)*[28].

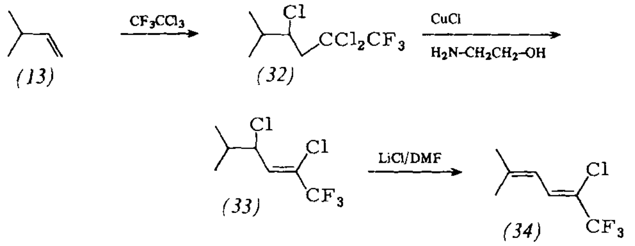


*(16) from dimethylbutenol derivatives:* A fourth synthetic method[29] starts from the acetate *(30)*. Addition of carbon tetrachloride to *(31)* gives 1,1-dichloro-4-methyl-1,3-pentadiene *(16)* *via* C—C bond cleavage under basic conditions.



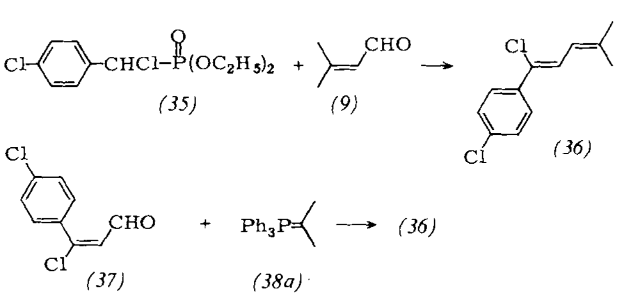
1.1.4. 2-Chloro-1,1,1-trifluoro-5-methyl-2,4-hexadiene *(34)*

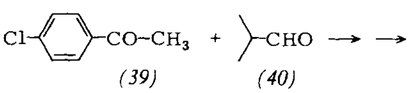
The diene *(34)* is, in principle, obtained by the same fundamental process as 1,1-dichloro-4-methyl-1,3-pentadiene *(16)* from 3-methyl-1-butene *(13)*, but special conditions had to be found for the dehydrochlorination of *(32)* and *(33)*[30] (DMF = dimethylformamide).

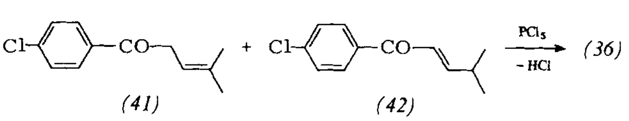


1.1.5. 1-Chloro-1-(4-chlorophenyl)-4-methyl-1,3-pentadiene *(36)*

The diene *(36)* can be obtained *e.g.* by a Wittig reaction[31], or by the reaction of *p*-chloroacetophenone *(39)* with isobutyraldehyde *(40)*[31]. A dimeric condensation product is obtained, which can be resolved into a mixture of the isomeric monomers *(41)* and *(42)*, which can in turn be converted into *(36)*.

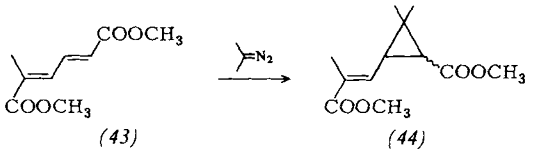






### 1.2. Diazopropane Synthesis

Whereas the introduction of C-1 by diazoacetic ester is one of the most important syntheses for pyrethroid acid components, there are only a few examples of the introduction of C-2. We shall, therefore, only mention the synthesis of the pyrethrate ester *(44)*[32,33] from diazopropane and (*E,E*)-α-methyl muconate *(43)*[34]. The pyrazoline intermediate can be isolated[33].



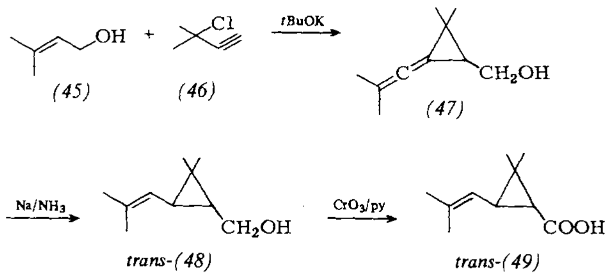
### 1.3. Intramolecular Diazo Syntheses

*cis*-Chrysanthemic acid and *cis*-permethrinic acid were obtained by an intramolecular cyclopropane ring closure of diazoketone[35] or of a diazoacetic ester[36] (see Section C).

### 1.4. Other Carbene and Carbenoid Additions

Further examples of carbene- and carbenoid-addition demonstrate the preparative range of this method, although this does not surpass or even reach the importance of the diazoacetic ester method.

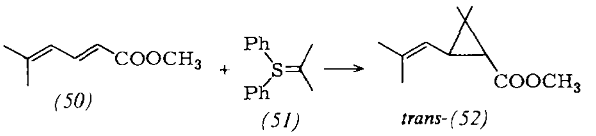
The *cis-trans* chrysanthemic acid ester *(7)* can be prepared from the diene *(5)* and diiodoacetic ester *via* a Simmons-Smith variant[38]. 1-Cyanopermethrinic acid ester was obtained by reacting the dichlorodiene *(16)* with activated acetonitriles such as cyanoacetic ester in the presence of copper(II) salts[39]. The reaction of α-halomalonic acid derivatives with copper or with copper salts and a base has also led to permethrinic acid derivatives[40]. Using dimethylallenecarbene it was possible to synthesize the alcohol *(48)*, a precursor of chrysanthemic acid *(49)*, from prenol *(45)*[41].



## 1.5. Ylide Additions

### 1.5.1. Sulfuranes

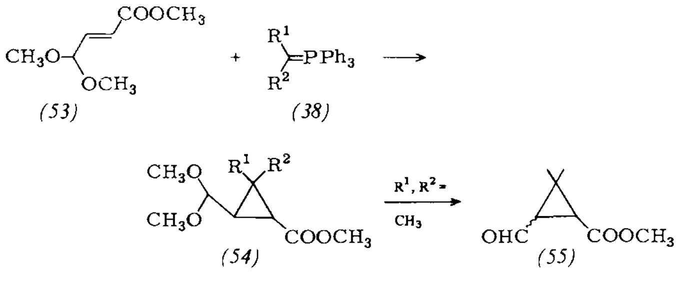
The possibility of using sulfuranes, such as *(51)*, for the synthesis of pyrethroids was demonstrated at an early stage using the chrysanthemic ester *(52)*[42]. Other pyrethroid acids[43] and intermediate products[44] have also been obtained with sulfuranes (see Section D).



*(50)* *(51)* *trans-(52)*

### 1.5.2. Phosphoranes

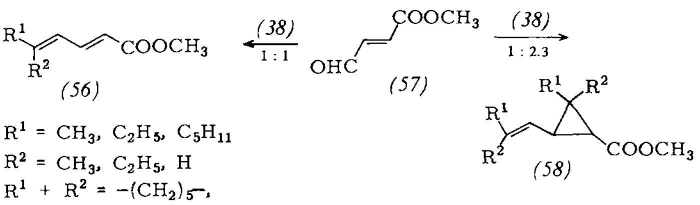
Three-membered ring formation in this series, using phosphoranes, was first reported by *Krief et al.*, who reacted methyl 4,4-dimethoxycrotonate *(53)*[45] with phosphoranes *(38)* to obtain the cyclopropanes *(54)*, which following hydrolysis to aldehydes constitute important intermediates for further pyrethroids (see Section B6).



*(53)* *(38)* *(54)* *(55)*

$R^1, R^2 = CH_3$; $R^1 + R^2 = -(CH_2)_4-$

Depending on the molecular ratio and the substituents, the dienecarboxylic ester *(56)* or the vinylcyclopropanecarboxylic ester *(58)* can be obtained from the aldehyde *(57)* and phosphoranes *(38)*[46]. However, the cyclopropanization to *(58)* was only possible with the isopropylidene and the cyclopentylidene phosphoranes *(38)*[45], the other phosphoranes *(38)* yielding the dienecarboxylic ester *(56)* exclusively. According to a mechanistic study, the chrysanthemic acid derivatives *(58)* are formed from the aldehyde *(57)* *via* a betaine[47]. On the basis of this finding, a single-vessel process for the production of the vinylcyclopropanecarboxylic ester *(58)* from two different phosphoranes has been developed[48].

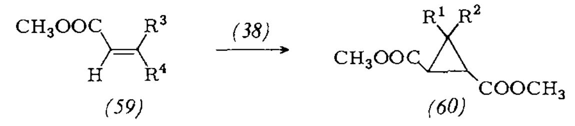


*(56)* *(57)* *(58)*

$R^1 = CH_3, C_2H_5, C_5H_{11}$
$R^2 = CH_3, C_2H_5, H$
$R^1 + R^2 = -(CH_2)_5-, -(CH_2)_4-$

$R^1, R^2 = CH_3$ [≡*(52)*]
$R^1 + R^2 = -(CH_2)_4-$

The cyclopropanization of fumaric or maleic esters *(59a)* and *(59b)*[49] with phosphoranes *(38)* opens up a stereospecific route to *trans*- and *cis*-caronaldehyde esters. In both cases the *trans*-1,2-cyclopropanedicarboxylic ester *(60)* is obtained, which is selectively converted into the *trans*- or *cis*-formylcyclopropanecarboxylic ester (see Section C).



*(59)* *(60)*

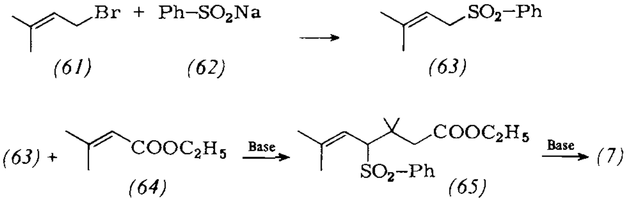
*(a)*, $R^3 = H$, $R^4 = COOCH_3$
*(b)*, $R^4 = COOCH_3$, $R^4 = H$

$R^1, R^2 = CH_3, C_2H_5$
$R^1 + R^2 = -(CH_2)_4-, -(CH_2)_5-$

## 1.6. Ring Closure by Addition-Elimination Reactions

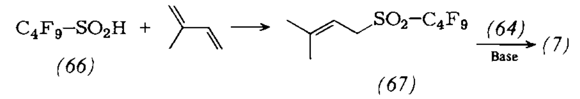
This section summarizes the methods in which the three-membered ring is produced by an addition-elimination reaction, although from the mechanistic point of view a strict separation of the ylide reactions is impossible.

*Martel et al.*[50] reacted the allyl sulfone *(63)*, obtained by alkylation of sodium benzenesulfinate *(62)*, with methyl crotonate derivatives such as *(64)* in the presence of bases. Depending on the quantity of base, *trans*-chrysanthemic acid ester *(7)* could be obtained in two separate steps or in a one-pot process. This process has subsequently been used for the preparation of numerous homologues[51,52] of chrysanthemic acid.



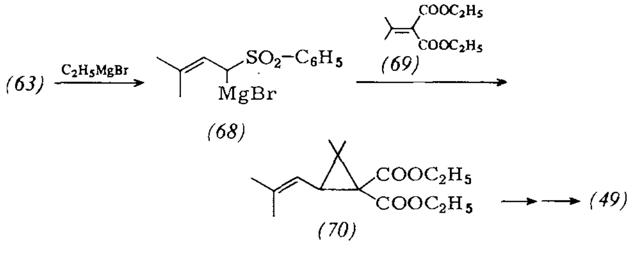
*(61)* *(62)* *(63)* *(64)* *(65)*

A more elegant access to allyl sulfones, the addition of perfluoroalkanesulfinic acids[53] to isoprene, simplifies the entire synthesis.



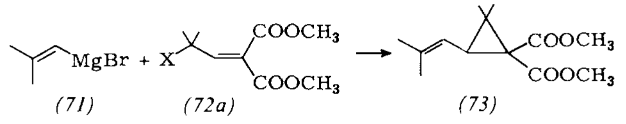
*(66)* *(67)*

A special variant of this process is the addition-elimination of the Grignard reagents *(68)*[54] to the isopropylidenemalonic ester derivatives *(69)* and subsequent conversion of the adduct *(70)* by hydrolysis and decarboxylation into chrysanthemic acid *(49)* (see Section B5.3). One variant is the reaction of the allyl sulfone *(63)* with 3-bromo-3-methylbutyric acid esters and potassium *tert*-butoxide to give *(7)*[55].



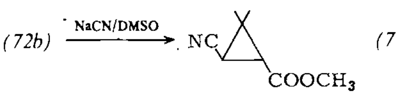
*(68)* *(70)*

The reaction of 2-methyl-1-propenylmagnesium bromide *(71)* with the (2-chloro-2-methylpropylidene)malonic ester *(72a)*[56], in which methyl 1-methoxycarbonylchrysanthemate *(73)* is formed as the main product, proceeds by a different course. The corresponding 2-bromide *(72b)* is largely reduced to the (2-methyl-1-propenyl)malonic ester.



*(a)*, X = Cl; *(b)*, X = Br

*Krief et al.*[57] similarly synthesized the *trans*-caronaldehyde ester. 3-Cyano-2,2-dimethylcyclopropanecarboxylic acid ester *(74)* was prepared from the bromo ester *(72b)* and sodium cyanide in a one-pot procedure, and this was then converted into the aldehyde *via* two routes (DMSO = dimethyl sulfoxide).



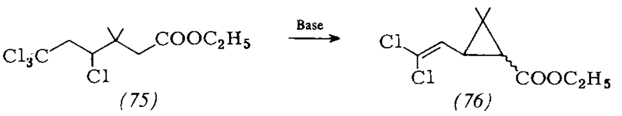
## 2. Nucleophilic Substitution

The most important processes for the preparation of vinylcyclopropanecarboxylic acids are based on ring closure by 1,3-elimination between C-1 as the nucleophilic center and C-2 or C-3 as the site of the substitution. For preparative reasons the connection between C-1 and C-3 is the more important.

### 2.1. Ring Closure between C-1 and C-3

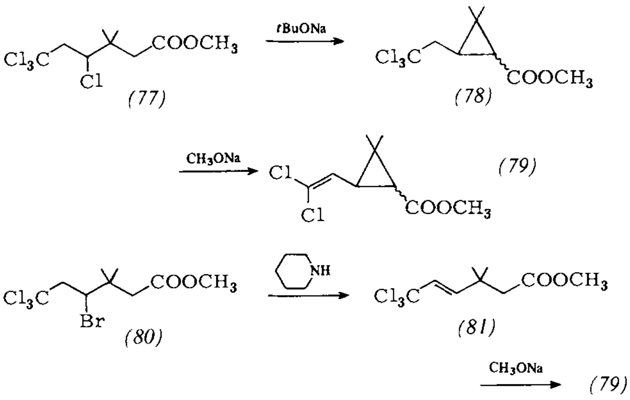
### 2.1.1. 1,3- and Vinylogous 1,5-Elimination

As a result of the activating influence of a carboxy group the action of bases on C-1 leads to formation of a carbanion, which upon ring formation substitutes a leaving group on C-3[58] or vinylogously on C-5[59]. Halogen atoms dominate the nucleofugal groups, in this case again chlorine. In many cases dehydrogenation often accompanies this cyclization, as shown by the final stage of the Sagami process[60].

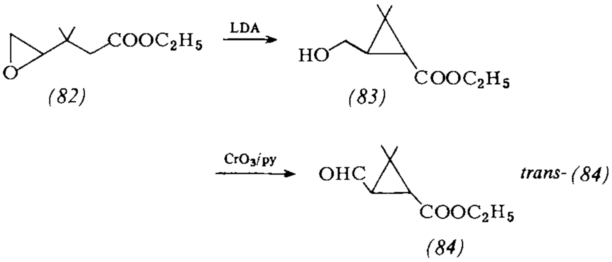


In many syntheses this reaction principle is applied with a modification of the carboxy group[61,62], the substituents on the vinyl group[37,63,64], the bases, and the solvent. Under special conditions the two steps can be carried out separately and consecutively[65,66].

The presence of another activating group facilitating the ring closure[67], such as carboxy, alkoxycarbonyl, cyano, or acyl on C-1, is determined by the accessibility of the initial products. The conversion into the monocarboxylic acid takes place in successive steps (see Section B 5).



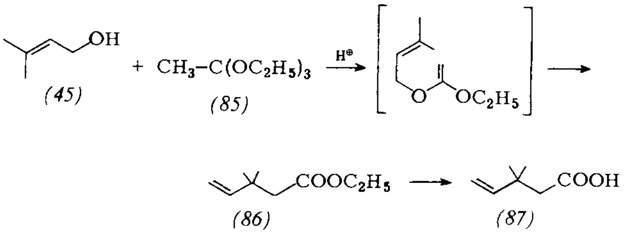
Cyclopropane ring closure with simultaneous opening of an epoxide *(82)* is used for the synthesis of the caronaldehyde ester *(84)*[68] (LDA = lithium diisopropylamide).



The intermediates capable of cyclization are essentially obtained by radical addition of polyhalogenated alkanes to 3,3-dimethyl-4-pentenoic acid derivatives, by Claisen rearrangement of corresponding halogenated allyl vinyl ethers, and by ring opening of lactones (see Sections B2.1.2—2.1.4).

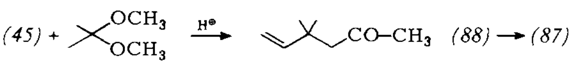
### 2.1.2. Addition of Polyhalogenated Alkanes to 3,3-Dimethyl-4-pentenoic Acid *(87)* and Derivatives

*Syntheses of (87):* 3,3-Dimethyl-4-pentenoic acid *(87)* and its derivatives are intermediates of central significance for a great number of pyrethroid syntheses. The acid was first prepared by a malonic ester synthesis[69]. Several new routes were opened up in the 'seventies. The synthetic route of the Sagami Chemical Research Center afforded direct access[60] from prenol *(45)* and orthoacetic ester *(85)* or ketene acetal *via* a Claisen rearrangement.



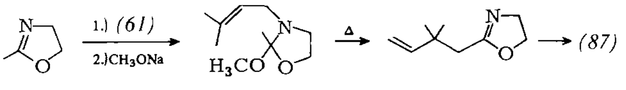
A Claisen rearrangement had already been used earlier to make other 3,3-dimethyl-4-pentene derivatives[70,71].

This reaction has become the starting point for many variants of the process[72]. The hexenone *(88)*[73], which is also an important intermediate for permethrinic acid, can be obtained in this way.



The synthesis of *N,N*,3,3-tetramethyl-4-pentenoic acid thioamide from prenyl chloride and *N,N*-dimethylthioacetamide is based on a thia-Claisen rearrangement[74].

Starting from 2-methyloxazoline *(89)* and prenyl bromide *(61)*, a 2-methoxyoxazolidine *(90)* can be prepared and which undergoes rearrangement into 2-(2,2-dimethyl-3-butenyl)oxazoline *(91)* upon pyrolysis[75].

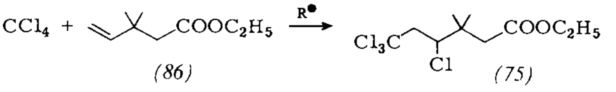


*(89)* *(90)* *(91)*

The radical addition of ethanol[76] and of acetaldehyde[77] to 3-methylcrotonic acid derivatives should similarly result in derivatives of *(87)*.

Further methods for the preparation of pentenoic acid *(87)* include the oxidation of 3,3-dimethyl-4-pentenal[78] with silver oxide, the addition of vinylmagnesium chloride to 3-methylcrotononitrile[79], and the combined substitution and elimination reactions of cyanide with 2,2-dimethyl-1,3-butanedisulfonates[80].

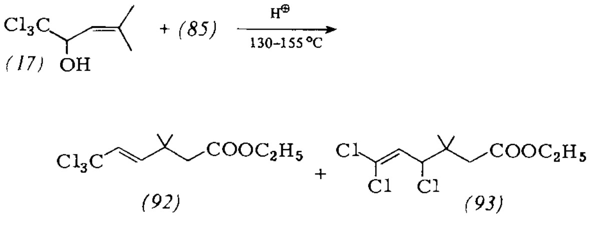
*Addition to (87) and derivatives:* The radical addition of polyhalogenated alkanes to derivatives of 3,3-dimethyl-4-pentenoic acid *(87)* is performed in a known fashion[81] *via* initiation by peroxides, metal salts, metal complexes, or light[60,72,82].



The most frequently used polyhalogenated alkanes are tetrahalogenomethanes such as carbon tetrachloride and chlorotribromomethane, although chlorinated and/or brominated higher alkanes[83] and fluorinated alkanes[37,64] have also been used. Instead of the dimethylpentenoic acid derivatives[84] their analogues, such as 4,4-dimethyl-5-hexen-2-one *(88)*[85], 3,3-dimethyl-4-pentenal[86], or isopentenyl malonic ester derivatives[87], can also be used, the conversion into monocarboxylic acid taking place at a later stage (see Section 5).

### 2.1.3. Claisen Rearrangement of Halogenated Allyl Vinyl Ethers

The reactions discussed in this section proceed *via* intermediate halogenated allyl vinyl ethers. Reference may also be made to a non-halogenated analogue arising in the formation of *(86)* from *(45)* and *(85)* (Section B 2.1.2).

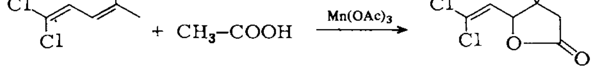


Whereas in the Sagami process the halogen is introduced after the Claisen rearrangement, this step is taken before the rearrangement in the synthetic procedure of the Kuraray company. The alcohol mixture, obtainable from chloral and isobutene (see Section B 1.1.1), is converted into the trichlorodimethylhexenoic esters *(92)* and *(93)*, after isomerization to *(17)*, by the action of orthoacetic ester *(85)* or ketene acetals[88]. This reaction is not restricted to chloral as educt, and gives rise to homologous permethrinic acids with other halogenated aldehydes[89].

### 2.1.4. Preparation and Ring Opening of Secondary Lactones

Since the ring opening of γ-lactones with halogenating reagents leads to γ-halogenated carboxylic acid derivatives[90], this constitutes a good method for the preparation of the precursors of the cyclopropane ring closure. Both secondary and tertiary lactones are suitable for this process, but intermediate products are obtained for coupling C-1 and C-2 from the tertiary lactones, as discussed in Section B 2.2. Only the secondary lactones, which can be prepared in many possible ways, can be used for ring closure between C-1 and C-3.

Lactones such as *(94)* are obtained from 1,1-dichloro-4-methyl-1,3-pentadiene *(16)* and carboxylic acids[91] by oxidation.



*(16)* *(94)*

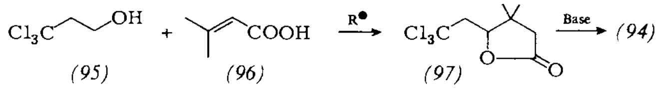
A novel route to *(94)* consists in the reaction of 1,1,1-trichloro-4-methyl-3-penten-2-ol *(17)* or its isomer *(18)* with 1,1-dichloroethene[92] in sulfuric acid.

$$(17) + CH_2{=}CCl_2 \xrightarrow{H_2SO_4} (94)$$

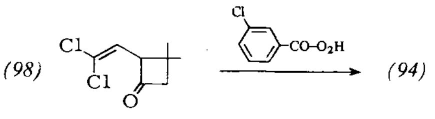
At high temperatures Claisen rearrangement of the alcohol *(17)* similarly gives the lactone *(94)*[93].

$$(17) + (85) \xrightarrow[100\text{-}190\ ^\circ C]{H^\oplus} (94)$$

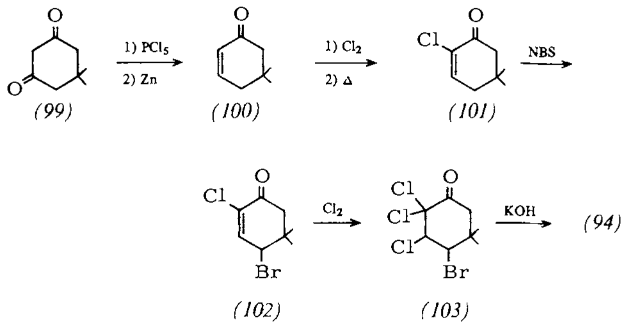
Radical addition of 3,3,3-trichloro-1-propanol *(95)* to 3-methylcrotonic acid *(96)* leads to the trichloroethyl lactone *(97)*, which can be dehydrohalogenated to *(94)*[94].



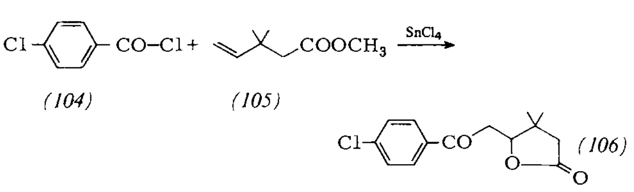
The cyclobutanone *(98)*, important as an intermediate for the Favorskii rearrangement (see Section 3), provides access to the lactone *(94)* by Baeyer-Villiger oxidation[95].



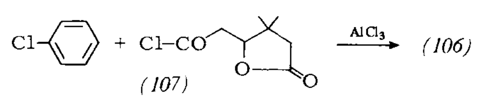
The diversity of the syntheses is demonstrated by another route that starts from 5,5-dimethyl-1,3-cyclohexanedione (dimedone) *(99)*, *via* the alkaline cleavage of tetrahalocyclohexanone *(103)*[96] (NBS = *N*-bromosuccinimide).



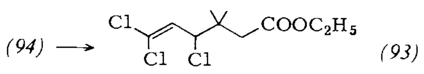
Acylation of the 3,3-dimethyl-4-pentenoic ester *(105)* with acid chlorides catalyzed by $SnCl_4$ yields secondary lactones *(106)*, whose ring cleavage permits the preparation of (styryl)cyclopropanecarboxylic acids[97].



The lactone *(106)* is similarly accessible by Friedel-Crafts acylation[97].

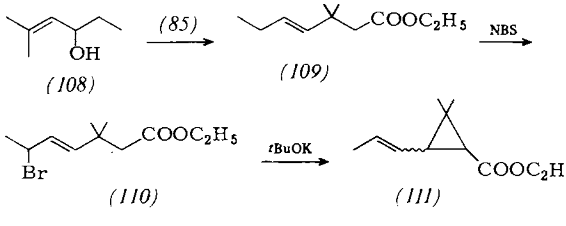


The cleavage of the lactone ring, *e.g.* in *(94)*, proceeds in conventional fashion with hydrogen chloride and alcohols or with inorganic acid halides and alcohols[91,98].

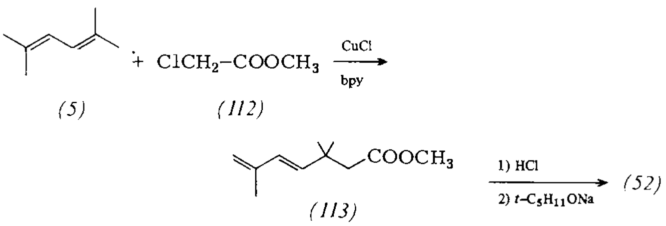


### 2.1.5. Other Halogenations

The allyl halogenations[63,99] of 4-alkenoic acid esters such as *(110)*, which also proceed *via* a Claisen rearrangement, must be regarded as exceptions. This halogenation makes it possible to prepare chrysanthemumic acid analogues such as *(111)*.

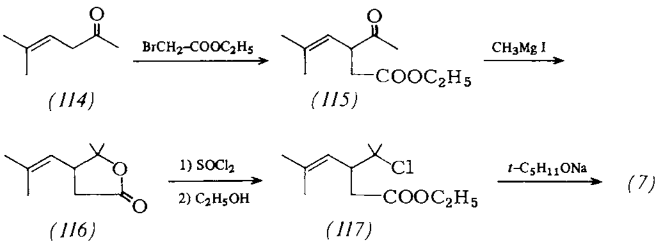


As a special method for the formation of methyl chrysanthemate *(52)*, *Julia et al.*[100] described the addition of methyl chloroacetate *(112)* to 2,5-dimethyl-2,4-hexadiene *(5)* with redox catalysis to give the diene ester *(113)*, which is then cyclized by alkoxide to *(52)* after hydrogen chloride addition. The yield of the process is low.



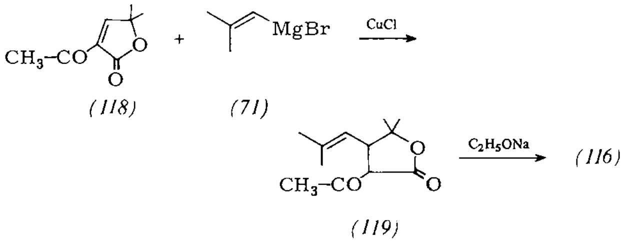
## 2.2. Ring Closure between C-1 and C-2

The bond between C-1 and C-2 in the pyrethroid ring can be formed in a similar manner by nucleophilic 1,3-elimination, the use of phase-transfer catalysts giving yields comparable to those in ring closures between C-1 and C-3. The γ-halogenated carboxylic acids required for this purpose are obtained from tertiary lactones such as *(116)*. Chrysanthemic acid syntheses, in particular, have been developed in this manner by ***Julia***, who prepared pyrocine *(116)* using isobutyraldehyde and acetone and after ring opening and cyclization obtained ethyl *trans*-chrysanthemate *(7)*[101].

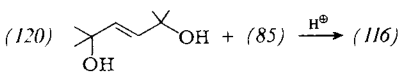


A similar synthesis, but based on a Claisen rearrangement, has been described[70].

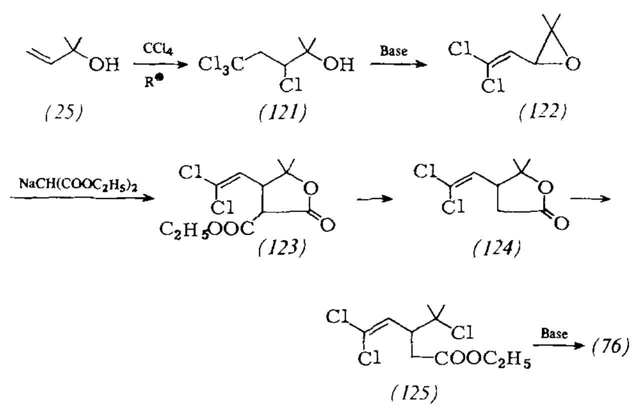
Japanese authors[102] have found a new route to the lactone *(116)*, preparing the acyl lactone *(119)* by a Michael addition from the butenolide *(118)* and cleavage of the ketone.



Claisen rearrangement of the butenediol *(120)* with orthoacetic ester *(85)* also gives rise to the pyrocine *(116)*[103].

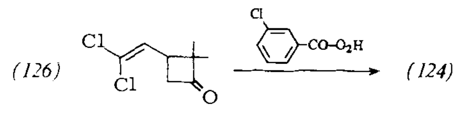


Processes for the preparation of (halovinyl)cyclopropanecarboxylic acids *via* tertiary lactones as intermediates were developed in parallel by ***Baeyer*** and ***Cheminova***[104]. To this end, 2-methyl-3-buten-2-ol *(25)* is used as the starting material and the tetrachloromethane adduct *(121)* converted with base into the epoxide *(122)*[105]. The reaction with malonic ester gives the lactone *(123)*, which after decarboxylation *via* the γ-chloro ester *(125)* yields the permethrinic acid ethyl esters *(76)*.



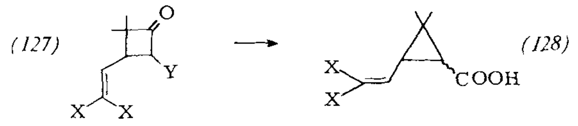
Chrysanthemic acid is synthesized in the same manner starting from 4,5-epoxy-2,5-dimethyl-2-hexene[106] and styrylcyclopropanoic acids[107] can be synthesized in an analogous manner.

The tertiary lactone *(124)* can also be obtained by Baeyer-Villiger oxidation from 3-(2,2-dichlorovinyl)-2,2-dimethylcyclobutanone *(126)*[108].



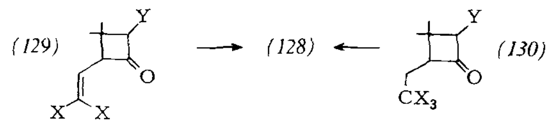
## 3. Favorskii Rearrangement

*Conia et al.*[109] found that α-halogenated cyclobutanones generally react to give cyclopropanecarboxylic acids in very good yields, and consequently this route has also been used for the preparation of pyrethroid acids of the general type *(128)*[110, 111].



X = $CH_3$, Cl, Br; Y = Cl, Br, O–Tosyl

The cyclobutanones *(129)* isomeric with *(127)* and their analogues *(130)* having a saturated side chain also react to give the cyclopropanecarboxylic acids *(128)*[112].

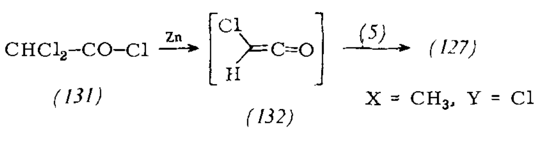


X = Cl, Br; Y = Cl, Br, O-Tosyl

In the case of *(130)* the Favorskii rearrangement and dehydrohalogenation are carried out in one step using aqueous sodium hydroxide.

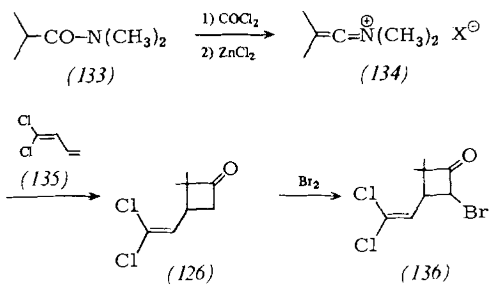
### 3.1. Preparation of Cyclobutanones of Type *(127)* and *(130)*

There are several possibilities for the preparation of the cyclobutanones but the process is fundamentally one of [2+2]-cycloaddition:

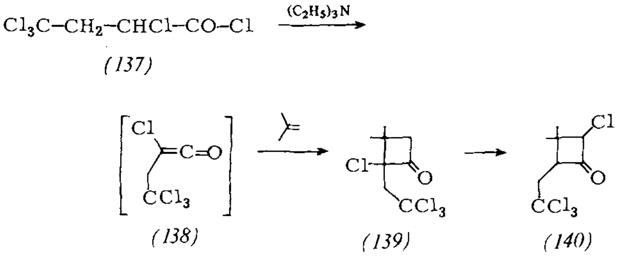


X = $CH_3$, Y = Cl

The relatively difficultly accessible monohaloketenes such as *(132)* are needed for the synthesis of *(127)*, Y = halogen. In the preparation of the derivative *(127)*, X = Cl, Y = Br [≡*(136)*] this is avoided by reacting 1,1-dichloro-1,3-butadiene *(135)*[113] with the alkenylideneammonium salt *(134)* to give *(126)*[111, 114]. The 4-bromine atom is introduced subsequently.



One route for the synthesis of the type *(130)* starts out from the addition product *(137)* of carbon tetrachloride and acrylic acid chloride[115].

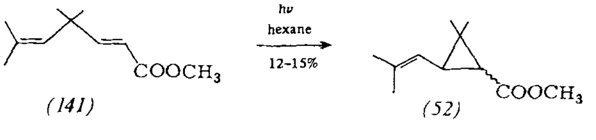


The rearrangement *(139)*→*(140)* [≡*(130)*, X = Y = Cl] proceeds with tertiary amines or quaternary ammonium salts[112].

## 4. Photochemical Formation of the Cyclopropane Ring

### 4.1. Di-π-methane Rearrangement

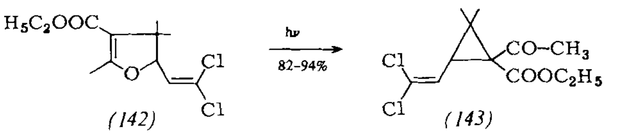
This relatively broadly applicable photochemical reaction leading to cyclopropane derivatives[116] has also been used for the synthesis of chrysanthemic acid methyl ester *(52)* from the dienoic ester *(141)*[117].



*cis* : *trans* = 1 : 2

### 4.2. Dihydrofuran Rearrangement

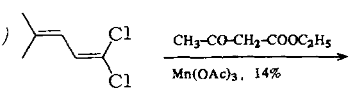
Irradiation of ethyl 5-(2,2-dichlorovinyl)-2,4,4-trimethyl-4,5-dihydrofuran-3-carboxylate *(142)*[118, 119] gives excellent yields of the ester *(143)*, a precursor of permethrinic acid.



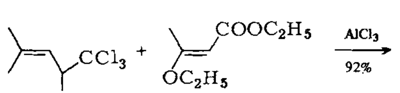
*(142)* *(143)*

Chrysanthemic acid has also been prepared in this way[118]. *(142)* is obtained by oxidative coupling of *(16)* with acetoacetic ester[120]. The reaction of *(17)* with the isocrotonic acid derivative *(144)* leads to better yields of *(142)*.

*(16)*



*(142)*



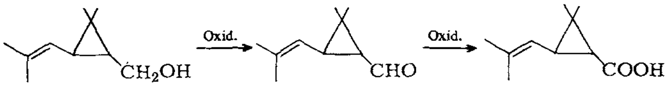
*(17)* *(144)* *(142)*

## 5. Reactions at C-1

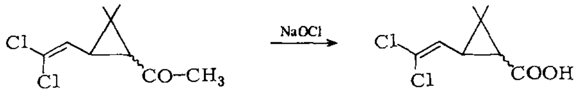
In some syntheses vinylcyclopropanes are formed after the ring closure and a further reaction at C-1 is required to obtain vinylcyclopropanemonocarboxylic acids. This is achieved by oxidation (Section B 5.1), hydrolysis (Section B 5.2), or decarboxylations and carboxylations (Section B 5.3).

### 5.1. Oxidation

Vinylcyclopropanemethanols and -carbaldehydes, which can be oxidized to the corresponding carboxylic acids, are accessible by the methods described in Sections B 1.4 and B 2.1 *via* addition of carbene and polyhalogenated methane or from natural products such as 3-carene[122]. Oxidation of the alcohol *(48)* with oxygen on a platinum catalyst[123] or with chromium trioxide[124] leads to the aldehyde *(145)*. With sodium periodate and ruthenium dioxide, mixtures of aldehyde and acid *(49)* are obtained[125]. Chromium trioxide/pyridine[41, 126], Jones' reagent[126], and silver oxide[123, 126] are suitable for selective oxidation of the aldehyde *(145)* to chrysanthemic acid *(49)*. Alkaline hydrogen peroxide has also been described as an oxidizing agent for the permethrinaldehyde[122]. The permethrinaldehyde can be converted into the carbonitrile *via* an intermediate oxime[127].



*(48)* *(145)* *(49)*



*(146)* *(147)*

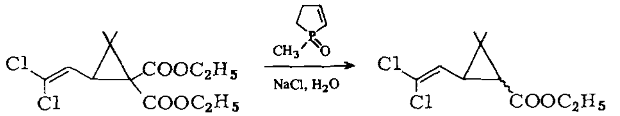
Methyl ketones such as *(146)* are converted into permethrinic acid *(147)* or its esters[128] by oxidative degradation (haloform reaction).

### 5.2. Hydrolysis

Nitriles often serve as precursors, and are formed by ring closure between C-1 and C-3 (Section B 2.1), by dehydration of oximes, or by decarboxylation of 1-cyanocyclopropanecarboxylic acids (Section B 5.3). Solvolysis of the nitriles yields both acids and esters[35, 129].

### 5.3. Decarboxylation and Carboxylation

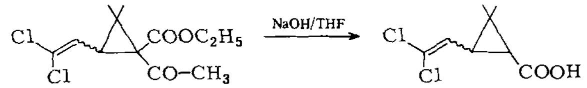
The 1,1-difunctional cyclopropanes, based on malonic acid derivatives and acetoacetic ester (Section B 2), must be degraded at the end of the synthesis of cyclopropanemonocarboxylic acid derivatives. Thermal decarboxylation of the dicarboxylic acids leads, *via* opening of the cyclopropane ring, to lactones of the type of *(124)*. The desired products can be obtained by heating in quinoline in the presence of copper[130]. Cleavage of diesters such as *(148)* can be carried out in $DMSO/H_2O$ using alkali metal salts[131] and with cyclic amidines and amines[132], and especially advantageously on heating with alkali metal salts in phospholine oxides[133].



*(148)* *(76)*

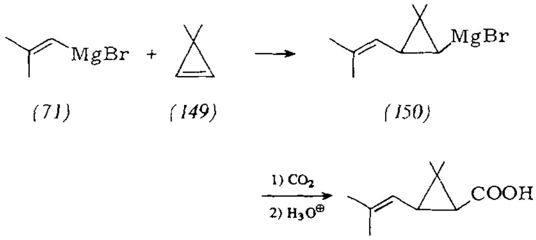
1-Cyanocyclopropanecarboxylic acids and esters are decarboxylated under analogous conditions to give mononitriles[67a, 134].

1-Acetylcyclopropanecarboxylic acid esters such as *(143)* are converted into permethrinic acid *(147)* by acid cleavage (THF = tetrahydrofuran)[67b, 118].



*(143)* *(147)*

Addition of the alkenyl Grignard compounds *(71)*[135] to 3,3-dimethylcyclopropene *(149)*, which is accessible *e.g.* from isobutene and chloroform, opens up a selective route to *cis*-chrysanthemic acid *(49)*. Carboxylation of the addition product leads to (*Z*)-chrysanthemic acid *(49)*.



*(71)* *(149)* *(150)*

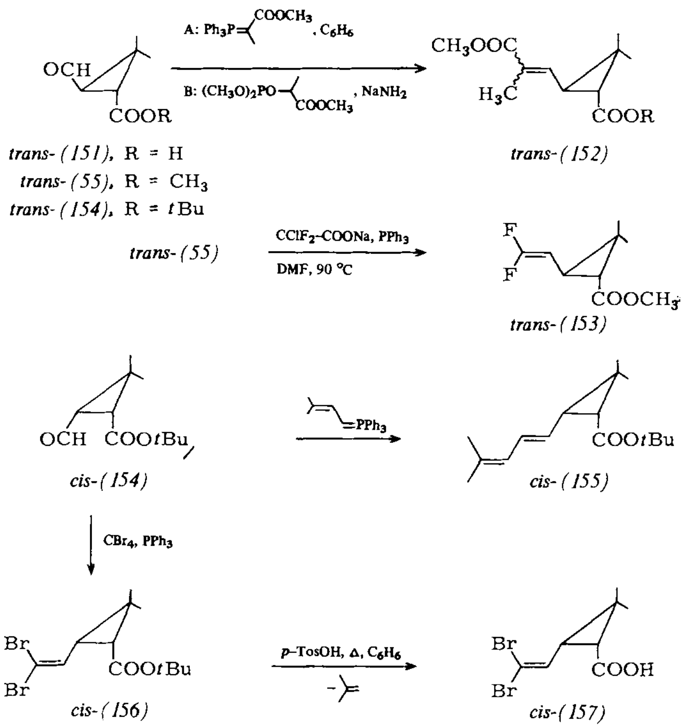
*cis-(49)*

## 6. Reactions at C-3

### 6.1. Syntheses Proceeding from Caronaldehydic Acid *(151)*

3-Formyl-2,2-dimethyl-1-cyclopropanecarboxylic acid *(151)* and its esters *(55)* and *(154)* are intermediates from which any pyrethroid acid with a (substituted) vinyl group in the 3-position can be made.

The Wittig reaction in its various forms[136a–f] and analogous olefinations[137] lead without any problems to the desired products (*E*:*Z* see [136g]). The production of the central building blocks of the synthesis, *e.g.* *(151)*, *(55)* and *(154)*, is time-consuming and elaborate. The addition of phosphoranes and sulfuranes to suitably substituted unsaturated compounds has already been mentioned as a synthetic route to these compounds (see Section B 1.5.2) and the extent that it is stereospecifically regulated is shown in Section C 4.5.

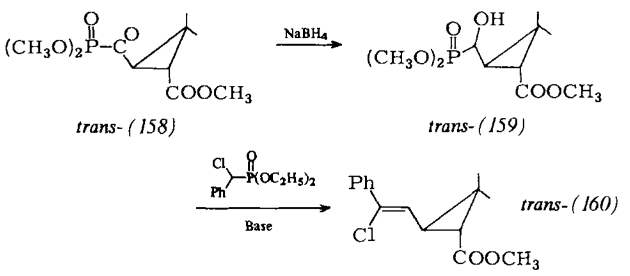


*trans-(151)*, R = H
*trans-(55)*, R = $CH_3$
*trans-(154)*, R = *t*Bu
*trans-(152)*
*trans-(55)*
*trans-(153)*
*cis-(154)*
*cis-(155)*
*cis-(156)*
*cis-(157)*

Ozonization of chrysanthemic esters had been used repeatedly for the preparation of caronaldehydic acid esters such as the particularly useful *tert*-butyl ester *(154)*. *Martel*[166] developed this process into a method for making enantiomerically pure *cis*- and *trans*-pyrethroid acids accessible from enantiomerically pure chrysanthemate (see Section C 4.5).

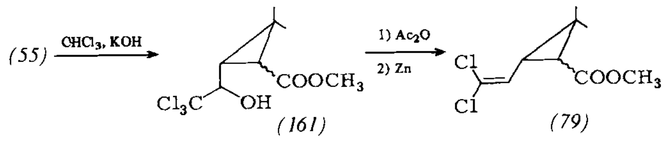
Other caronaldehydic acid syntheses (see *e.g.* Sections B 1.6 and C 4.5) also demand multistage and sometimes elaborate reaction sequences, so that equivalent synthesis elements have also recently been used for olefination reactions[138]. The ester *(158)* is obtained by reacting a caronic acid half-ester chloride and a phosphorous ester.

Aldol condensations of caronaldehydic acid esters such as *(154)* are also used with appropriate reaction partners, *e.g.* methyl propionate, for the preparation of pyrethroid acids[139].



*trans-(158)*
*trans-(159)*
*trans-(160)*

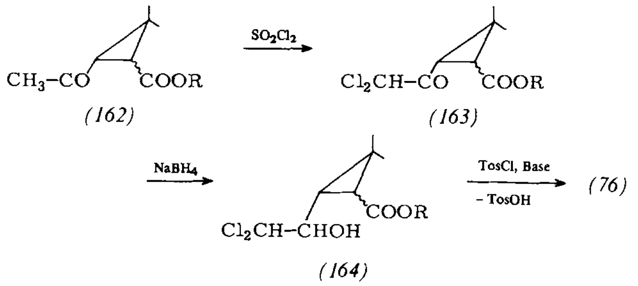
An alternative to the synthesis of 3-(2,2-dihalovinyl)-pyrethroid acids such as *(79)* by the Wittig reaction is the haloform addition to caronaldehydic acid (ester) in the presence of alkali metal hydroxides[140]. *(79)* is obtained in 65% yield [relative to *(151b)*].



*(161)*
*(79)*

### 6.2. Syntheses Proceeding from 3-Acetyl-2,2-dimethyl-1-cyclopropanecarboxylic Acid *(162)*

The ester *(162)* can be obtained by addition of alkoxycarbonylmethylenesulfuranes to mesityl oxide[141]. Selective halogenation to *(163)*, subsequent reduction to *(164)*, and elimination convert this precursor into important dihalovinylpyrethroid acids *e.g.* *(76)*[142].

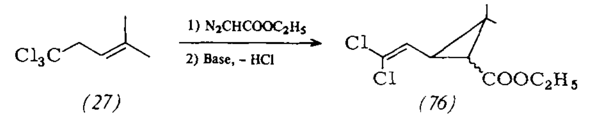


*(162)*
*(163)*
*(164)*

### 6.3. Pyrethroid Acids from Elimination Reactions on Alkyl Groups in the 3-Position

Eliminations leading to the production of the vinyl group in the 3-position are associated with many pyrethroid acid syntheses under basic conditions. Such secondary reactions are shown in the corresponding ring syntheses (see Sections B 2.1.1, B 2.1.4, B 2.2, B 3, C 4.2, and C 4.3).

It can sometimes prove advantageous to perform the elimination at the end of the synthesis if unsaturated precursors which are more expensive to make can thereby be avoided. Thus, the diazoacetic ester synthesis (see Section B 1.1) can also be carried out with *(27)* instead of the diene *(16)*, the cycloadduct being readily dehydrohalogenated at the end[142].

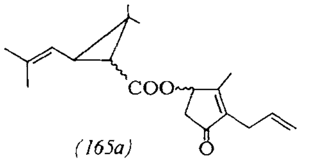


*(27)*
*(76)*

## C) Stereochemistry

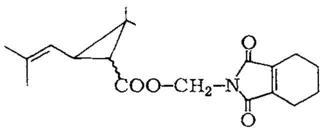
### 1. Superior Activity of Certain Enantiomers

The superior activity of *trans*-chrysanthemic esters, and especially of the enantiomers having the *trans*-(1*R*,3*R*) configuration, in combination with the natural pyrethroid alcohol components and in synthetic chrysanthemates such as allethrin *(165a)*[143] and tetramethrin *(165b)* has long been known. In contrast to this, it has been found that the 3-phenoxybenzyl esters of chrysanthemic acid have a superior activity when the *cis*-acid, and especially its (1*R*,3*S*)-enantiomer, is used as the acid component[144].



*(165a)*

Allethrin



*(165b)*

Tetramethrin

Analogous steric structure-activity relationships have been found for the insecticides derived from the dihalovinyl(dimethyl)cyclopropanecarboxylic acids. The first enantiomerically pure active principle introduced into practice [decamethrin, Decis®, *(4)*] contains as the acid component the *cis*-(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethyl-1-cyclopropanecarboxylic acid (decamethrinic acid). It was found that the esters of other (1*R*)-acids[145] are also several times more active than their enantiomers, and thus major efforts have been made to develop methods of preparation of sterically uniform pyrethroid acids.

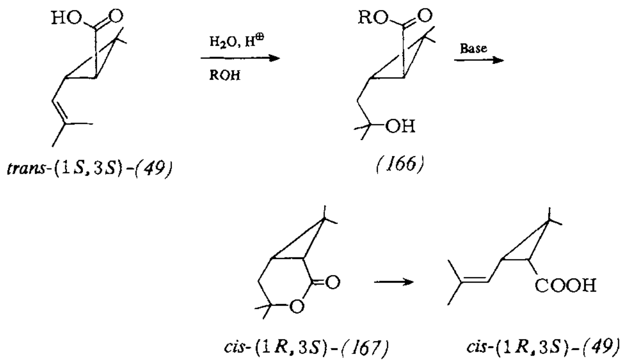
### 2. Methods of Separation

The resolution of *cis/trans*-mixtures and racemates by fractional crystallization of the *cis/trans*-acids or their diastereomeric salts with optically active bases has often been used for the preparation of the desired isomers[146]. Differences in the reactivity of the *cis*- and *trans*-acids permit separation techniques making use of a selective ester hydrolysis of *trans*-chrysanthemic acid[147] or a selective salt formation of *trans*-permethrinic acids[148]. The *cis*- and *trans*-acids can also be resolved by distillation[149].

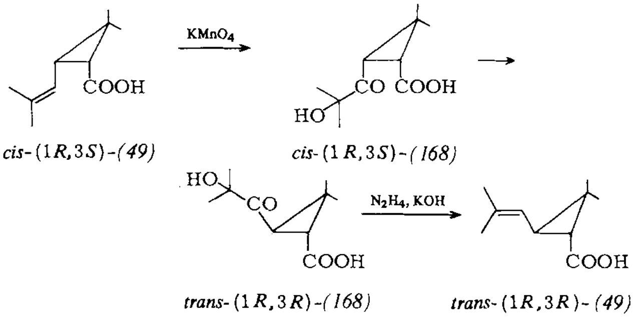
### 3. Isomerizations and Analogous Reactions

*cis*-Chrysanthemic acid *cis-(149)* can be isomerized to the *trans*-compound by basic catalysts[150] and by the action of Lewis acids on the acid chloride[151]. Similar isomerizations take place on heating permethrinic acid anhydrides in the presence of Lewis acids[152].

The *trans*-chrysanthemic acid *trans-(49)* can be converted into the *cis*-compound by hydration of the dimethylvinyl group and esterification to *(166)*[153], subsequent epimerization at C-1 with simultaneous lactone formation to give *(167)*, followed by elimination[154].



A method comprising oxidation of the dimethylvinyl group of the chrysanthemic acid to a ketol *(168)*, its epimerization and subsequent reduction with simultaneous elimination, has been used for the preparation of optically active *trans*-acid from optically active *cis*-acid *(49)*[155].



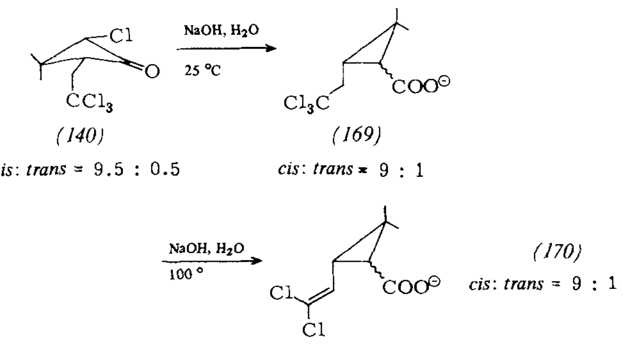
### 4. Stereoselective Syntheses

#### 4.1. Diazoacetic Ester Additions

Much effort has justifiably been expended on the stereoselective and enantioselective syntheses of pyrethroid acids by the application of special reaction conditions to known methods that do not proceed very selectively without suitable modification. Thus, in the reaction of *tert*-butyl diazoacetate with 2,5-dimethyl-2,4-hexadiene *(5)* the *trans*-chrysanthemic ester was obtained in high yield[156]. In the presence of copper(II) complexes with chiral ligands as catalysts the reaction of *(5)* proceeds enantioselectively both with diazoacetic esters[157] and with diazomalonic esters[158]. The synthesis of the *trans*-(1*R*)-acid was carried out by the addition of (−)-menthyl diazoacetate to *(5)*, using chiral catalysts, with an enantioselectivity of approximately 90%[159]. With rhodium(II) salts of carboxylic acids as catalysts, *e.g.* the pivalate, *cis*-enriched pyrethroid acid esters are obtained by diazoacetic ester addition to 1,1-dihalo-4-methyl-1,3-pentadienes[160].

#### 4.2. Favorskii Rearrangement

A Favorskii rearrangement of the *cis*-compound *(140)*[112] leads predominantly to the *cis*-carboxylate *(169)*, which on elimination without steric changes in the cyclopropane system, yields permethrinic acid *(147)* of predominantly *cis*-configuration[161] *via (170)*.



(140) cis: trans = 9.5 : 0.5

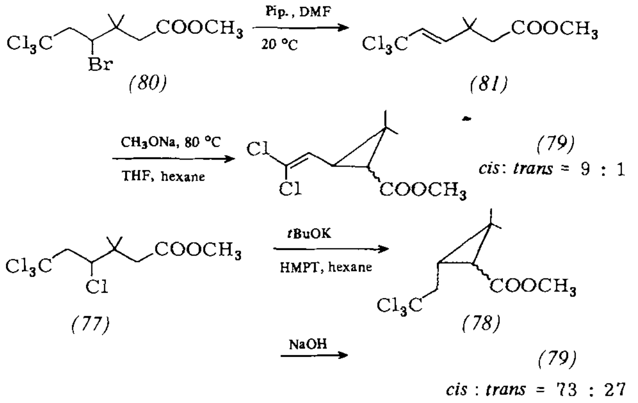
(169) cis: trans = 9 : 1

(170) cis: trans = 9 : 1

This route can also be used for the synthesis of enantiomerically pure acids when cyclobutanones, prepared by racemate resolution of the cyclobutanone hydrogen sulfite adducts, are used as educts[162].

### 4.3. 1,3-Ring Closure

The 1,3-ring closure of 4,6,6,6-tetrahalo-3,3-dimethylhexanoic acid esters such as (80) and (77) can be stereoselectively controlled using special reaction conditions[65, 163] (Pip. = piperidine, HMPT = hexamethylphosphoric triamide).



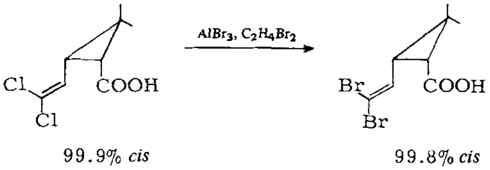
(80) (81)

(79) cis: trans = 9 : 1

(77) (78)

(79) cis : trans = 73 : 27

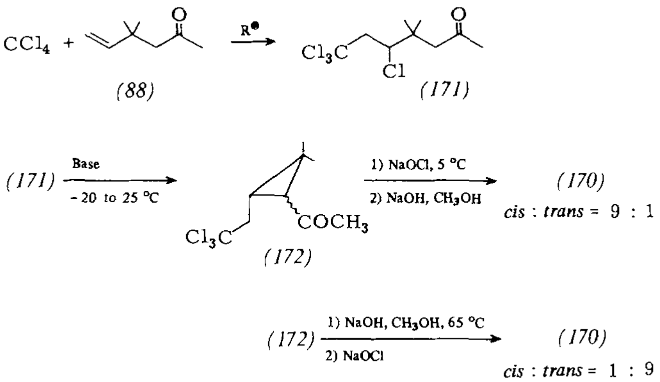
The chlorine atoms of the permethrinic acid (147) can be replaced by bromine atoms without a steric alteration of the cyclopropane system[163].



99.9% cis (147)

99.8% cis (157)

Stereoselective regulation of an analogous 1,3-ring closure proceeding from the ketone (171) leads to a cis-enriched isomeric mixture of the isomeric cyclopropyl methyl ketone (172). By varying the reaction conditions, this mixture can be further reacted to cis- or trans-rich permethrinic acid mixtures via the carboxylate (170)[164]. An alternative stereoselective synthesis is thus available, based on 4,4-dimethyl-5-hexen-2-one (88).



(88) (171)

(171) → (172) → (170) cis : trans = 9 : 1

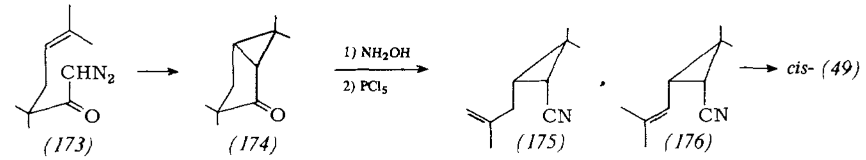
(172) → (170) cis : trans = 1 : 9

### 4.4. Intramolecular [2 + 1]-Addition

Intramolecular [2 + 1]-addition made possible the synthesis of cis-substituted cyclopropane precursors, which lead in one case (A) to the cis-chrysanthemic acid cis-(49)[150a] and in the other (B) to cis-3-(2,2-dihalovinyl)-2,2-dimethylcyclopropanecarboxylic acids cis-(147), X = Cl or cis-(157), X = Br[163].

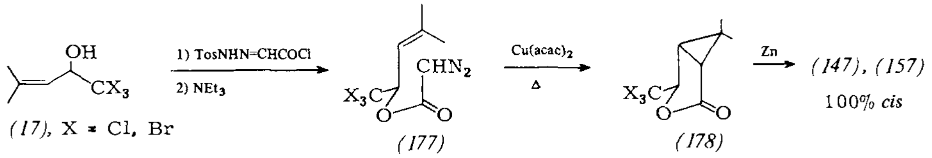
If synthesis B is carried out using (2R)-1,1,1-trichloro-4-methyl-3-penten-2-ol (17) as the educt, cis-(1R,3R)-permethrinic acid cis-(147) is obtained in 98% optical purity[163].

A



(173) (174) (175) (176)

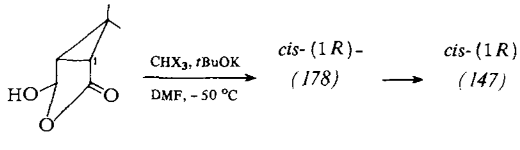
B



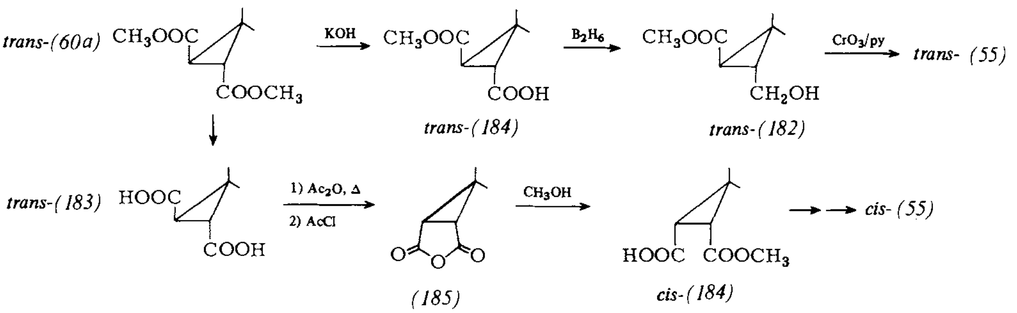
(17), X = Cl, Br (177) (178)

### 4.5. Isomerically Pure Precursors

The lactones (178) had already been used earlier by *Martel et al.*[165] as intermediates for the preparation of pyrethroid acids; in this case the haloform addition[140] to hemiacylals (179) of cis-caronaldehydic acid or pure enantiomers of this compound leading to the desired product.



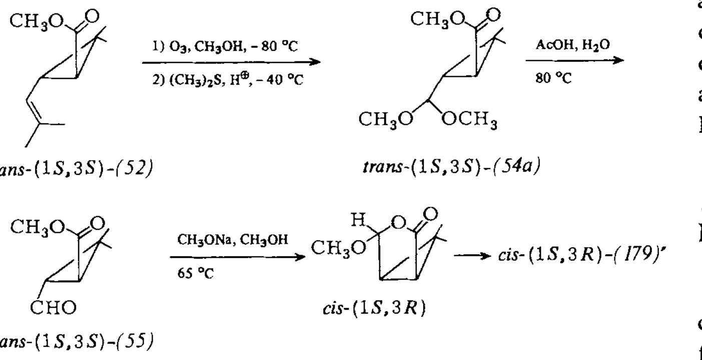
cis-(1R)-(179)



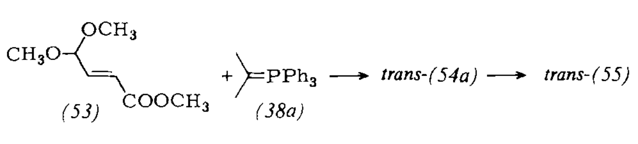
Derivatives of 3-formyl-2,2-dimethyl-1-cyclopropanecarboxylic acid (caronaldehydic acid) such as *(179)*, as pure stereoisomers or enantiomers, are probably the most valuable building blocks for the syntheses of sterically homogeneous pyrethoid acids. A Wittig reaction[136] and analogous olefinations[137, 138] lead directly to the target products with conservation of the configuration of the three-membered ring.

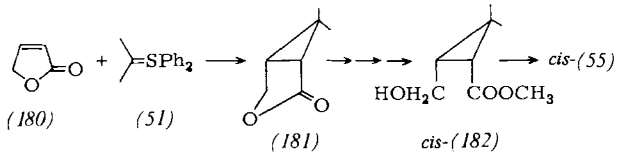
The educts probably used most commonly for sterically homogeneous caronaldehydes are the natural or synthetic sterically pure chrysanthemates, their ozonolysis leading directly to the desired intermediates.

*Martel* introduced this synthetic method for caronaldehydes and at the same time showed that by epimerization at C-3 4-hydroxy-6,6-dimethyl-3-oxabicyclo[3.1.0]hexan-2-one *(179)*, a synthetic equivalent of *cis*-caronaldehyde can be prepared from the *trans*-compound[166].



*Krief et al.* have devised several synthetic pathways to *trans*- and *cis*-caronaldehydes *(55)*: the starting material is the 4,4-dimethoxycrotonic ester *(53)*[45] or the butenolide *(180)*[167], whose reaction with isopropylidene(diphenyl)sulfurane *(51)* leads stereoselectively to the *trans*- or *cis*-substituted cyclopropane derivatives *(54a)* and *(181)*, which are converted into isomerically pure caronaldehydes by hydrolysis and if necessary by oxidation.





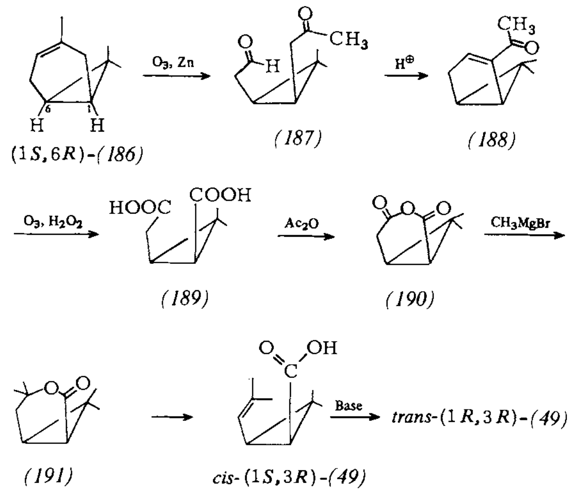
In another case, *trans*-caronic acid diester *(60a)* (see Section B 1.5.2) serves as an intermediate. This compound can be obtained both by an ylide addition to fumaric or maleic ester *(49)* or to 3-methylcrotonic ester[43], and by a 1,3-ring closure of α-bromoglutaric esters. A further synthesis proceeds *via* the caronic acid hemiester *(184)*, which is reduced selectively to the hydroxy acid *(182)* and finally oxidized to (*trans*-)caronaldehyde *(151b)*. The analogous synthesis of the *cis*-aldehyde is preceded by an isomerization of the *trans*-acid *(183)*[168].

These novel methods also indicate the difficult accessibility of the important building block of the synthesis, caronaldehyde, especially when the synthesis is aimed at sterically homogeneous isomers. This applies still more to the preparation of enantiomerically pure caronaldehyde, *e.g.* from terpenes (see Section C 5).

Mention must also be made at this point of recently published methods for the preparation of *cis*-chrysanthemic acid *cis-(49)* by selective hydrogenation of the analogous cyclopropenecarboxylic acids obtained by diazopropane addition to an ene-yne-carboxylic ester[169] or by Grignard addition[135] to 3,3-dimethylcyclopropene (see Section B 5.3).

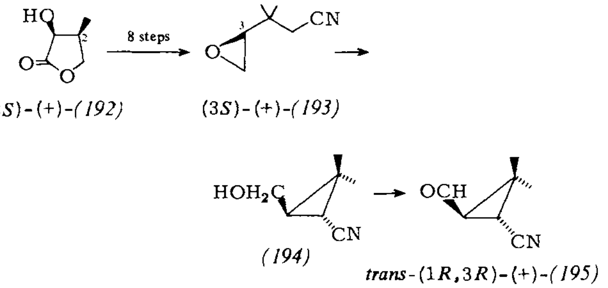
## 5. Pyrethroid Acids from Optically Active Natural Products

Enantiomerically pure pyrethroid acids—and especially chrysanthemic acid—have also been obtained starting from optically active natural products. (+)-3-carene, (1*R*, 5*R*)-(+)-α-pinene, and (2*R*)-(−)- and (2*S*)-(+)-pantolactone were used as starting materials.

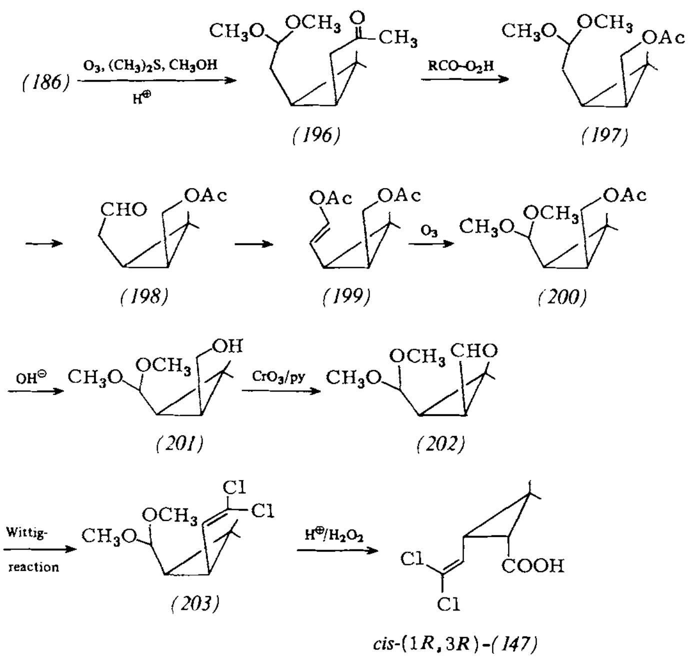


In this way *Matsui et al.*[170] obtained (1*R*,3*R*)-(+)-*trans*-chrysanthemic acid *(49)* from (+)-3-carene *(186)*. This synthetic route has since been improved by several working groups[171].

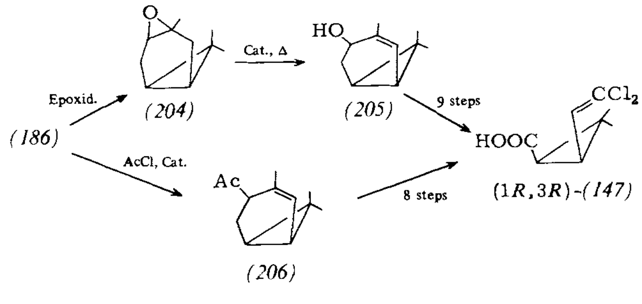
In the synthesis of (+)-*trans*-chrysanthemic acid from (1*R*,5*R*)-(+)-α-pinene[172] the decisive step is a Favorskii rearrangement. Synthesis from (2*S*)-(+)-pantolactone *(192)*[173] proceeds *via* the caronaldehydenitrile *(195)*.



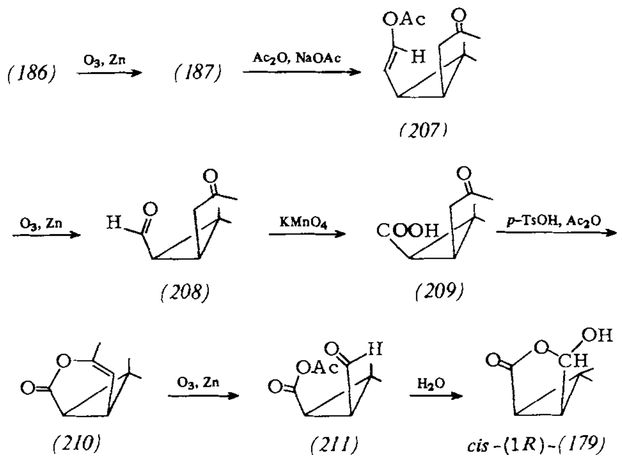
(+)-3-Carene *(186)* can also be used for the synthesis of (+)-*cis*-permethrinic acid *(147)*[122,174].



Two other synthetic routes start from the derivatives *(205)* and *(206)* of (+)-2-carene[175], which are obtained from (+)-3-carene *(186)*. These two multistage pathways[176,177] begin with an ozonization.



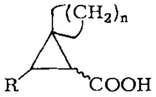
The cyclic hemiacetal *(179)* or *cis*-(1*R*)-caronaldehyde is also obtained from 3-carene as the starting substance.



## D) Synthetic Methods for other Pyrethroid Acids

### 1. Variation at C-2

The geminal dimethyl group is essential for the insecticidal action of the pyrethroid derivatives[179]. The substitution of even one methyl group by ethyl is enough to cause a sharp reduction in the action intensity[180]. Acid components with only one methyl group[181] and with spiroalkyl groups on C-2 *(212)* have been described[112b,182]. Such acids can be prepared by a Favorskii rearrangement or by diazoacetic ester synthesis.

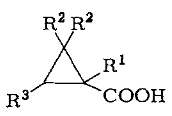


*(212)*, R = Alkyl, Dichlorovinyl
n = 0, 1, 2, 3

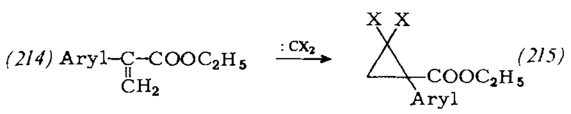
### 2. Variation at C-1

Additional substituents at C-1 have a stronger negative effect on the biological activity than a change at C-3[183].

However, esters of the acid type *(213)* with good insecticidal action are known. These include, above all, acids like *(215)* containing an aryl group at C-1 and hydrogen at C-3. The acids constitute a special case, since in place of the geminal methyl group at C-2 geminal halogen substituents also give rise to active esters[184]. The acids *(215)* can be prepared by Favorskii rearrangement or by carbene addition to atropic acid esters *(214)*.

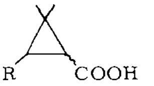


*(213)*, $R^1$ = Alkyl, Aryl, Phenoxy
$R^2$ = Methyl, Halogen
$R^3$ = Alkyl, Dihalovinyl



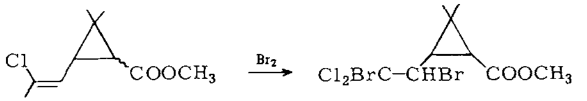
## 3. Variation at C-3

In the great majority of the acid components the substituents are varied at C-3. Compounds of the type *(216)* with a hydrogen atom at C-3 show the closest structural similarity to the vinylcyclopropanecarboxylic acids.



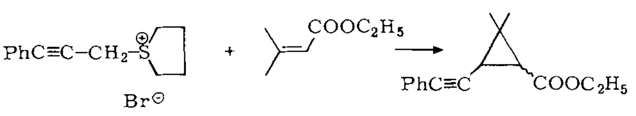
*(216)*, R = Alkyl, Aryl, Halogen, Alkoxy, Alkylthio

Acids *(216)* in which R = aryl are obtained by diazoacetic ester synthesis[185]. Aryl-substituted cyclopropanecarboxylic acids, which are claimed to have particularly good acaricidal action, are described in recent patent literature[186]. Acids with a heterocyclic residue R have also been patented[187]. Acids in which R is a saturated residue similarly give insecticidally active esters. R can be unsubstituted (methyl[188], isobutyl[189]) or it can be substituted by a halogen[190], alkoxy[191], or alkylthio[192] group. For example, haloethyl-substituted acids *(217)* are obtained by bromination of the permethrin ester *(79)*[193].



*(79)* *(217)*

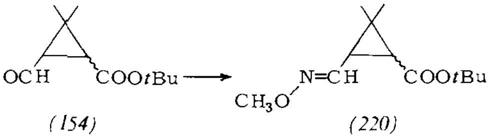
If R is an alkynyl group, as in *(219)*, the action is weaker than in the case of the corresponding vinyl-substituted esters. Acids with a triple bond are as a rule prepared by dehydrohalogenation[194]. The 2,2-dimethyl-3-(phenylethynyl)cyclopropanecarboxylic ester *(219)* was synthesized from the propargylsulfonium salt *(218)* and ethyl 3-methylcrotonate *(64)*[195]:



*(218)* *(64)* *(219)*

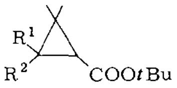
Finally, pyrethroid acid components in which R = halogen[196], alkoxy[183,197], and aryloxy[183,198] have been described.

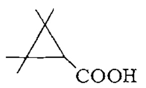
If the caronaldehyde-*tert*-butyl ester *(154)* [cf. *(151c)*] is reacted with hydroxylamine or an *O*-substituted hydroxylamine[199], the oxime ether *(220)* is obtained, from which esters with good "knock-down" activity can be made[179,199,200]: where the term "knock-down" activity means that the insects are rapidly paralyzed.



*(154)* *(220)*

Among the acids *(221)* in which there is no hydrogen atom at C-3, the 2,2,3,3-tetramethylcyclopropanecarboxylic acid *(222)*[201] has acquired particular significance. This acid is readily obtained by diazoacetic ester synthesis[202] or from 4-chloro-2,2,3,3-tetramethylcyclobutanone by a Favorskii rearrangement[110].

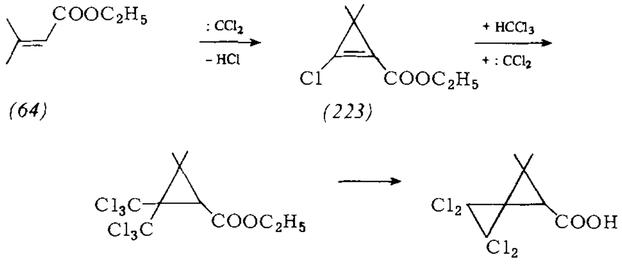
*(221)*




*(222)*

Wide variation of the structure *(221)* has only given rise to less effective compounds[183,203,204].

If $R^1$ and $R^2$ in *(221)* form a ring, spiro compounds are obtained, such as the 4,4,5,5-tetrachloro-2,2-dimethylspiropentane-1-carboxylic acid *(225)*[205], which is prepared from the ester *(64)* and dichlorocarbene with phase-transfer catalysis[206].

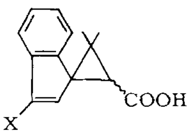


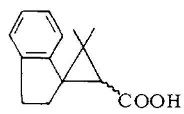
*(64)* *(223)*

*(224)* *(225)*

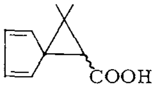
Greater importance attaches to spiro[2,4]heptanecarboxylic acids *(226)*–*(231)*[207], from which many esters have been synthesized.

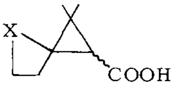
*(226)*, X = H
*(227)*, X = Cl





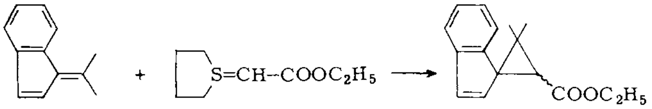
*(228)*

*(229)*




*(230)*, X = CH=CH
*(231)*, X = $CH_2$–$CH_2$

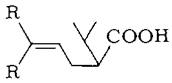
The ethyl ester *(234)* of the acid *(226)* is obtained from isopropylidenindene *(232)* and the sulfur ylide *(233)*[208].



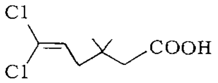
*(232)* *(233)* *(234)*

## 4. Pyrethroid Acid Components without a Cyclopropane Ring

Already in the 1920's *Staudinger* and *Ruzicka*[209] investigated whether the cyclopropane ring is absolutely necessary for the insecticidal action. Esters of "cut-up" chrysanthemic acid *(235)* proved to be inactive, though the esters *(236)* and *(237)* are said to have a certain insecticidal activity[210].



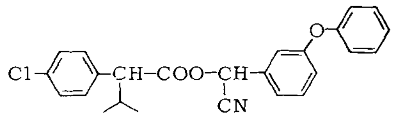
*(235)*, R = $CH_3$
*(236)*, R = Cl



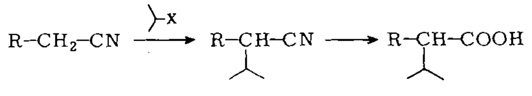
*(237)*

Fenvalerate *(238)* is a compound having an insecticidal activity of similar magnitude to that of permethrin *(3)*[211].

The 4-chlorophenyl-3-methylbutyric acid *(241)* is made by alkylation of 4-chlorophenylacetonitrile *(239)* and hydrolysis of the alkylated product[211,212]. The isopropyl group is essential for the insecticidal action: the methyl and isobutyl compounds are practically inactive, and the ethyl compound has only half the activity[211]. The analogous cyclopropyl compounds[212] also have a high activity.



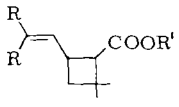
Fenvalerate *(238)*



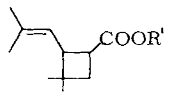
*(239)* *(240)* *(241)*

R = $p$-Cl–$C_6H_4$, X = Halogen

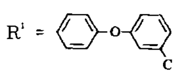
The substituents in the benzene ring can also be varied over a wide range, and the benzene ring itself can be replaced by a heterocycle, *e.g.* a furan[211], thiophene[211], or pyrrole ring[213].



*(242)*, R = $CH_3$; *(243)*, R = Cl



*(244)*



Cyclobutanecarboxylic acid esters such as *(242)* have only a weak activity[214], and the isomeric esters *(244)* have none[214]. The dichlorovinylcyclobutanecarboxylic acid esters *(243)* should also exhibit insecticidal activity[215].

## E) Future Prospects

The development of the new generation of insecticidal pyrethroids into a class of major economic significance is certainly not yet over. The essential task now is to find low-cost methods of production for the particularly active compounds.

The isomerically or enantiomerically pure active substances will only become an attractive proposition as agricultural chemicals when their manufacturing costs have been made comparable with those of their isomeric mixtures.

Evidently what is needed here is imagination and creativity. The future will undoubtedly demonstrate that stereoselective and enantioselective methods of synthesis can also be of great significance for industrial organic chemistry.

Received: February 13, 1981 [A 371 IE]
German version: Angew. Chem. *93*, 719 (1981)

[1] *H. Staudinger, L. Ruzicka,* Helv. Chim. Acta *7*, 177, 201, 212, 236, 245, 377 (1924).

[2] *H, Staudinger, L. Ruzicka,* Helv. Chim. Acta *7*, 448 (1924).

[3] *M. Elliott, A. W. Farnham, N. F. Janes, P. H. Needham, D. A. Pulman, J. T. Stevenson,* Nature *246*, 169 (1973).

[4] a) *J. Farkas, P. Kourim, F. Šorm,* Chem. Listy *52*, 688 (1958); b) Collect. Czech. Chem. Commun. *24*, 2230 (1959).

[5] *H. Staudinger, O. Muntwyler, L. Ruzicka, S. Seibt,* Helv. Chim. Acta *7*, 390 (1924).

[6] *I. G. M. Campbell, S. H. Harper,* J. Chem. Soc. *1945*, 283.

[7] *A. L. Henne, H. H. Chanan, A. Turk,* J. Am. Chem. Soc. *63*, 3474 (1941); *64*, 826 (1942); *66*, 395 (1944).

[8] *K. Y. Shim, D. J. Martin,* DOS 2123989 (1970), Stauffer Chem. Co.; *A. Nurrenbach, W. Böll,* DOS 2400188 (1974), BASF AG.

[9] *A. J. Hubert, A. F. Noels, A. J. Anciaux, P. Teyssie,* Synthesis *1976*, 600.

[10] *H. J. Sanders, A. W. Taff,* Ind. Eng. Chem. *46*, 414 (1954).

[11] *S. Przybytek,* Ber. Dtsch. Chem. Ges. *20*, 3239 (1887).

[12] DBP 886907 (1953), BASF AG; Chem. Abstr. *52*, 13799c (1958).

[13] *D. Holland, D. J. Milner,* Chem. Ind. (London) *1979*, 707.

[14] *B. Bogdanovic, S. Konstantinovic,* Synthesis *1972*, 481.

[15] *L. Crombie, S. H. Harpes, K. C. Sleep,* J. Chem. Soc. *1957*, 2743.

[16] *J. H. Wevers,* DOS 2624340 (1976), Shell Int. Res.

[17] *H. Pitt,* DOS 2751435 (1978), Stauffer Chem. Co.

[18] *A. Lupichuk,* US-Pat. 4070404 (1978), FMC Corp.

[19] *J. Colonge, A. Perrot,* Bull. Soc. Chim. Fr. *1957*, 204; cf. also: *H. Normant, J. Ficini, ibid. 1956*, 1441.

[20] a) *F. Mori, Y. Omura, T. Nishida, K. Itoi,* DOS 2542377 (1976), Kuraray Co. Ltd.; b) *P. J. V. Cleare,* DOS 2616681 (1976), ICI Ltd.; c) *I. T. Kay, A. G. Williams,* DOS 2657148 (1977), ICI Ltd.; d) *M. Alvarez, M. L. Fishman,* US-Pat. 4022672 (1977), FMC Corp.; e) *R. Voigtländer, H. Matschiner, H. Biering,* Z. Chem. *20*, 217 (1980).

[21] *R. L. Soulen, D. G. Kundiger, S. Earles, Jr., R. A. Sanchez,* J. Org. Chem. *32*, 2661 (1967).

[22] *E. Kysela, R. Lantzsch,* Bayer AG, unpublished results.

[23] *E. Kysela, R. Lantzsch, E. Klauke,* DOS 2536503 (1977), Bayer AG.

[24] *W. G. Scharpf,* DOS 2658283 (1977), FMC Corp.

[25] *J. B. Afanaser, J. V. Mamontora, T. M. Fillipora, G. J. Samokhalov,* J. Org. Chem. USSR *7*, 1 (1971).

[26] *Y. Fujita, Y. Omura, F. Mori, K. Hoi, T. Nishida, Y. Tamei, S. Aihara, T. Hosoga, F. Wada,* DOS 2616528 (1976), Kuraray Co. Ltd.

[27] *R. Lantzsch, D. Arlt, E. Kysela,* DOS 2536504 (1977), Bayer AG.

[28] *W. Hewertson, D. Holland, J. David,* DOS 2629868 (1977), ICI Ltd.; *W. Hewertson, D. Holland, D. J. Milner,* J. Chem. Soc. Perkin Trans. 2 *1978*, 1062; *D. Holland, D. J. Milner, P. J. Thomas,* J. Chem. Res. (S) *1979*, 149.

[29] *D. Arlt, M. Jautelat,* DOS 2756271 (1979), Bayer AG.

[30] *D. Holland, D. J. Milner, R. K. Huff,* DOS 2920536 (1979); *J. Crosby, B. W. H. Terry,* DOS 2920591 (1979); *J. Crosby,* Eur.-Pat. 10856 (1980), all ICI Ltd.

[31] *R. A. Fuchs, H. Harnisch, R. Lantzsch, K. Naumann, H. J. Riebel, R. Schröder,* DOS 2916343 (1980).

[32] *S. Takei, M. Ohno, Y. Inouye,* US-Pat. 3009946 (1961), Inst. Insect Control.

[33] *H. D. Scharf, J. Mattay,* Chem. Ber. *111*, 2206 (1978).

[34] *P. L. Stetter, S. A. Roman, C. L. Edwards,* Tetrahedron Lett. *1972*, 4071.

[35] *S. Julia, M. Julia, G. Linstrumelle,* Bull. Soc. Chim. Fr. *1966*, 3499.

[36] a) *C. E. Hatch, K. Konds, T. Takashima, D. Tunemoto,* Eur.-Pat. 3666 (1979), FMC Corp.; b) *K. Kondo, T. Takashima, A. Negishi, K. Matsui, T. Fujimoto, K. Sugimoto, C. E. Hatch III, J. S. Baum,* Pestic. Sci. *11*, 180 (1980).

[37] *K. R. Huff,* DOS 2802962 (1978), ICI Ltd.

[38] *K.-H. Büchel, F. Korte,* Z. Naturforsch. *B17*, 349 (1962).

[39] *P. J. V. Cleare, A. E. Kaye, D. J. Milner,* DOS 2730755 (1977), ICI Ltd.

[40] *A. E. Kaye, A. C. Tucker,* Eur.-Pat. 7154 (1979), ICI Ltd.

[41] a) *R. W. Mills, R. D. H. Murray, R. A. Raphael,* Chem. Commun. *1971*, 555; b) J. Chem. Soc. Perkin Trans. 1 *1973*, 133.

[42] *E. J. Corey, M. Jautelat,* J. Am. Chem. Soc. *89*, 3912 (1967).

[43] *Y. Kishida, M. Yoshimoto, N. M. Ishida,* DOS 2132761 (1971), Sankyo; *W. W. Brand,* DOS 2724734 (1977), Am. Cyanamid Co.

[44] a) *G. B. Payne,* US-Pat. 3397223 (1968), Shell Oil Co.; b) J. Org. Chem. *32*, 3351 (1967).

[45] *A. Krief,* DOS 2615160 (1976), Roussel-Uclaf; *M. J. Devos, L. Hevesi, P. Bayet, A. Krief,* Tetrahedron Lett. *1976*, 3911.

[46] *A. Krief,* DOS 2922961 (1979), Roussel-Uclaf.

[47] *M. J. Devos, A. Krief,* Tetrahedron Lett. *1979*, 1511.

[48] *M. J. Devos, A. Krief,* Tetrahedron Lett. *1979*, 1515.

[49] *M. J. Devos, J. N. Denis, A. Krief,* Tetrahedron Lett. *1978*, 1847.

[50] a) *J. Martel, C. Huynh*, Bull. Soc. Chim. Fr. *1967*, 985; b) *J. B. Martel, C. Huynh, E. Toromanoff, G. Nomine*, DAS 1289046 (1969), Roussel-Uclaf.

[51] *L. Velluz, J. Martel, G. Nomine*, C. R. Acad. Sci. Ser. *C 268*, 2199 (1969); *J. Martel, C. Huynh*, DAS 1668603 (1971), Roussel-Uclaf.

[52] *R. V. M. Campbell, L. Crombie, D. A. R. Findley, R. W. King, G. Pattenden, D. A. Whiting*, J. Chem. Soc. Perkin Trans. 1 *1975*, 897.

[53] *M. Hanack, T. Stoll*, DOS 2926671 (1981), Bayer AG.

[54] *M. Julia, A. Guy-Rouault*, Bull. Soc. Chim. Fr. *1967*, 1411.

[55] *Z. Csuros, R. Soos, E. Fogassy, J. Palinkas, G. Hernadi*, Hung. Teljes *1974*, 8014; Magy. Tud. Akad.; Chem. Abstr. *81*, 37316f (1974).

[56] *S. Torii, H. Tanaka, Y. Nagai*, Bull. Chem. Soc. Jpn. *50*, 2825 (1977).

[57] *M. J. Devos, A. Krief*, Tetrahedron Lett. *1979*, 1891.

[58] a) *M. Julia, S. Julia, B. Bemont*, Bull. Soc. Chim. Fr. *1960*, 304; b) *T. Sugiyama, A. Kobayashi, K. Yamashita*, Agric. Biol. Chem. *38*, 979 (1974); c) *J. Ficini, J. d'Angelo*, Tetrahedron Lett. *1976*, 2441.

[59] *J. P. Genet, F. Piau, J. Ficini*, Tetrahedron Lett. *1980*, 3183; *J. Ficini, J. P. Genet*, Eur. Pat. 13844 (1980), Roussel-Uclaf.

[60] *K. Kondo, K. Matsui, A. Negishi*, DOS 2539895 (1976), Sagami Chem. Res.; *K. Kondo, K. Matsui, A. Negishi*, ACS Symp. Ser. *42*, 128 (1977); *Y. Nakada, R. Endo, S. Muramatsu, J. Ide, Y. Yura*, Bull. Chem. Soc. Jpn. *52*, 1511 (1979).

[61] a) *M. Julia, S. Julia, B. Cochet*, Bull. Soc. Chim. Fr. *1964*, 1476; b) *N. Punja*, DOS 2621835 (1976), ICI Ltd.; c) *F. Mori, Y. Omura, T. Nishida, K. Itoi*, Jap. Pat. 77/125122 (1977), Kuraray Co. Ltd.; Chem. Abstr. *88*, 62006g (1978).

[62] *Y. Omura, F. Mori, T. Nishida, K. Itoi*, Jap. Pat. 77/14749 (1977), Kuraray Co. Ltd.; Chem. Abstr. *87*, 67906q (1977).

[63] a) *M. Julia, S. Julia, M. Langlois*, Bull. Soc. Chim. Fr. *1965*, 1007; b) *K. Kondo, K. Matsui, Y. Takahatake*, Tetrahedron Lett. *1976*, 4359; c) *F. Mori, Y. Omura, T. Nishida, K. Itoi*, Jap. Pat. 76/131857 (1976) and 77/83718 (1977), both Kuraray Co. Ltd.; Chem. Abstr. *86*, 189302q (1977) and *88*, 22208t (1978) respectively.

[64] a) *J. F. Engel*, Eur. Pat. 3336 (1979), FMC Corp.; b) *R. Lantzsch, H. Hagemann, I. Hammann, W. Behrenz, B. Homeyer*, DOS 2831193 (1980), Bayer AG.

[65] *K. Kondo, A. Negishi, K. Sugimoto*, Eur. Pat. 3683 (1979), FMC Corp.

[66] a) *K. Kondo, K. Matsui, A. Negishi, T. Kanagawa*, DOS 2658281 (1977); b) *K. Kondo, K. Matsui, A. Negishi, S. Dobashi, Y. Takahatake*, Jap. Pat. 76/82242 (1976), both Sagami Chem. Res.; Chem. Abstr. *85*, 176937e (1976); c) *F. Mori, Y. Omura, T. Nishida, K. Itoi*, Jap. Pat. 77/83438 (1977), Kuraray Co. Ltd.; Chem. Abstr. *88*, 6393u (1978); d) *T. Mizutani, N. Itaya, T. Matsuo, O. Magara*, Jap. Pat. 78/40741 (1978), Sumitomo Chem. Co.; Chem. Abstr. *89*, 108331k (1978).

[67] a) *N. Punja*, DOS 2621830 (1976), ICI Ltd.; b) *K. Kondo, K. Matsui, A. Negishi, Y. Takahatake, K. Sugimoto*, DOS 2649531 (1977) and DOS 2649856 (1977), both Sagami Chem. Res.; c) *H. Austermühle-Bertola*, DOS 2727613 (1977), Shell Int. Res.; d) *S. Omura, T. Hosogai, F. Mori, Y. Fujita, T. Nishida, K. Itoi*, Jap. Pat. 77/151148 (1977), Kuraray Co. Ltd.; Chem. Abstr. *88*, 136191n (1978).

[68] *J. H. Babler, A. J. Tortorello*, J. Org. Chem. *41*, 885 (1976).

[69] *N. R. Easton, R. D. Dillard*, J. Org. Chem. *27*, 3602 (1962).

[70] a) *M. Julia, S. Julia, M. Langlois*, C. R. Acad. Sci. *256*, 436 (1963); b) *M. Julia, S. Julia, M. Langlois*, Bull. Soc. Chim. Fr. *1965*, 1014; c) *M. Julia*, DAS 1263760 (1968), Rhone-Poulenc.

[71] *P. Cresson*, Bull. Soc. Chim. Fr. *1964*, 2618.

[72] a) *K. Kondo, K. Matsui, A. Negishi*, Jap. Pat. 76/131819 (1976), Sagami Chem. Res.; Chem. Abstr. *86*, 139416j (1977); b) *K. Kondo, A. Negishi, K. Matsui*, Jap. Pat. 77/05708 (1977) and 77/27711 (1977), both Sagami Chem. Res.; Chem. Abstr. *86*, 189231r (1977) and *87*, 52809m (1977) respectively; c) *M. Matsui, T. Matsuo*, Jap. Pat. 77/46012 (1977), Sumitomo Chem. Co.; Chem. Abstr. *87*, 84554r (1977); d) *Y. Omura, S. Aihara, F. Mori, Y. Tamai, T. Hosogai, Y. Fujita, F. Wada, K. Itoi*, Jap. Pat. 77/46013 (1977), Kuraray Co. Ltd.; Chem. Abstr. *87*, 84550m (1977); e) *Y. Omura, F. Yamamoto, T. Kawaguchi*, Jap. Pat. 77/111513 (1977), Kuraray Co. Ltd.; Chem. Abstr. *88*, 50311q (1978); f) *H. Austermühle-Bertola, R. v. Helden*, DOS 2649711 (1977), Shell Int. Res.

[73] a) *F. Fujita, N. Itaya, O. Magara*, Jap. Pat. 78/135917 (1978) und 78/135918 (1978), both Sumitomo Chem. Co.; Chem. Abstr. *90*, 151584c (1979) and *90*, 168065 (1979) respectively.

[74] *M. Jautelat*, DOS 2752366 (1979), Bayer AG.

[75] *M. Jautelat, D. Arlt*, Eur. Pat. 4070 (1979), Bayer AG.

[76] *Y. Ninagawa, T. Kawaguchi, T. Nishida, K. Itoi*, Jap. Pat. 77/83412 (1977) and 77/83413 (1977), both Kuraray Co. Ltd.; Chem. Abstr. *87*, 184003d (1977) and *87*, 200815c (1977) respectively.

[77] *Y. Ninagawa, T. Kawaguchi, T. Nishida, K. Itoi*, Jap. Pat. 77/83411 (1977), Kuraray Co. Ltd.; Chem. Abstr. *87*, 184019p (1977).

[78] *P. Hayden, H. W. B. Reed, N. Punja*, DOS 2728926 (1978), ICI Ltd.

[79] *N. Itaya, F. Fujita, H. Matsuo*, Jap. Pat. 77/111509 (1977), Sumitomo Chem. Co.; Chem. Abstr. *88*, 50289p (1978).

[80] *M. Jautelat, D. Arlt*, DOS 2732075 (1979), Bayer AG.

[81] a) *Houben-Weyl:* Methoden der Organischen Chemie. Thieme, Stuttgart 1962, Bd. V/3, S. 971; b) *M. Asscher, D. Vofsi*, J. Chem. Soc. *1963*, 1887; c) *H. Matsumoto, N. Toshimi, N. Yoichiro*, J. Org. Chem. *41*, 396 (1976).

[82] a) *Y. Yura, Y. Nakada, R. Endo*, Jap. Pat. 77/83505 (1977) and 77/83522 (1977), both Sankyo; Chem. Abstr. *87*, 200806a (1977) and *88*, 22210n (1978) respectively; b) *F. Mori, Y. Omura, T. Nishida, K. Itoi*, Jap. Pat. 77/125121 (1977), Kuraray Co. Ltd.; Chem. Abstr. *88*, 61998v (1978).

[83] *J. Ide, Y. Nakata, R. Endo*, Jap. Pat. 78/103415 (1978), Sankyo; Chem. Abstr. *90*, 22342y (1979).

[84] *N. Punja*, DOS 2621831 (1976), ICI Ltd.

[85] *T. Matsuo, N. Itaya, O. Magara*, DAS 2605398 (1976), Sumitomo Chem. Co.

[86] *P. J. V. Cleare*, DOS 2650584 (1978), ICI Ltd.

[87] *T. Hosogai, Y. Omura, F. Mori, K. Itoi, T. Nishida, Y. Tamai, S. Aihara, Y. Fujita, F. Wada*, Jap. Pat. 76/131820 (1976), Kuraray Co. Ltd.; Chem. Abstr. *86*, 139415h (1977); *N. Punja*, Brit. Pat. 1520024 (1978), ICI Ltd.; Chem. Abstr. *90*, 151603h (1979); *H. Austermühle-Bertola, F. Baardman, A. Reinink*, DOS 2730359 (1978), Shell Int. Res.; *R. A. Sheldon, M. Anderson, H. Verbrugge, J. L. M. Syrier*, Eur. Pat. 3857 (1979), Shell Int. Res.

[88] a) *F. Mori, Y. Omura, T. Nishida, K. Itoi*, DOS 2544150 (1976), Kuraray Co. Ltd.; b) *K. Kondo, K. Matsui, A. Negishi, Y. Takahatake*, DOS 2552615 (1976), Kuraray and Sagami; c) *F. Mori, Y. Omura, T. Nishida, K. Itoi*, Jap. Pat. 76/141812 (1976), Kuraray Co. Ltd.; Chem. Abstr. *87*, 38905h (1977); d) *T. Misutani, N. Itaya, T. Matsuo, O. Magara*, Jap. Pat. 76/149221 (1976), Sumitomo Chem. Co.; Chem. Abstr. *87*, 38908m (1977).

[89] *F. Mori, Y. Omura, T. Nishida, K. Itoi*, Jap. Pat. 76/131815 (1976) and 76/131821 (1976), both Kuraray Co. Ltd.; Chem. Abstr. *87*, 5374 (1977) and *86*, 139417k (1977) respectively.

[90] *Houben-Weyl:* Methoden der Organischen Chemie. Thieme, Stuttgart 1963, Vol. VI/2, p. 807, 808.

[91] a) *W. Costain, B. W. H. Terry, N. Punja, P. J. V. Cleare*, DOS 2630981 (1977), ICI Ltd.; b) *T. Hosogai, Y. Omura, F. Mori, S. Aihara, F. Wada, Y. Fujita, T. Onishi, T. Nishida*, Jap. Pat. 77/57163 (1977), Kuraray Co. Ltd.; Chem. Abstr. *88*, 37598u (1978).

[92] a) *N. Itaya, F. Fujita*, DOS 2707104 (1977), Sumitomo Chem. Co.; b) *N. Itaya, T. Matsuo, N. Ohno, T. Mizutani, F. Fujita, H. Yoshioka*, ACS Symp. Ser. *42*, 45 (1977).

[93] *P. Martin*, DOS 2731483 (1978), Ciba-Geigy.

[94] *Y. Ninagawa, T. Kawaguchi, T. Nishida, K. Itoi*, Jap. Pat. 77/83456 (1977), Kuraray Co. Ltd.; Chem. Abstr. *87*, 200816d (1977).

[95] *H. Greuter, P. Martin, D. Bellus*, DOS 2813336 (1978), Ciba-Geigy.

[96] *R. A. Raphael*, DOS 2623777 (1976), ICI Ltd.

[97] *M. Jautelat, D. Arlt, R. Lantzsch, R. A. Fuchs, H.-J. Riebel, R. Schröder, H. Harnisch*, DOS 2916375 (1980) and DOS 2916417 (1980), both Bayer AG.

[98] a) *T. Matsuo, N. Itaya, O. Magara*, DOS 2624351 (1977), Sumitomo Chem. Co.; b) *F. Mori, Y. Omura, T. Nishida, K. Itoi*, Jap. Pat. 77/125150 (1977), Kuraray Co. Ltd.; Chem. Abstr. *88*, 62039v (1978).

[99] *K. Kondo, K. Matsui, A. Negishi, S. Dobashi, Y. Takahatake*, Jap. Pat. 76/82217 (1976), Sagami Chem. Res.; Chem. Abstr. *85*, 142679g (1976); *K. Kondo, K. Matsui, Y. Takahatake*, Jap. Pat. 77/116440 (1977), Sagami Chem. Res.; Chem. Abstr. *88*, 74106c (1978).

[100] *M. Julia, L. Saussine, G. Le Thillier*, J. Organomet. Chem. *174*, 359 (1979).

[101] *M. Julia, S. Julia, C. Jeanmart*, C. R. Acad. Sci. *251*, 249 (1960); *M. Julia, S. Julia, C. Jeanmart, M. Langlois*, Bull. Soc. Chim. Fr. *1962*, 2243; *M. Matsui, M. Uchiyama*, Agric. Biol. Chem. *26*, 532 (1962).

[102] *A. Takeda, T. Sakai, S. Shinohara, S. Tsuboi*, Bull. Chem. Soc. Jpn. *50*, 1133 (1977).

[103] *K. Kondo, F. Mori*, Chem. Lett. *1974*, 741; with ketene-*O,N*-acetal: *W. Sucrow, W. Richter*, Tetrahedron Lett. *1970*, 3675.

[104] *P. D. Klemmensen, H. Kolind-Andersen, H. B. Madsen*, DOS 2702222 (1977), Cheminova; *R. Lantzsch*, DOS 2710151 (1978) and 2710174 (1978), beide Bayer AG; *P. D. Klemmensen, H. Kolind-Andersen, H. B. Madsen*, DBP 2723447 (1977); *P. D. Klemmensen, H. Kolind-Andersen*, DBP 2732455 (1978) und 2732456 (1978), all Cheminova; *P. D. Klemmensen, H. Kolind-Andersen, H. B. Madsen, A. Svendsen*, J. Org. Chem. *44*, 416 (1979); *R. Lantzsch*, DBP 2747824 (1979), Bayer AG.

[105] *N. Itaya, F. Fujita, O. Magara*, Jap. Pat. 77/113907 (1977), Sumitomo Chem. Co.; Chem. Abstr. *88*, 50269g (1978).

[106] *M. J. Devos, A. Krief*, Tetrahedron Lett. *1978*, 1845.

[107] *M. Jautelat, D. Arlt, R. Lantzsch, R. A. Fuchs, H.-J. Riebel, R. Schröder, H. Harnisch*, DOS 2916401 (1980) and 2916321 (1980), both Bayer AG.

[108] *H.-G. Heine, A. Hübner, W. Hartmann*, DOS 2740849 (1979), Bayer AG.

[109] *J. M. Conia, J. R. Salem*, Acc. Chem. Res. *5*, 33 (1972).

[110] *M. J. van den Brink, H. Austermühle-Bertola, P. A. Kramer*, DOS 2539048 (1976), Shell Int. Res.

[111] *H. G. Heine, W. Hartmann,* DOS 2638356 (1978) and 2654062 (1978), both Bayer AG.

[112] a) *P. Martin, H. Greuter, D. Bellus,* DOS 2909665 (1979), Ciba-Geigy; J. Am. Chem. Soc. *101*, 5853 (1979); b) *P. Martin, H. Greuter, E. Steiner, D. Bellus,* DOS 2813337 (1978), Ciba-Geigy; c) *P. Martin, H. Greuter, D. Bellus,* DOS 2842601 (1980).

[113] *R. Lantzsch, E. Kysela,* DOS 2642006 (1978) and 2655007 (1978), both Bayer AG.

[114] *H. G. Heine, W. Hartmann,* DOS 2654060, 2654061 and 2715336 (1978), all Bayer AG.

[115] *M. Assher, D. Vofsi, A. Katschalski,* Isr. Pat. 18771 (1965); Chem. Abstr. *63*, 13089e (1965).

[116] *S. S. Hixson, P. S. Mariano, H. E. Zimmerman,* Chem. Rev. *73*, 531 (1973).

[117] *M. J. Bullivent, G. Pattenden,* J. Chem. Soc. Perkin Trans. 1 *1976*, 256; *P. Baeckström,* J. Chem. Soc. Chem. Commun. *1976*, 476; Tetrahedron *34*, 3331 (1978).

[118] *K. Ohkata, T. Isako, T. Hanafusa,* Chem. Ind. (London) *1978*, 274.

[119] *H. G. Schmidt,* DOS 2812672 (1979), Dynamit Nobel.

[120] *E. I. Heiba,* J. Org. Chem. *39*, 3456 (1974).

[121] *H. G. Schmidt,* DOS 2740479 and 2825363 (1979), both Dynamit Nobel.

[122] *P. A. Verbrugge, P. A. Kramer, J. van Berkel, H. C. Kelderman,* Eur. Pat. 2850 (1979), Shell Int. Res.

[123] *A. I. Dalton,* DBP 2642672 (1977), Air Products.

[124] *T. Sasaki, S. Eguchi, M. Ohno, T. Umemura,* J. Org. Chem. *38*, 4095 (1973).

[125] *A. I. Dalton, H. J. Doran, R. D. H. Murray,* DBP 2642671 (1977), Air Products.

[126] *S. C. Welch, T. A. Valdes,* J. Org. Chem. *42*, 2108 (1977).

[127] *N. Punja,* DBP 2621832 (1976), ICI Ltd.

[128] a) *T. Matsuo, N. Itaya, O. Magara,* DBP 2605398 (1976) and Jap. Pat. 77/57143 (1977), both Sumitomo Chem. Co.; Chem. Abstr. *87*, 134029w (1977); b) *P. J. V. Cleare,* DBP 2621833 (1976), ICI Ltd.

[129] a) *R. J. Lindsay, J. Ferguson, A. T. Costello,* DBP 2751610 (1978), ICI Ltd.; b) *J. L. M. Syrier,* DBP 2831555 (1979) and Eur. Pat. 2077 (1979), both Shell Int. Res.; c) *A. T. Costello, R. J. Lindsay,* DBP 2926890 (1980), ICI Ltd.

[130] *R. Lantzsch, D. Arlt,* DBP 2606635 (1977), Bayer AG.

[131] *N. Punja,* DBP 2536145 (1976), ICI Ltd.

[132] *R. Lantzsch,* DBP 2623848 (1977), Bayer AG.

[133] *R. Lantzsch, H. Hoffmann,* DBP 2638453 (1978), Bayer AG.

[134] *P. A. Kramer, H. Austermühle-Bertola,* DBP 2727612 (1978), Shell Int. Res.; *A. T. Costello, R. J. Lindsay,* DBP 2926852 (1980), ICI Ltd.

[135] Shell Int. Res., Niederl. Pat. 74/02879 (1974); Chem. Abstr. *83*, 27684b (1975); *H. Lehmkuhl, K. Mehler,* Justus Liebigs Ann. Chem. *1978*, 1841.

[136] a) Roussel-Uclaf, Fr. Pat. 2032526 (1970); b) *J. Martel,* DOS 1807091 (1969), Roussel-Uclaf; c) *M. Elliott, N. F. Janes, D. A. Pulman,* DOS 2439177 (1975), NRCD; d) *M. Elliott, N. F. Janes, P. H. Needham, D. A. Pulman,* Nature *244*, 456 (1973); e) *M. Elliott, N. F. Janes, D. A. Pulman,* DOS 2326077 (1974), NRCD; f) J. Chem. Soc. Perkin Trans. 1 *1974*, 2470; g) *T. Sugiyama, A. Kobayashi, K. Yamashita,* Agric. Biol. Chem. *36*, 565 (1972).

[137] *W. G. Taylor,* Synthesis *1980*, 554.

[138] *H. Hoffmann, F. Maurer, U. Priesnitz, H. J. Riebel,* DOS 2917620 (1980), Bayer AG.

[139] *J. Martel, J. Buendia,* DOS 2024614 (1970), Roussel-Uclaf.

[140] *N. Itaya, T. Matsuo, N. Ohno, T. Mizutani, F. Fijita, H. Yoshioka,* ACS Symp. Ser. *42*, 51 (1977).

[141] *G. R. Lee,* DOS 2639777 (1977), Wellcome Found. Ltd.

[142] a) Kuraray Co. Ltd., Jap. Pat. 76/145168 (1975) and 76/146442 (1975); Chem. Abstr. *87*, 140782 (1977) and *87*, 52854 (1977) respectively.

[143] *M. Elliott* et al., J. Sci. Food Agric. *5*, 509 (1954).

[144] *Y. Okuno, T. Masachika, H. Takeda, N. Itaya,* DOS 2432951 (1975), Sumitomo Chem. Co.

[145] *J. Warnant, V. Prost-Marechal, P. Cosquer,* DOS 2718039 (1977), Roussel-Uclaf.

[146] a) *J. G. M. Campbell et al.,* J. Sci. Food Agric. *2*, 421 (1951); *3*, 189 (1952); b) *J. Martel, B. Goffinet, A. Locatelli,* DAS 1768847 (1969), Roussel-Uclaf; c) *M. Elliott et al.,* Pestic. Sci. *1971*, 245; d) *P. E. Burt et al., ibid. 1974*, 791; e) *K. Okada et al.,* Agric. Biol. Chem. *37*, 2235 (1973); f) *C. Pavan, J. Bulidon,* DOS 2949384 (1980), Roussel-Uclaf; g) *T. Honda, N. Itaga, F. Horiuchi, O. Magara, T. Mitsutani,* Jap. Pat.-Anm. 040563 (1975); Chem. Abstr. *84*, 164251 (1976); *T. Honda, N. Itaga, O. Magara, T. Mitsutani,* Jap. Pat.-Anm. 108984 (1976); Chem. Abstr. *85*, 108340 (1976); *M. Matsui, F. Horiuchi,* Jap. Pat.-Anm. 005772 (1974); Chem. Abstr. *83*, 10504 (1975); *F. Horiuchi, H. Yoshioka,* Jap. Pat.-Anm. 097576 (1974), all Sumitomo Chemical Co.; Chem. Abstr. *81*, 120093 (1974); h) *K. Naumann,* DOS 2800922 (1979) and 2826952 (1980), both Bayer AG.

[147] *T. Nagase, G. Suzukamo, M. Fukao, H. Yoshioka,* DOS 2356702 (1974), Sumitomo Chem. Co.

[148] *K. Naumann,* DOS 2713538 (1978), Bayer AG.

[149] *K. Naumann,* DOS 2716898 (1978), Bayer AG.

[150] a) *S. Julia, M. Julia, G. Linstrumelle,* Bull. Soc. Chim. Fr. *1964*, 2693; b) *M. Julia,* Fr. Pat. 1203902 (1959), Rhone-Poulenc; c) *T. Nagase et al.,* DAS 2324473 (1973), Sumitomo Chem. Co.

[151] a) *G. Suzukamo, T. Nagase,* DOS 2723383 (1977), b) *T. Nagase, G. Suzukamo,* DOS 2453639 (1976), both Sumitomo Chem. Co.

[152] *T. Mizutani, N. Itaya, T. Honda,* Brit. Pat. 1464327 (1977), Sumitomo Chem. Co.

[153] *S. H. Harper, R. A. Thompson,* J. Sci. Food Agric. *3*, 230 (1952).

[154] *J. Martel, J. Buendia,* DOS 2010182 (1970), Roussel-Uclaf.

[155] *M. Matsui, K. Yoshioka,* DOS 1225171 (1966), Sumitomo Chem. Co.

[156] *T. Matsumoto, A. Nagai, Y. Takahashi,* Bull. Chem. Soc. Jpn. *36*, 481 (1963).

[157] a) *T. Aratani, S. Nakamura,* DAS 2240257 (1973), Sumitomo Chem. Co.; b) *T. Aratani, Y. Yoneyoshi, F. Fujita, T. Nagase,* DOS 2634633 (1975), Sumitomo Chem. Co.; c) *T. Aratani, Y. Yoneyoshi, T. Nagase,* Tetrahedron Lett. *1975*, 1707.

[158] *T. Aratani, S. Nakamura,* Jap. Pat. 49066-660 (1974), Sumitomo Chem. Co.; Chem. Abstr. *82*, 43007 (1975).

[159] *T. Aratani, Y. Yoneyoshi, T. Nagase,* Tetrahedron Lett. *1977*, 2599.

[160] *D. Holland, D. J. Milner,* J. Chem. Res. (S) *1979*, 317.

[161] *P. Martin, H. Greuter, D. Bellus,* Pestic. Sci. *11*, 141 (1980).

[162] *J. G. Dingwall, H. Greuter, P. Martin, P. Ackermann, L. Gsell,* Eur. Pat.-Anm. 0012722 (1980), Ciba-Geigy.

[163] *K. Kondo, T. Takashima, A. Negishi, K. Matsui, T. Fujimoto, K. Sugimoto, C. E. Hatch III, J. S. Baum,* Pestic. Sci. *11*, 180 (1980).

[164] *T. Matsuo, N. Itaya, O. Magara,* DOS 2605398 (1976), Sumitomo Chem. Co.

[165] *J. Martel, J. Tessier, J.-P. Demonte, J. Tolly,* DOS 2827627 (1979), Roussel-Uclaf.

[166] a) *J. Martel,* DOS 1935320 (1970), 1935321 (1970), 1935386 (1970), 1966839 (1969), all Roussel-Uclaf.

[167] *M. Sevrin, L. Hevesi, A. Krief,* Tetrahedron Lett. *1976*, 3915.

[168] *A. Krief,* DOS 2758624 (1978), Roussel-Uclaf.

[169] a) *M. Franck-Neumann, C. Dietrich-Buchecker,* Tetrahedron Lett. *21*, 671 (1980); b) *M. Franck-Neumann, C. Dietrich-Buchecker, M. Miesch,* Eur. Pat. 7828 (1980), Roussel-Uclaf.

[170] *M. Matsui, H. Yoshioka, H. Sakamoto, Y. Yamada, T. Kitahara,* Agric. Biol. Chem. *29*, 784 (1965); *31*, 33, 1143 (1967).

[171] a) *R. Sobti, S. Dev,* Tetrahedron *30*, 2927 (1974); b) *Y. Gopichand, A. S. Khanra, R. B. Mitra, K. K. Chakravarti,* Indian J. Chem. *13*, 433 (1975); c) *A. S. Khanra, R. B. Mitra, ibid. 14*, 716 (1976); d) *W. Cocker, H. S. J. Lander, P. V. R. Shannon,* J. Chem. Soc. Perkin Trans. 1 *1975*, 337; *1974*, 194; e) *F. Horiuchi, N. Itaya, H. Yoshioka,* DOS 2261611 (1973), Sumitomo Chem. Co.

[172] *R. B. Mitra, A. S. Khanra,* Synth. Commun. *7*, 245 (1977).

[173] *T. Matsuo, K. Mori, M. Matsui,* Tetrahedron Lett. *1976*, 1979.

[174] *S. A. Roman,* DOS 2942618 (1980), Shell Int. Res.

[175] a) *K. Arata, J. O. Bledsoe, K. Tanabe,* Tetrahedron Lett. *1976*, 3861; b) *B. B. Mutherjee, D. G. Brown, I. D. Hill,* US-Pat. 3708528 (1973), Tenneco Chem. Inc.

[176] a) *R. A. Sheldon,* DOS 2928840 (1980); b) *J. L. M. Syrier,* DOS 2928833 (1980) and 2928839 (1980); c) *J. van Berkel, H. C. Kelderman, P. A. Verbrugge, P. A. Kramer, J. L. M. Syrier,* Eur. Pat. 7142 (1980); d) *J. L. M. Syrier,* DOS 2928834 (1980); e) *J. van Berkel, H. C. Kelderman, J. L. M. Syrier,* DOS 2928835 (1980) and 2928836 (1980), all Shell Int. Res.

[177] *P. A. Verbrugge, P. A. Kramer,* DOS 2907730 (1979), 2917508 (1979) and 2917591 (1979), all Shell Int. Res.

[178] *S. A. Roman,* US-Pat. 4132717 (1979) and 4156692 (1979), both Shell Oil Comp.

[179] *M. Eliott, N. F. Janes,* Chem. Soc. Rev. *8*, 473 (1979).

[180] *R. Lantzsch,* Bayer AG, unpublished results.

[181] *J. Drabek, L. Gsell, F. Karrer, W. Meyer,* DOS 2614648 (1976), Ciba-Geigy.

[182] a) *R. H. Davis, R. J. G. Searle,* DOS 2447735 (1975) and 2553991 (1976), both Shell Int. Res.; b) *H. Greuter, S. Faroog, L. Gsell, P. Martin,* DOS 2856791 (1979), Ciba-Geigy; c) *R. H. Davis, R. J. G. Searle,* US-Pat. 4118510 (1978), Shell Oil Comp.

[183] *H. Greuter, P. Bissig, P. Martin, V. Flück, L. Gsell,* Pestic. Sci. *11*, 148 (1980).

[184] a) *G. Holan, R. A. Walser,* US-Pat. 4220591 (1980), CSIRO; b) *G. Holan, D. F. O'Keefe, C. Virgona, R. Walser,* Nature *272*, 734 (1978).

[185] a) *J. Farkas, P. Kourim, F. Šorm,* Collect. Czech. Chem. Commun. *24*, 2460 (1959); b) *S. Takei,* Bochu-Kagaku *27*, 51 (1962).

[186] a) *K. Ozawa, S. Ishii, M. Hayashi, M. Hirose, K. Hirata,* DOS 2935575 (1980); b) *K. Ozawa, S. Ishii, M. Hayashi, M. Hirose, R. Nonaka,* DOS 2949342 (1980), both Nissan Chem. Ind. Ltd.

[187] *K. Ozawa, S. Ishii, M. Hayashi, M. Hirose, R. Nonaka,* Jpn. Kokai Tokkyo Koho *79*, 151, 961 (1979), Nissan Chem. Ind. Ltd.

[188] *K. Okada, K. Fujimoto, Y. Okuno, M. Matsui,* Agric. Biol. Chem. *37*, 2235 (1973).

[189] *J. Drabek, S. Faroog, L. Gsell, O. Kristiansen, W. Meyer,* DOS 2731033 (1978), Ciba-Geigy.

[190] a) *J. Martel, J. Tessier, J. P. Demonte,* DOS 2742546 und 2742547 (1978), Roussel-Uclaf; b) *J. Drabek, P. Ackermann, S. Faroog, L. Gsell, O. Kristiansen, W. Meyer,* DOS 2805193, 2805226, 2805274 and 2805312 (1978); c) *H. Greuter, P. Martin, L. Gsell,* DOS 2843073 (1979), all Ciba-Geigy.

[191] *Y. Katsuda, Y. Minamide,* Jap. Kokai Tokkyo Koho *79,* 130, 534 (1979); Chem. Abstr. *92,* 75952v (1980).

[192] *S. A. Roman,* US-Pat. 4219562 (1980), Shell Oil Co.

[193] *M. Hirano, T. Ohsumi, K. Kasamatsu, T. Kato,* DOS 3006922 (1980), Sumitomo Chem. Co.

[194] a) *Y. Oomura, Y. Fujii, F. Mori, Y. Tamai, T. Hosogei, F. Wada, S. Aihara, T. Nishida, K. Itoi,* Jap. Kokai 77, 14748 (1977), Kuraray Co. Ltd.; Chem. Abstr. *87,* 52857a (1977); b) *N. Soma, Y. Nakata, R. Endo, Y. Inoue, S. Ohno, T. Mizuno,* Jap. Kokai 77, 122, 345 (1977); Sankyo Co. Ltd.; Chem. Abstr. *88,* 62038u (1978); c) *P. Piccardi, F. Corda, F. Gozzi, A. Mauconi, A. Longoni,* DOS 2907609 (1979), Montedison S.p.A.

[195] *Y. Kishida, M. Yoshimoto, I. Noburo,* DOS 2132761 (1972), Sankyo Co. Ltd.

[196] *J. H. Davis, M. J. Bull,* DOS 2813552 (1978), Shell Int. Res.

[197] a) *Y. Katsuta,* Jap. Kokai Tokkyo Koho 80, 22, 635 (1980); Chem. Abstr. *93,* 39533w (1980); b) *Y. Katsuda, Y. Minamite,* DOS 2851428 (1979), Dainippon Jochugiku K.K.

[198] *P. Bissig, H. Greuter, L. Gsell,* Eur. Pat. 7446 (1980) and 4316 (1979), Ciba-Geigy.

[199] *M. Elliott, N. F. Janes, D. A. Pulman,* US-Pat. 3922269 (1975), NRDC.

[200] a) *M. Elliott, A. W. Farnham, N. F. Janes, P. H. Needham, D. A. Pulman,* Pestic. Sci. *1976,* 492; b) *S. A. Roman, S. B. Soloway,* Eur. Pat. 5882 (1979), Shell Int. Res.

[201] a) *R. J. G. Searle, R. E. Woodall,* DOS 2407024 (1974), Shell Int. Res.; b) *T. Sugiyama, A. Kobayashi, K. Yamashita,* Agric. Biol. Chem. *39,* 1483 (1975).

[202] *M. Matsui, T. Kitahara,* Agric. Biol. Chem. *31,* 1143 (1967).

[203] *Y. Katsuta, Y. Minamide,* Jap. Kokai Tokkyo Koho 79, 132, 554 (1979); Chem. Abstr. *92,* 197997j (1980).

[204] a) *K. Tsushima, N. Kasamatsu, N. Ono, T. Matsuo, M. Mizutani,* Jap. Kokai Tokkyo Koho *80,* 38341 (1980), Sumitomo Chem. Co. Ltd.; Chem. Abstr. *93,* 167731w (1980); b) *R. J. G. Searle, R. E. Woodall, M. J. Bull,* DOS 2422977 (1974), Shell Int. Res.; c) *F. Karrer, S. Faroog,* DOS 2732811 (1978), Ciba Geigy; d) *T. Kitahara, K. Fugimoto, M. Matsui,* Agric. Biol. Chem. *38,* 1511 (1974).

[205] *R. A. Fuchs, I. Hammann, W. Stendel,* DOS 2825314 (1979).

[206] a) *E. V. Dehmlow,* Justus Liebigs Ann. Chem. *758,* 148 (1972); b) *E. V. Dehmlow, G. Höfle,* Chem. Ber. *107,* 2760 (1974).

[207] a) *R. W. Addor, M. S. Schrider,* DOS 2605828 (1976), Am. Cyanamid Co.; b) *S. Faroog, J. Drabek, L. Gsell, F. Karrer, W. Meyer,* DOS 2642814 (1977), 2642850 (1977) and 2642861 (1977), all Ciba-Geigy; c) *M. S. Schrider,* US-Pat. 4078080 (1978); d) *D. G. Brown,* US-Pat. 4203918 (1980), both Am. Cyanamid Co.; e) *I. Ohno, H. Takeda, M. Hirano, T. Umemura, T. Nishioka, N. Haya, T. Matsuo,* Jap. Kokai *76,* 148024 (1976), Sumitomo Chem. Co. Ltd.; Chem. Abstr. *86,* 166407P (1977); f) *S. Faroog, J. Drabek, L. Gsell, O. Kristiansen, W. Meyer,* DOS 2723236 (1977) and 2727909 (1978), both Ciba-Geigy.

[208] *W. W. Brand,* DOS 2724734 (1977), Am. Cyanamid Co.

[209] *H. Staudinger, L. Ruzicka,* Helv. Chim. Acta *7,* 393, 405 (1924).

[210] a) *J. Drabek, S. Faroog, L. Gsell, O. Kristiansen, W. Meyer,* DOS 2750182 (1978), Ciba-Geigy; b) *P. Winternitz,* DOS 2800073 (1978), Hoffmann-La Roche; c) *F. Mori, Y. Omura,* DOS 2810031 (1978), Kuraray Co. Ltd.

[211] a) *N. Ohno, K. Fujimoto, Y. Okuno, T. Mizutani, M. Hirano, N. Itaya, T. Honda, H. Yoshioka,* Agric. Biol. Chem. *38,* 881 (1974); b) *K. Fujimoto, N. Ohno, T. Mizutani, I. Ohno, M. Hirano, N. Itaya, T. Matsuo,* DAS 2335347, DOS 2365555 (1974), both Sumitomo Chem. Co.

[212] a) *P. A. Verbrugge, E. W. Uurbanus, P. A. Kramer, W. Terlouw,* DOS 2630633 (1977), Shell Int. Res.; b) *N. Ohno, I. Ohno, T. Nishioka, H. Takeda, K. Kasamatsu,* DOS 2647366 (1977), Sumitomo Chem. Co.; c) *M. Elliott, N. F. Janes, D. A. Pulman,* DOS 2717414 (1977), NRDC.

[213] *S. Faroog, J. Drabek, L. Gsell, W. Meyer, F. Karrer,* DOS 2647368 (1977), Ciba-Geigy.

[214] *H. D. Scharf, J. Janus, E. Müller,* Tetrahedron *35,* 25 (1979).

[215] *H. Greuter, D. Bellus,* DOS 2747616 (1968), Ciba-Geigy.

# Inorganic Pigments: Bases for Colored, Uncolored, and Transparent Products[**]

By Franz Hund[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Colored and uncolored inorganic pigments have been obtained since prehistoric times from natural minerals, at first empirically, then by specially developed methods. Since the beginning of the 18th century they have also gradually come to be studied scientifically, and today such research makes use of the latest techniques of solid-state physics and chemistry. On the basis of our knowledge of technically and aesthetically important properties, it has been possible in the last seventy years to make synthetic pigments superior to the natural ones, to increase production drastically while maintaining the pigment properties unchanged or improving them, and to broaden the range by the addition of new synthetic pigments. Nowadays it is in principle possible to write down a specification for many fields of application, taking into account aesthetic, technical, economic, and ecological aspects, and to make the corresponding inorganic pigment in adequate amounts. In what follows I shall discuss the dependence of the scattering and absorption constants of pigments on the refractive index, the wavelength of the light and the particle size, the properties of pigmented systems that depend on the particle geometry, and also some of the optical characteristics determined by the arrangement of the atoms in the crystal lattice.

## 1. Historical

Deliberate coloring by the use of natural or synthetic pigments is one of the oldest human activities, and because of the high stability of inorganic pigments the latter's preparation and use can be traced back over millenia. As has been shown by *Noll et al.*[1], pigments were already made synthetically in the city and river cultures of antiquity. More than 5 million tons of synthetic inorganic pigments *per annum* are nowadays produced industrially all over the world, and they have therefore become an important economic product[2].

## 2. Basic Concepts

An inorganic pigment[3a] is a colored or hueless colorant, practically insoluble in solvents and binders. The color produced by inorganic pigments[3b] is a sense-impression evoked by rays of light entering the eye. If the light source itself is standardized, the optical properties of a pigmented layer of lacquer or paint depend on the optical properties of the pigment particles, their size, their shape, and their volume concentration, and also on the optical properties of the (usually colorless) dispersion medium. Within certain limits, the pigment particle size and shape, and their distribution curves can be freely selected by the manufacturer so that the pigment properties that depend on these parameters can be varied, optimized, or developed in a desired direction. Aesthetic points of view apart, the most important properties for white pigments are the tinting strength and hiding power, and for black, gray, and colored pigments the tinctorial strength and hiding power. These properties[4] are determined by the scattering and absorption constants ($S_\lambda$ and $K_\lambda$) of the pigmented systems. In the case of white pigments the influence of the scattering constants predominates, and in the case of black pigments the influence of the absorption constant, with practically no wavelength dependence. Colored pigments are characterized by the ratio of the wavelength-dependent $S_\lambda$ and $K_\lambda$. Generally speaking, the tinting strength and hiding power of white pigments depend quite overwhelmingly on the scattering constant, and the tinctorial strength and hiding power of black and colored pigments are determined overwhelmingly by the absorption constant.

## 3. Dependence of the Scattering and Absorption Constants on the Refractive Index, Wavelength of the Light, and Particle Size

A relationship between the reflectivity $\beta_\lambda$ of a very thick pigmented coating and the absorption constant $K_\lambda$, together with the scattering constant $S_\lambda$ (both in the units of $\mu m^{-1}$), is given by the Kubelka-Munk equation[5a]:

$$\frac{(1-\beta_\lambda)^2}{2\beta_\lambda}=\frac{K_\lambda}{S_\lambda}$$

From *Mie*'s theory[5b], using simplified assumptions, we can calculate how the relative scattering cross section ($Q_S$) and the absorption cross section ($Q_A$), which are proportional to the scattering and absorption constants, depend on the (spherical) pigment particle size and the wavelength if we know the wavelength-dependent complex refractive

---

[*] Dr. F. Hund
Bayer AG, D-4150 Krefeld-Uerdingen
Address for correspondence: Scheiblerstrasse 89, D-4150 Krefeld 1 (Germany)

[**] From a principal lecture at the GDCh-Hauptversammlung, München, Sept. 13, 1977.

*0570-0833/81/0909-0723 $ 02.50/0*

index ($m_\lambda = n_\lambda - i \cdot k_\lambda$) of the pigment and dispersion medium under parallel illumination. Table 1 gives the mean refractive indices of the most important inorganic pigments and some dispersion media. The real component $\bar{n}$ of the refractive index varies between 1.5000 and 3.0805.

Table 1. Refractive indices of the most important pigments and dispersion media (mean values for $Na_D$ radiation).

| Trivial name | Formula | $\bar{n}$ |
|---|---|---|
| Ultramarine | $Na_8(Al_6Si_6O_{24})S_2$ | 1.500 |
| Cobalt blue | $CoAl_2O_4$ | 1.76 |
| Titanite | $CaTiSiO_5$ | 1.947 |
| Zircon | $ZrSiO_4$ | 1.9548 |
| Lead white | $2\,PbCO_3 \cdot Pb(OH)_2$ | 2.015 |
| Zincite | $ZnO$ | 2.021 |
| Cassiterite | $SnO_2$ | 2.0489 |
| Goethite | α-FeOOH | 2.366 |
| Wurtzite | $ZnS$ | 2.367 |
| Zinc blende | $ZnS$ | 2.3676 |
| Pseudobrookite | $Fe_2TiO_5$ | 2.385 |
| Magnetite | $Fe_3O_4$ | 2.42 |
| Minium | $Pb_3O_4$ | 2.42 |
| Crocoite | $PbCrO_4$ | 2.45 |
| Chromium oxide | $Cr_2O_3$ | 2.50 |
| Greenockite | $CdS$ | 2.5175 |
| Anatase | $TiO_2$ | 2.5246 |
| Rutile | $TiO_2$ | 2.7462 |
| Hematite | α-$Fe_2O_3$ | 2.873 |
| Cinnabar | $HgS$ | 3.0805 |
| Linseed oil | | 1.5000 |
| Water | | 1.333 |
| Alkyd resins | | 1.500 |
| Enamel frit (glass) | | 1.500 |
| Flint glass | | 1.575 |

Figure 1 shows the spectral variation of the refractive index for two white pigments and one colored pigment. Figure 2 shows the relative scattering cross section $Q_S/\alpha$ as a function of the particle diameter, calculated by *Völz* from *van de Hulst*'s data[6] for $TiO_2$, $ZnS$, and $BaSO_4$ dispersed in linseed oil for a wavelength of 550 nm. The course of the curve shows that with increasing refractive index of the pigment the optimal particle diameter (maximum of the scattering cross section) is displaced in the direction of smaller values and the absolute contribution of the scattering maximum increases considerably. Of the inorganic white pigments, $TiO_2$ in the rutile form has the smallest optimal particle diameter (0.19 μm) and the largest relative scattering cross section.

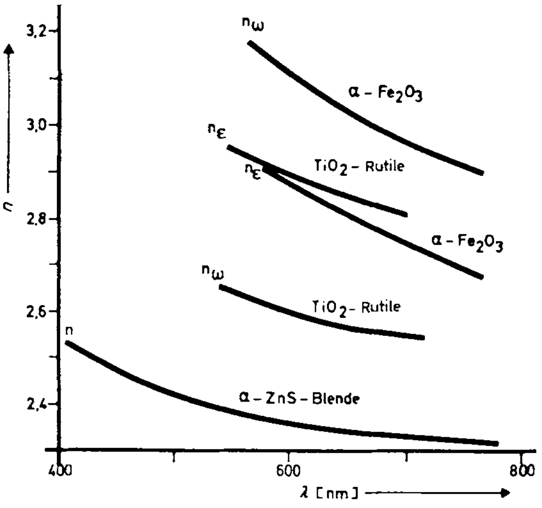


Fig. 1. Refractive index $n$ and wavelength $\lambda$.

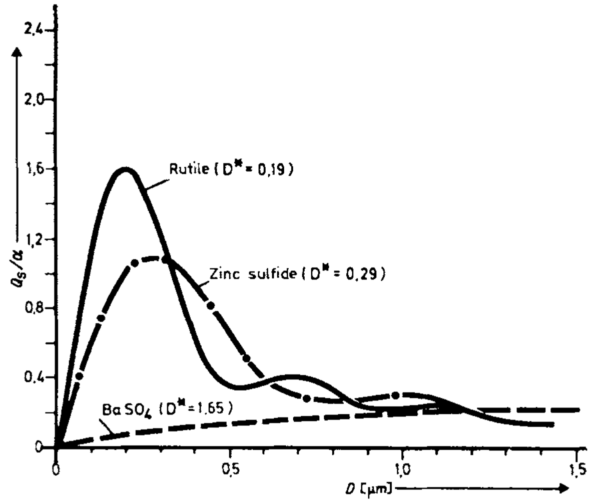


Fig. 2. Scattering curves of $Q_S/\alpha$ for $\lambda = 550$ nm, $D^*$ = optimal particle diameter [μm].

For α-$Fe_2O_3$, which crystallizes in the hematite lattice and is manufactured in very large amounts, Figure 3 shows, on the basis of *Brockes*'[7] data, the change in the relative effective cross sections for scattering ($Q_S/2\alpha$) and absorption ($Q_A/2\alpha$) as a function of the dimensionless particle size parameter $\alpha$[8]. With decreasing particle size the two cross sections at first increase up to a maximum. With a further reduction in the size of the pigment particles the relative scattering cross section falls very rapidly to zero, while the relative absorption cross section, after a shallow maximum, reaches finite high values at atomic dimensions. Thus, for colored inorganic pigments there are particle size regions in which scattering has disappeared and the wavelength-dependent absorption constant reaches finite values (transparent pigments!).

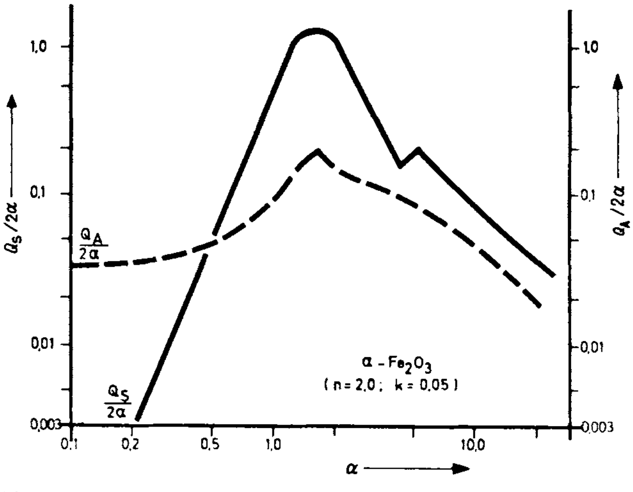


Fig. 3. Scattering, absorption, and particle size ($\alpha$ [8] ~ $D$ [μm]).

## 4. Properties of Inorganic Pigments that Depend on the Geometry of the Particles

For a given chemical composition, crystal structure, pigment volume concentration, and distribution in a dispersion medium, the optical and many other properties of *e. g.* an ideally pigmented lacquer coating are substantially determined by the size and shape of the particles and by their distributions about certain mean values. Important properties of pigmented systems, such as these, depend on the real geometry of the individual particles or their actual distribution in the dispersion medium and will be dealt with on the basis of individual examples.

### 4.1. Dependence of the Color of Red $\alpha$-$Fe_2O_3$ Pigments on Their Particle Size

The color of lacquer dispersions pigmented with isometric red $\alpha$-$Fe_2O_3$ particles can be determined numerically and unambiguously according to *Helmholtz*[9] from the dominant wavelength $\lambda_f$, the colorimetric purity $p_c$, and the radiance factor $A$.

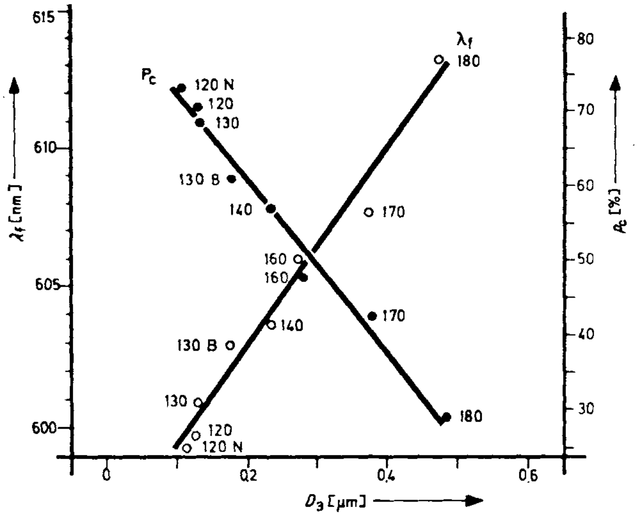


Fig. 4. Hue $\lambda_f$, color purity $p_c$, and particle diameter $D_3$ [10] of red iron oxides.

Figure 4 shows values of $\lambda_f$ (hue) and $p_c$ (color purity) of various colored iron oxide red pigments (commercial products) plotted against their diameter $D_3$[10]; with increasing diameter $\lambda_f$ rises and $p_c$ falls linearly, as previously described[11]. At the beginning, middle, and end of this series of pigments it can be seen in Figure 5a how the hue changes from a yellow-red to a blue-red with increasing particle diameter, and how the color purity decreases; the lower part shows, for a 1 : 5 mixture of iron oxide red and rutile, the extraordinarily strong coloring action (tinting strength) of these colored pigments. Figure 5b shows their spectral reflectance.

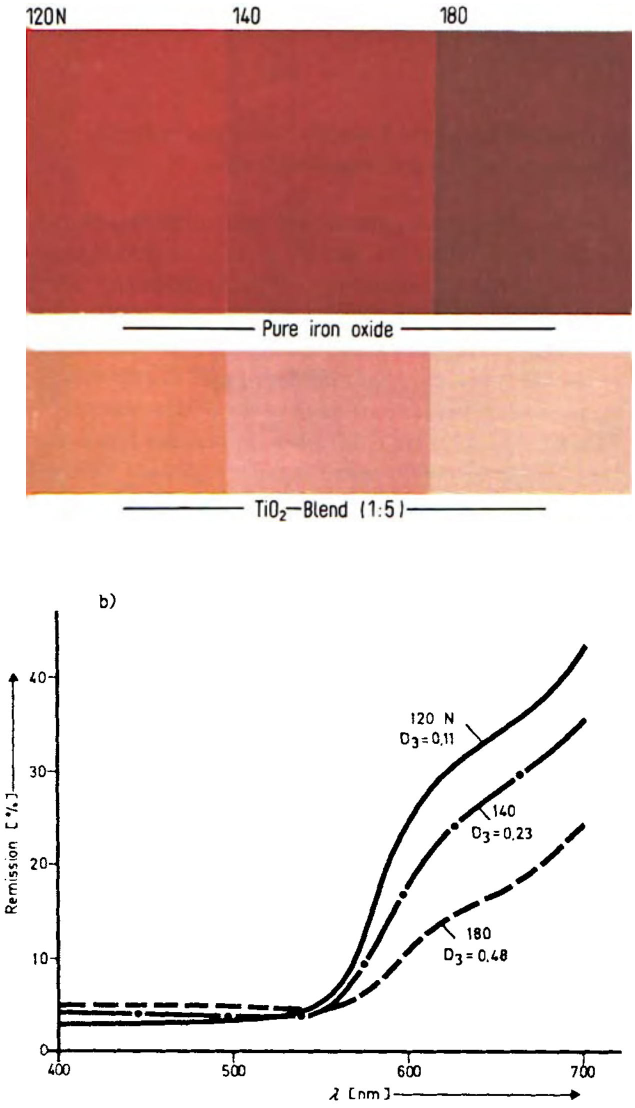


Fig. 5. a) Hue and tinting strength of red iron oxides (see Fig. 4 and text). b) Spectral reflectance and particle size.

### 4.2. Dependence of the Color of Red $\alpha$-$Fe_2O_3$ Pigments on the Particle Shape

Figure 6 presents the reflectance curves of two iron oxide pigments having the same crystal structure and same mean diameter $D_3$[10] but different particle shapes[12]. The acicular red iron(III) oxide 1130 shows a substantially higher reflectance in the long-wave region (600—700 nm), and therefore a higher scattering power, than pigment 730

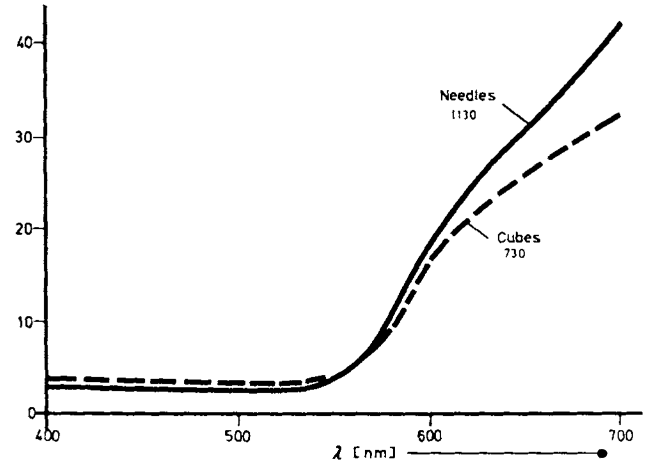
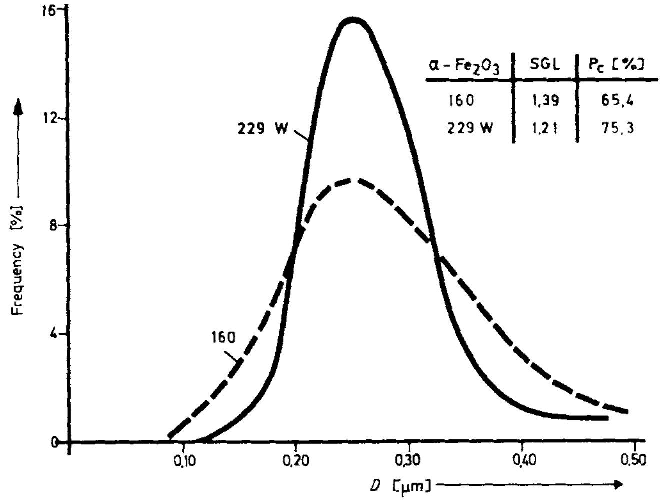


Fig. 6. Spectral reflectance and particle size of red iron oxides.

with its isometric particles; it therefore also has a yellower hue ($\lambda_f$), a higher color purity ($p_c$), and a higher radiance factor ($A$).

### 4.3. Dependence of the Color Purity of Red α-$Fe_2O_3$ Pigments on the Particle Size Distribution

For the same mean particle size, same isometric particle shape, and therefore the same hue ($\lambda_f$), an investigation was carried out to determine how the color purity ($p_c$) of red iron oxide pigments depends on the actual particle size distribution (SGL) about the mean value. The highest purity should occur only with monodisperse distributions[13] but because of the laws of nucleus formation, the growth of nuclei, and solid-state diffusion, in practice it is hardly ever possible to obtain monodisperse pigments. The particle size frequencies have Gaussian or log-normal distributions in which the deviation from monodispersity is described numerically by the standard deviations SG or SGL, respectively. Figure 7 shows particle size distribution curves with practically the same mean value but different widths of distribution. The calculated standard deviations SGL and color purities ($p_c$) derived from color measurements are plotted. With decreasing width of the distribution (decreasing SGL) and the same mean particle size, the color purity of the red iron oxide pigments increases considerably.



| α-$Fe_2O_3$ | SGL | $P_c$ [%] |
|---|---|---|
| 160 | 1,39 | 65,4 |
| 229 W | 1,21 | 75,3 |

Fig. 7. Particle size distribution and colorimetric purity.

### 4.4. Dependence of Tinting Strength on the Particle Size and the Particle Size Distribution

The relative tinting strength[14] or the tinctorial strength of colored or black pigments is a measure of the capacity of the inorganic pigment, on the basis of its absorption constant $K_\lambda$, to impart color to other light-scattering substances. The relationship of the tinting strength to $K_\lambda$, and therefore to the relative absorption cross section, also depends on the mean particle size and the widths of the particle size distribution. In Figure 8, the color intensity determined photometrically for a series of isometric α-$Fe_2O_3$ pigments[14] has been plotted against the volume-surface diameter $D_3$[10]. As a function of the particle size, the measured tinting strength follows a similar course to that of the relative absorption cross section ($Q_A/2\alpha$) in Figure 3 calculated by *Brockes*[7] after *Mie*[5b]. The luminosity of the pigment increases linearly with decreasing particle diameter $d_3$.

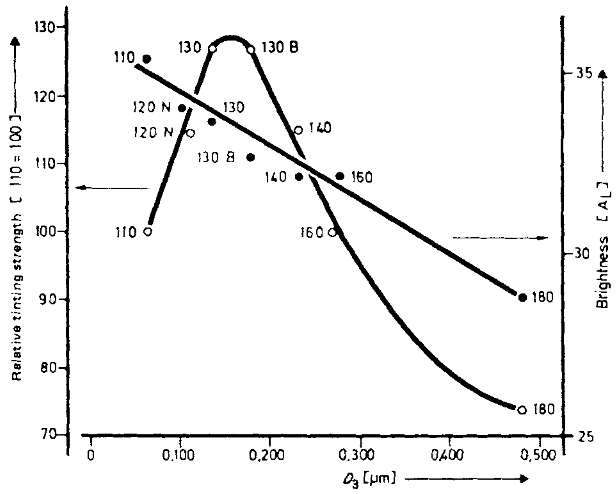


Fig. 8. Relative tinting strength, luminosity, and particle size of red iron oxides (see Fig. 4 and text).

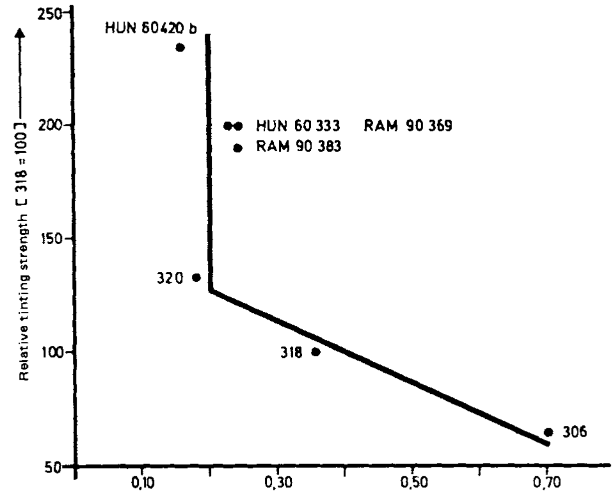


Fig. 9. Tinting strength and mean particle size of black iron oxides.

In Figure 9 the tinting strength of various isometric black iron oxide pigments ($Fe_3O_4$) has been plotted against the central value of the volume distribution curve (DZVL) from ultramicroscopic counts. In the upper range of particle sizes—as shown in Figure 8 for red α-$Fe_2O_3$ pigments—the tinting strength increases with decreasing particle size. At a certain small particle size it continues to rise markedly for some black pigments without a further reduction of the particle size. It can be seen from Figure 10, in which the real particle size distribution curves of these pigments are presented, that the further increase in the tinting strength with approximately constant particle diameter is due to the narrowing width of distribution of these pigments. From the degree of polydispersity of these pigments as a function of the logarithmic standard deviation SGL,

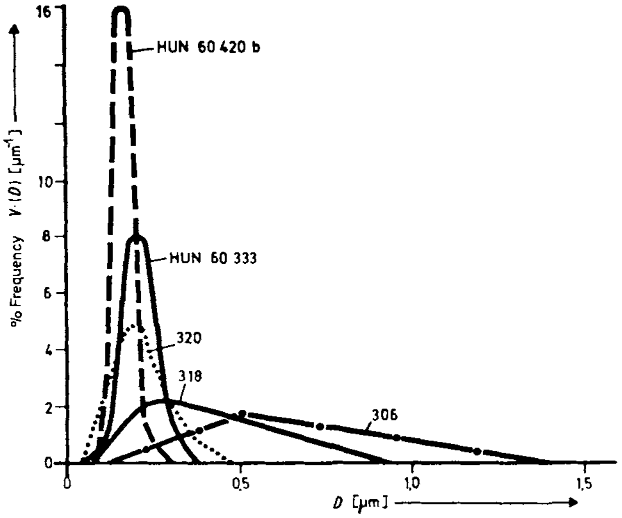


Fig. 10. Particle size distribution of various $Fe_3O_4$ pigments (see Fig. 9).

calculated from counts in Figure 11, it follows that the tinting strength increases approximately linearly with decreasing width of distribution (SGL) with the same mean particle size and the same particle shape.

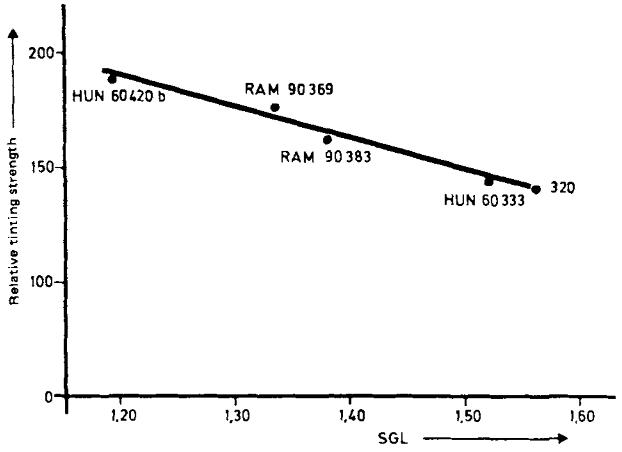


Fig. 11. Tinting strength (standardized $Fe^{3+}/Fe^{2+}$) and standard deviations of iron oxide black (see text).

### 4.5. Transparency of Red $\alpha$-$Fe_2O_3$ Pigments[15] and Particle Size

Figure 3 shows the dependence of the scattering and absorption of red iron oxides on the particle size. In the region to the left of the optimal particle diameter for the relative scattering cross section ($Q_S/2\alpha$), the scattering should decrease with further reduction of the particle diameter and finally disappear. Hence, the transparency of transparent dispersion media colored with such pigments should increase. Since $K_\lambda$ for $\alpha$-$Fe_2O_3$ disappears in the red wavelength region (600—700 nm), a transparent red coloration appears here as can be seen from Figure 12. It can also be seen how the transparency of the dispersion increases with decreasing particle diameter $D_3$ and how the original black and white checkered pattern becomes more recognizable with increasing transparency.

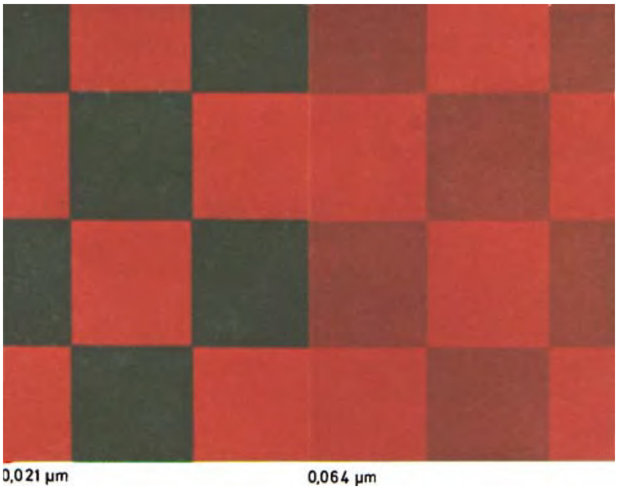


Fig. 12. Transparent iron oxide red ($D_3$=0.021 and 0.064 µm).

### 4.6. Tinting Strength of White Pigments: Dependence on the Refractive Index and Particle Size

The tinting strength of a white pigment[16] is its capacity to increase the reflectance of a dispersion medium that is intrinsically black or colored or one that has been made such through the inclusion of black or colored substances. The tinting strength of white pigments depends, through the scattering constant $S_\lambda$ and the relative scattering cross section ($Q_S/2\alpha$), on the refractive index and particle size.

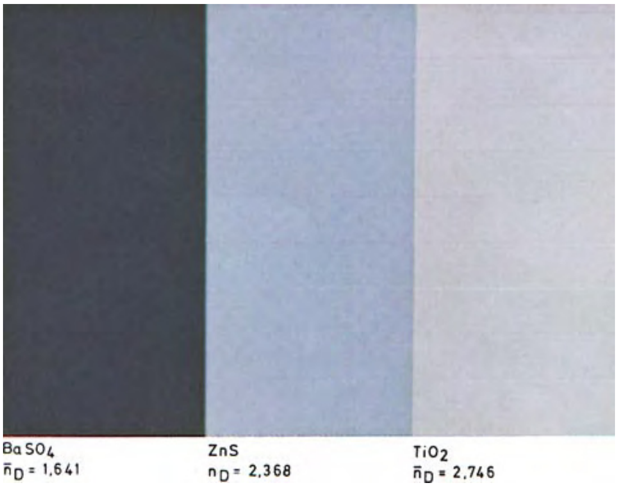


Fig. 13. Tinting strength (scattering constant) and refractive index of white pigments (5 : 1 with ultramarine).

Figure 13 shows the dependence of the tinting strength of various white pigments on their refractive indices. With equal weight proportions of white and blue pigments, the brightening action of the white pigments varies qualitatively with their refractive indices. The tinting strength of $TiO_2$ (rutile) with its optimal particle diameter of 0.19 µm is greater than that of ZnS (zinc blende) with its optimal diameter of 0.29 µm and much greater than that of $BaSO_4$ (barite) with its optimal diameter of 1.65 µm. The tinting strength of white pigments, like that of colored and black pigments, is a tinctorial property—the higher the numerical values, the smaller are the amounts necessary.

### 4.7. Hiding Power[17] of White Pigments: Dependence on Refractive Index and Particle Size

The hiding power of a pigmented lacquer film is its capacity to mask colors or color differences of the substrate. It follows from the Mie and Kubelka-Munk theory[5] that an increase of both the scattering constant $S_\lambda$ and the absorption constant $K_\lambda$ increases the hiding power. The white pigments $TiO_2$, ZnS, and $BaSO_4$ (see Section 4.6), having different refractive indices, were applied in a lacquer film, under the same conditions, to a black and white checkered pattern (Fig. 14). Since in the case of white pigments the absorption constant can be neglected, the hiding power of the three white pigments show a sequence similar to that of the tinting (Fig. 13). This is understandable, because both the hiding power and the tinting strength depend in the same way, through the scattering constant $S_\lambda$, on the refractive index of the white pigments.

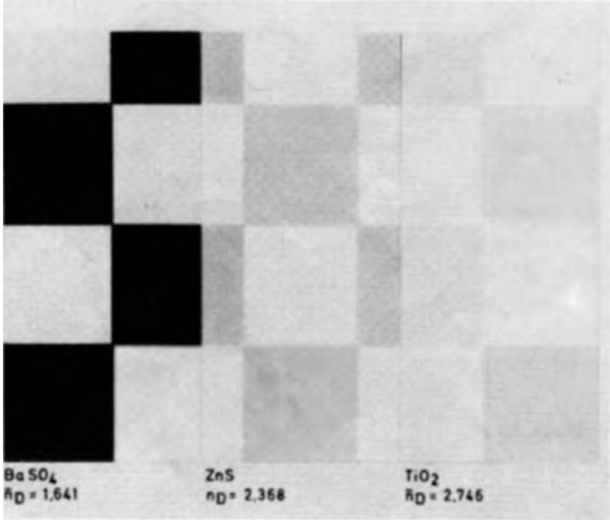


Fig. 14. Hiding power (scattering constant) and refractive index of white pigments.

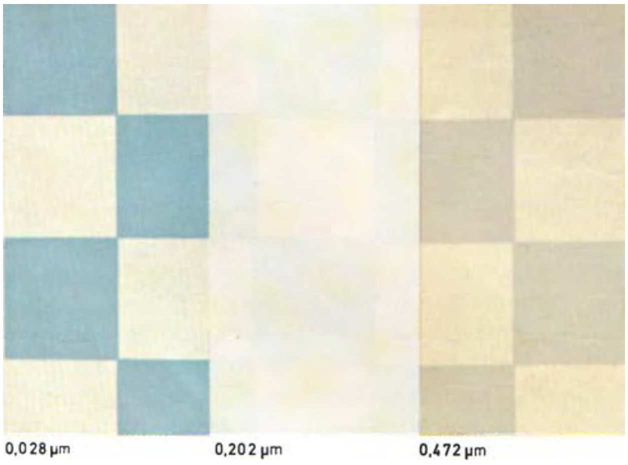


Fig. 15. Hiding power (scattering constant) and particle size $D_3$ of $TiO_2$.

In Figure 15, dispersions of $TiO_2$ pigments with different particle diameters $D_3$[10] were applied to a black and white checkered substrate under identical conditions. In agreement with *Völz*'s calculations (see Fig. 2), the hiding power determined by the relative cross section ($Q_S/\alpha$) of $TiO_2$ is very low for very small particles ($D_3 = 0.028$ µm) and very large at almost the optimal particle diameter (0.20 µm); it falls off again at still larger diameters (0.472 µm).

### 4.8. Dispersibility[18,19] (Dispersion Hardness) of Pigments

The "dispersion hardness" is a characteristic of the amount of pigment that must be dispersed in a dispersion medium; it is a quality characteristic that can be varied by the pigment manufacturer within certain limits by aftertreatment. A numerical value for the dispersion hardness is obtained from the rate of development of the tinting strength of pigments in a given binder. In the ideal final state of the dispersion all pigment agglomerates have been broken down into primary particles and aggregates, both of which are distributed statistically in each volume fraction of the medium. In Figure 16 the development of the tinting strength of a red iron oxide pigment has been plotted against the milling time.

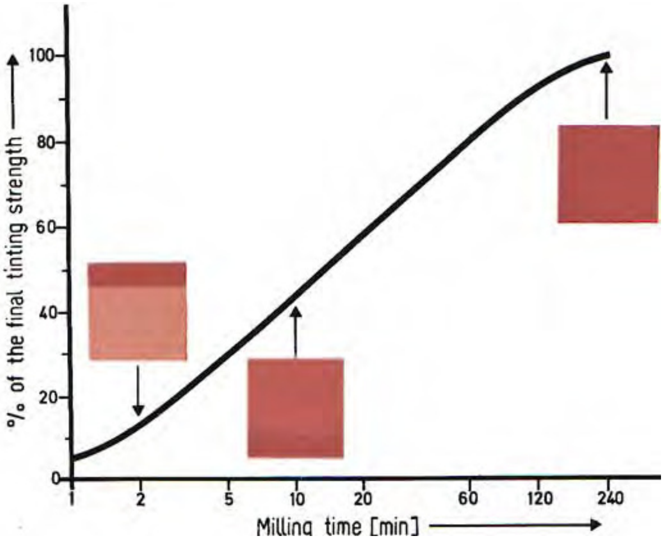


Fig. 16. Dispersibility of iron oxide red (110).

### 4.9. Dependence of the Oil Absorption[20] on the Particle Size and Particle Shape

The "oil absorption" of a pigment is the quantity of oil (in gram) needed to convert 100 g of the pigment into a putty-like mass under specified conditions. This characteristic, which is important for the practical application of pigments, depends on the particle size, particle size distribution, and most importantly on the particle shape; it increases with decreasing particle size and as their shape becomes more acicular.

## 5. Properties of Inorganic Pigments Depending on the Actual Atomic Arrangement

Until now the optical properties of inorganic pigments have been explained essentially on the basis of the real part $n_\lambda$ of the complex refractive index $m_\lambda = n_\lambda - i \cdot k_\lambda$, and its relationship to the size and shape of the particles have been considered. From a theoretical point of view, this exhausts the possibilities of modifying pigment properties by variations in the particle size and shape. Since the light absorption $K_\lambda$ retains finite high values down to atomic dimensions, the task arises of increasing the activity of colored pigments whose color is due to the presence of d- and f-elements in anions, with respect to hue, color purity, and tinting strength by changing the ligand field on an atomic scale. The motivation for this is the relatively high price and the limited natural occurrence of these elements.

### 5.1. Incorporation of d- and f-Elements in a Host of High Refractive Index

Using *Mie*'s theory[5b], *Brockes*[7] calculated how the relative absorption cross section ($Q_A/2\alpha$) changes when a substance with low $K_\lambda$ (small amount of a d-element in a colorless host) is incorporated into a pigment ($n_1$)/dispersion medium ($n_0$) system with $n_1/n_0 = 1.0$ and 2.0.

The relative absorption cross section has been plotted against the size of the pigment particles for the two cases in Figure 17. According to this, above a certain particle size the optical activity of the absorption constant ($Q_A/2\alpha$) of d- and f-elements in colorless hosts, with a large real part of the complex refractive index, is substantially larger than that in colorless hosts with a correspondingly low value. This situation has been observed in the incorporation of coloring $Ni^{2+}$ ions into spinel ($n \approx 1.0$) and rutile ($n \approx 1.83$) mixed phases; with the same amount of nickel and the optimal particle diameter, the tinting strength in the rutile phase is almost twice as high. All d- and f-elements can be incorporated into colorless hosts by application of the laws of heterotypic mixed-phase formation[21-24].

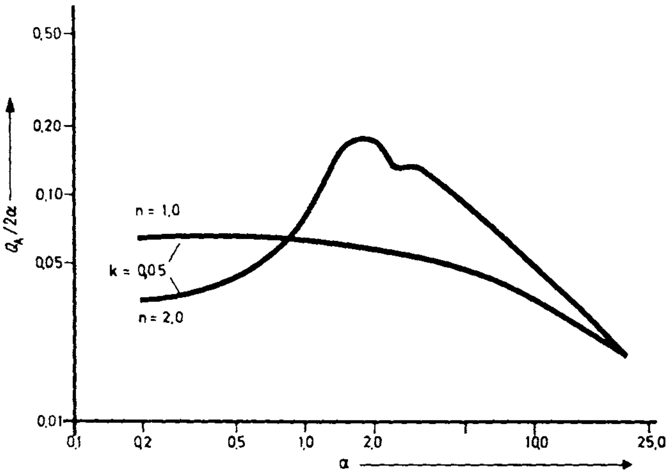


Fig. 17. Absorption, particle size ($\alpha$ [8]), and refractive index ratio ($n = 1.0$ or 2.0, $k = 0.05$).

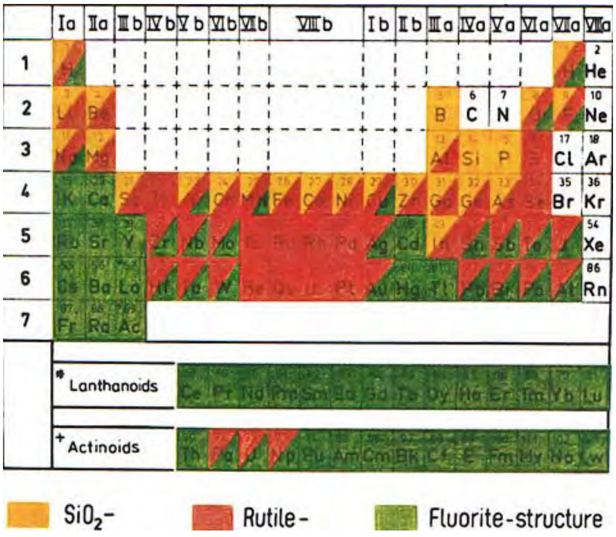


Fig. 18. Incorporation of elements in mixed phases.

Figure 18 shows the ability of the various elements of the periodic system to incorporate into $AO_2$ hosts with $SiO_2$-, rutile-, and fluorite-structures. Many new colored pigments[25] with $TiO_2$, $SnO_2$, and $ZrO_2$ as colorless host and coloring d- and f-elements have been developed on the basis of this principle in the last few years.

### 5.2. Lowering the Cation Coordination Number and Symmetry-Distortion of the Coordination Polyhedron

A further limited possibility of increasing the activity of d- and f-elements involves their incorporation into hosts by lowering the normal coordination number (in the case of oxides, this is determined essentially by the radius ratio of the cation and anion). Figure 19 shows that the molar extinction coefficient for cobalt increases by almost two orders of magnitude when the coordination number is lowered from 6 to 4. With the same coordination number of 6, for example for $Co^{2+}$, the absorption constant rises considerably when the polyhedron is distorted, as can be observed on going from (Mg,Co)O- to (Mg,Co)$TiO_3$-mixed phases[26].

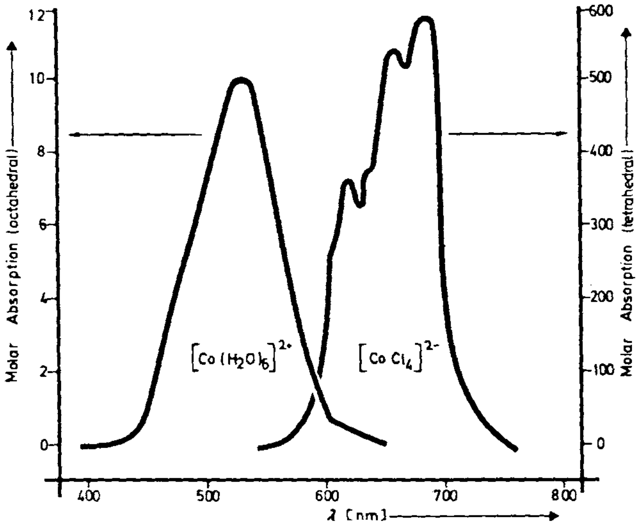


Fig. 19. Absorption and coordination of $Co^{2+}$ ions.

### 5.3. Change in the Ligand Field Strength

In the case of transition metal and lanthanoid ions the energy difference between the ground and excited states, the term difference $\Delta$, is so small that the absorption of light takes place in the visible part of the spectrum. This is responsible for the appearance of color. When d- and f-elements are coordinated with oxide, sulfide, or hydroxide ions, a ligand field forms round the coloring central cation, and the intensity of this field—inversely proportional to the distance—affects the term energy difference $\Delta$ of the cation[27]. Figure 20 shows the term-splitting for an octahedral oxygen ligand field around a $d^1$ cation as a function of the ligand field strength. The splitting increases with the strength of the ligand field, *i. e.* as the distance between the cation and the anion decreases. The effect of a change in the ligand field strength can be demonstrated for cadmium pigments crystallizing in the wurtzite lattice. A reduction of the distance by partial substitution of $Cd^{2+}$ (1.03 Å) by $Zn^{2+}$ (0.83 Å) increases the ligand field strength, displaces the absorption toward shorter wavelengths, and produces a green-yellow color. Increasing the distance by partial replacement of $S^{2-}$ (1.74 Å) by $Se^{2-}$ (1.91 Å) lowers the ligand field strength, displaces the absorption toward longer wavelengths, and changes the hue from yellow to a dark red. Figure 21 shows the spectral reflectance curves of pure CdS and of (Cd,Zn)S and Cd(S,Se) mixed phases, together with the color patterns.

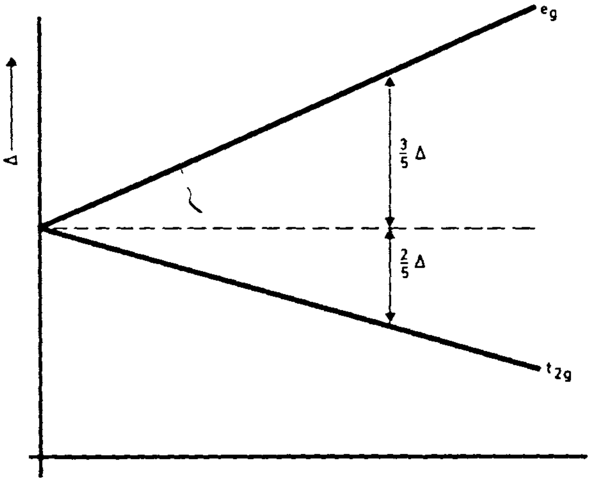


Fig. 20. Term splitting and ligand field (field strength $L$ proportional to the reciprocal distance between a $d^1$-cation and $O^{2-}$ligands, octahedral coordination).

Received: January 21, 1980 [A 378 IE]
German version: Angew. Chem. 93, 763 (1981)

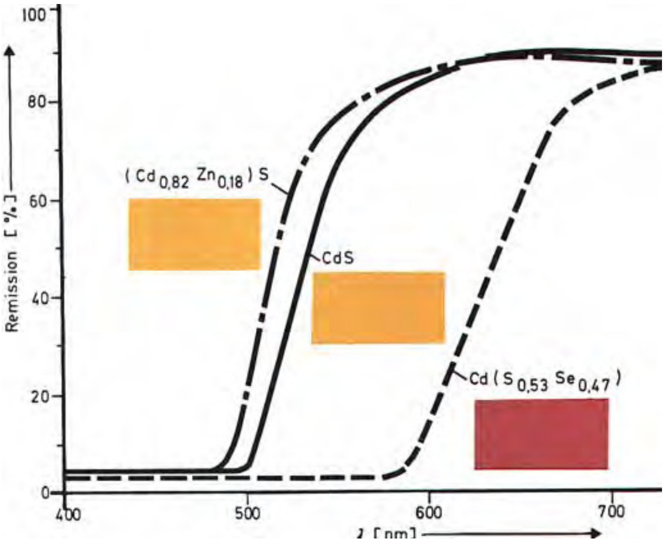


Fig. 21. Spectral reflectance of cadmium pigments.

---

[1] *W. Noll, R. Holm, L. Born,* Angew. Chem. *87,* 639 (1975); Angew. Chem. Int. Ed. Engl. *14,* 602 (1975).

[2] See also *K. Bittler, W. Ostertag,* Angew. Chem. *92,* 187 (1980); Angew. Chem. Int. Ed. Engl. *19,* 190 (1980).

[3] Cf. a) DIN 55945 (November 1968), DIN 55944 (June 1971); b) DIN 5033 (July 1970).

[4] For checking and evaluation, see *H. G. Völz,* Angew. Chem. *87,* 721 (1975); Angew. Chem. Int. Ed. Engl. *14,* 688 (1975).

[5] a) *P. Kubelka, F. Munk,* Z. Tech. Phys. *12,* 593 (1931); b) *G. Mie,* Ann. Phys. (Leipzig) *45,* 377 (1908); see also [4].

[6] *H. C. van de Hulst:* Light Scattering by Small Particles, Wiley, New York 1957; *H. G. Völz,* unpublished results.

[7] *A. Brockes,* Optik (Stuttgart) *21,* 550 (1964).

[8] $\alpha = 2\pi r n_0/\lambda$; $r$ = particle radius, $n_0$ = refractive index of the dispersion medium, $\lambda$ = wavelength of light.

[9] Cf. DIN 5033 (April 1972).

[10] $D_3 = 6/\rho \cdot S$; $\rho$ = density, and $S$ = specific surface.

[11] *F. Hund,* Chem. Ing. Tech. *38,* 423 (1966).

[12] *F. Hund* in Ullmanns Encyklopädie der technischen Chemie, 3. Ed., Vol. 13, Urban & Schwarzenberg, München 1962, p. 740; 4. Ed., Vol. 18, Verlag Chemie, Weinheim 1979, S. 554.

[13] *G. Kämpf,* Farbe + Lack *71,* 353 (1965).

[14] DIN 53234 (June 1971); Relative tinting strength is the percentage ratio of the color intensity of the specimen to the color intensity of a reference pigment; see also [4].

[15] For quantitative measurement of the transparency of inorganic pigments, see *H. G. Völz,* XIII. Fatipec Congress 1976, Juan-les-Pins, Congress Report, p. 639.

[16] DIN 53191, DIN 53192 (both August 1960): The tinting strength of a reference white pigment is taken as 100; see also [4].

[17] DIN 53162 (July 1967); cf. also [4].

[18] DIN 53238 (March, 1974): Determination of the dispersion hardness form the development of the color intensity.

[19] *L. Gall, U. Kaluza,* DEFAZET Dtsch. Farben-Z. *29,* 102 (1975).

[20] DIN 53199 (August 1965).

[21] *F. Hund,* Angew. Chem. *74,* 23 (1962); Angew. Chem. Int. Ed. Engl. *1,* 41 (1962).

[22] *F. Hund,* Z. Anorg. Allg. Chem. *321,* 2 (1963).

[23] *F. Hund,* Ber. Dtsch. Keram. Ges. *42,* 251 (1965).

[24] *F. Hund,* Farbe + Lack *73,* 111 (1967).

[25] *F. Hund,* US-Pat. 3022186 (1962), Bayer AG.

[26] *O. Schmitz-Du Mont et al.,* Forschungsber. des Landes Nordrhein-Westfalen Nr. *1389,* 50 (1964).

[27] *L. E. Orgel:* An Introduction to Transition-Metal Chemistry, Methuen, London 1960.

# Phospha-alkenes and Phospha-alkynes, Genesis and Properties of the (p-p)π-Multiple Bond

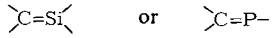
By Rolf Appel, Fritz Knoll, and Ingo Ruppert[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Just as the octet rule had prevented the discovery of the inert-gas compounds, the systematic search for phosphorus-carbon- and phosphorus-nitrogen-compounds having (p-p)π-multiple bonds was hindered by the double bond rule. The first successful synthesis of mesomeric-stabilized phosphorus-carbon compounds with coordination number 2, seventeen years ago, was followed nine years later by the preparation of the imino-phosphanes whose intensive investigation has continued to the present day. A dramatic development has now begun in the phospha-alkene and -alkyne fields, and a large variety of preparative methods have been found. Several compounds of this type are amazingly stable, however they do not participate in typical ylide reactions such as the Wittig reaction. In contrast, the PC double bond is more comparable to that of olefins, which has been confirmed by the occurrence of *E,Z*-isomers and pericyclic reactions of phospha-1,5-hexadienes.

## 1. Introduction

Even today the double bond rule, according to which compounds with (p-p)π-bonds between elements of the first and those of higher periods should not exist, can be found in many text-books[1,2]. Compounds of carbon with silicon or phosphorus, containing this structural element



should exist at best as short-lived intermediates but never as stable species. Studies over the last two decades have revealed that this rule is no longer valid for phosphorus and silicon in its combination with carbon and nitrogen.

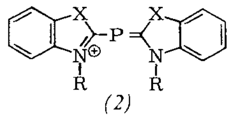
Numerous reports have appeared on the amino(imino)phosphanes, —N=P—N<[3], and mesomerically stabilized phosphorus-carbon compounds, in which the phosphorus has the coordination number 2[4,5]. In this article we have therefore only considered the most recent developments in the field of phospha-alkenes and -alkynes. We start with a brief historical review, sketching out the most important highlights on the way to PC-multiple bonds of lower coordinated, trivalent phosphorus.

The first experiment which led to the postulation of (p-p)π-interactions was carried out by *Gier*[6] in 1961 who obtained the phospha-acetylene *(1)* as a gas, stable only at low temperatures, by passing $PH_3$ through an electric arc between graphite electrodes. In 1964 *Dimroth* and *Hoffmann* described the first compound which is stable at room temperature because of the mesomeric structures of the phosphorus-carbon double bond of the two-coordinate phosphorus[7]. The actual existence of a delocalized (C2p—P3p)π-bond in the phosphamethine cyanine cations *(2)* could be determined by X-ray structure analysis[8]. In 1966 *Märkl* published the synthesis of the 2,4,6-triphenylphosphabenzene *(3a)*[9], and in 1971 *Ashe* succeeded in a very elegant synthesis of the unsubstituted phosphabenzene *(3b)*[10], in which the (p-p)π-bonds are also stabilized by resonance with the aromatic ring.

The breakthrough to isolable, acyclic compounds with localized (PC)-double-bond was initiated six years later by *Becker*[11]: Working on the synthesis of *P*-silylated acylphosphanes he observed a silyl migration from P to O and obtained the derivative *(4)*, the first example of a new structural type.

$P{\equiv}C{-}H$

*(1)*



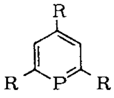
*(2)*

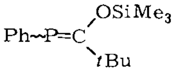
–X– = –CH=CH–, –S–, –NR–

R = $CH_3$, $C_2H_5$

*(3a)*, R = Aryl

*(3b)*, R = H





$$Ph{-}P{=}C\begin{matrix}OSiMe_3\\ tBu\end{matrix}$$

*(4)*

Since that time several important contributions to this dynamic field of research have also stemmed from the groups of *Issleib, Bickelhaupt,* and *Nixon*. Our group in Bonn first encountered this class of compounds in the chlorination of silyl-substituted methyldiphenylphosphanes with carbon tetrachloride[12,13]. Since then we have studied the mode of action of chlorocarbon compounds, especially $CCl_4$, $C_2Cl_6$, phosgene, and isocyanide dichlorides on tertiary phosphanes. The chronological presentation will now be left and a systematic survey of the available preparative methods for phospha-alkenes will be given: their properties and reactivity will also be discussed and compared with well known phenomena of the chemistry of hydrocarbons. Finally, the phospha-alkynes will be discussed.

## 2. Synthetic Routes to Phospha-alkenes

### 2.1. 1,2-Elimination

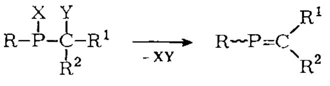
By analogy to the usual procedures in olefinic chemistry, a 1,2-elimination reaction at organophosphanes having

---

[*] Prof. Dr. R. Appel, Dr. F. Knoll, Dr. I. Ruppert
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)

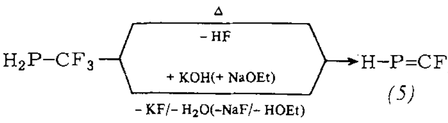
functional substituents X at phosphorus and Y at the α-C atom presents a good possibility of generating a PC-double bond. Substituents of opposite polarity which combine to a thermodynamically favored leaving molecule XY, are advantageous but not necessary.

The following possibilities have been verified to date: X = H, Y = F[14,15]; X = Cl, Y = H[14,16-19]; X = Br or I, Y = H[20]; X = Cl, Y = $SiMe_3$[12,13,21] and X = Y = Cl[20].



$$R{-}\overset{X}{P}{-}\overset{Y}{\underset{R^2}{C}}{-}R^1 \xrightarrow{-XY} R{\sim}P{=}C\begin{smallmatrix}R^1\\ R^2\end{smallmatrix}$$

A comparison of the distinct procedures demonstrates that as in the synthesis of *(5)* it is possible to choose either the thermal or base-induced elimination[14,15].



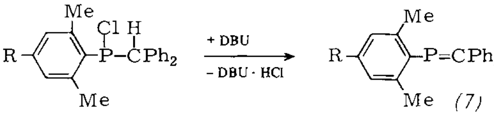
$$H_2P{-}CF_3 \xrightarrow[\text{+ KOH(+ NaOEt)}\ /\ \text{- KF/- }H_2O\text{(-NaF/- HOEt)}]{\Delta\ /\ \text{- HF}} H{-}P{=}CF_2$$

*(5)*

When the polarity of the substituents is reversed, *e.g.* X = Cl and Y = H, both pathways of synthesis can be used as shown in equations *(a)* to *(d)* (DBU = 1,5-diazabicyclo[5.4.0]undec-5-ene; DBO = 1,4-diazabicyclo[2.2.2]octane).

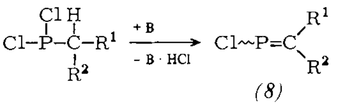
$$Cl_2P{-}CH_3 \xrightarrow[-HCl]{\Delta} Cl{-}P{=}CH_2 \qquad \text{(a)}$$

*(6)*



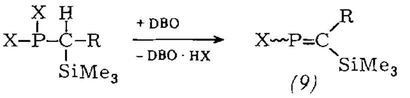
*(7)* (b)

*(7a)*, R = Me; *(7b)*, R = H



$$Cl{-}\overset{Cl}{P}{-}\overset{H}{\underset{R^2}{C}}{-}R^1 \xrightarrow[-B\cdot HCl]{+B} Cl{\sim}P{=}C\begin{smallmatrix}R^1\\ R^2\end{smallmatrix} \qquad \text{(c)}$$

*(8)*

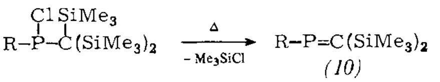


$$X{-}\overset{X}{P}{-}\overset{H}{\underset{SiMe_3}{C}}{-}R \xrightarrow[-DBO\cdot HX]{+DBO} X{\sim}P{=}C\begin{smallmatrix}R\\ SiMe_3\end{smallmatrix} \qquad \text{(d)}$$

*(9)*

| *(8)* | $R^1$ | $R^2$ | B | *(9)* | | R |
|---|---|---|---|---|---|---|
| *(a)* | H | Ph | DBO | *(a)* | Br | Ph |
| *(b)* | Ph | Ph | $NEt_3$ | *(b)* | Br | $SiMe_3$ |
| *(c)* | Ph | $SiMe_3$ | DBO or $NEt_3$ | *(c)* | I | Ph |
| *(d)* | $SiMe_3$ | $SiMe_3$ | DBO | | | |

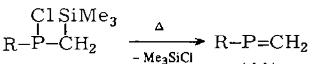
Looking at the different methods of preparation more closely it has to be pointed out that in contrast to the thermolytic HCl-elimination (eq. (a))[14], only the dehydrohalogenation in solution according to eqs. (b)—(d)[16-19] allows the isolation of marked amounts of pure phospha-alkenes. The use of suitable bases renders accessible not only the methylenephosphanes *(7a)* and *(7b)*[16], which are blocked at the phosphorus atom by bulky substituents, but even—extending the principle of synthesis to selected primary halogenophosphanes—*P*-halogen derivatives [eq. (c) and (d)][17-20]. The assumption[16] that PC-double bonds of the (p-p)π-type are stabilized above all by steric hindrance at the phosphorus atom is refuted by these results. Whereas the thermal HCl-elimination is inefficient, from a preparative point of view, the corresponding halosilane-elimination can be used synthetically. The action of heat on *P*-chloro(organo)phosphanes, with different silyl substituents at the methyl group, under conditions of reduced pressure, yields the *C*-silylated phospha-alkene *(10)*[21] and, surprisingly, also the carbon-unsubstituted phospha-alkene *(11)*[22] in pure form.



$$R{-}\overset{Cl}{P}{-}\overset{SiMe_3}{C}(SiMe_3)_2 \xrightarrow[-Me_3SiCl]{\Delta} R{-}P{=}C(SiMe_3)_2$$

*(10)*

*(10a)*, R = *t*Bu; *(10b)*, R = Ph



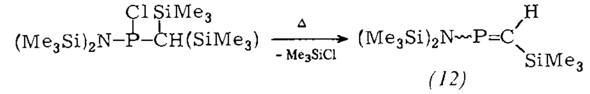
$$R{-}\overset{Cl}{P}{-}\overset{SiMe_3}{C}H_2 \xrightarrow[-Me_3SiCl]{\Delta} R{-}P{=}CH_2$$

*(11)*

R = 2, 4, 6-$tBu_3C_6H_2$

Methylenephosphanes which only possess small substituents also exhibit extraordinary stability. In the case of *(11)*, however, the shielding is due to the extremely bulky 2,4,6-tri-(*tert*-butyl)phenyl substituent on the phosphorus atom.

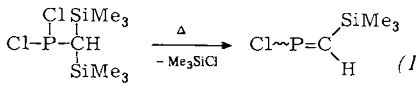
The amino-substituted chlorophosphanes also undergo a selective thermolysis, and this has been used in a one-pot synthesis of *(12)*[23].



$$(Me_3Si)_2N{-}\overset{Cl}{P}{-}\overset{SiMe_3}{C}H(SiMe_3) \xrightarrow[-Me_3SiCl]{\Delta} (Me_3Si)_2N{\sim}P{=}C\begin{smallmatrix}H\\ SiMe_3\end{smallmatrix}$$

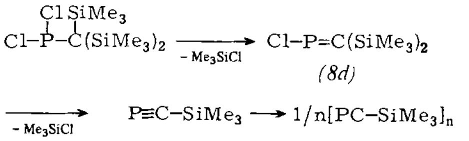
*(12)*

The extension to dichlorophosphanes, having several possibilities of elimination, leads to consecutive reactions. *(13)* can be formed by vapor phase pyrolysis and trapped at low temperatures[20]; the action of heat on the corresponding *C*-persilylated compound *(8d)* results in polymerization[21], due to the instability of the final product of the double elimination (see Section 5).



$$Cl{-}\overset{Cl}{P}{-}\overset{SiMe_3}{\underset{SiMe_3}{C}}H \xrightarrow[-Me_3SiCl]{\Delta} Cl{\sim}P{=}C\begin{smallmatrix}SiMe_3\\ H\end{smallmatrix}$$

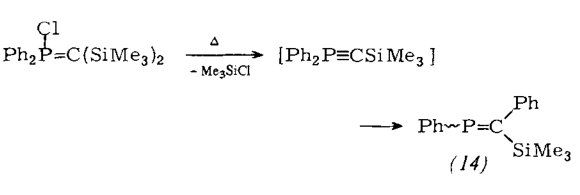
*(13)*



$$Cl{-}\overset{Cl}{P}{-}\overset{SiMe_3}{C}(SiMe_3)_2 \xrightarrow[-Me_3SiCl]{} Cl{-}P{=}C(SiMe_3)_2 \xrightarrow[-Me_3SiCl]{} P{\equiv}C{-}SiMe_3 \longrightarrow 1/n[PC{-}SiMe_3]_n$$

*(8d)*

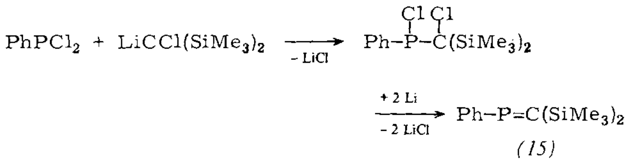
A surprising exception is the $Me_3SiCl$-elimination at the pentavalent phosphorus in the disilylated *P*-chloro(methylene)phosphorane in eq. (e). In this case the formation of *(14)* can be explained only by a subsequent reductive 1,2-(P,C)-shift of the phenyl group[12,13,20].



$$Ph_2\overset{Cl}{P}{=}C(SiMe_3)_2 \xrightarrow[-Me_3SiCl]{\Delta} [Ph_2P{\equiv}CSiMe_3] \longrightarrow Ph{\sim}P{=}C\begin{smallmatrix}Ph\\ SiMe_3\end{smallmatrix} \qquad \text{(e)}$$

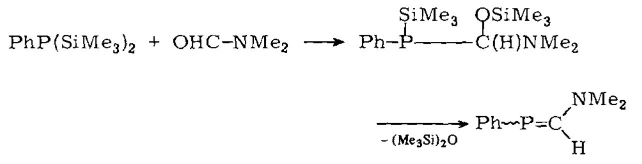
*(14)*

By analogy to the dehalogenation of vicinal dihaloalkanes with base or electropositive metals, the dechlorination of a *P*-chloro-α-chloroalkylphosphane with lithium offers another procedure for the introduction of the PC-double bond[20]. Certainly the general scope of application is restricted by the availability of the starting material.

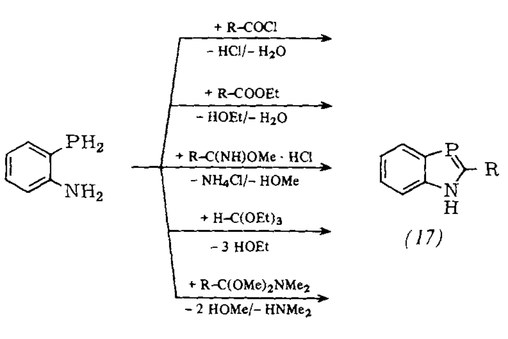

*(15)*

## 2.2. Condensation

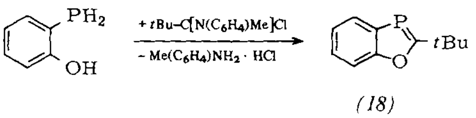
The reactions in which the P—C-bond—involved in the 1,2-elimination step—must first be formed are to be distinguished from the procedures previously mentioned. The P—C-bond may be formed by addition of a silylphosphane or a phosphane having a P—H bond to a carbonyl group, followed by the elimination-step. In principal, this has to be considered as a condensation reaction, as demonstrated by the example of siloxane-elimination in the preparation of *(16a)*[24].


*(16a)*

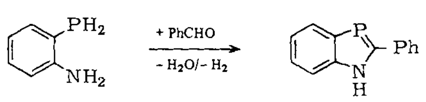
The formation of a PC-double bond is particularly favored, if this is incorporated into a stabilizing ring skeleton. Accordingly, the condensation of *o*-phosphinoaniline with carboxylic acid derivatives, such as chlorides, esters, imidoesters, orthoformic acid esters or aminals, leads to the 1,3-benzazaphospholes *(17)*[22,25].

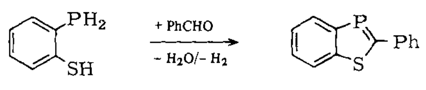

*(17)*

*o*-Phosphinophenol condenses with imidochlorides analogously to the 1,3-benzoxaphosphole *(18)*[22].

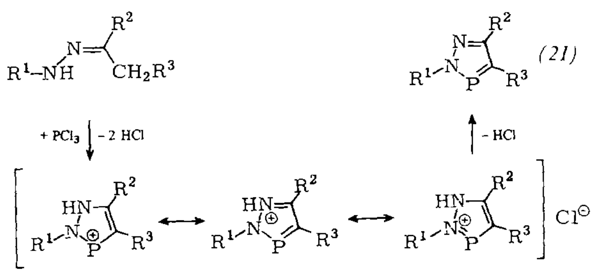

*(18)*

The addition compounds of *o*-phosphinoaniline and -thiophenol with benzaldehyde undergo hydrogen and water cleavage, either spontaneously or by oxidation[22]. 2-Phenyl-1,3-benzazaphosphole *(17c)* and 2-phenyl-1,3-benzothiaphosphole *(19c)* are formed respectively.


*(17c)*


*(19c)*

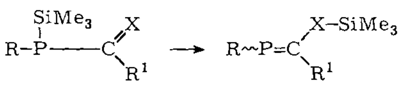
Hereby, the palette of elimination reactions was extended to the example of dehydration with dehydrogenation. Finally, the action of *N*-substituted hydrazones with α-CH-acidity on phosphorus trichloride, leading to the new heterocyclic compound *(21)*[26,27], belongs to this group of condensations. The cyclic 6π-electron system of the phosphenium chloride *(20)*[28] could be identified as an intermediate of the dehydrohalogenation.


*(21)*

*(20)*

## 2.3. 1,3-Trimethylsilyl Migration

An entirely different principle for the generation of the PC-double bond is based on the migration of a *P*-silyl-group to an element such as nitrogen, oxygen or sulfur which is bonded in the α-position. According to eq. (f) the double bond is hereby shifted to the phosphorus. The driving force of this "silatropy" could be the formation of a very stable N—Si-, O—Si- or S—Si-bond.

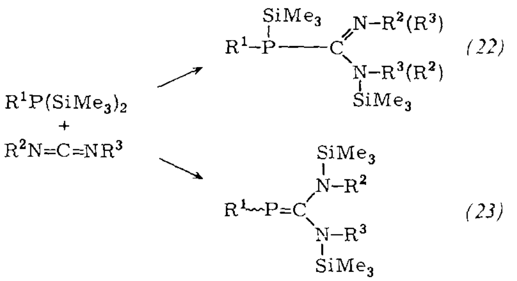

(f)

$X = NR^2, O, S$

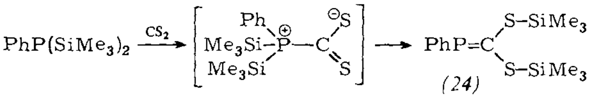
### 2.3.1. Addition with Silyl Migration

To date two examples, in which addition of silylphosphanes to double-bonds takes place prior to the silyl migration, are known. Monoorganobis(trimethylsilyl)phosphanes react with carbodiimides by insertion into the PSi-bond to give phosphaguanidines[29].

Depending on the substituents $R^2$, $R^3$ either the *N,P*-bis-silylated derivatives *(22)* or, by double silyl migration, the isomeric phospha-alkenes *(23)* are formed [*(23a—e)*, see Table 1; $R^2$, $R^3$ should preferably be phenyl].

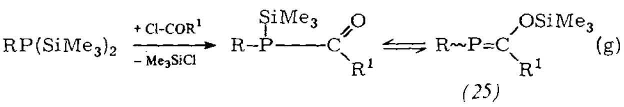


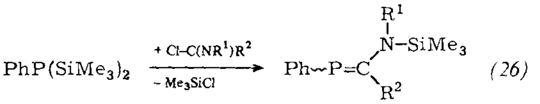
An analogous reaction with formation of a primary adduct was observed when phenyl(bistrimethylsilyl)phosphane was treated with $CS_2$[30]. The phospha-alkene *(24)* is formed.



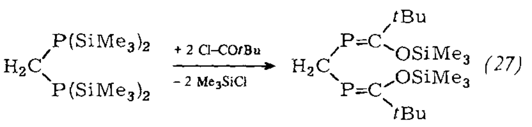
2.3.2. Condensation with Silyl Migration

The very first introduction of a stable PC-double-bond ensued from a halosilane condensation between disilylated phosphanes and carboxylic acid derivatives[11,31,32] and their aza analogues[33]. This synthetic procedure for *(25)* and *(26)* is very advantageous from the preparative point of view because of the ready availability of the starting materials. The primary condensation to the *p*-silylacylphosphane is usually followed by a rapid, irreversible migration of the silyl group with formation of the methylenephosphane structure. Depending on the acyl moiety both silatautomers have occasionally been found in equilibrium[11] [eq. (g)] [*(25a–f)* and *(26a–j)* see Table 1].

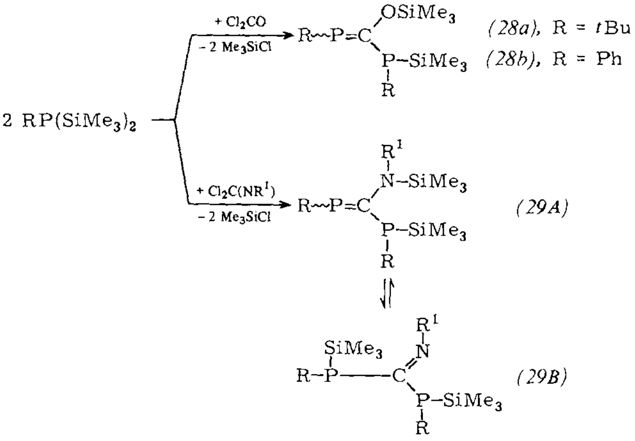




Methylenebis(disilylphosphane) behaves in a similar manner and yields *(27)*, whose structure was determined by X-ray structure analysis[34].



Carbonic acid halides, as *e.g.* phosgene[35,36] and isocyanide dichlorides[37,38] undergo double substitution to give the *C*-phosphinomethylenephosphanes *(28)* and *(29)*, respectively, without isolable intermediates. The isomeric phosphaguanidines *(29B)* can be identified by NMR in minor amounts in solutions of *(29A)*[39] in a similar manner to the acylphosphanes in eq. (g) [*(29a—n)*, see Table 1].



## 3. Properties and Reactivity of Phospha-alkenes

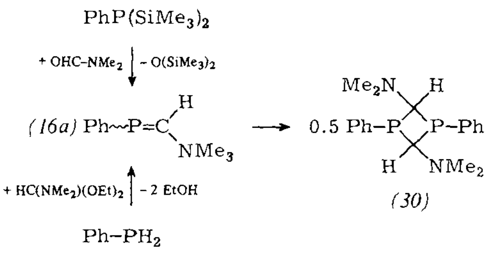
The phospha-alkenes hitherto synthesized on a preparative scale are mainly oily, often yellow-colored substances, which show only a small tendency to crystallize. They are readily or very readily soluble in the usual polar or nonpolar solvents. So far, typical reactions of phosphanes such as oxidations and alkylations, except for the sulfuration of the particularly reactive compound *(12)* (cf. Section 3.3) have not been reported. Up to now no tendency for Wittig-reactions has been be observed.

As far as is known the phospha-alkenes can react in two ways: at the PC-double-bond or at the periphery.

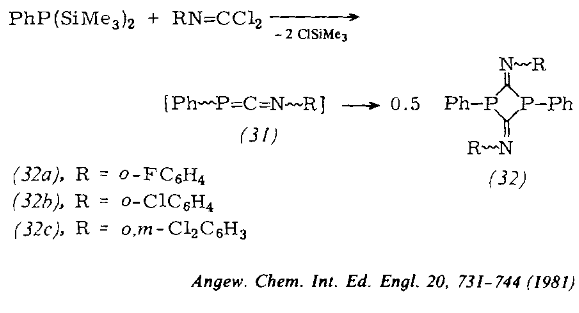
### 3.1. Reactions at the PC-Double Bond

3.1.1. Self-Addition

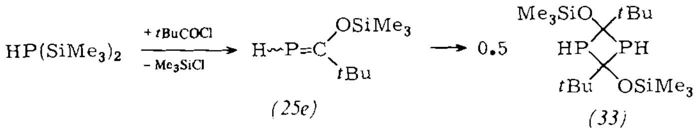
It is well known that molecules with double-bonds have a tendency to dimerize. The phospha-alkene *(16a)* (cf. Section 2.2), which can be prepared *via* different pathways, undergoes [2+2]-cycloaddition (head-to-tail condensation) to give the 1,3-diphosphetane *(30)* according to the expected differences in polarity[22,24].



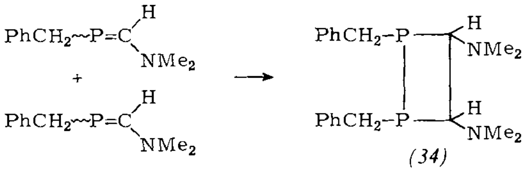
1,3-Diphosphetanes *(32)* are also obtained by reaction of isocyanide dichlorides with disilylphosphanes. The products *(32)* are probably formed by dimerization of the not yet isolated monophosphacarbodiimide *(31)*[38,40].



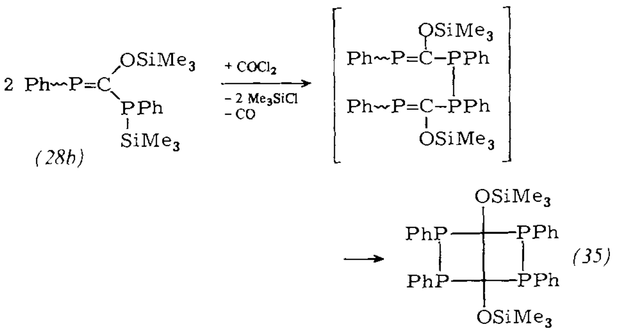
Also *(25e)*, the condensation product of bis(trimethylsilyl)phosphane and pivaloyl chloride, is slowly converted into the 1,3-diphosphetane *(33)* under the influence of light[32].

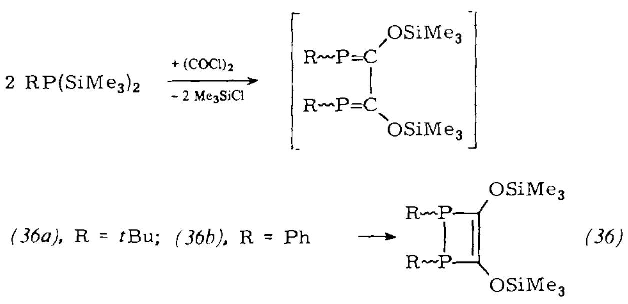


The cyclization of two methylenephosphane-units to the isomeric 1,2-diphosphetanes *(34)* can be observed with the *P*-benzylated aminomethylenephosphane[41].



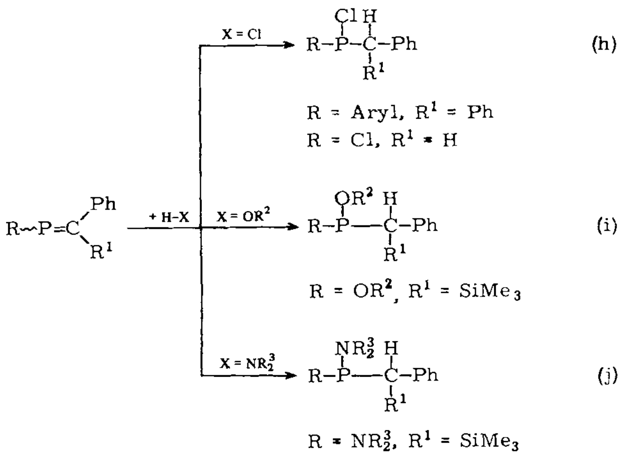
This surprising head-to-head and tail-to-tail addition may also be responsible for the formation of the bicyclo[2.2.0]hexane structure *(35)* when the phosphino-substituted methylenephosphane *(28b)* is treated with phosgene[35,36]. As in the synthesis of the 1,2-phosphetenes *(36)* from disilylphosphanes and oxalyl chloride[42], the corresponding intermediates cannot be isolated.





### 3.1.2. Addition of H-Acidic Reagents

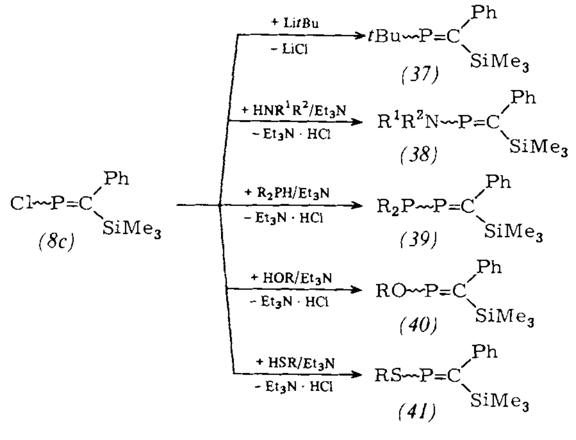
Directed addition reactions of polar reagents to phospha-alkenes have only been investigated to a limited extent up to now and have been restricted to the hydrogen halides[16], alcohols and amines[43]. The anionic part of the HX always adds to the P-atom, while the proton adds to the C-atom [eq. (h)—(j)].



## 3.2. Substitution with Preservation of the PC-Double Bond

### 3.2.1. Derivatization of *P*-Chloro(methylene)phosphanes

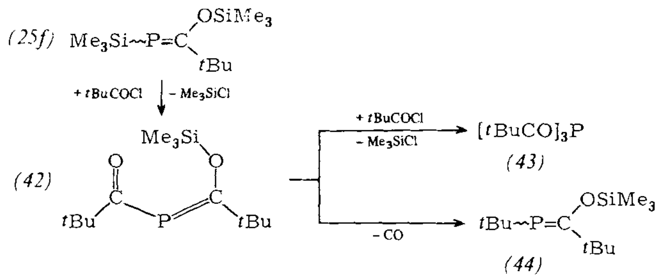
*P*-halogenated methylenephosphanes such as *(8c)*[17] allow derivatization at the phosphorus. They are therefore valuable key compounds for the preparation of a large variety of novel methylenephosphanes, such as the phosphino-, alkoxy- and alkylthio-substituted compounds with unknown atomic sequence[43]. The condensations of *(8c)* with *tert*-butyllithium to give the *P*-organo derivative *(37)*, with secondary amines to give the *P*-amino(methylene)phosphanes *(38)* and with secondary phosphanes to give the group of *P*-phosphino(methylene)phosphanes *(39)* having the diphosphane partial structure may be cited as examples. The alkoxy or alkylthio groups can be introduced by alcoholysis or thiolysis to give *(40)* and *(41)*, respectively [*(38)*, $R^1$, $R^2$=alkyl and/or aryl; *(39a)*, R=*t*Bu; *(39b)*, R=Ph; *(40)*, R=alkyl and/or aryl; *(41)*, R=alkyl; cf. also Table 1].



In this connection *(8c)* has a reactivity which is comparable to that of the secondary chlorophosphanes with the coordination number three. However, it must be borne in mind that after the primary substitution an addition to the PC-double bond has been observed with an excess of the *N,O*-acidic reagents (eq. (i) and (j)).

### 3.2.2. Derivatization of *P*-Silyl(methylene)phosphanes

The silyl derivative *(25f)* with the reversed reactivity (umpolung) of the *P*-chloro(methylene)phosphane *(8c)* oc-

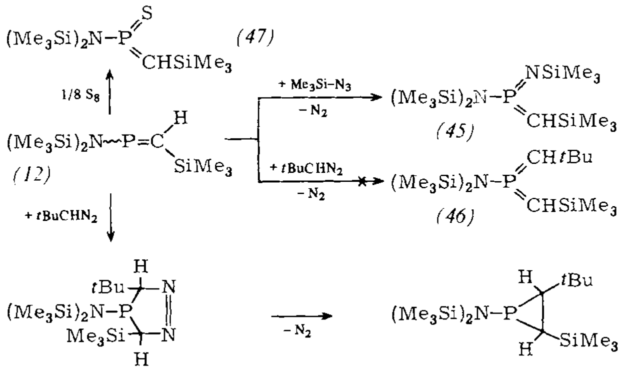


cupies a special position[31]. According to eq. (g), *(25f)* is formed by the reaction of tris(trimethylsilyl)phosphane with pivaloyl chloride. The *P*-acylated derivative *(42)* is formed *via* another halosilane condensation under more vigorous conditions, and reacts in part with further acid chloride to give the triacylphosphane *(43)*, and in part *via* decarbonylation to give *(44)*[31].

### 3.3. Oxidative Extension of the Coordination of the Methylenephosphane Phosphorus

The reaction of trimethylsilylazide or diazaalkanes with the bis(trimethylsilyl)amino(trimethylsilylmethylene)phosphane *(12)*, in order to synthesize the double ylides *(45)* or *(46)* with three coordinated phosphorus was studied; only the imination to *(45)*, however, succeeded[44]. A compound with the skeleton *(45)* had already been obtained by methylenation of the (N—P=N)-system[45a].

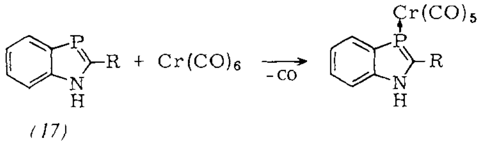
Recently, however, we have succeeded in introducing a second PC double bond at the same P atom[45b]. Starting from *(12)*, instead of the double ylide, only the isomeric phosphirane was formed from the detectable $1,2,4\lambda^3$-diazaphospholidine intermediate *via* $N_2$-elimination[23].



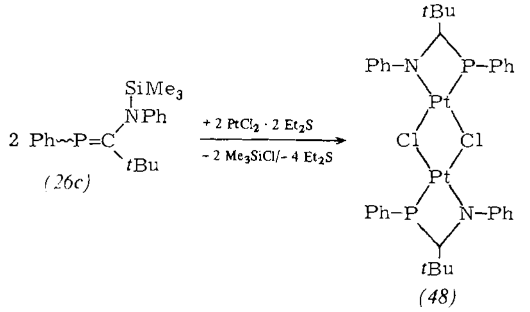
The special position of the methylenephosphane *(12)*, which can be sulfurized to *(47)*, has however been recorded in the literature[45c].

### 3.4. Complexes with Transition Metals

Tertiary phosphanes are valuable and widely used ligands in complex-chemistry. Initial experiments indicate that methylenephosphanes such as *(17)* are also able to displace carbon monoxide from carbonylmetal compounds[22,46]. The question arises whether the complex may be formed only with the lone-pair electrons of the trivalent phosphorus or also with the π-electrons of the double bond. This problem may be elucidated by further studies with varied substitution pattern at the methylenephosphane.



The 1,3-condensation of an amino-substituted phosphaalkene at d$^8$-metal salts (using the stabilizing chelate effect) is demonstrated in eq. (k)[33].



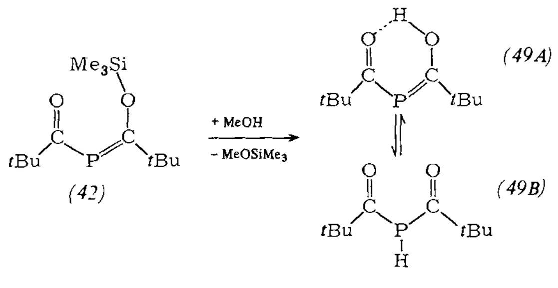
(k)

### 3.5. Reactions at the Periphery

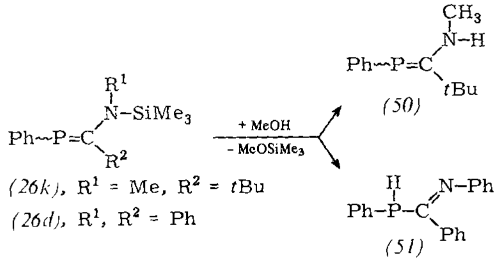
This section deals with reactions at the α-position to the methylene carbon which can affect the double bond. These reactions include cleavage of the *O*-, *N*- or *P*-silyl groups[32,47] with reagents such as methanol and phosgene. Usual derivatizations, such as acylations, in which the molecular structure is retained will not be dealt with here[33].

#### 3.5.1. Desilylations

The cleavage of a silyl group bonded to oxygen or nitrogen, may (but must not necessarily) influence the PC-double bond. Both possibilities have been verified in the keto-enol equilibrium, *(49B)*⇌*(49A)*, after methanolysis of *(42)*[48]. As with the β-diketones, both species are observed in solution; however, according to the X-ray structure determination in the solid state, only the H-bridged enol-form *(49A)* exists.



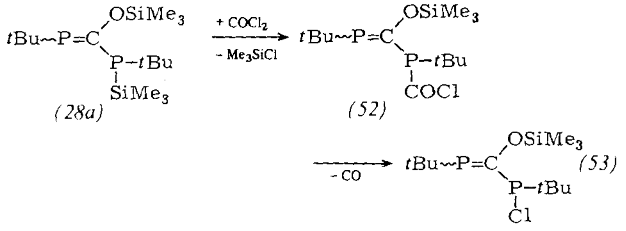
The protonolysis of the silylamino-substituted methylenephosphane is controlled by the competitive basicity of the amino- and phosphino centers of the molecule. In the *N*-methylderivative *(26k)* the position of the double bond remains fixed, even after alcoholysis to *(50)*; in the acidic phenyl derivative *(26d)* the imide *(51)* is formed by an (*N,P*)-prototropy[33].



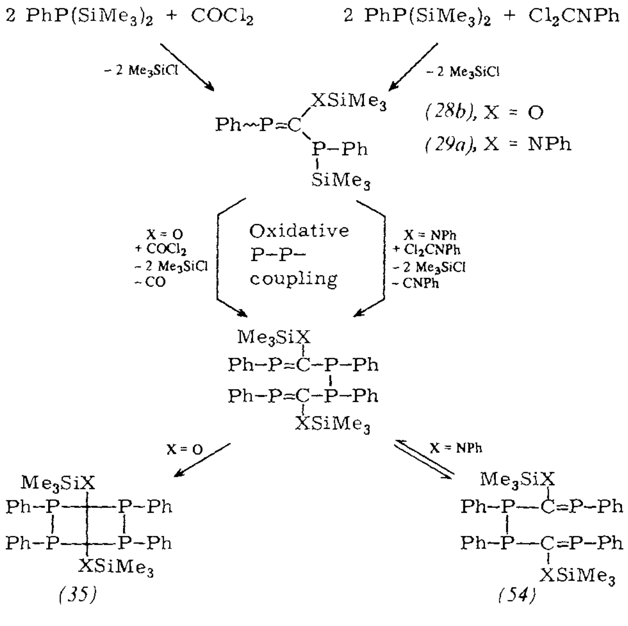
### 3.5.2. Particular Condensations with Phosgene and Isocyanide Dichlorides

The action of phosgene and isocyanide dichlorides on silylphosphino-substituted phospha-alkenes can be distinguished from pure derivatizations which do not affect the methylenephosphane bond and reactions which cause a fundamental change in the bond-system.

$COCl_2$ reacts with the *tert*-butyl compound *(28a)* according to the first pattern, whereby the *P*-silyl function of *(28a)* is converted into the *P*-chloro function of *(53)* following CO-elimination from the detectable mono-condensation product *(52)*[49].



Upon replacing the *tert*-butyl group of *(28a)* by the smaller phenyl group, the phosgenation takes another course. The P—P-linkage in *(28b)* to the 1,3,4,6-tetraphospha-1,5-hexadiene is no longer hindered[37,38]. The bis(siloxy)-analogue of *(54)*, thus obtained, is unstable and undergoes cyclization at the PC-double bond to the stable 2,3,5,6-tetraphosphabicyclo[2.2.0]hexane derivative *(35)*[35,36].



A similar reaction pathway—halosilane condensation and elimination of an isonitrile—is observed up to the penultimate step in the aza-analogues of phosgene, the isocyanide dichlorides. *(54)* shows no tendency to cyclize. It is stable at higher temperatures and undergoes an identical Cope-rearrangement, as discussed in Section 4.3[37,38].

## 4. Structural Characteristics of the PC-Double Bond

Structural problems connected with the PC-double bond are discussed using $^{31}$P-NMR data and X-ray structure determinations.

### 4.1. Influence of the Substitution Pattern on the $^{31}$P-NMR Spectrum

The values of the chemical shifts of the $^{13}$C- or $^{31}$P-atom arise from the state of hybridization of the elements. Both the P- and C-nuclei of the PC-double bond show the characteristic sp$^2$-downfield shift, which is decisively different from that of sp$^3$- or sp-hybridized atoms. The downfield shift of the P-atom of the double bond mainly reflects the deshielding, which probably arises from the lone-pair electrons[50].

Table 1. $^{31}P\{^1H\}$-NMR shifts of phospha-alkenes as a function of the substitution pattern. (A), (B): isomer A or B respectively.

| Phospha-alkene $R^1$ | $R^2$ or X | | δ | Ref. |
|---|---|---|---|---|
| $R^1P{=}C(SiMe_3)_2$ | | | | |
| tBu | | (10a) | +439 | [21] |
| Ph | | (10b) | +376 | [21] |
| Cl | | (8d) | +343 | [20] |
| $R^1P{=}C(SiMe_3)Ph$ | | | | |
| $tBu_2P$ | | (39a) | +331 | [55] |
| tBu | | (37) | +328 (A)<br>+290 (B) | [43] |
| PhO | | (40c) | +323 (A)<br>+291 (B) | [43] |
| MeO | | (40a) | +305 | [43] |
| nBuS | | (41) | +301 | [43] |
| tBuO | | (40b) | +291 | [43] |
| I | | (9c) | +280 | [20] |
| Br | | (9a) | +278 | [20] |
| Ph | | (14) | +277 | [12, 13] |
| Cl | | (8c) | +273 | [17] |
| MePhN | | (38d) | +254 | [43] |
| $Me_2N$ | | (38a) | +248 | [43] |
| Piperidino | | (38c) | +242 | [43] |
| $iPr_2N$ | | (38b) | +238 | [43] |
| $R^1P{=}CPh_2$ | | | | |
| Cl | | (8b) | +235 | [17] |
| Mesityl | | (7a) | +233 | [16] |
| $R^1P{=}C(SiMe_3)H$ | | | | |
| Cl | | (13) | +312 | [20] |
| $(Me_3Si)_2N$ | | (12) | +309 | [23] |
| $ClP{=}CHPh$ | | (8a) | +274 (A)<br>+272 (B) | [17] |
| $2,4,6\text{-}tBu_3C_6H_2{-}P{=}CH_2$ | | (11) | +290 | [22] |
| $R^1P{=}C(OSiMe_3)tBu$ | | | | |
| tBu | | (25b) | +176 | [11] |

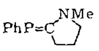
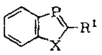
| | | | | |
|---|---|---|---|---|
| $C_6H_{11}$ | | *(25c)* | +154 | [11] |
| Ph | | *(25d)* | +137 | [11] |
| *t*BuC(O) | | *(42)* | +131 | [31] |
| $CH_2P{=}C(OSiMe_3)$*t*Bu | | *(27)* | +124 | [34] |
| Me | | *(25a)* | +120 | [11] |
| $Me_3Si$ | | *(25f)* | +120 | [31] |
| H | | *(25e)* | + 54 (A)<br>+ 38 (B) | [32] |
| $R^1P{=}C[N(SiMe_3)Ph]_2$ | | | | |
| *t*Bu | | *(23b)* | +170 | [29] |
| $C_6H_{11}$ | | *(23c)* | +148 | [29] |
| *p*-$Me_2NC_6H_4$ | | *(23e)* | +126 | [29] |
| Ph | | *(23d)* | +121 | [29] |
| Me | | *(23a)* | +116 | [29] |
| $PhP{=}C(SSiMe_3)_2$ | | *(24)* | +262 | [30] |
| $R^1P{=}C(NMe_2)H$ | | | | |
| Ph | | *(16a)* | + 70 (A)<br>+ 68 (B) | [24] |
| Mesityl | | *(16b)* | + 57 | [22] |
| $HP{=}CF_2$ | | *(5)* | − 62 | [15] |
| *t*Bu$P{=}C(OSiMe_3)[P(SiMe_3)R^1]$ | | | | |
| *t*Bu | | *(28a)* | +277 (A)<br>+231 (B) | [49] |
| COCl | | *(52)* | +255 | [49] |
| Cl | | *(53)* | +252 | [49] |
| COMe | | | +241 | [49] |
| COPh | | | +236 | [49] |
| H | | | +232 | [49] |
| *n*Bu | | | +223 | [49] |
| Me | | | +222 | [49] |
| $PhP{=}C(OSiMe_3)[P(SiMe_3)Ph]$ | | *(28b)* | +164 | [35] |
| $PhP{=}C[P(SiMe_3)Ph][N(SiMe_3)R^1]$ | | | | |
| Ph | | *(29a)* | +214 | [38, 39] |
| *p*-$ClC_6H_4$ | | *(29j)* | +221 | [38, 39] |
| *p*-$BrC_6H_4$ | | *(29k)* | +220 | [38, 39] |
| *p*-$FC_6H_4$ | | *(29i)* | +201 | [38, 39] |
| *p*-$MeC_6H_4$ | | *(29h)* | +204 | [38, 39] |
| *m*-$ClC_6H_4$ | | *(29g)* | +229 (A)<br>+142 (B) | [38, 39] |
| *o*-$ClC_6H_4$ | | *(29e)* | +140 | [38, 39] |
| *o*-$FC_6H_4$ | | *(29d)* | +157 | [38, 39] |
| *o,m*-$Cl_2C_6H_3$ | | *(29l)* | +143 | [38, 39] |
| *o*-$MeC_6H_4$ | | *(29b)* | +136 | [38, 39] |
| *o*-$MeOC_6H_4$ | | *(29f)* | +141 | [38, 39] |
| *o*-$CF_3C_6H_4$ | | *(29c)* | +137 | [38, 39] |
| EtOCO | | *(29n)* | +244 (A)<br>+180 (B) | [38, 39] |
| PhCO | | *(29m)* | +155 | [38, 39] |
|  | | | + 49 | [22] |
| $PhP{=}CR^1[N(SiMe_3)R^2]$ | | | | |
| Ph | Ph | *(26d)* | +225 (A)<br>+144 (B) | [33] |
| *p*-$ClC_6H_4$ | Ph | *(26e)* | +220 (A)<br>+152 (B) | [33] |
| *p*-$MeOC_6H_4$ | Ph | *(26f)* | +215 (A)<br>+146 (B) | [33] |
| Mesityl | Ph | *(26g)* | +122 | [33] |
| *t*Bu | Ph | *(26c)* | +249 | [33] |
| Ph | *p*-$ClC_6H_4$ | *(26h)* | +236 (A)<br>+149 (B) | [33] |
| Ph | *p*-$MeOC_6H_4$ | *(26i)* | +138 | [33] |
| Ph | Me | *(26a)* | +122 | [33] |
| Ph | $C_6H_{11}$ | *(26b)* | +178 | [33] |
| Ph | 2,6-$Et_2C_6H_5$ | *(26j)* | +126 | [33] |
| $PhP{=}C[N(SiMe_3)R^1]{-}PPh{-}PPh[R^1(Me_3Si)N]C{=}PPh$ | | | | |
| Ph | | *(54)* | +258 (A) *meso*<br>+235 (B) *rac* | [37]<br>[37] |
| 3-$Cl(C_6H_4)$ | | | +259 | [38] |
| 4-$Cl(C_6H_4)$ | | | +261 | [38] |
|  | | | | |
| H | NH | *(17a)* | + 77 | [25] |
| Me | NH | *(17b)* | + 70 | [25] |
| Ph | NH | *(17c)* | + 72 | [25] |
| H | S | *(19a)* | + 79 | [22] |
| Me | S | *(19b)* | + 71 | [22] |
| Ph | S | *(19c)* | + 70 | [22] |
| *t*Bu | O | *(18)* | + 76 | [22] |

Table 1, classified according to substance classes, shows the effect of the vicinal groups at the PC-double bond on the $^{31}P$-NMR shifts. In this context there are parallels to the $^{13}C$-NMR shifts of the alkenes (α-increments[50]) as well as to the $^{31}P$-NMR shifts of the corresponding phosphanes. These values can be correlated with the corresponding values for the phospha-alkanes, when the electronic interaction of the substituents (H, alkyl, aryl) with the π-system of the PC-double bond is prevented or reduced. Substituents with an electron pair capable of mesomerism (Cl, OR, $NR_2$) at the $P{=}C$ unit, cause a shift to higher field, $Si(CH_3)_3$ however, shifts to lower field[16] (Fig. 1). The $^{31}P$-shifts are not affected if the last mentioned groups are attached to the *P*- or *C*-atom.

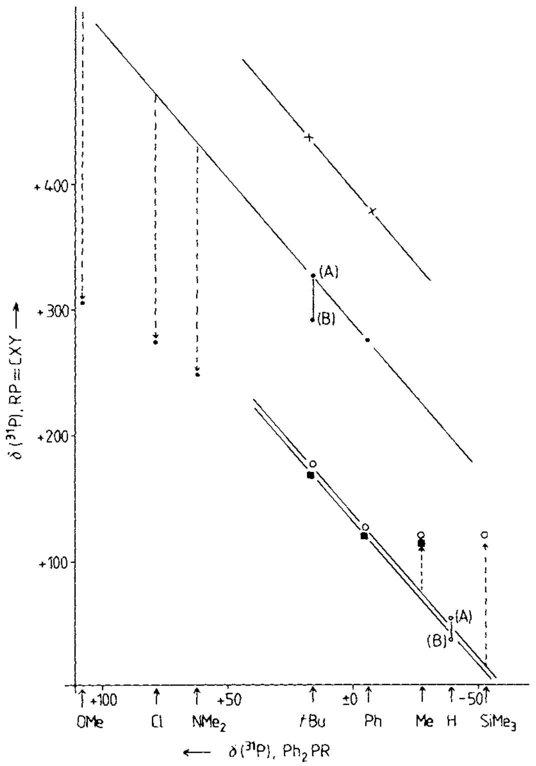


Fig. 1. Correlation of chemical shifts ($^{31}P$-NMR) in phosphanes ($Ph_2PR$) and phospha-alkenes $RP{=}CXY$ with the same substituents R.
x: $RP{=}C(SiMe_3)_2$; ● $RP{=}C(SiMe_3)Ph$, ○ $RP{=}C(OSiMe_3)$ *t*Bu;
■ $RP{=}C[N(SiMe_3)Ph]_2$. (A), (B): isomer A or B respectively.

### 4.2. Geometry of the PC-Double Bond: NMR and X-Ray Results

Taking into account the lone-pair electrons of the two coordinate phosphorus, geometrical isomers analogous to the alkenes are to be expected. In both cases the double bond prevents the mutual conversion of the *cis-trans*-isomers[51]. It is thus possible to obtain both forms (*E/Z*-pairs) and in certain cases to seperate them.

Depending on the substitution pattern the isomeric pairs (summarized in Table 2) can also be detected in the $^{31}$P- as well as in the corresponding $^{13}$C-NMR spectrum.

Table 2. $^{31}$P-NMR shift differences between (*E,Z*)-isomeric pairs.

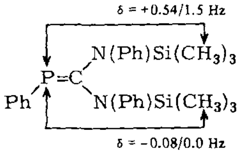
| (*E,Z*)-Phospha-alkene | | $\Delta\delta$ | Ref. |
|---|---|---|---|
| $\mathrm{Cl{\sim\sim}P{=}C(H)Ph}$ | *(8a)* | 2 | [17] |
| $\mathrm{H{\sim\sim}P{=}C(OSiMe_3)}t\mathrm{Bu}$ | *(25e)* | 3 | [35] |
| $\mathrm{PhO{\sim\sim}P{=}C(SiMe_3)Ph}$ | *(40c)* | 32 | [43] |
| $t\mathrm{Bu{\sim\sim}P{=}C(SiMe_3)}Ph$ | *(37)* | 38 | [31] |
| $t\mathrm{Bu{\sim\sim}P{=}C(OSiMe_3)[P(SiMe_3)}t\mathrm{Bu]}$ | *(28a)* | 45 | [49] |
| $\mathrm{Ph{\sim\sim}P{=}C[N(SiMe_3)COOEt][P(SiMe_3)Ph]}$ | *(29n)* | 63 | [39] |
| $\mathrm{Ph{\sim\sim}P{=}C[N(SiMe_3)Ph]Ph}$ | *(26d)* | 81 | [33] |
| $\mathrm{Ph{\sim\sim}P{=}C[N(SiMe_3)}m\mathrm{\text{-}ClC_6H_4][P(SiMe_3)Ph]}$ | *(29g)* | 86 | [38, 39] |

A small shift difference in the $^{13}$C-NMR spectra can also be observed for the corresponding pairs of Schiff-bases and oximes. Differences of up to $\Delta\delta(^{31}P) = 86$ ppm, as in the phospha-alkenes in Table 2 cannot, however, be accounted for in terms of the different position of the substituents at the double bonds.

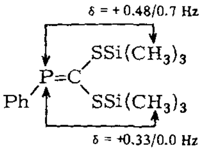
Up to now two theories have been proposed to account for the correlation of the NMR spectroscopic data with the E- and/or Z-isomers defined. From a stereochemical point of view, the phospha-amidines *(26)*, absorbing between $\delta(^{31}P) = +215$ and $+249$ are assigned to the *E*-, and those having signals between $+120$ and $+152$ ppm are assigned to the *Z*-configuration[33].

The structural predictions were also confirmed by the $^{1}$H-NMR parameters.

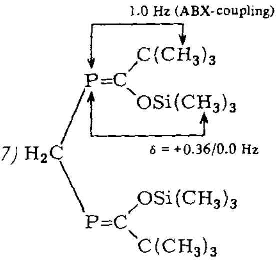
In the case of the phosphaguanidines *(23d)*[29] and of phenylbis(trimethylsilylthio)methylenephosphane *(24)*[30], two signals from the methyl groups are observed; the one at lower field is usually split by coupling with phosphorus. This low field signal is assigned (based on its stereoelectronic properties[29] or on an X-ray structure determination of *(Z,Z)-P,P'*-methylenebis[neopentylidene(trimethylsiloxy)phosphane] *(27)*[34]) to the silyl group on the same side of the double bond as the lone-pair electrons at phosphorus[32].



*(23d)*



*(24)*



*(27)*

This hypothesis has been generalized in later publications and the configuration deduced from the magnitude of the ($^{31}$P-$^{1}$H)-interaction between the P-electron pairs and the coupling group.

The NMR results and several X-ray structure determinations on phosphinomethylenephosphanes *(39a)*[52], *(29e)*[53], *(55)*[54] and *(54A)*[52], studied in our group, restrict the general application of the previously discussed theory.

Hence, no coupling can be detected in the $^{1}$H-NMR spectrum of compound *(39a)* with *E*-configuration, where a *cis*-interaction between the electron pair and the silyl group has been confirmed by X-ray analysis[55]. Similarly, no long range interaction of the methylenephosphane-phosphorus with the *P*-silyl group can be seen in *(29e)*. The doublet from the *N*-trimethylsilyl group results from the phosphano-phosphorus, according to double-resonance experiments.

The hypothesis of a correlation of the $\delta(^{31}P)$-values with the geometry at the PC-double bond is questionable because two other compounds with the comparable substituents exist.

On the one hand, compounds *(29e)* and *(54A)* although having the same configuration, show different $^{31}$P-NMR shifts and, on the other, similar $\delta(^{31}P)$-values are observed with *(29c)* and *(55)* despite different configurations.

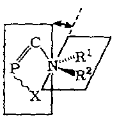
These results indicate another factor which influences the $^{31}$P-NMR data far more than the arrangement of the substituents at the double bond: Primarily the interaction between the lone-pair electrons of the group capable of mesomerism and the double bond (see stereoplots) seems to be decisive for the $^{31}$P-NMR shift[16]. If this orbital is orientated approximately parallel to the double bond (*e.g.* *(55)*), a displacement to high field is observed. The $\delta(^{31}P)$-value for the isolated double bond occurs when the overlap is hindered or restricted (Table 3). The downfield shift of *(39a)* results from a double bond which does not overlap with the filled lone-pair orbital of the phosphino phosphorus, as evident from the *trans*-conformation of the diphosphane unit in the stereo pair of *(39a)*[52].

### 4.3. Pericyclic Reactions of Phospha-1,5-hexadiene Derivatives

Another important argument for the existence of real PC-double bonds due to overlap of the C2p- and P3p-orbitals are the pericyclic reactions of the 1,3,4,6-tetraphospha-1,5-hexadiene derivative *(54)*[37]. The $^{31}$P-NMR spectrum of *(54)*, whose analysis leads to these conclusions, will be discussed in more detail because of the crucial importance of this phenomenon for the characterization of the bonding interactions.

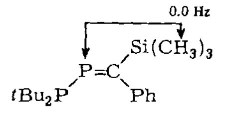
At 30 °C the characteristic substructure of a 4-spin-system of the AA'XX'-type is observed. The left signal group at $\delta = +258$ is assigned to the phosphorus atom with the coordination number 2, the right group at $-12.3$ to the trivalent diphosphane phosphorus. In addition a broad sig-

Table 3. Correlation of the $^{31}$P-NMR shift data with structural parameters. Assignments after



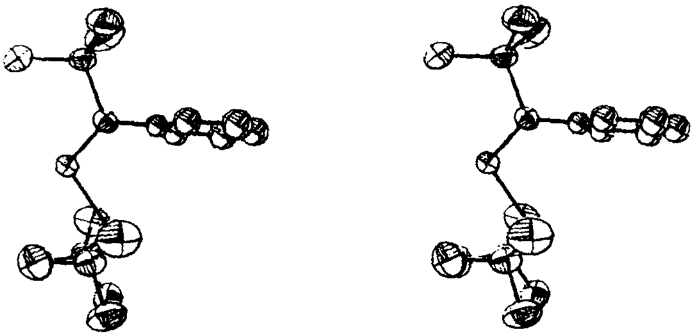
| Phospha-alkene | Configu-ration | δ(P=C) | Dihedral Angle [°] | P=C [pm] | | X—P=C [°] | N—C [a] [pm] |
|---|---|---|---|---|---|---|---|
| *(55)* | *Z* | +113 | 0 [b] | 172.1(12) | X=Ph | 100.9(6) | 136.9(14) |
| *(29e)* | *E* | +140 | 15.5 [b] | 170.2 | X=Ph | 113.7 | 141.1 |
| *(54A)* | *E,E* | +258 | 68.6 [b] | 168.6(9) | X=Ph | 108.1(3) | 144.8(9) |
| *(39a)* | *E* | +331 | 91.1 [c] | 168 | X=*t*Bu$_2$P | 104.7 | 223 |

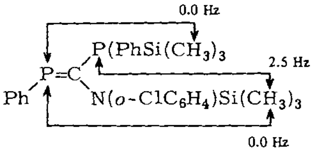
[a] P—P bond length in the diphosphane unit in *(39a)*. [b] To the free N-electron pair. [c] To the free electron pair of the *t*Bu$_2$P group.



*(E)-(39a)*

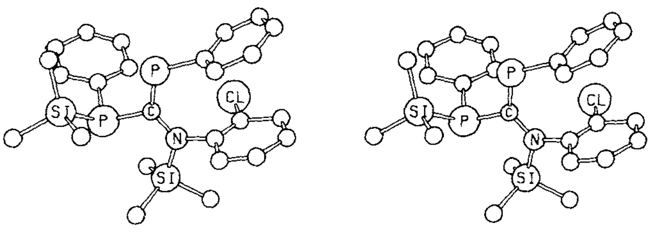
$^{31}$P{$^1$H}-NMR: δ = +331 (P=C)

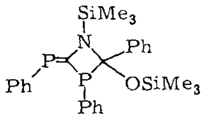




*(E)-(29e)*

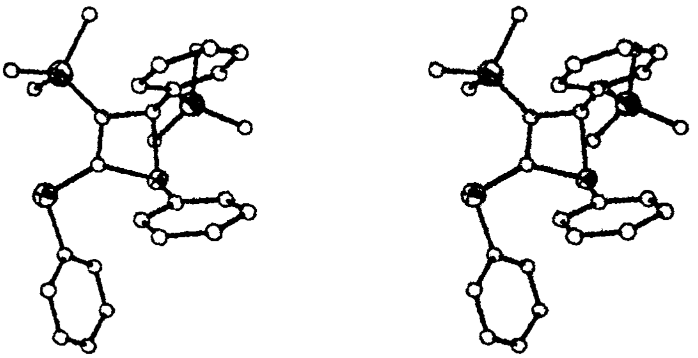
$^{31}$P{$^1$H}-NMR: δ = +140 (P=C)

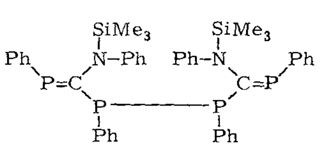




*(Z)-(55)*

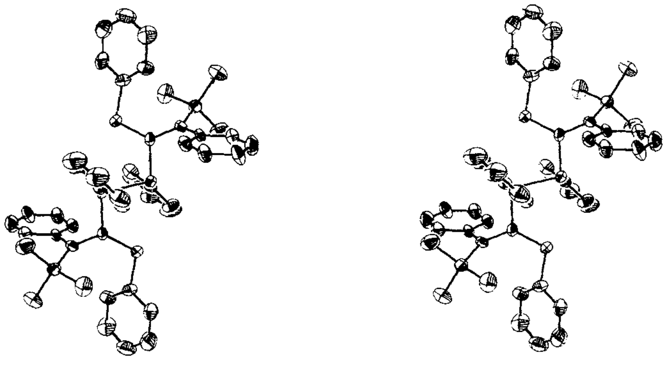
$^{31}$P{$^1$H}-NMR: δ = +113 (P=C)





*(E,E)-meso-(54A)*

$^{31}$P{$^1$H}-NMR: δ = +258 (P=C)



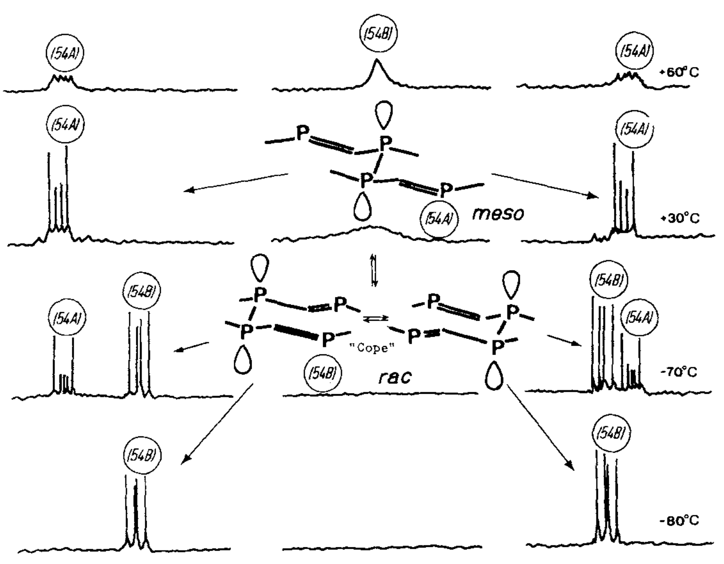


Fig. 2. Temperature dependence of the $^{31}P\{^{1}H\}$-NMR spectrum of the 1,3,4,6-tetraphospha-1,5-hexadiene derivative *(54)*.

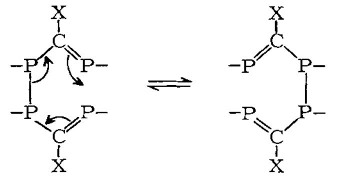
nal at +115.7 occurs which sharpens on heating to 60 °C, while the other signals simultaneously broaden. Cooling to 70 °C results in a splitting of the broad signal. In addition to the signals already present, another 4-spin-system of the same type appears, with the left part arising from the phosphorus with the coordination number 2 and the right hand signals at $\delta = -3.2$ from the diphosphane-phosphorus. Heating the sample to 30 °C results in coalescence of the two inner groups, and the broad absorption reappears at $\delta = +115.8$. This process is reversible.

Upon cooling down to −80 °C or lower, the outer group of signals, designated *(54A)*, disappear completely, since *(54A)* crystallizes out below −80 °C. If the crystals are filtered off at low temperature and redissolved, the spectrum of *(54A)*, followed by the slow conversion of *(54A)* into the *rac*-form *(54B)* can be recorded. At 30 °C the spectrum originally recorded at this temperature is obtained. These results allow the following conclusions to be drawn:

Because *(54)* is homogeneous, according to elemental analysis and molecular mass determination, the compound indicated by the broad absorption at $\delta = +115$ must have the same composition. The splitting of the broad absorption into another AA'XX'-multiplet also indicates that this species must be a diastereomeric tetraphosphahexadiene derivative, since the characteristic signal groups of the diphospane- and the methylenephosphane-phosphorus appear.

These assumptions raise the following questions: what is the reason for the reversible coalescence of the two inner multiplets as a function of temperature and why does only one diastereomer, *(54B)*, show this phenomenon? This may be answered as follows: Only a pericyclic reaction—which is observed at the hexadiene as well and is generally known as the Cope rearrangement—is in complete accord with the coalescence phenomenon [eq. (1)].

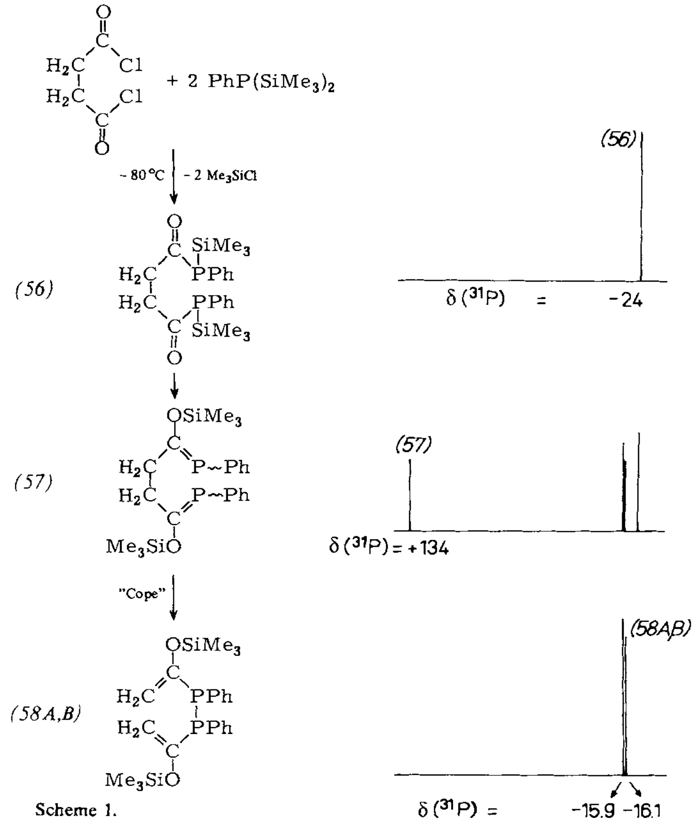
In a [3.3]-sigmatropic reaction the PP-bond in *(54B)* opens and a simultaneous shift of the PC-double bond with formation of a PP-bond takes place. Since the identical rearrangement occurs in *(54B)* and the bonding changes occur on the NMR-time scale, the original signals of the P atoms in *(54B)* with coordination number 2 and 3 coalesce in the middle at room temperature.



(1)

The fact that only one diastereomer shows the coalescence may be explained since it is well known that symmetrical, unequally substituted diphosphanes, which have the same substitution pattern as presented here, have two centers of chirality. The synthesis usually yields a 1 : 1 proportion of the *meso*- and the *rac*-forms, which can be distinguished by their $^{31}$P-NMR shifts. The outer set of multiplets must be assigned to the diastereomer *(54A)*, and the inner set to *(54B)*. The rapid exchange process in the $^{31}$P-NMR spectrum of one isomer at room temperature—which is not observed for the other—leads to the conclusion that only the *rac*-form *(54B)* has a configuration which fulfills the stereochemical demands of the Cope rearrangement. The result of an X-ray structure analysis on the crystals of *(54A)*, filtered off a low temperature and not exhibiting the coalescence phenomenon, is in complete agreement with this assumption. As shown in the stereoplot, this diastereomer presents the *meso*-form with a *trans*-orientation of the substituents at the P—P bond.

The rapid equilibration (compared to carbon compounds) of the *meso*- and *rac*-forms is no exception in phosphorus compounds with chiral, pyramidal P atoms. This has been observed with diphosphanes on several occasions[56].

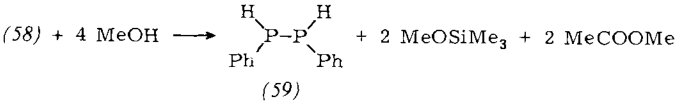


Scheme 1.

Of course, care must be exercised in applying the concepts of pericyclic reactions to elements of the second octet period of the periodic table; nevertheless, interactions are involved between the 2p- and the energetically considerably higher 3p-levels. The bridge connecting the fields of carbon and phosphorus chemistry can, however, be seen in the following experiment.

Succinyl dichloride reacts with bis(trimethylsilyl)phenylphosphane at −80 °C *via* halosilane cleavage to the succinylbis(phosphane) *(56)*. At −10 °C the 1,6-diphospha-1,5-hexadiene *(57)* results from a double 1,3-silyl migration, and at −8 °C a spontaneous [3,3]-sigmatropic rearrangement leads to the corresponding 1,2-diphenyl-1,2-divinyldiphosphane *(58)*[55] (Scheme 1).

The surprising cleavage of a C—C-bond and two PC-double bonds in favor of a P—P-bond, and two olefinic double-bonds, is confirmed not only by unequivocal $^{31}$P-NMR-data but also by a classical decomposition reaction of *(58)*.



$$(58) + 4\,\text{MeOH} \longrightarrow \text{PhHP–PHPh}\ (59) + 2\,\text{MeOSiMe}_3 + 2\,\text{MeCOOMe}$$

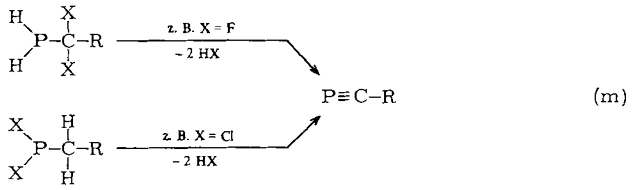
Instead of the $C_4$-unit of succinic acid the methanolysis yields two $C_2$-units (methyl acetate), in addition to the 1,2-diphenyldiphosphane *(59)* and the trimethylsilyl methyl ether.

## 5. Phospha-Alkynes

The early identification of the simplest phospha-alkyne, the phospha-acetylene *(1)*[6], stimulated the search for the more stable phosphorus-carbon combinations with (p-p)π-multiple bonds.

| $P{\equiv}C{-}H$ | $P{\equiv}C{-}F$ | $P{\equiv}C{-}CH_3$ | $P{\equiv}C{-}CF_3$ | $P{\equiv}C{-}C{\equiv}N$ |
|---|---|---|---|---|
| *(1)* | *(60)* | *(61)* | *(62)* | *(63)* |

Besides phospha-acetylene, its derivatives *(60)*[15], *(61)*[57], *(62)*[46] and *(63)*[58] have been reported, all of which were synthesized by repeated hydrogen halide-elimination from primary α-halophosphanes or dihalophosphanes with two hydrogens in α-position. Both pathways are shown in eq. (m).

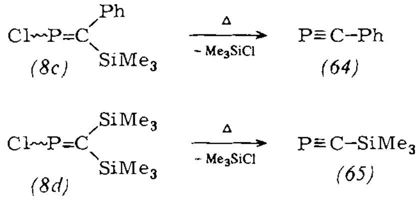


Only the cyanophosphaethyne *(63)*[58] is accessible *via* a condensation reaction.

$$\underset{(1)}{P{\equiv}C{-}H} + N_3{-}CN \xrightarrow[-HN_3]{} \underset{(63)}{P{\equiv}C{-}C{\equiv}N}$$

All the hitherto described phospha-alkynes have been prepared by vapor phase pyrolysis. The phospha-alkynes are obtained as mixtures and identified by their PE-, NMR-, or microwave-spectra; their thermolability, however, has hindered their separation from by-products and their isolation in preparatively useful amounts.

The stepwise synthesis of the triple bond from the double bond of phospha-alkenes suggests itself.

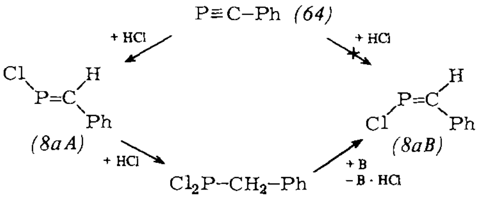


$$\underset{(8c)}{\text{Cl–P=C(Ph)SiMe}_3} \xrightarrow[-\text{Me}_3\text{SiCl}]{\Delta} \underset{(64)}{P{\equiv}C{-}Ph}$$

$$\underset{(8d)}{\text{Cl–P=C(SiMe}_3)_2} \xrightarrow[-\text{Me}_3\text{SiCl}]{\Delta} \underset{(65)}{P{\equiv}C{-}SiMe_3}$$

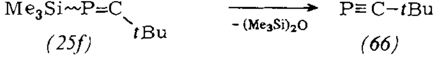
The vicinal chloro- and trimethylsilyl-substituted methylenephosphanes *(8c)* and *(8d)* selectively eliminate chlorotrimethylsilane when heated to *ca.* 700 °C in an Hg-diffusion pump vacuum and the phospha-alkynes *(64)*[18] and *(65)*[19] can be obtained almost quantitatively in a cold-trap placed directly after the pyrolysis apparatus. *(64)* only exists at low temperatures in its monomeric form, above −50 °C slow decomposition takes place. Its half-life, as determined by $^{31}$P-NMR spectroscopy amounted to 7 minutes at 0 °C. As expected, the silyl compound *(65)* is more stable (half-life at room temperature *ca.* 50 minutes).

Apart from the $^{13}$C-NMR data, the presence of a PC-triple bond is confirmed by stepwise HCl-addition.



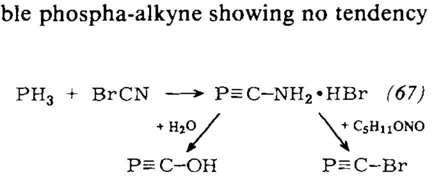
The previously mentioned preparation of *(8a)* *via* dehydrochlorination always yields, besides *(8aA)*, the *Z*-isomer *(8aB)*. After addition of HCl to *(64)*, *(8aA)* is not formed, and this may be explained by a *cis*-addition to the triple bond. Repeated hydrohalogenation leads to benzyldichlorophosphane.

The *tert*-butyl derivative *(66)* with coordination number 1 is stable at room temperature[59]. The PC-triple bond was introduced very smoothly by NaOH-catalyzed siloxane-elimination.



$$\underset{(25f)}{\text{Me}_3\text{Si–P=C(OSiMe}_3)t\text{Bu}} \xrightarrow[-(\text{Me}_3\text{Si})_2\text{O}]{(\text{NaOH})} \underset{(66)}{P{\equiv}C{-}t\text{Bu}}$$

The direct synthesis of the stable hydrobromide *(67)* from phosphane and cyanogen bromide seems to be questionable and conversion to the monomeric hydroxy bromo derivatives very dubious[60], since to date only *(66)* has proven to be a stable phospha-alkyne showing no tendency to polymerize.



Due to the limited number of examples, the hitherto obtained NMR-data cannot be interpreted completely. The effects of the substituents on the $^{31}$P-NMR shifts seem to be similar to those of the phospha-alkenes (Section 4.1).

Compared to *(1)* and *(64)* the silyl substituted phospha-alkyne *(65)* is registrated at a lower field, the halogen derivatives, such as *(60)*, at higher field.

Just as the position of the signal of the phosphorus varies between $\delta = -200$ and $+100$ (rel. to 85% $H_3PO_4$), the values of the methine-C signal vary over a large range and are thereby not significant from a structural point of view. Compared to alkynes or nitriles the phospha-alkyne signals occur at a lower field in the $^{13}$C-NMR.

Table 4. NMR-parameters of phospha-alkynes. $J$ in Hz.

| Phospha-alkyne | | $^{31}P\{^1H\}$ $\delta$ | $^{13}C\{^1H\}$ $\delta(P{\equiv}C)$ | $J$(PC) | Ref. |
|---|---|---|---|---|---|
| PC—H | *(1)* | − 32 | + 154.0 d | 54.0 | [61] |
| PC—*t*Bu | *(66)* | − 69 | + 184.8 d | 38.5 | [59] |
| PC—Ph | *(64)* | − 32 | + 164.9 d | 48.3 | [18] |
| PC—F | *(60)* | − 207 | — | — | [15] |
| PC—SiMe$_3$ | *(65)* | + 96 | + 201.4 d | 13.9 | [19] |

## 6. Summary and Conclusion

Research over the last five years has shown that stable compounds with phosphorus-carbon (p-p)π-multiple bonds can be prepared even without stabilizing mesomeric effects. The introduction of the double bond preferably ensues from 1,2-elimination or from silyl group migration; different methods are available for both pathways.

From the point of view of a preparative chemist hardly any argument can be found against the assumption of real PC-multiple bonds analogous to those of the alkenes and alkynes. The relationship to this type of bond cannot be denied and this is proven by the detection of *E,Z*-stereoisomers, as well as by the existence of a "phospha(keto-enol)-tautomerism". The fluxional structures of the tetraphosphahexadiene derivative *(54B)* may be regarded as completely analogous to the olefinic systems. In agreement with this conception of the double bonds, the $^{13}$C-NMR spectra prove that the methylene carbon atoms of the phospha-alkenes—comparable to the Schiff-bases—are sp$^2$-hybridized.

The reactivity of these new substances is different from that of the homologous CN-compounds, the Schiff-bases and carbonitriles, as demonstrated by the addition of H-acidic reagents to the double bond which occurs in an opposite sense. From this point of view the terms phospha-alkenes and -alkynes, instead of phospha-imines or -nitriles are preferred.

There are some indications that the development of research in the field of (p-p)π-multiple bonds between elements of the first and second octet rows of the periodic table is just beginning. The synthesis of analogous silicon compounds has been repeatedly reported in recent times[62,63]. In a recent report on the synthesis of a stable diphosphaethene RP=PR[64] even a homo-nuclear double-bond between elements of the second octet period can no longer be excluded.

Stimulating topics of future research can only be indicated under keyword headings. They can be found in the field of synthesis of conjugated double bond systems and in the combination of PC-double bonds with olefinic bonds. Can we achieve, for instance, a Diels-Alder synthesis?[*]

Furthermore, it may be worthwhile to use the new structural elements for the synthesis of heterocyclic compounds. In addition, only a small amount of information is available on the field of complex-formation.

Only the future will tell whether these hopes of a new chapter in phosphorus-carbon chemistry will be fulfilled.

*We are indebted to the coworkers mentioned in this article, for their dedicated work and their valuable assistance, and to Dr. M. Halstenberg and Dr. R. Sievers for the X-ray analyses. Financial support was provided by the Deutsche Forschungsgemeinschaft as well as by the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen, for which we are very grateful.*

Received: July 23, 1981 [A 380]
German version: Angew. Chem. *93*, 771 (1981)

---

[*] This question has already been answered in a positive sense after submission of the manuscript. Certain phospha-alkenes can function as diene [65] and also as dienophile [66] in Diels-Alder reactions.

[1] *K. S. Pitzer*, J. Am. Chem. Soc. *70*, 2140 (1948).

[2] *R. S. Mulliken*, J. Am. Chem. Soc. *72*, 4493 (1950).

[3] *E. Niecke, O. J. Scherer*, Nachr. Chem. Tech. *23*, 395 (1975).

[4] *K. Dimroth*, Fortschr. Chem. Forsch. *38*, 1 (1973).

[5] *E. Fluck*, Top. Phosphorus Chem. *10*, 193 (1980); review up to 1977.

[6] *T. E. Gier*, J. Am. Chem. Soc. *83*, 1769 (1961).

[7] *K. Dimroth, P. Hoffmann*, Angew. Chem. *76*, 433 (1964); Angew. Chem. Int. Ed. Engl. *3*, 384 (1964).

[8] *R. Allmann*, Angew. Chem. *77*, 134 (1965); Angew. Chem. Int. Ed. Engl. *4*, 150 (1965).

[9] *G. Märkl*, Angew. Chem. *78*, 907 (1966); Angew. Chem. Int. Ed. Engl. *5*, 846 (1966).

[10] *A. J. Ashe*, J. Am. Chem. Soc. *93*, 3293 (1971).

[11] *G. Becker*, Z. Anorg. Allg. Chem. *423*, 242 (1976).

[12] *R. Appel, V. Barth, J. Peters*, lecture delivered at the International Conference on Phosphorus Chemistry, Halle 1979.

[13] *R. Appel, J. Peters, R. Schmitz*, Z. Anorg. Allg. Chem. *475*, 18 (1981).

[14] *M. J. Hopkinson, H. W. Kroto, J. F. Nixon, N. P. C. Simmons*, J. Chem. Soc. Chem. Commun. *1976*, 513.

[15] *H. E. Eshtiagh-Hosseini, H. W. Kroto, J. F. Nixon*, J. Chem. Soc. Chem. Commun. *1979*, 653.

[16] *Th. C. Klebach, R. Lourens, F. Bickelhaupt*, J. Am. Chem. Soc. *100*, 4886 (1978).

[17] *R. Appel, A. Westerhaus*, Angew. Chem. *92*, 578 (1980); Angew. Chem. Int. Ed. Engl. *19*, 556 (1980).

[18] *R. Appel, A. Westerhaus*, Angew. Chem. *93*, 215 (1981); Angew. Chem. Int. Ed. Engl. *20*, 197 (1981).

[19] *R. Appel, A. Westerhaus*, Tetrahedron Lett. *1981*, 2159.

[20] *R. Appel, A. Westerhaus, J. Peters*, Tetrahedron Lett., in press.

[21] *K. Issleib, H. Schmidt, C. Wirkner*, Z. Anorg. Allg. Chem. *473*, 85 (1981).

[22] *K. Issleib*, lecture delivered at the International Conference on Phosphorus Chemistry, Durham (USA) 1981.

[23] *E. Niecke, W. Schöller, D. Wildbredt*, Angew. Chem. *93*, 119 (1981); Angew. Chem. Int. Ed. Engl. *20*, 131 (1981).

[24] *G. Becker, O. Mundt*, Z. Anorg. Allg. Chem. *462*, 130 (1980).

[25] *K. Issleib, R. Vollmer, H. Oehme, H. Meyer*, Tetrahedron Lett. *1978*, 441.

[26] *A. F. Vasil'ev, L. V. Vilkov, N. P. Ignatova, N. N. Mel'nikov, V. V. Negrebeckij, N. I. Svecov-Silovskij, L. S. Chajkin*, J. Prakt. Chem. *314*, 806 (1972).

[27] *J. Luber, A. Schmidpeter*, J. Chem. Soc. Chem. Commun. *1976*, 887.

[28] *J. Luber, A. Schmidpeter*, Angew. Chem. *88*, 91 (1976); Angew. Chem. Int. Ed. Engl. *15*, 111 (1976).

[29] *K. Issleib, H. Schmidt, H. Meyer*, J. Organomet. Chem. *192*, 33 (1980).

[30] *G. Becker, G. Gresser, W. Uhl*, Z. Anorg. Allg. Chem. *463*, 144 (1980).

[31] *G. Becker*, Z. Anorg. Allg. Chem. *430*, 66 (1977).
[32] *G. Becker, M. Rössler, W. Uhl*, Z. Anorg. Allg. Chem. *473*, 7 (1981).
[33] *K. Issleib, H. Schmidt, H. Meyer*, J. Organomet. Chem. *160*, 47 (1978).
[34] *G. Becker, O. Mundt*, Z. Anorg. Allg. Chem. *443*, 53 (1978).
[35] *R. Appel, V. Barth*, Angew. Chem. *91*, 497 (1979); Angew. Chem. Int. Ed. Engl. *18*, 469 (1979).
[36] *R. Appel, V. Barth, M. Halstenberg, G. Huttner, J. Seyerl*, Angew. Chem. *91*, 935 (1979); Angew. Chem. Int. Ed. Engl. *18*, 872 (1979).
[37] *R. Appel, V. Barth, F. Knoll, I. Ruppert*, Angew. Chem. *91*, 936 (1979), Angew. Chem. Int. Ed. Engl. *18*, 873 (1979).
[38] *R. Appel, B. Laubach*, Tetrahedron Lett. *1980*, 2497.
[39] *R. Appel, F. Knoll*, lecture delivered in Durham, see [22].
[40] *R. Appel, A. Kirfel, M. Halstenberg*, unpublished results.
[41] *G. Becker*, Chemisches Kolloquium, Universität Köln, June 24, 1981.
[42] *R. Appel, V. Barth*, Tetrahedron Lett. *1980*, 1923.
[43] *R. Appel, U. Kündgen*, Angew. Chem., in press.
[44] *R. J. Thoma, R. H. Neilson*, lecture delivered in Durham, see [22].
[45] *E. Niecke, D. A. Wildbredt*, Angew. Chem. *90*, 209 (1978); Angew. Chem. Int. Ed. Engl. *17*, 199 (1978).
[45] a) *E. Niecke, D. A. Wildbredt*, Angew. Chem. *90*, 209 (1978); Angew. Chem. Int. Ed. Engl. *17*, 199 (1978); b) *R. Appel, J. Peters, A. Westerhaus, ibid.*, in press; c) *E. Niecke, D. A. Wildbredt*, J. Chem. Soc. Chem. Commun. *1981*, 72.
[46] *J. F. Nixon*, lecture delivered in Durham, see [22].
[47] *G. Becker, M. Rössler, E. Schneider*, Z. Anorg. Allg. Chem. *439*, 121 (1978).
[48] *G. Becker, H. P. Beck*, Z. Anorg. Allg. Chem. *430*, 77 (1977).
[49] *W. Paulen*, Diplomarbeit, Universität Bonn 1980.
[50] *E. Breitmaier, W. Voelter*: $^{13}$C-NMR Spectroscopy, 2nd ed., Verlag Chemie, Weinheim 1978, p. 72.
[51] *C. Thomson*, J. Chem. Soc. Chem. Commun. *1977*, 322.
[52] *R. Appel, M. Halstenberg*, unpublished results.
[53] *R. Appel, R. Sievers*, unpublished results.
[54] *R. Appel, M. Halstenberg, P. Stegemann*, unpublished results.
[55] *R. Appel*, opening lecture in Durham, see [22].
[56] *I. F. Lutsenko, M. V. Proskurnina*, Usp. Khim. *47*, 1648 (1978).
[57] *M. J. Hopkinson, H. W. Kroto, J. F. Nixon, N. P. C. Simmons*, Chem. Phys. Lett. *42*, 460 (1976).
[58] *T. A. Cooper, H. W. Kroto, J. F. Nixon, O. Ohashi*, J. Chem. Soc. Chem. Commun. *1980*, 333.
[59] *G. Becker, G. Gresser, W. Uhl*, Z. Naturforsch. *B 36*, 16 (1981).
[60] *I. S. Matveev*, Khim. Tekhnol. (Kiev) *1974*, 49; Chem. Abstr. *83*, 97470c (1975).
[61] *S. P. Anderson, H. Goldwhite, D. Ko, A. Letsou*, J. Chem. Soc. Chem. Commun. *1975*, 744.
[62] *A. G. Brook*, Chem. Eng. News *59*, Nr. 13, S. 18 (1981).
[63] *G. Maier, G. Mihm, H.-P. Reisenauer*, Angew. Chem. *93*, 615 (1981); Angew. Chem. Int. Ed. Engl. *20*, 597 (1981) and literature cited therein; *P. Rosmus, H. Bock, B. Solouki, G. Maier, G. Mihm, ibid. 93*, 616 (1981) and *20*, 598 (1981), literature cited therein.
[64] *M. Yoshifuji, I. Shima, N. Inamoto*, lecture delivered in Durham, see [22].
[65] *Y. Kobayashi, S. Fujino, I. Kumadaki*, J. Am. Chem. Soc. *103*, 2465 (1981).
[66] *R. Appel, M. Halstenberg, S. Korte*, unpublished results.

# Chemistry and Biochemistry of Microbial α-Glucosidase Inhibitors

**By Ernst Truscheit, Werner Frommer, Bodo Junge, Lutz Müller, Delf D. Schmidt, and Winfried Wingender**[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

α-Glucosidases are among the most important carbohydrate-splitting enzymes. They catalyze the hydrolysis of α-glucosidic linkages. Their substrates are—depending on their specificity—oligo- and polysaccharides. Microbial inhibitors of α-amylases and other mammalian intestinal carbohydrate-splitting enzymes studied during the last few years have aroused medical interest in the treatment of metabolic diseases such as diabetes. Moreover, they extend the spectrum of microbial secondary metabolites which comprises an enormous variety of structures. They also contribute considerably to a better understanding of the mechanism of action of α-glucosidases. These inhibitors belong to different classes of substances. Those studied most thoroughly are microbial α-glucosidase inhibitors which are members of a homologous series of pseudooligosaccharides of the general formula *(4)*. They all have a core in common which is essential for their inhibitory action, a pseudodisaccharide residue consisting of an unsaturated cyclitol unit, and a 4-amino-4,6-dideoxyglucose unit. The—in many respects—most interesting representative of this homologous series is acarbose *(5)*, a pseudotetrasaccharide exhibiting a very pronounced inhibitory effect on intestinal α-glucosidases such as sucrase, maltase and glucoamylase. The present paper will review this new field of microbial α-glucosidase inhibitors which has been studied with particular intensity during the past ten years.

## 1. Introduction

Natural enzyme inhibitors, especially inhibitors of hydrolases are found in many plants and animals as well as in bacteria and fungi. Some of them have been known for a long time. The ubiquitous protease inhibitors[1-4] have been studied most thoroughly with respect to their structure, function and mechanism of action. Publications on protease inhibitors of the serum[5,6] already appeared at the end of last century. Reports on natural α-glucosidase inhibitors date back to the early thirties of this century. In 1933 *Chrzaszcz* and *Janicki*[7] described a protein-like substance

---

[*] Dr. E. Truscheit, Prof. Dr. W. Frommer, Dr. B. Junge, Dr. L. Müller, Dr. D. D. Schmidt, Dr. W. Wingender
Chemisch-wissenschaftliches Labor Pharma der Bayer AG
Postfach 101709, 5600 Wuppertal 1 (Germany)

0570-0833/81/0909-0744 $ 02.50/0

practically insoluble in water which is found in the malts of various kinds of grain, especially in buckwheat malts. Because of its malt α-amylase inactivating properties this substance was called "sistoamylase". Later *Kneen* and *Sandstedt*[8,9] described water-soluble preparations with protein character and α-amylase inhibiting properties which they had isolated from rye and wheat germ flour. These substances were potent inhibitors of α-amylases from human saliva and bacteria. Pancreatic amylase, *e.g.* porcine, was inhibited to a lesser degree. Potent inhibitors of α-amylase were later discovered also in other plants, *e.g.* bean seeds[10-14] and the tuberous root of Colocasia[15], and found to be proteins and glycoproteins. The α-amylase inhibitors of plant origin, especially those from wheat, have been studied very closely by several investigators[16] since about 1970. By means of special methods of isolation using aqueous-alcoholic solutions at acidic pH, preparations were obtained from wheat germ flour or preferably glutens, which proved to be potent inhibitors of both salivary and pancreatic α-amylases[17,18]. Such a preparation was even able to inhibit pancreatic amylase *in vivo*. As was demonstrated by starch loading tests carried out with rats, dogs, and healthy volunteers, the inhibitor, administered orally, reduces the postprandial hyperglycaemia[*] and hyperinsulinaemia dose-dependently[17,19]. These findings provided experimental evidence for a new concept developed by *Puls*[19,20] for the treatment of metabolic disorders such as diabetes mellitus, adiposity and hyperlipoproteinaemia, Type IV, and gave rise to a screening for α-glucosidase inhibitors of microbial origin in the course of which new interesting active substances were isolated from microorganisms of the order *Actinomycetales*[21]. Among these were inhibitors of α-glucosidases found to be members of a homologous series of complex oligosaccharides (pseudooligosaccharides)[22,23].

The wide distribution of microbial α-amylase inhibitors, especially in organisms of the genus *Streptomyces*, has been confirmed by various teams of investigators during the past few years (cf. Table 4). We have found that new methods for microbiological screening tests will lead to new substance classes with interesting biochemical properties so that the spectrum of microbial metabolites, showing a great structural variety and so far exhibiting predominantly antibiotic effects, is extended. Systematic studies which have been carried out by the *Umezawa* group[24] since the second half of the sixties have yielded similar results. These investigators searched and found above all microbial inhibitors of proteases, esterases, aminopeptidases and enzymes involved in the biosynthesis of epinephrine[24-26].

α-Glucosidases are hydrolases that occur ubiquitously in bacteria, fungi, plants and animals. By definition, they catalyze the hydrolysis of α-glucosidic linkages. Depending on their specificity, their substrates are oligo- and polysaccharides.

At present, there is practically no evidence that the microbial inhibitors of α-glucosidases dealt with in this paper have a biological function. However, on the one hand they are of pharmaceutical interest, on the other they contribute decisively to a better understanding of the mechanism of action of α-glucosidases. The inhibitors of this type have so far been studied mainly with regard to the effect on α-glucosidases occurring in the intestinal tract of mammals. Our interest, therefore, centers on α-amylase produced in the pancreas and secreted into the small intestine and also on oligo- and disaccharidases located in the brush border of the small intestine. These glucoamylase, maltase, isomaltase, and sucrase activities may function as reaction partners of microbial α-glucosidase inhibitors.

## 2. Amylases and Enzymatic Starch Hydrolysis

The natural substrate of the amylases is starch, the main storage form of carbohydrate in most of the higher plants. Detailed reviews have been published[27-29] on its structure, which was determined especially by enzymatic methods, and on its metabolism. Starch is composed of two polysaccharides, amylose and amylopectin. Partial molecular structures of these two constituents (generally 15—25% amylose and 75—85% amylopectin) are shown in Figure 1 and their most important properties are listed in Table 1.

Table 1. Properties of starch-type polysaccharides, according to *Manners* [28].

| Property | Amylose | Amylopectin |
|---|---|---|
| General structure | essentially unbranched | branched |
| Average chain length [a] | ≈ $10^3$ | 20—25 |
| Degree of polymerization [a] | ≈ $10^3$ | $10^4$—$10^5$ |
| Conversion into maltose [%] | | |
| a) with α-amylase | ≈ 100 | ≈ 90 |
| b) with β-amylase | 70—100 | ≈ 55 |
| c) with β-amylase after pretreatment with a debranching enzyme [b] | 100 | ≈ 75 |

[a] D-glucose residues. [b] Yeast isoamylase.

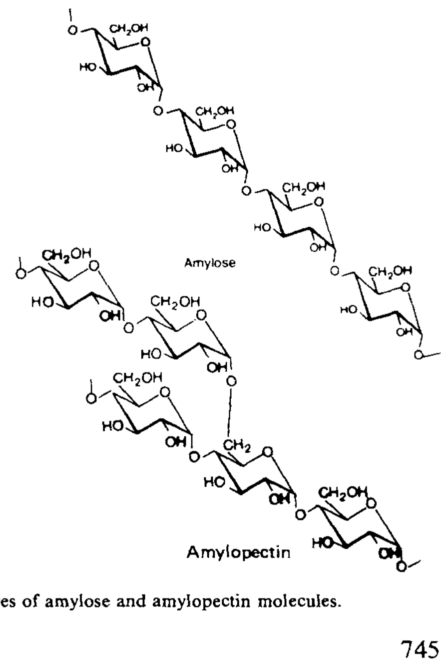


Fig. 1. Partial structures of amylose and amylopectin molecules.

---

[*] postprandial = occurring after a meal; hyperglycaemia = excessively increased blood glucose values; hyperinsulinaemia = excessively increased blood insulin values; adiposity = obesity.

Amylose is a linear (1→4)-α-glucan consisting of helically arranged chains of polysaccharides with an average degree of polymerization of about 1000 glucose residues. Amylopectin, on the other hand, is a branched polysaccharide the molecules of which have a much higher molecular weight (up to about $10^7$). The molecules have a treelike structure[30] consisting of two types of (1→4)-α-glucan chains with an average length of 20 and of over 50 D-glucose residues, resp. that are connected by α(1→6)-linkages. A molecule of amylopectin can contain up to 100000 D-glucose residues and 4000—5000 inter-chain α(1→6)-glucosidic linkages (and the same number of individual chains) (Figs. 1 and 2)[*].

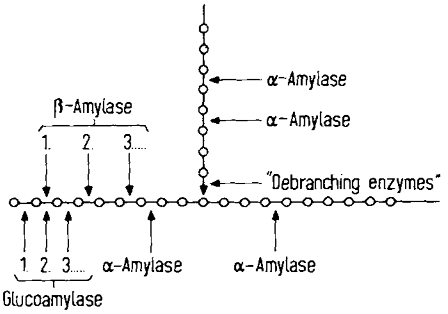
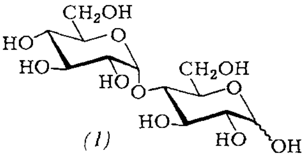


Fig. 2. Sites of action of various starch-degrading enzymes (partial structure of an amylopectin molecule).

α-Amylases (1,4-α-D-glucan glucanohydrolases, EC 3.2.1.1) attack the substrate molecule—as can be seen schematically in Figure 2 for the example of amylopectin—from inside acting as "endoenzymes", and split off maltose residues released in the α-configuration. Amylose is thus degraded mainly to maltose *(1)* by up to 100%, amylopectin by up to about 90%. In addition, slight amounts of maltotriose and glucose may result.



*(1)*

When amylopectin is degraded, so called α-dextrins[28] (see diagram in Fig. 3) are also formed which still contain the original inter-chain α(1→6)-glucosidic linkages not cleaved by α-amylases.

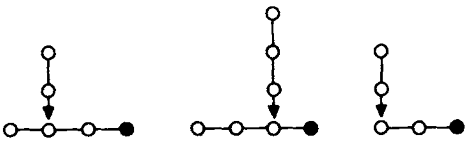


Fig. 3. Typical α-dextrin structures according to *Manners* [28]. ○: α(1→4)-linked D-glucose residue; ↓: α(1→6)-inter-chain linkage; ●: free reducing group.

β-Amylases (1,4-α-D-glucan maltohydrolases, EC 3.2.1.2) are found preferentially in plants but are not produced by the mammalian organism. They act as "exoenzymes", splitting successive maltose residues (which due to inversion are released in the β-configuration) from amylose and amylopectin from the non-reducing end (cf. Fig. 2). The degradation of amylose is sometimes complete only after pretreatment with a so-called "debranching enzyme" (*e.g.* microbial isoamylase, glycogen 6-glucanohydrolase, EC 3.2.1.68) (cf. Table 1)[28] due to the presence of a very small number of branch points. The β-amylolytic degradation of amylopectin, on the other hand, remains incomplete even under these conditions (cf. Table 1), since the outermost branching sites can be neither split nor bypassed[27-29].

Glucoamylases (1,4-α-D-glucan glucohydrolase, EC 3.2.1.3) also known as exo-α-(1→4)-glucosidases, amyloglucosidases or γ-amylases are found preferentially in microorganisms but also occur as enzyme complexes (see Section 3) in the intestinal wall of mammals. They successively split off glucose residues from the non-reducing end (Fig. 2).

The "debranching enzymes" which split α(1→6)-glucosidic linkages in the native amylopectin molecule, occur preferentially in microorganisms and plants. Corresponding enzymes of the mammalian organisms are not active in the intestinal tract. Here the intestinal oligo- and disaccharidases (Section 3) act on the α-(1→6)-glucosidic linkages of degradation products of amylopectin.

The α-amylases, the mode of action of which has already been described, are the starch-degrading enzymes investigated most thoroughly. Highly purified preparations have been obtained from a great variety of microbes, plants and animals and have been biochemically characterized. The main sources for animal α-amylases are pancreatic juice and saliva. Different forms (isoenzymes) of both human salivary amylase[31] of molecular weights between 50000 and 53000 and pancreatic amylase of hogs[32] of molecular weights between 51000 and 54000 have been

Principle of determination according to *Bernfield* [33]:

1) Hydrolysis of soluble starch, 5 min at 35°C, pH 6.9 (0.02 M sodium glycerophosphate buffer, 0.001 M $CaCl_2$).
2) Determination of the reducing groups formed by reaction with 3,5-dinitrosalicylic acid reagent and measurement of the extinction at 540 nm.

Definition of amylase unit (AU):
1 AU = 1 μVal maltose/min.

Definition of amylase-inhibitor unit AIU:
1 AIU: amount of inhibitor which after previous incubation with the enzyme inhibits 2 AU by 50%.

Scheme 1. Activity of α-amylase.

Principle of determination according to F.I.P. [34]; modification of the test according to *Willstätter* (*R. Willstätter, G. Schudel*, Ber. Dtsch. Chem. Ges. *51*, 780 (1918)):

1) Hydrolysis of soluble starch at pH 6.8 and 25°C (in the presence of NaCl).
2) Titration of the reducing groups with iodine in alkaline solution.

Definition of amylase unit according to F.I.P. (FIP-AU):
1 FIP-AU: that amount of enzyme which, under the test conditions, splits starch at such an initial rate that 1 micro-equivalent of glucosidic linkages is hydrolyzed per minute.

Definition of "F.I.P. amylase inhibitor unit (FIP-AIU)":
1 FIP-AIU: that amount of inhibitor which after previous incubation with the enzyme inhibits 2 FIP-AU by 50%.

Scheme 2. Activity of α-amylase.

---

[*] One amylopectin molecule contains only 1 reducing glucose residue.

described. Partial sequences of the polypeptide chain, made up of approximately 470 amino acid residues, are known.

Various methods are used to determine the activity of α-amylases and their inhibitors. We refer to two test methods which are briefly described in Schemes 1 and 2.

The first of these methods introduced by *Bernfeld*[33] is used frequently, though in many modified forms. The second method, the so-called "FIP-Test" is recommended by the "Commission on Enzymes" of the Fédération Internationale Pharmaceutique for the determination of activity of pancreatic α-amylase[34]. The inhibitory tests outlined in Schemes 1 and 2 have been described in detail[21]. Other tests, especially to determine the activity of α-amylase inhibitors of plant origin, have been described in detail by *Whitaker*[35] and *Marshall*[36].

## 3. Intestinal Oligo- and Disaccharidases, Their Substrates and the Determination of Their Activity

While after food intake pancreatic α-amylase is secreted by the pancreas into the duodenum and—apart from a partial adsorption at the intestinal wall—exerts its effect (the initiation of intestinal starch digestion) in the lumen of the small intestine, the intestinal oligo- and disaccharidases are fixed components of the cell membrane of the "brush border region" of the wall of the small intestine. These glycoside hydrolases of the intestinal wall, of which only slight amounts are released into the intestinal lumen, act mainly in a membrane-bound form. Their properties and mode of action and the molecular mechanism of action of sucrase are described in detail in a review by *Semenza*[37]. These enzymes are listed in Table 2.

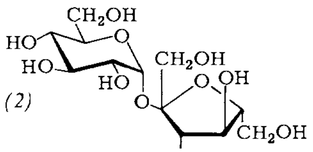
Table 2. Oligo- and disaccharidases of the small intestine [37].

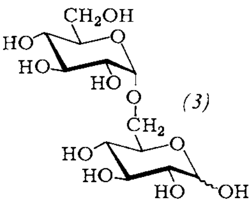
| Designation | EC number |
|---|---|
| 1 Maltases-glucoamylases (γ-amylases) | 3.2.1.20 or 3.2.1.3. |
| 2 Sucrase-maltase | 3.2.1.48 or 3.2.1.20 |
| 3 Isomaltase-maltase | 3.2.1.10 or 3.2.1.20 |
| 4 α-Limit dextrinase [40] | |
| 5 Trehalase | 3.2.1.28 |
| 6 Lactase and hetero-β-glucosidase (phlorizine hydrolase) | 3.2.1.23 and 3.2.1.62 |

Trehalase, lactase and hetero-β-glucosidase have been included for the sake of completeness.

Like the other membraneous glucosidases, maltase-glucoamylases—also known as γ-amylases—can be obtained in a homogeneous form by solubilization of an intestinal mucosa preparation with papain and subsequent chromatography. A preparation of human origin is a glycoprotein with a carbohydrate content of 32—38% and a molecular weight of the protein portion of about 220000[38]. Substrates are maltose *(1)*, maltotriose and higher α(1→4)-glucans including amylose and amylopectin, *viz.* starch. By cleaving linkages from the non-reducing end (cf. Fig. 2) glucose in the α-pyranose form is produced. The process of splitting is the faster, the smaller the substrate molecule—in contrast to the splitting of poly- and oligosaccharides by pancreatic α-amylase which is already slightly inhibited by maltose. Maltase-glucoamylases thus improve the effectivity of pancreatic amylase. These enzymes are competitively inhibited by 2-amino-2-hydroxymethyl-1,3-propanediol (tris).

The sucrase-isomaltase complex, which among the intestinal oligo- and disaccharidases has been characterized in greatest detail, can be obtained by solubilizing the mucosa material of the small intestine with either proteases (papain) or detergents (Triton X-100, sodium dodecylsulfate (SDS)). This complex is a glycoprotein with a carbohydrate content of 15% and a molecular weight for the protein component of about 220000. The complex can be split into 2 sub-units by various methods: into a sucrase-maltase and an isomaltase-maltase. Both units have an active center with sucrase and maltase specificity and with isomaltase and maltase specificity, respectively. The sucrase-isomaltase complex from the mucosa of human small intestine can be split using β-mercaptoethanol and urea[39]. The 2 sub-units are very much alike: their amino acid composition is similar. Both liberate glucose in the α-pyranose form. The sucrase-maltase complex splits sucrose *(2)*, maltose *(1)*, maltotriose and higher oligosaccharides. Substrates for the isomaltase-maltase sub-unit are, besides maltose *(1)* and isomaltose *(3)*, other oligosaccharides with α(1→6)-glucosidic linkages such as isomaltulose, isomaltotriose, α-dextrins (cf. Fig. 3) and higher limit dextrins.


*(2)*


*(3)*

Both sub-units are competitively inhibited by tris. According to recent studies by *Marshall et al.*[40], a further α-glucosidase activity of the small intestinal wall, designated limit dextrinase, which splits α(1→6)-glucosidic linkages is required in addition to the isomaltase-maltase complex.

The function of the intestinal α-glucosidases described in this section is, on the one hand, the further degradation of oligosaccharides (maltose, maltotriose, α-dextrins, isomaltose *etc.*), that are produced by pancreatic α-amylase from starch, to absorbable glucose which is introduced into the intermediary metabolism. On the other hand, they also break down oligosaccharides such as sucrose ingested with the food to absorbable monosaccharides such as glucose and fructose. *In vivo,* these processes are rather complex and have not yet been clarified in all detail. A recent review by *Semenza*[41] presents a critical evaluation of the present state of knowledge and of open questions in this field.

When determining the activities of intestinal oligo- and disaccharidases and their inhibitors, mostly enzyme preparations obtained by solubilizing mucosa of the small intestine *e.g.* from hogs[42] are used. The specificity of the test applied depends on the substrate (sucrose[23,43b], maltose[44], isomaltose[44], soluble starch[44], "dextrin" (obtained by the exhaustive degradation of glycogen with pancreatic amylase)[45,46]). The methods of determining the activity of sucrase and its inhibition are outlined in Scheme 3[43b].

Principle of determination [43b]:

1) Hydrolysis of 0.2 M sucrose, 20 min at 37 °C, pH 6.25 (0.1 M sodium maleinate buffer).
2) Determination of released glucose, using glucose dehydrogenase reagent (in 0.5 M trisbuffer, pH 7.6), 30 min at 37 °C, and determination of absorption at 340 nm.

Principle of sucrase inhibition test [43b]:
Determination of residual activity after 10 minutes of pre-incubation of the enzyme with the inhibitor at 37 °C, pH 6.25.

Scheme 3. Activity of sucrase.

## 4. Survey of the Occurrence and Composition of Microbial α-Glucosidase Inhibitors

In a screening for microbial α-glucosidase inhibitors started about 10 years ago, inhibitory activities, especially against pancreatic α-amylase and small intestinal sucrase from hogs, were found in almost all genera of the order *Actinomycetales*, of which many strains were available[21,25]. These inhibitors occur especially in strains of the family *Actinoplanaceae*[*], above all of the genera *Actinoplanes*, *Ampullariella* and *Streptosporangium*. Table 3 presents some of the results of these studies[25]. The relatively high frequency of activities for *Actinoplanes* and *Streptosporangium* is striking.

Table 3. Occurrence of α-amylase and sucrase inhibitors in strains of various genera [25].

| Genus | No. of strains tested | Strains active against amylase from hog pancreas | Strains active against sucrase from small intestine of hogs |
|---|---|---|---|
| *Streptomyces* | 85 | 3 | 2 |
| *Actinoplanes* | 220 | 43 | 24 |
| *Streptosporangium* | 161 | 18 | 24 |

Some strains showed effects on individual α-glucosidases, the others were effective against several enzyme activities. The preparation of α-amylase inhibitors resulted in two different groups of active substances[23,25]:

a) inhibitors of a polypeptide character which are heat-labile, hard to dialyze if at all, and can be inactivated by treatment with trypsin, urea or β-mercaptoethanol.
b) inhibitors which are complex oligosaccharides and have been studied most thoroughly (see Section 5). They are stable to heat (at pH 7), acid (up to pH 2), alkali (up to pH 12) and some are dialyzable. Besides α-amylase inhibitors this group includes inhibitors of oligo- and disaccharidases of the mammalian intestinal tract.

The occurrence of α-amylase inhibitors, which will be described in detail in the following sections, has during the past few years been confirmed by various groups of investigators especially for *Streptomycetes sp.* (Table 4).

Table 4. Occurrence and composition of microbial inhibitors of mammalian α-glucosidases (arranged in chronological order of publication).

| Occurrence | Composition | Specificity | Ref. |
|---|---|---|---|
| Actinomycetes of various genera | proteins, complex oligosaccharides | salivary and pancreatic α-amylases, glucoamylases, intestinal oligo- and disaccharidases | [21, 23] |
| *Streptomyces flavochromogenes* | carbohydrate-containing polypeptides (inhibitors A,B,B′,C) | salivary, pancreatic amylase; bacterial α-amylases, *Rhizopus* glucoamylase | [47–50] |
| *Streptomyces diastaticus var. amylostaticus* | N-containing oligosaccharide (amylostatin, S-AI) | salivary, pancreatic amylase;<br>microbial α-amylases, malt amylase, *Rhizopus* amylase | [51–53] |
| *Streptomyces fradiae* | acidic polypeptide, mol. weight ≈6500 (inhibitor X2) | α-amylases | [54] |
| Bacilli, *Streptomyces sp.* | nojirimycin,<br>1-deoxynojirimycin | intestinal mammalian oligo- and disaccharidases;<br>plant and fungal β-glucosidases | [44, 55–63] |
| *Streptomyces sp.* | glucose-containing oligosaccharide, mol. weight ≈600 | salivary α-amylase, glucoamylase | [64] |
| *Streptomyces calidus* | glycopeptide, rich in lysin and glucose | α-amylases, maltase and sucrase of digestive tract | [65] |
| *Streptomyces tendae* | polypeptide, mol. weight ≈7400 | animal α-amylases | [66, 67] |
| *Streptomyces sp.* | N-containing oligo-saccharides ("amino sugars") | α-amylase, sucrase, maltase | [68] |
| *Streptomyces calvus* | N-containing oligosaccharides, mol. weight 950–1050, 650–700 (inhibitors TAI-A and TAI-B, resp.) | microbial and mammalian α-amylases, microbial glucoamylase | [69] |
| *Streptomyces dimorphogenes* | "amino sugar derivatives" (trestatins A, B, C) | α-amylase | [70] |
| *Streptomyces griseosporeus* | proteins, mol. weight ≈8500 (inhibitors Haim I and II) | pancreatic α-amylase | [71,72a] |
| *Streptomyces myxogenes* | weakly basic oligosaccharides (SF-1130-$X_1$, -$X_2$, -$X_3$) | intestinal mammalian α-glucosidase and sucrase | [72b] |

## 5. Acarbose and Homologous Pseudo-oligosaccharidic α-Glucosidase Inhibitors

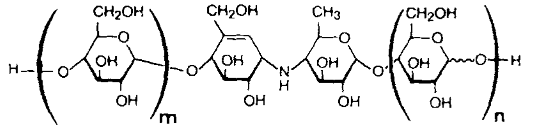
As mentioned in Section 4 a totally new substance class of secondary metabolites marked by a very pronounced inhibitory effect mainly against intestinal α-glucosidases of mammals has been found in culture filtrates[21–23]. These inhibitors are members of a homologous series of pseudo-oligosaccharides the general formula *(4)* of which is presented in Table 5.

A characteristic of these inhibitors is that they have a core essential for their inhibitory action composed of

---

[*] These strains, until that date hardly exposed to testing for secondary metabolite formation, were isolated by *A. Henssen* and *D. Schäfer*, Fachbereich Botanik, Universität Marburg (Germany).

Table 5. Pseudo-oligosaccharidic α-glucosidase inhibitors of the general formula *(4)*.



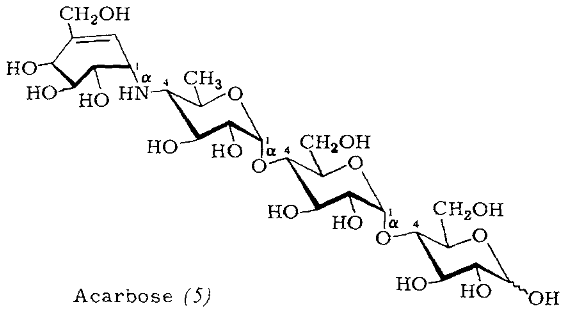
(4)

| Designation | *m* | *n* | Structural formula | Ref. |
|---|---|---|---|---|
| "Component 2" | 0 | 1 | *(6)* | [25, 46] |
| "Component 3" (acarbose, BAY g 5421) | 0 | 2 | *(5)* | [23, 25, 43b, 46] |
| "Component 4" [a] | 1 | 2 | *(27)* | [25, 46] |
| "Component 5" [b] | 2 | 2 | *(28)* | [25, 46] |
| "Component 6" [c] | 3 | 2 | *(30)* | [25, 46] |

[a] Predominant isomer with $m+n=3$. [b] Predominant isomer with $m+n=4$. [c] Predominant isomer with $m+n=5$.

a cyclitol unit (hydroxymethylconduritol residue) and a 4-amino-4,6-dideoxy-D-glucopyranose unit (4-amino-4-deoxy-D-chinovose residue). This core is linked to a varying number of glucose residues. The linkage of the individual elements is an α(1→4)-linkage as in the natural substrates (*e.g.* amylose, maltose) of the α-glucosidases. In the cyclitol unit the arrangement of the substituents is stereochemically similar to that in an α-D-glucopyranose unit.

Individual members of this homologous series have been isolated either in a homogeneous form or in the form of hardly separable isomer mixtures and been characterized in detail (Table 5). The substance investigated most thoroughly—both with regard to its microbiology[25], chemistry, biochemistry[43b,46,73] and pharmacology[45,74,100] and to its clinical use[75,76]—is component 3 *(5)*. It was given the test designation BAYg5421 and the generic name acarbose[45].



Acarbose *(5)*

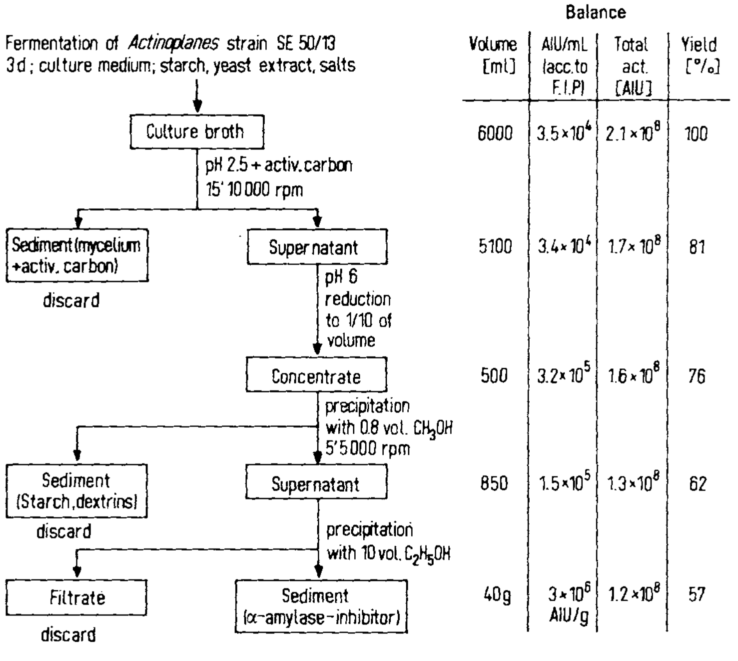
Pseudo-oligosaccharidic α-glucosidase inhibitors were first detected in culture broths of the *Actinoplanes* strain SE 50[*]. Inhibitors of both α-amylase from porcine pancreas and of a sucrase preparation from the small intestinal mucosa of hogs were found. The inhibitory activities of the culture broths against α-amylase or sucrase can vary widely, depending on the conditions of cultivation[25].

As can be seen from Table 6, the composition of the carbon source of the culture medium is of decisive importance for the inhibitory activities produced. Media containing glucose and maltose will yield especially high titers of sucrase inhibition while media containing starch will result in a very high content of α-amylase inhibitors[25]. An amplification of this trend was achieved by the selection of suitable natural variants of the SE 50 strain. In a starch-containing medium, sub-strain SE 50/13 produces amylase inhibitor titers of around 35000 FIP-AIU/mL and only very low sucrase inhibitor activities. Strain SE 50/110, on the other hand, produces sucrase inhibitor titers of around 60 SIU/mL in a maltose-containing medium while producing an amylase inhibitor titer of only about 760 FIP-AIU/mL[25].

Table 6. Influence of carbon source in the medium on inhibitor production of the *Actinoplanes* Strain SE 50 [25].

| Carbon source | Titer after 4 d | | |
|---|---|---|---|
| | SIU/L | AIU/mL | $\frac{\text{SIU}}{\text{AIU}} \times 10^{-3}$ |
| glycerol 3% | 160 | 100 | 1,6 |
| galactose 3% | 1100 | 100 | 11 |
| maltose 3% | 5500 | 1000 | 5,5 |
| cellobiose 3% | 1300 | 220 | 6 |
| glycerol 1% + glucose 2% | 2700 | 120 | 22 |
| galactose 1% + glucose 2% | 2700 | 120 | 22 |
| maltose 1% + glucose 2% | 6600 | 200 | 33 |
| cellobiose 1% + glucose 2% | 2200 | 105 | 21 |

The diagram in Figure 4 shows how a purified inhibitor mixture is obtained which consists mainly of such members of the homologous series of the general formula *(4)* with a very pronounced inhibitory activity against α-amylase. The actinoplanes strain SE 50/13 was cultured in a starch-containing medium. The preparation obtained by fractional precipitation of the culture filtrate with methanol and ethanol inhibits α-amylases from human saliva and pancreas and from hog pancreas to a high degree[25]. This substance (designated BAYe 4609) served, ***inter alia***, as a standard preparation for pharmacological[45,77] and clinical[78] studies. The molecular weight range of this pre-



Balance

| Volume [ml] | AIU/mL (acc. to F.I.P) | Total act. [AIU] | Yield [%] |
|---|---|---|---|
| 6000 | $3.5\times10^4$ | $2.1\times10^8$ | 100 |
| 5100 | $3.4\times10^4$ | $1.7\times10^8$ | 81 |
| 500 | $3.2\times10^5$ | $1.6\times10^8$ | 76 |
| 850 | $1.5\times10^5$ | $1.3\times10^8$ | 62 |
| 40g | $3\times10^6$ AIU/g | $1.2\times10^8$ | 57 |

Fig. 4. Microbiological production of an α-amylase inhibitor standard preparation (BAYe4609) [21, 85].

---

[*] This strain was isolated by *A. Henssen* and *D. Schäfer*, Fachbereich Botanik, Universität Marburg (Germany).

paration is determined by the conditions of precipitation (soluble in 50% $CH_3OH$, precipitable from a mixture of $C_2H_5OH$, $CH_3OH$ and $H_2O$ (84 : 8 : 8)).

The analysis of the oligomer distribution of this mixture consisting of oligosaccharides with inhibitory activity and inert sugars by gel chromatography (using Bio-Gel P-6)[22] resulted in a separation into two fractions with inhibitory activity with different molecular weight ranges[25,46].

The high-molecular fraction with an estimated molecular weight range of 6000 to 8000 has not been examined thoroughly yet. Rechromatography on Bio-Gel P-2 of the low-molecular weight fraction indicated a clear-cut maximum of inhibitory activity for the elution volume of a maltononaose (molecular weight 1477). This portion was shown to consist mainly of a mixture of isomers of component 7 (cf. *(4)*: ($m+n=6$)) and component 8 ($m+n=7$). In addition, it contains small amounts of components 3 to 6 ($m+n=2$, 3, 4, 5)[22]. By re-chromatography of this fraction, using strongly acidic ion exchangers (Dowex 50 W), a preparation of the inhibitor mixture was obtained which is largely free from inert carbohydrates and exhibits a specific activity of $15 \times 10^6$ FIP-AIU/g. This corresponds to about a 5-fold enrichment of the initial material (BAYe4609)[46].

When the crude mixture of this α-amylase inhibitor (BAYe4609) is subjected to a mild acid hydrolysis with 0.5 N hydrochloric acid at 100 °C, a gradual decrease in α-amylase inhibitory activity occurs in the course of hydrolysis which is accompanied by a corresponding increase in sucrase inhibitory activity[23,43b,80]. This sucrase inhibitory activity reaches its maximum about 45 min after the start of hydrolysis after which it slowly falls to minimum values which can be interpreted as a total disintegration of the inhibitors. It was shown by thin-layer chromatography and high-pressure liquid chromatography that with consistent increase of cleavage of glucose residues the whole homologous series of inhibitory components is passed through[43b] in the course of hydrolysis. A solution with a high sucrase-inhibiting and minimal α-amylase-inhibiting activity obtained after one hour of hydrolysis has been studied closely[46].

A separation of the components with inhibitory activity from the other products of hydrolysis (mainly glucose and maltose) was achieved by adsorption on activated carbon and fractional desorption with increasing concentrations of ethanol. Four different pure components (1—4: component 1 from fraction 1, component 2 from fraction 2, *etc.*) were obtained by means of partition chromatography using cellulose (cf. Fig. 5) and after further purification by gel chromatography using Sephadex G-15. The individual components showed different inhibitory effects against sucrase, that of component 1 being very weak. Components 2—4 can—as is shown in Figure 6 by the example of component 3 (acarbose *(5)*)—be converted into the component one unit smaller by further acid hydrolysis, *i.e.* cleavage of one additional glucose residue. The end product of acid hydrolysis, component 1 *(8)*, cannot be transformed further under these conditions[23,46,79].

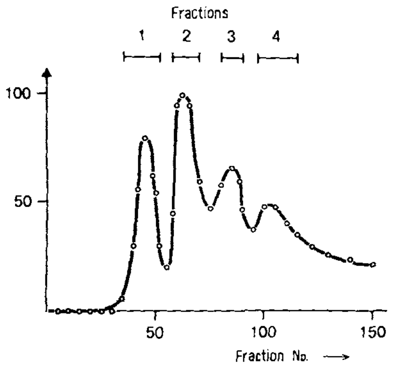


Fig. 5. Chromatography (on cellulose) of a hydrolyzate of the α-amylase inhibitor preparation BAYe4609 [46]. Solvent: pyridine/ethyl acetate/acetic acid/water (36/36/7/21); column: 1.6 × 185 cm; flow rate: 25 mL/h; fractions of 8 mL. Ordinate: Percentage of sucrase inhibition by 10 µL of each fraction.

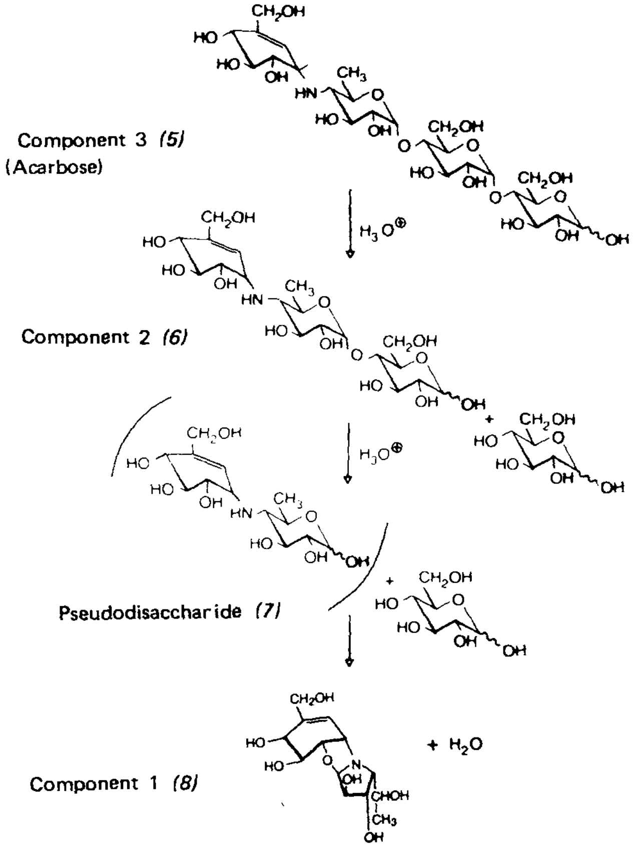


Fig. 6. Acid hydrolysis of component 3 (acarbose) *(5)* [46].

The complete acid hydrolysis of 100 g of the crude preparation BAYe4609 will yield about 500 mg of component 1 *(8)*. The yield of higher components produced after incomplete hydrolysis is within the same range[46]. Component 1 *(8)* is a tricyclic compound, whose structure was determined by degradation reactions, derivatization and spectroscopic analysis[46,73,79]. *(8)* is formed in the following way: after one glucose residue is split off from component 2 *(6)*, the amino sugar *(7)* released is not stable in the pyranose form. It is well known that 4-aminopyranoses such as *(7)* undergo a rearrangement to a pyrrolidine form and readily split off water in acid solution (Fig. 7). The un-

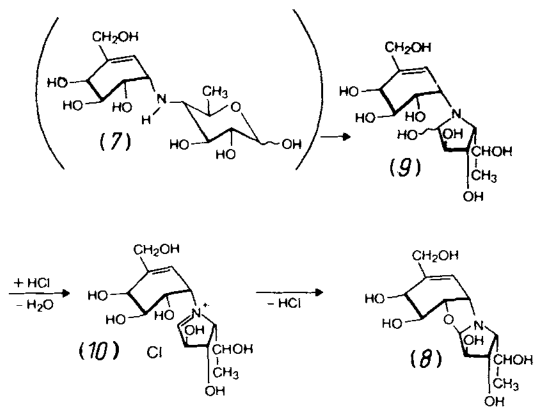


Fig. 7. Conversion of the unstable pseudodisaccharide *(7)* into a pyrrolidine derivative *(9)* and its dehydration to component 1 *(8)*.

saturated compound *(10)* is stabilized by the addition of an adjacent hydroxyl group of the cyclitol unit to the C=N double bond. The non-crystalline tricyclic product of condensation *(8)* is very easily reduced with $NaBH_4$. As a result, the 1,3-oxazolidine ring opens (Fig. 8). The resulting aminocyclitol *(11)* is ineffective against α-amylase and sucrase although the cyclitol unit of the molecule has remained unchanged compared to the highly active components 2—6 of the homologous series. This means that the unsaturated hydroxymethylconduritol unit *alone* will not produce the desired inhibitory effect. The product *(11)* obtained by $NaBH_4$-reduction can be split into the cyclitol unit and the pyrrolidine unit by hydrogenolysis at a platinum contact. The main products thus obtained are validatol *(12)*[81] and the derivative *(13)*[73]. Validatol *(12)* was also obtained by degrading the antibiotic validamycin A *(14)*[81,82].

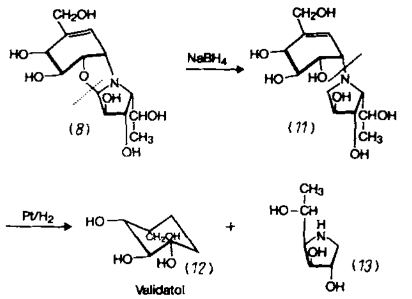
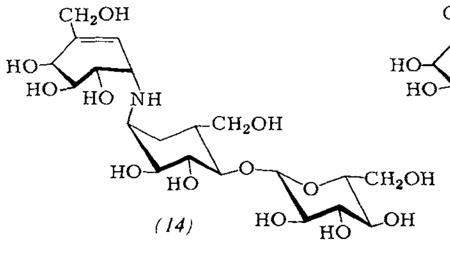
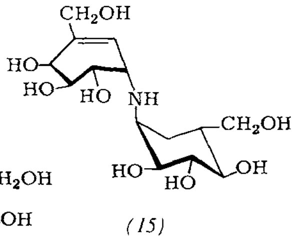


Fig. 8. Reduction of component 1 *(8)* with $NaBH_4$ to an aminocyclitol *(11)* and its catalytic hydrogenation[73].

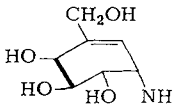


(14)



(15)

Neither validamycin A *(14)* nor validoxylamine A *(15)*[83] inhibit α-amylase or sucrase, although, as constituents of the molecule, they contain the unsaturated hydroxymethylconduritol unit. Valienamine *(16)*[84] obtained by the microbial degradation of validamycin A *(14)* with *Pseudomonas maltophila* proved to be a weak inhibitor of sucrase[73][*].



(16)

By selecting suitable strains and optimizing culture conditions the individual components of the homologous series of pseudo-oligosaccharidic α-glucosidase inhibitors can be obtained much more easily and in higher quantities[25,85,86] than by the acid hydrolysis of the preparation BAY e 4609 described above. The use of glucose or maltose in the culture medium of the *Actinoplanes* strain SE 50/110[86] will result in high sucrase inhibitor titers in the culture broths from which the inhibitors can be adsorbed by activated carbon.

Desorption with successively increasing concentrations of ethanol led to a crude preparation which was purified further by ion-exchange chromatography[46] (Fig. 9). Fractions C to E are partly identical with components 2—4 (obtained by acid hydrolysis of BAY e 4609). The main fraction, approximately 80% of the sucrase inhibitors obtained from this fermentation (Fraction D, Fig. 9), proved to be identical with component 3 (acarbose) *(5)*. The yield of acarbose from fermentation was around 600 mg/L of culture broth. Fraction E was found to have one glucose unit less and identified as component 2. Fraction C has the same composition as component 4 and fractions A and B contain isomeric mixtures of the higher components 6 and 5.

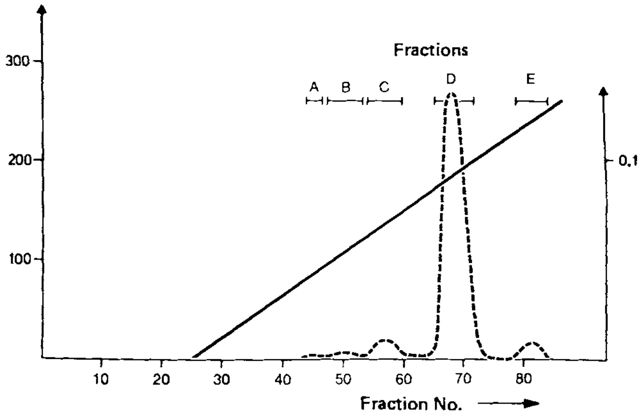


Fig. 9. Ion exchange chromatography of a crude sucrase-inhibitor preparation of the strain SE 50/110 [46]. Dowex 50 W×4H® (200—400 mesh); column: 0.9×60 cm; elution with $10^{-3}$ N HCl up to fraction No. 20; then linear gradient with increasing NaCl concentrations in $10^{-3}$ N HCl; flow rate: 30 mL/h, fractions of 7.5 mL; Left ordinate: SIU/mL (---); Right ordinate: NaCl concentration (M) (——).

Further information about the constituents essential for α-glucosidase inhibition in acarbose and in the other components was provided by hydrogenolysis with $Pt/H_2$, during which the cyclitol residue can be removed by cleaving the C—N bond in allyl position to the double bond without changing the remaining molecule[73]. The basic trisac-

---

[*] For inhibition of other α-glucosidases see [84b].

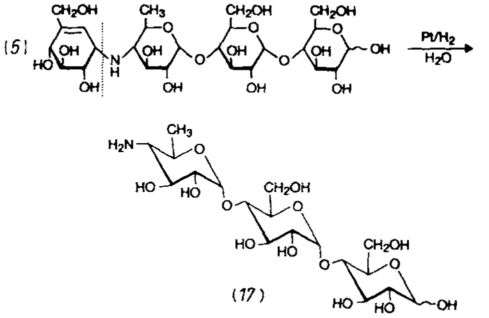


Fig. 10. Hydrogenolytic cleavage of the basic trisaccharide *(17)* during the catalytic hydrogenation of acarbose *(5)* [73].

charide obtained in this way *(17)*[*] has no inhibitory activity against α-amylase or sucrase, which means that the amino sugar *alone* is not essential for the inhibitory effect. As previously mentioned, the unsaturated cyclitol residue alone does not suffice for the inhibitory effect, either.

This leads us to the conclusion that the pseudodisaccharide unit composed of both constituents is essential for the effect. The splitting of the C—N bond in allyl position to the double bond is only one, though preferred, possibility of molecular reaction. The two C—O bonds in allyl position to the double bond are easy to split by hydrogenolysis, too (Fig. 11). Moreover, the double bond is saturated

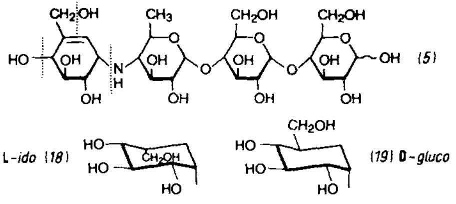


Fig. 11. Possible reactions of acarbose *(5)* during catalytic hydrogenation with maintenance of the pseudotetrasaccharide structure [73].

during hydrogenation. This will result in the formation of two diastereomeric products with an L-*ido* *(18)* or D-*gluco*-configuration *(19)*. Since there may be several of these reactions at the same time, it is easy to imagine how complex a product mixture is obtained by catalytic hydrogenation of acarbose *(5)*. The hydrogenation mixture was first separated into basic and non-basic constituents by fractionation on cation exchangers in the $H^{\oplus}$ form. Each of the two main fractions was then purified further by chromatography.

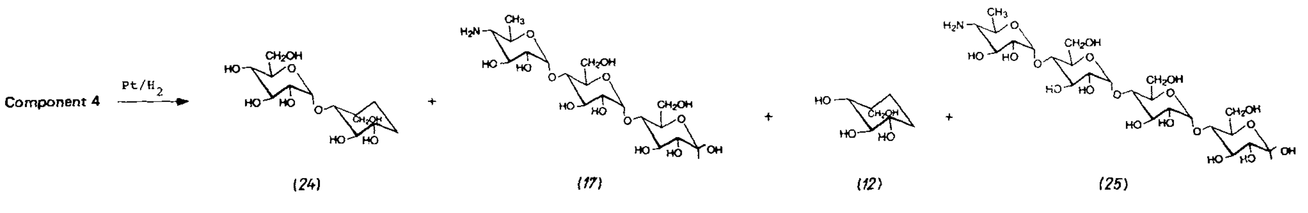


Fig. 13. Catalytic hydrogenation of component 4 [73].

The basic reaction products (Fig. 12) isolated were, apart from the ineffective trisaccharide *(17)* mentioned, two products showing a pseudotetrasaccharide structure which had resulted from simple saturation of the double bond in the cyclitol unit. The compound *(20)* with an L-*ido*-configuration in the cyclitol unit had no inhibitory effect against either α-amylase or sucrase any more, while the other compound with a D-*gluco*-configuration in the cyclitol unit was ineffective against α-amylase but had a very pronounced effect on sucrase. A further product of hydrogenation *(22)* in which the primary hydroxyl group of the cyclitol residue had been additionally removed by reduction had no inhibitory effect on either of the enzymes.

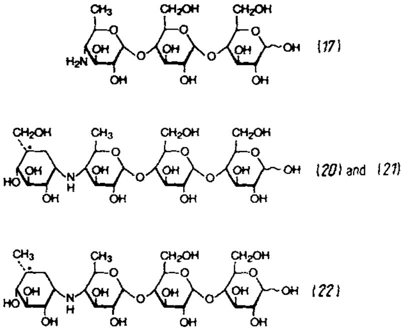
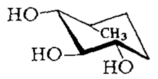


Fig. 12. Basic reaction products of the catalytic hydrogenation of acarbose *(5)* [73].

Consequently, the double bond in the cyclitol unit is—quantitatively—important for the effect. The non-basic products were examined by thin-layer chromatography and found to be derivatives of the cyclitol.

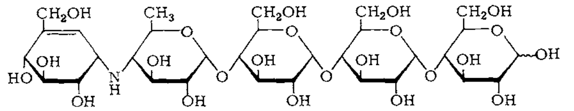
Validatol *(12)* and 7-deoxyvalidatol[81] *(23)* were isolated and identified[73].


*(23)*

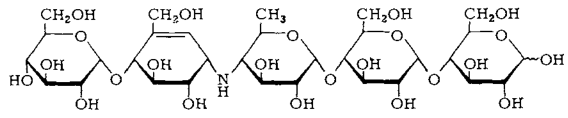
The higher components were also subjected to hydrogenolysis in the form described. As can be seen in Figure 13, "component 4" yields mainly validatol glucoside *(24)* in addition to the basic trisaccharide *(17)* mentioned. However, validatol *(12)* and a basic tetrasaccharide *(25)*[46] are also obtained. Component 4 thus consists of two isomers *(26)* and *(27)*. The isomer with the terminal cyclitol residue *(26)* constitutes only a small proportion. A separation of both isomers was achieved using strongly acidic ion exchangers.

---

[*] *(17)* was acetylated, split into the three monosaccharide constituents by acetolysis and thus correlated to known compounds [73].



(26)



(27)

Both have inhibitory activity against α-amylase and sucrase, isomer *(26)* being slightly more effective. Components 5 and 6 (cf. Table 4) were also found to be isomer mixtures. When the main isomer *(28)* of component 5 is subjected to hydrogenolysis, validatol maltoside *(29)* and the basic trisaccharide *(17)* are formed (cf. Fig. 14).

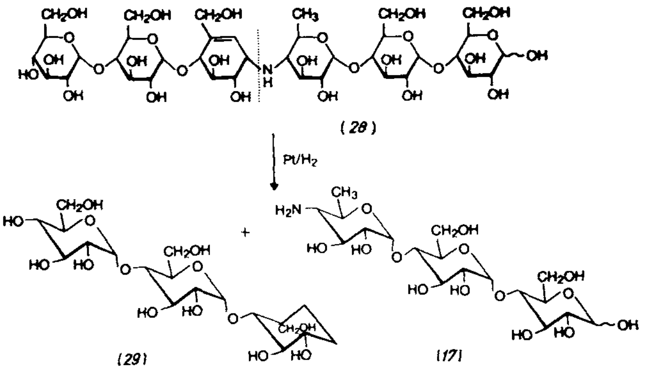
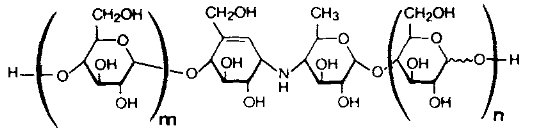


Fig. 14. Catalytic hydrogenation of the predominant isomer *(28)* of component 5 [73].

These data relating to the constitution of individual members of the homologous series of pseudo-oligosaccharidic α-glucosidase inhibitors of the general formula *(4)* have been confirmed and extended by reactions of enzyme degradation using β-amylase which is inhibited by the individual components to a much lesser degree than other α-glucosidases. As is shown in Figure 15, a maltose residue is split off from each of the two main isomers *(28)* and *(30)* of the isomer mixtures contained in components 5 and 6. Further products of reaction are component 3 (acarbose) *(5)* and the component 4 isomer *(27)*.

## 6. Inhibitory Spectrum of Acarbose and of Homologous Pseudo-oligosaccharides

The individual components of the homologous series described in detail in the previous Section differ with regard to their inhibitory activities against α-amylase from porcine pancreas and sucrase from hog small intestine (Fig. 16).



(4), m+n = 1-7

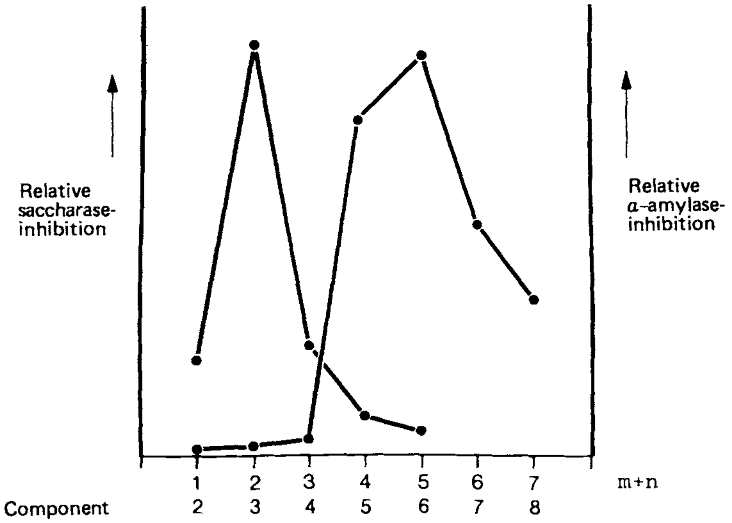


Fig. 16. Relative inhibition of sucrase and α-amylase by "components 2—8" [43].

The highest specific inhibitory activity against α-amylase is exhibited by a component 6 preparation with minimum inhibitor activity against sucrase. (The inhibition of α-amylase by the component 6 preparation is linear up to 70%. By extrapolation the amount of inhibitor for the 100% inhibition can be determined and a 1 : 1 stoichiometric relationship between enzyme and inhibitor is estimated.)

The inhibitory activity against α-amylase decreases with the higher components, while component 3 (acarbose) *(5)* shows maximum inhibitory activity against sucrase (Fig. 16). Table 7 lists the inhibitory activities of different components against α-amylase from porcine pancreas and the intestinal oligo- and disaccharidases from hog small intestine. As a measure of inhibitory activity, that amount of inhibitor is given which produces a 50% inhibition under test conditions. From Table 7 it is obvious that component 3

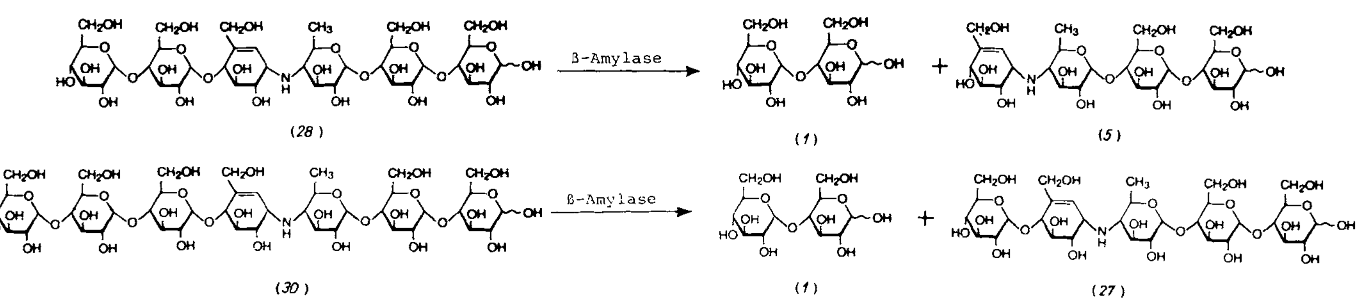


Fig. 15. Enzymatic hydrolysis of component 5 (predominant isomer *(28)*) and component 6 (predominant isomer *(30)*) using β-amylase (sweet potato) [46].

Table 7. Amounts (in ng) of acarbose *(5)* and homologues of the general formula *(4)* [45] necessary for inhibition ($ID_{50}$ [a]) of the activity of intestinal α-glucosides *in vitro* [b].

| Component | No. of glucose residues $m+n$ in *(4)* | Maltase 10 mU [c] | Isomaltase 10 mU | "Dextrinase" 29 mU | Glucoamylase 10 mU | α-Amylase 100 mU | Sucrase 10 mU |
|---|---|---|---|---|---|---|---|
| 2 | 1 | 100 | 43500 | 205 | 83 | 855 | 500 |
| 3 (acarbose) | 2 | 15 | 42000 | 64 | 9.3 | 680 | 74 |
| 4 | 3 | 80 | 54500 | 93 | 39 | 1135 | 455 |
| 5 | 4 | 236 | > 100000 | 100 | 110 | 4.7 | 700 |
| 6 | 5 | 1000 | ≫ 100000 | 93 | 410 | 2.8 | 700 |
| BAY e 4609 | 7-30 | 8250 | ≫ 100000 | 810 | 8000 | 14.5 | 60000 |

[a] Amount of inhibitor in ng per test, required for 50% inhibition. [b] Assays for glucose-releasing enzymes: Pre-incubate 0.01 ml inhibitor solution in multiple dilutions with 0.1 mL enzyme preparation for 10 minutes, incubate with 0.1 mL substrate solution, stop with 1 mL glucose dehydrogenase reagent in 0.5 M tris-buffer, develop for 30 min for determination of glucose and determine absorption at 340 nm. Substrate solutions and incubation periods: 0.4 M sucrose for 20 min, 50 mM maltose for 10 min, 40 mM isomaltose for 10 min, 5% soluble starch for 20 min. Assay for destrinase: Pre-incubate 0.01 ml inhibitor solution in multiple dilutions with 0.1 ml enzyme preparation for 10 minutes, incubate with 0.1 mL 5% limit dextrin solution for 20 minutes, mix with 0.5 mL dinitrosalicylic acid reagent [33], heat to 95 °C for 5 min, dilute with 1.5 mL water and determine absorption at 540 nm. Assay for α-amylase: Pre-incubate 0.01 mL inhibitor solution in multiple dilutions with 0.2 mL enzyme preparation (α-amylase from hog pancreas) for 10 min, incubate with 0.2 mL 5% starch solution for 5 min, mix with 0.5 mL dinitrosalicylic acid reagent [33], heat to 95 °C for 5 min, dilute with 2.5 mL water and determine absorption at 540 nm. [c] 1 U is that amount of enzyme which converts 1 μmol of substrate per min under standard conditions. 1 U = 16.67 nkat.

(acarbose) *(5)* has the highest specific inhibitory activity also against the other α-glucosidases located in the wall of the small intestine. The isomaltase activity of the enzyme preparation from the small intestine of hogs is inhibited to a very small degree by the lower components (in comparison with nojirimycin and 1-deoxynojirimycin (see Section 8, Table 10)) and practically not at all by the higher components. However, the activity of the enzyme preparation referred to as "dextrinase" (substrate: glycogen degraded to limit dextrins by α-amylase from porcine pancreas) is inhibited to a high degree.

A number of bacterial, fungal and plant enzymes (cf. Table 8) were tested for inhibition by acarbose *(5)*[87]. Table 8 indicates that α-amylases from *Bacillus subtilis* and *Aspergillus oryzea* and glucoamylase from *Aspergillus niger* and α-glucosidase from yeast *(Saccharomyces sp.)* are inhibited. As can be seen from Table 9 glucoamylase of *Aspergillus* origin is the most sensitive of all enzymes tested in this study[87]. Furthermore, cyclodextrin-glucosyl-transferase is inhibited, while muscle phosphorylase is not affected[87].

Table 8. Inhibitory spectrum of acarbose *(5)* for enzymes from bacteria, fungi and plants [87].

| Enzyme | Origin | Substrate | Inhibition [a] |
|---|---|---|---|
| α-amylase | *B. subtilis* | starch | + |
| α-amylase | *A. oryzae* | | + |
| α-amylase | barley malt | | + |
| β-amylase | "sweet potato" | | – |
| β-amylase | B. polymyxa | | – |
| glucoamylase | A. niger | | + |
| invertase | *Saccharomyces sp.* | sucrose | – |
| α-glucosidase | | maltose | + |
| β-glucosidase | almonds | cellobiose | – |
| β-galactosidase | *Saccharomyces fragilis* | lactose | – |
| dextran sucrase | *Leuconostoc mesenteroides* | sucrose | – |
| pullulanase | *Aerobacter aerogenes* | pullulan | – |
| isoamylase | *Cytophaga sp.* | glycogen | – |
| cyclodextrin-glucosyl transferase | *B. macerans* | starch | + |

[a] Inhibition: +, no inhibition: –.

By reacting the reducing glucose unit of acarbose *(5)* a number of semisynthetic glycoside derivatives were produced and tested[73]. In a few cases an increase of up to a factor of three in the inhibitory activity against sucrase was found, but none of the derivatives offered any convincing advantages over acarbose[73]—especially when considering their costly production.

Table 9. Concentrations of acarbose *(5)* required for a 50% inhibition of various α-glucosidases [87].

| Enzyme | Origin | Concentration of inhibitor [μg/mL] |
|---|---|---|
| α-Amylase | "Bacterial saccharifying" | 0.3 |
| | "Bacterial liquefying" | 40.9 |
| | Aspergillus oryzae | 180.0 |
| | Porcine pancreas | 3.8 |
| | Barley malt | 83.5 |
| Glucoamylase | *Aspergillus niger* | 0.04 |
| α-Glucosidase | *Saccharomyces sp.* | 70.0 |

## 7. Further Pseudo-oligosaccharadic α-Amylase Inhibitors

A short time ago microbial α-amylase inhibitors became known from the patent literature which are obviously also members of a homologous series and assumed to have the same "core" as the pseudo-oligosaccharides (acarbose series) (Section 5). Three basic amino sugar derivatives were isolated from culture broths of *Streptomyces dimorphogenes* NR-320-OM7HB and NR-320-OM7HBS. These derivatives, which were separable by high-pressure liquid chromatography, were called trestatins A *(31)*, B *(32)* and C[70]. Their molecular weights as determined by osmometry are 1470, 975 and 1890, respectively. The structures proposed for trestatins A and B on the basis of spectroscopic analysis on the one hand and examinations of products of hydrolysis (4 N HCl, 3 h at 80 °C) on the other are shown in Figure 17.

The products of hydrolysis of the three trestatins are glucose and an amine ($pK_a = 3.9$) of the empirical formula $C_{13}H_{21}NO_7$[*]. All three trestatins have one trehalose residue as a common structural characteristic. Trestatin A *(31)*

---

[*] "Component 1" *(8)* has the same molecular formula.

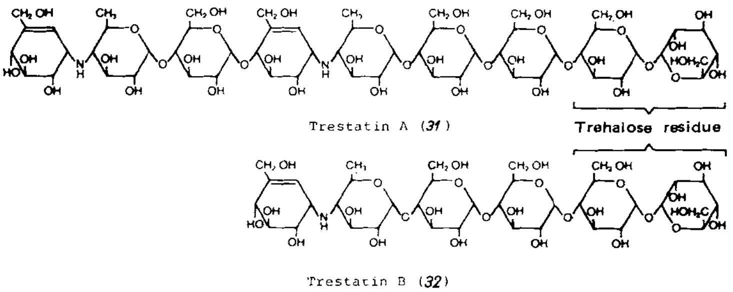
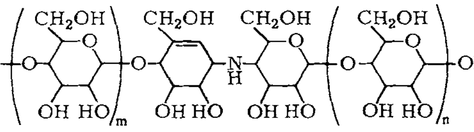


Fig. 17. Proposed structures of trestatins A *(31)* and B *(32)* [70].

contains two and trestatin C three pseudodisaccharide residues per molecule. Both show relatively high specific inhibitor activity against pancreatic α-amylase from hog ($7.1 \times 10^7$ IU/g and $4.9 \times 10^7$ IU/g, respectively)[*]. Trestatin B *(32)* has only one pseudodisaccharide residue per molecule and a lower specific activity of $1.5 \times 10^6$ IU/g[*].

In a patent application[68] inhibitors of α-glucosidase are described which are also members of a homologous series of the general formula *(33)*. The microorganisms producing these inhibitors are said to be strains of the genus *Streptomyces* (*e.g.* A 2396)[68]. The only structural difference from the acarbose series of the general formula *(4)* is that the 4-amino-4,6-dideoxyglucose residue is replaced by a 4-amino-4-deoxyglucose residue. In the patent application mentioned above[68] amino sugars of the general formula *(33)* with $m = 0$ to 8, $n = 1$ to 8 are claimed, $m+n$ having a value of 1 to 8. The structure of these inhibitors was derived mainly from spectroscopic data. The higher compounds of the homologous series are more effective against α-amylase than the lower ones. Furthermore, inhibitory action on sucrase and maltase is mentioned.


*(33)*

*Murao et al.*[51–53] carried out detailed investigations on a pseudo-oligosaccharidic α-amylase inhibitor (amylostatin, S-AI) isolated from culture broths of *Streptomyces diastaticus subsp. amylostaticus* No. 2476. Its structure has not yet been completely identified, but shows a striking similarity to members of the homologous acarbose series of the general formula *(4)*. This inhibitor was isolated by chromatography followed by purification *via* an enzyme-inhibitor complex with "bacterial liquefying α-amylase" (BLA)[52]. A molecular weight of about 1500 was determined. S-AI *(34)* is called a "substrate analog inhibitor"[53]. Its inhibitory spectrum covers not only human salivary amylase and pancreatic amylase from hogs but also a number of bacterial and fungal α-amylases. Moreover, ***Rhizopus niveus*** glucoamylase and malt α-amylase are inhibited, while mammalian intestinal sucrase, β-amylase of plant origin and a number of microbial α-glucosidases are not. S-AI *(34)* has a reducing terminal glucose residue and five more glucose residues connected by 1,4-glucosidic linkages. Two maltose residues can be split off with β-amylase. The remaining molecule was named "glucosyl-S-AI-X-glucose"[53]. A further derivative, S-AI-XG[72] (molecular weight approximately 500) was obtained from S-AI *(34)* by enzymatic and/or chemical methods. This derivative consists of that part of the molecule containing nitrogen and a reducing glucose residue. Figure 18 shows a schematic attempt at representing the structure[53] of S-AI *(34)*, according to which the active center of BLA interacts with 8–10 glucose residues and the catalytic center of the enzyme "fits" the unknown part of the molecule S-AI-X of S-AI *(34)* which is obviously essential to the inhibitory effect.

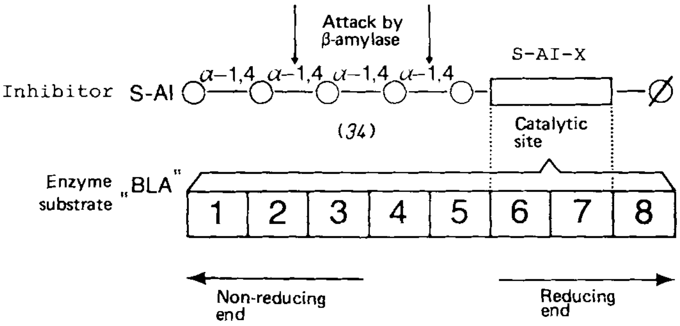


Fig. 18. Structure suggested for the microbial α-amylase inhibitor S-AI *(34)* and postulated binding mechanism between S-AI and "bacterial liquifing amylase (BLA)" according to *Murao* and *Ohyama* [53] (∅: reducing glucose residue).

Additional N-containing oligosaccharidic α-amylase inhibitors, TAI-A and TAI-B, were isolated from culture broths of *Streptomyces calvus* TM-521[69]. These inhibitors have a molecular weight of 950 to 1050 and 650 to 700, respectively, and contain two or several glucose residues and, as a basic residue, probably an amino sugar unit. TAI-A and TAI-B differ from the compounds of the homologous acarbose series of the general formula *(4)* by the absence of methyl groups. Their inhibitory spectrum covers human salivary amylase, porcine pancreatic amylase, ***Rhizopus niveus*** glucoamylase, Taka amylase[*] (only TAI-A) and "bacterial saccharifying α-amylase" but not BLA.

A glucoamylase and α-amylase inhibitor, NCGAI, was isolated from culture broths of *Streptomyces sp.* No. 33[64]. Its molecular weight is approximately 600 and it is assumed to consist mainly of glucose residues. NCGAI exhibits a pronounced inhibitory effect on glucoamylase while inhibiting pancreatic amylase and BLA to a lesser degree.

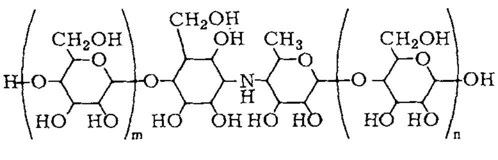
A short while ago a patent application became known[72a] in which three α-glucosidase inhibitors (isolated from *Streptomyces myxogenes* SF-1130, ATCC 31305) of the general formula *(34a)* are described. They are said to be weakly basic oligosaccharides. Apart from their inhibitory activity against mammalian intestinal α-glucosidase and sucrase, these substances are referred to as antibiotics

---

[*] Because of different test conditions these values are not comparable with those stated in Section 5.

[*] Taka amylase is a commercially available crude product from cultures of *A. oryzae* which degrades starch to glucose.

SF-1130-$X_1$, -$X_2$ and -$X_3$. SF-1130-$X_3$ (molecular weight *ca.* 830) is a particularly potent inhibitor of α-glucosidase.



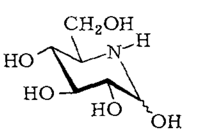
(34a)

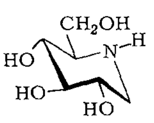
Antibioticum SF-1130-$X_1$, m + n = 5
Antibioticum SF-1130-$X_2$, m + n = 4
Antibioticum SF-1130-$X_3$, m = o, n = 3

## 8. Nojirimycin and 1-Deoxynojirimycin

Nojirimycin *(35)* was first described as an antibiotic produced by *Streptomyces roseochromogenes* R-468 and *Streptomyces lavendulae*-SF-425[56,58].

(35)





(36)

1-Deoxynojirimycin *(36)* was obtained from *(35)* by catalytic hydrogenation at the platinum contact or by reduction with $NaBH_4$[56,58]. There are also fully synthetic ways to prepare nojirimycin[58] and 1-deoxynojirimycin[57]. Later *(35)* was found to be a potent inhibitor of β-glucosidases (emulsin, fungal β-glucosidases)[59,60]. *(36)* is a much weaker inhibitor of emulsin than *(35)*[59]. *(35)* also inhibits microbial α-glucosidases, but to a much lesser degree than β-glucosidases[59,60].

A screening for inhibitors of intestinal mammalian α-glucosidases reveals that *(35)* and *(36)* are also produced by many strains of the genus *Bacillus*[44,55]. After 4- to 6-day fermentation in nutrient solutions usually containing starch or maltose, culture filtrates with relatively high titers of sucrase inhibitor units were obtained from the strains *B. amyloliquefaciens* (DSM 7), *B. polymyxa* (DSM 365), *B. subtilis* (DSM 704)[*] and *B. subtilis var. niger* (DSM 675). The inhibitors were bound to strongly acidic cation exchangers ($H^{\oplus}$ form) and subsequently eluted with aqueous ammonia. They were purified further by chromatography using CM-cellulose and gel-filtration using Sephadex LH-20. From the concentrated fractions with inhibitory activity, *(36)* crystallized in the form of colorless scales (m.p. 206 °C). *(36)* was also isolated from mulberry tree leaves[61] and called moranoline. Later *(36)* was also obtained by fermentation of the *Streptomyces lavendulae* strains SEN-158[62] and *subsp. trehalostaticus* No. 2882[63]. *(35)* and *(36)* were found to be potent inhibitors of intestinal oligo- and disaccharidases of mammals (Table 10)[44]. Pancreatic α-amylase is practically not inhibited. It was recently discovered that *(36)* is also a potent inhibitor of trehalases (rabbit and *Chaetomium aureum* MS-27) and of *Rhizopus niveus* glucoamylase and *exo*-β-1→3-glucanase *(Penicillium)*[63].

Table 10. Molar concentrations of nojirimycin *(35)* and 1-deoxynojirimycin *(36)* required for a 50% inhibition of intestinal α-glucosidases [44].

| Inhibitor | Sucrase | Maltase | Isomaltase | Glucoamylase |
|---|---|---|---|---|
| Nojirimycin | $5.6\times10^{-7}$ M | $1.7\times10^{-6}$ M | $2.5\times10^{-7}$ M | $7.6\times10^{-7}$ M |
| 1-Deoxynojirimycin | $2.2\times10^{-7}$ M | $1.3\times10^{-7}$ M | $1.3\times10^{-7}$ M | $9.6\times10^{-8}$ M |
| mU Enzyme in 0.21 mL incubation volume at 37 °C | 11.1 | 11.8 | 11.5 | 10.1 |

Assays: Pre-incubate 0.01 mL inhibitor solution in multiple dilutions with 0.1 mL enzyme preparation for 10 min, incubate with 0.1 mL substrate solution, stop with 1 mL glucose dehydrogenase reagent in 0.5 M tris-buffer, develop during 30 min for determination of glucose and determine absorption at 340 nm. Substrate solutions and incubation periods: 0.4 M sucrose for 20 min, 50 mM maltose for 10 min, 40 mM isomaltose for 10 min, 5% soluble starch for 20 min. Nojirimycin is released from the bisulfite adduct using barium hydroxide, determined quantitatively using glucose dehydrogenase reagent and used immediately for the inhibition test.

## 9. Carbohydrate-Containing Polypeptides as Inhibitors of α-Amylase

*Ueda et al.* obtained carbohydrate-containing, peptide-like substances from culture broths of *Streptomyces sp.* No. 280, a variant form of *Streptomyces flavochromogenes*. These crude substances were found to inhibit quite a number of α-glucosidases, glucosyl transferases and phosphorylases (cf. Table 11)[47-50]. By combining several methods of separation (paper chromatography, paper electrophoresis) it was possible to isolate four homogeneous glycopeptide fractions A, B, B′ and C[49]. The carbohydrate portion consists mainly of glucose and the molecular weights range from 1300 (for C) to 4000. In a purified form the inhibitors had different activities against the enzymes listed in Table 11[49].

Recently the authors were able to show that the carbohydrates contained in the inhibitors are degraded enzymatically by *Streptomyces* amylase in the course of culturing the organism (in a medium containing 3% oatmeal)[50]. An additional proteolysis during fermentation cannot be excluded. An amylase preparation was isolated from the inhibitor-producing strain and used for degradation experiments with a crude inhibitor obtained after fermentation for 24 hours (probably glycopeptide fraction A, molecular

Table 11. Enzymes which are inhibited by a crude α-glucosidase inhibitor preparation of *Streptomyces flavochromogenes* [47-50].

| Enzyme | Inhibition |
|---|---|
| Glucoamylase (Rhizopus) | strong |
| α-Amylase (saliva, human) | strong |
| α-Amylase (pancreas, human) | strong |
| α-Amylase (Bacillus) | weak |
| α-Amylase (Bacillus, "bacterial saccharogenic") | strong |
| α-Amylase (Aspergillus) | weak |
| α-Glucosidase (sucrase, intestinal mucosa of rat) | strong |
| α-D-Glucosidase (mucor) | strong |
| α-D-Glucosidase (yeast) | strong |
| Cycloamylose glucosyltransferase | strong |
| Phosphorylase A (rabbit muscle) | strong |
| Phosphorylase (potato) | strong |

---

[*] This strain was isolated by *U. Heber*, Botanisches Institut, Universität Düsseldorf (Germany).

weight approximately 4000). The products of hydrolysis were mainly maltose besides traces of maltotriose and glucose. The inhibitory activity of the resulting "residual inhibitors" remained practically unchanged against *Rhizopus* glucoamylase while slightly decreasing against amylase from hog pancreas and sucrase from rat small intestine. The inhibitory activity against phosphorylase A from rabbit muscle was lost almost completely. This effect thus appears to be dependent to a high degree on the chain length of the carbohydrate unit. Amylase from porcine pancreas and Taka-amylase showed a similar degrading effect on the inhibitor as *Streptomyces* amylase. The above-mentioned glycopeptide inhibitors A, B, B′ and C must therefore be regarded as multiple forms of a native inhibitor formed by bioconversion.

In a patent application[65] a glycopeptide obtained from culture broths of *Streptomyces calidus* DS 26320 and having a molecular weight between 10000 and 20000 is described. This preparation inhibits pancreatic amylase and the sucrase and maltase activities of an enzyme preparation from rat small intestine. Acid hydrolysis yields lysine and monosaccharides consisting mainly of glucose.

## 10. Protein Inhibitors

An inhibitor of mammalian α-amylases (HOE 467), an oligopeptide having a molecular weight of approximately 7400, was isolated from the culture broths of *Streptomyces tendae*[66, 67a]. The inhibition of α-amylase is irreversible. The only lysine residue in the molecule is possibly part of the active center of the inhibitor. Later, the inhibitor was separated into two fractions (A and B) and the amino acid sequence of the fraction HOE467A was elucidated[67b].

Two further very similar protein inhibitors free from carbohydrates and of a molecular weight of approximately 8500, Haim I and II[*], were isolated from culture broths of *Streptomyces griseosporeus* (probable identity) YM-25[71, 72]; they were isolated by precipitation with ammonium sulfate and subsequent chromatography. The inhibitors show about the same specific activity against α-amylase from porcine pancreas. They differ electrophoretically and in their isoelectric points (pH 4.0 and 3.8, respectively). In addition, pancreatic amylases from other species and human salivary amylase are inhibited, while microbial and plant glucosidases are not. The inhibition of amylase from porcine pancreas is linear up to 80% inhibition. There is no complete inhibition. By extrapolation to 100% inhibition a molar ratio of enzyme to inhibitor of 1 : 1 is found. The mechanism of inhibition is explained by a protein-protein interaction, a linkage near to the active center of the α-amylase being assumed. Both inhibitors have a similar arrangement of amino acids and a high content of aspartic acid (15.4 and 15.0 mol%, respectively) and alanine (12.8 and 12.5 mol%, respectively). They contain neither lysine nor methionine.

An α-amylase inhibitor was obtained from culture filtrates of *Streptomyces fradiae* (FERM-P 2303) by precipitation with ammonium sulfate and subsequent chromatography[54]. This preparation designated as X-2 has a molecular weight of approximately 6500 and is a carbohydrate-free acidic polypeptide with *N*-terminal aspartic acid (or asparagine).

## 11. Mechanism of Inhibition of Sucrase by Acarbose, Nojirimycin and 1-Deoxynojirimycin

The most thorough investigations into the inhibition mechanism of α-glucosidase by microbial inhibitors have so far been carried out by *Semenza et al.*[88] on the isolated sucrase-isomaltase complex from rabbit small intestine[89]. Acarbose *(5)* inhibits the sucrase activity of disaccharidase preparations from the small intestine of various species by a fully competitive mechanism[23, 88, 90, 91]. The inhibitor constants ($K_i$ values) listed in Table 12 range, depending on the species, between $10^{-6}$ and $10^{-7}$ mol/L. The $K_i$-value of component 2 *(6)* is $7.0 \times 10^{-7}$ mol/L (sucrase from porcine pancreas; method: "Dixon plot").

Table 12. Sucrase inhibitor constants ($K_i$) of acarbose *(5)*; substrate: sucrose.

| Origin of intestinal disaccharidase preparation | $K_m$ [mol/L] | $K_i$ [mol/L] | pH | Method | Ref. |
|---|---|---|---|---|---|
| Man | $1.9 \times 10^{-2}$ | $1.3 \times 10^{-6}$ | 6 | "Dixon plot" | [90, 91] |
| Hog | $1.9 \times 10^{-2}$ | $2.6 \times 10^{-7}$ | 6.25 | | [23] |
| Rat | | $\sim 4 \times 10^{-7}$ | | | [91] |
| Rabbit [a] | $8 \times 10^{-3}$ | $4.7 \times 10^{-7}$ | 6.8 | "Henderson plot" | [88] |

[a] $K_m$ value according to [92, 93].

Nojirimycin *(35)* and 1-deoxynojirimycin *(36)* are also fully competitive inhibitors of sucrase. Their $K_i$-values (enzyme preparations from rabbit; method: "Henderson plots" ("steady state" rates)) are $1.3 \times 10^{-7}$ mol/L and $3.2 \times 10^{-8}$ mol/L, respectively, at pH 6.8, the optimum of sucrase activity[88]. Consequently, these four substances can be regarded as the, so far, most potent unusually tight-binding sucrase inhibitors. Their affinity for the enzyme is 5 to 6 orders of magnitude greater than that of the substrate sucrose ($K_m$: approximately $8.0 \times 10^{-3}$ mol/L[92, 93]).

According to thorough kinetic studies[88] the reaction of *(5)*, *(35)* and *(36)* with the enzyme is slow: the steady state is reached within five minutes. In view of the structure of these inhibitors and the pH-dependence of their $K_i$-values, an interaction with the active center of the sucrase sub-unit can be assumed which would confirm the mechanism of action of sucrase suggested by *Cogoli* and *Semenza*[92]. The individual steps of the effect of sucrase are shown schematically in Figure 19. In simplified terms we can say that in a first step (A) the substrate molecule which consists of a glucose and a fructose residue is bound by the active center of the enzyme and the glucose pyranose ring is deformed. In a second step (B and C) the glucosidic oxygen function in the 1-position is protonated (possibly by the carboxyl groups in γ-position of a glutamic acid residue in the active center of the enzyme[94]). In a third step (C) the fructose residue is detached and an oxonium/carbenium cation formed which is stabilized by a carboxylate group

---

[*] Haim = hog pancreatic α-amylase inhibitor of microbes.

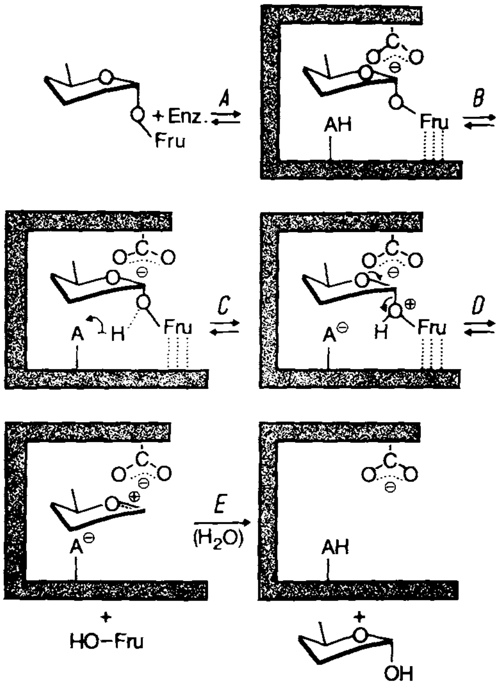


Fig. 19. Mechanism of action of enzymatic hydrolysis of sucrose by intestinal sucrase according to *Cogoli* and *Semenza* [92].

of the active center. In all probability, this is a carboxylate group in β-position of an aspartic acid residue[88,94,95]. In a last step (E) the oxonium/carbenium cation stabilized in the way described reacts with water to form D-glucopyranose—possibly *via* a covalent intermediary stage.

It is most likely that the unsaturated cyclitol unit of acarbose *(5)* interacts with the glucopyranosyl binding center of sucrase, the axially arranged nitrogen atom taking the position of the glycosyl-oxygen atom in the substrate molecule. The 4-amino-4,6-dideoxyglucose unit interacts with the so-called "aglucon" binding center. This interpretation is based on the following facts:

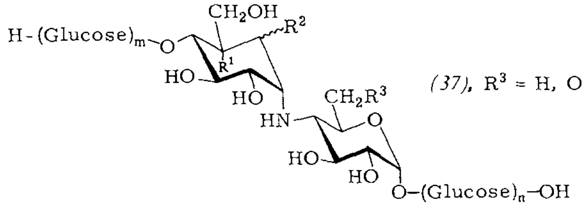
a) The unsaturated cyclitol unit has a half-chair conformation. Three of its four coplanar C atoms correspond with positions C2—C1—O—C5 in the oxonium/carbenium ion (cf. Fig. 19). However, the structural correspondence of cyclitol unit and carbenium cation is not so complete that the saturation of the double bond would lead to a drastic loss of efficacy.

b) Of greater importance for the pronounced inhibitory effect is the replacement of the glycosidic oxygen function of the substrate by the more basic NH function in the inhibitor. The p$K_a$ value of the NH group in *(5)* is about 5[96]. This means that protonation is unlikely to occur at any of the pH values tested (5.85; 6.8; 7.45)[88]. Since this group corresponds with the glycosidic oxygen of the substrate molecule, it will probably interact with the same carboxyl group of the active center. The p$K_a$ value of that group is about 7.3[88]. Actually, the affinity of acarbose *(5)* decreases when the carboxyl group is deprotonated ($K_i$ at pH 6.8: $4.7 \times 10^{-7}$ mol/L compared to $1.0 \times 10^{-6}$ mol/L at pH 7.45)[88].

c) Also important for the high affinity for the enzyme is a marked interaction of the 4-amino-4,6-dideoxyglucose residue in *(5)* with the "aglucon" binding center, for valienamine *(16)* is a weaker inhibitor of sucrase than acarbose by 2 to 3 orders of magnitude. In addition, the α(1→4)-like linkage of cyclitol unit and amino sugar contributes to a specifity of inhibition. Consequently, acarbose inhibits neither the isomaltase sub-unit—which is closely related to the sucrase sub-unit—nor the similarly acting β-glucosidase from almonds to any appreciable degree.

All these findings are consistent with the concept of the mechanism of action of sucrase and demonstrate that the pseudosaccharide "core" of the individual members of the homologous acarbose series is essential to the inhibitory effect.

On account of the results of our own studies (see Section 5) with products of the hydrogenation of acarbose *(5)*[73] and the properties of saturated microbial inhibitors[72b] related to acarbose *(5)* described by Japanese authors, the double bond has probably only quantitative significance. According to the present state of knowledge and further references in the patent literature[68] the general structural formula *(37)* follows for these pseudo-oligosaccharidic α-glucosidase inhibitors; here $R_1 = H$, $R_2 = H$ or OH, or $R_1$ and $R_2$ form a double bond, and $R_3 = H$ or OH.



*(37)*, $R^3$ = H, OH

Nojirimycin *(35)* and 1-deoxynojirimycin *(36)* have a similar molecular size and, to a certain extent, also a structure similar to D-glucose—in contrast to acarbose *(5)*. They inhibit quite a number of both α-glucopyranosidases (including isomaltase from small intestine[*], cf. Table 10) and β-glucopyranosidases[59,60,97,98]. They are likely to react with that part of the active center of sucrase which is the "glucopyranosyl subcenter", and neither with the "aglucon subcenter" nor the carboxyl group that protonates the glucosidic oxygen (p$K_a$ approximately 7.3). Accordingly, the $K_i$ values for both substances are practically equal at pH values 6.8 and 7.45[88]. On the basis of the data availa-

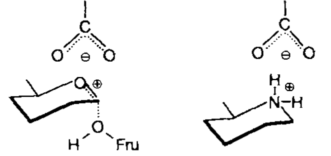


Fig. 20. Binding of the protonated 1-deoxynojirimycin molecule *(36)* to a carboxylate group of the active center of sucrase, in comparison with the stabilization of the oxonium/carbenium cation transition state of the substrate (see also Fig. 19).

---

[*] $K_i$ for 1-deoxynojirimycin *(36)*: $4.8 \times 10^{-8}$ mol/L at pH 6.25 (isomaltase from porcine small intestine, method: "Dixon plot").

ble the mechanism of action of nojirimycin *(35)* and deoxynojirimycin *(37)* is not as easy to explain as that of acarbose *(5)*. After a thorough discussion of all facts, including also the results obtained with other weaker inhibitors of sucrase (such as D-glucono-1,5-lactone and D-glucono-1,5-lactam), and considering hypotheses possibly applicable, *Semenza et al.*[88] arrive at the conclusion that *(35)* and *(36)* are bound to the active center in a non-protonated form and are subsequently protonated. In this case, a diagram as shown in Figure 20 could be drawn up for *(36)*.

## 12. Pharmacological and Clinical Aspects

For a long time dietetic rules have been a basic treatment of metabolic diseases such as diabetes mellitus, obesity or Type IV hyperlipoproteinaemia. As a rule, these regimens require a reduced intake of carbohydrates and a partition of daily meals into many small portions eaten through the day. If these instructions are followed, hyperglycaemia (excessive blood glucose values), hyperinsulinaemia (excessive blood insulin values) and hypertriglyceridaemia (increased triglyceride blood levels) can be prevented in many cases. However, in daily practice the observance of such restrictions is often hindered by unfavorable circumstances and inner resistance[45].

Carbohydrates are a main component of human food, 80—90% consisting of starch and sucrose[99]. In general more than 250 g of di- and polysaccharides—as is described in detail in Sections 2 and 3—must be enzymatically split in the intestinal tract before they can be utilized by the organism. According to the concept by *Puls*[19,20,45]—referred to in the introduction—a pharmacological interference with the intestinal carbohydrate digestion by suitable α-glucosidase inhibitors should be a feasible way to regulate and retard carbohydrate digestion, control the rate of absorption of monosaccharides and by this way influence the intermediary metabolism of the carbohydrates. As already mentioned in the introduction this concept was supported by an α-amylase inhibitor (BAY d 7791), a protein obtained from wheat germ flour[17,18], by experimental and clinico-pharmacological studies[17,19,77], which induced the search for more potent inhibitors of α-glucosidases. The pseudo-oligosaccharidic inhibitors of the general formula *(4)* proved to be particularly suitable. The results obtained with various homologues from *in vivo* experiments with rats are compared to the *in vitro* inhibitory activities against α-amylase and sucrase (Table 13, see also Table 7)[43,45,74,77].

Table 13. Inhibition of α-glucosidase activity *in vitro* and *in vivo* by acarbose *(5)* and homologues of the general formula *(4)* [45].

| Component | *In vitro* 50% inhibition of 100 mU α-amylase [a] [ng] | *In vivo* $ED_{50}$ [b] with starch [mg/kg rat] | *In vitro* 50% inhibition of 10 mU saccharase [a] [ng] | *In vivo* $ED_{50}$ with sucrose [mg/kg rat] |
|---|---|---|---|---|
| 2 | 855 | 1.1 | 560 | 1.0 |
| 3 (acarbose) | 680 | 1.5 | 74 | 1.1 |
| 4 | 1135 | 1.4 | 455 | 3.3 |
| 5 | 4.7 | 1.0 | 700 | 10.0 |
| 6 | 2.8 | 0.4 | 700 | ~25.5 |
| BAY e 4609 | 14.5 | 6.1 | 60000 | >75.0 |

[a] See footnote [b], Table 7. [b] $ED_{50}$ is the dose necessary to reduce the integrated postprandial increase in blood glucose by 50% [100].

The *in vivo* activity of the inhibitors is determined by loading tests with rats using the substrates starch and sucrose. After the administration of a defined amount of carbohydrates postprandial blood glucose concentrations are determined at various times, plotted and integrated.

The blood glucose concentrations of rats treated with physiological saline are used as a baseline. The *in vivo* activity is expressed numerically as $ED_{50}$. Comparison of the data for the *in vivo* activity in the sucrose loading tests for the first five members of the homologous series and the high-molecular preparation BAY e 4609 (given in Table 13) with the *in vitro* data of sucrase inhibitors shows that *in vitro* and *in vivo* activities are very much parallel—with the exception of component 2 *(6)*, the values of which cannot be satisfactorily explained at present.

Acarbose *(5)* stands out against the other compounds as the most effective inhibitor both *in vivo* and *in vitro*. It is striking that—according to Table 13—components 2—6 inhibit the degradation of starch *in vivo* to a very similar degree while there are considerable differences in the inhibition of α-amylases *in vitro* (Fig. 19 and Table 7). We can conclude from this that the *in vitro* inhibition test, using pure α-amylase as the enzyme, does not reflect the real course of the intestinal degradation of starch *in vivo*. As already mentioned in Section 3, the intestinal degradation of starch is a complex process involving a great number of enzymes. Table 7, according to which components 2—5 and especially acarbose *(5)* inhibit maltase, "dextrinase" and glucoamylase to a considerable degree, gives an idea of feasible mechanisms of the *in vivo* effects. If it were possible to exactly define the involvement of the various enzymatic activities in the *in vivo* degradation of starch to glucose, one might be able to explain the mechanism of *in vivo* action of acarbose and its homologues. It can be seen from Table 13 that the $ED_{50}$ for acarbose *(5)* in the starch loading test is 1.5 mg/kg in the rat, thus only slightly higher than the $ED_{50}$ determined in the sucrose loading test. This finding contributed to our selecting acarbose for clinical trials and thus for practical use. On account of its broader spectrum of inhibitory action *in vivo* acarbose proved to be clearly superior to the α-amylase inhibitor BAY e 4609 which was also subjected to in-depth pharmacological[77] and clinical studies[78].

Acarbose does not only produce a dose-dependent inhibition of the postprandial rise in blood sugar values in rats in starch and/or sucrose loading tests, but also inhibits the reactive postprandial hyperinsulinaemia[45,100]. Therapy-related clinico-pharmacological studies on healthy test persons have yielded similar results as the rat experiments described above[45,75,100].

Moreover, acarbose was found to reduce the weight of genetically obese "Zucker" rats that had received a sucrose-containing diet—in a dose-dependent manner—; this can be attributed to a reduced food intake by the animals treated. These animals also had significantly lower serum levels of triglycerides and free fatty acids. The reduction of carbohydrate-induced hyperlipoproteinaemia is considered to be due to a decrease in the excessive secretion of high-triglyceride lipoproteins, the so-called "VLDL fraction", from the liver. Analyses of the animals' trunks (carcasses) revealed a reduced accumulation of fat in the body but unchanged protein content[45,100] in comparison with controls.

Acarbose *(5)* is the clinically most thoroughly tested compound especially in the indication diabetes mellitus. The results of the numerous large-scale studied carried out so far can be summarized as follows[75,76,101]:

Acarbose clearly improves the metabolic condition of insulin-dependent diabetics. Blood glucose levels are lowered so that the dose of insulin can be reduced. However, if there is a deficiency of insulin, acarbose cannot replace insulin. In non-insulin-dependent diabetics the improvement of the metabolic condition is the greater the longer acarbose is administered. On account of its mechanism of action, acarbose may produce transient intestinal symptoms which, however, are usually tolerated by the patient. These symptoms are reduced, *i.e.* tolerability improves, especially when the drug is taken over a prolonged period. Haematological and clinical-biochemical studies have furnished evidence for the preparation's objectively very good tolerability. Acarbose—which has not yet been put on the market—can thus be regarded as a new active principle in the treatment of diabetes mellitus. The efficacy of this preparation in hyperlipoproteinaemia and adiposity is under clinical investigation.

In order to establish additional indications for microbial $\alpha$-glucosidase inhibitors investigations were performed with test persons into the inhibition of oral starch degradation as effected mainly by salivary amylase[102]. It was shown that the addition of the $\alpha$-amylase inhibitor BAY e 4609 to starch results in a reduction of oral starch degradation. After administration of starch, telemetry can be used to follow the rapid drop of pH which is caused by the bacteria within the "plaques" on the teeth. A smaller pH drop was observed in the presence of the amylase inhibitor. This effect was amplified by the combination of BAY e 4609 with acarbose. These results support the idea that microbial $\alpha$-glucosidase inhibitors might reduce the cariogenic potential of starch during its degradation in the oral cavity[102].

We have seen by the example of acarbose and the other $\alpha$-glucosidase inhibitors discussed in this article that new active substances from the far-from-exhausted reservoir of microbial secondary metabolites can be discovered by means of practice-related screening tests.

*We are indebted to Prof. Dr. G. Semenza, Biochemical Laboratory of ETH Zürich, for the extremely valuable discussions of the mechanism of action of the $\alpha$-glucosidase inhibitors and for making his manuscript[88], still unpublished when the present paper was submitted, available to us. We also express our gratitude to Dr. J. J. Marshall, Miles Laboratories Inc., Elkhart, Indiana (USA) for permitting the use of the data listed in Tables 8 and 9 which are part of a manuscript[87] still unpublished when this paper was written.*

Received: January 19, 1981 [A 372 IE]
German version: Angew. Chem. 93, 738 (1981)

[1] *H. Fritz, H. Tschesche:* Proceedings of the International Research Conference on Proteinase Inhibitors, de Gruyter, Berlin 1971.

[2] *H. Fritz, H. Tschesche, L. J. Greene, E. Truscheit:* Bayer-Symposium V, Proteinase Inhibitors, Springer, Berlin 1974.

[3] Review: *H. Tschesche,* Angew. Chem. *86,* 21 (1974); Angew. Chem. Int. Ed. Engl. *13,* 10 (1974).

[4] Review: *M. Laskowski, Jr., I. Kato,* Annu. Rev. Biochem. *49,* 593 (1980).

[5] *C. Fermi, L. Pernossi,* Z. Hyg. Infektionskr. *18,* 83 (1894).

[6] Summary by *N. Heimburger, H. Haupt, H. G. Schwick* in [1], p. 1.

[7] *T. Chrzaszcz, J. Janicki,* Biochem. Z. *260,* 354 (1933); *264,* 193 (1933).

[8] *E. Kneen, R. M. Sandstedt,* J. Am. Chem. Soc. *65,* 1247 (1943).

[9] *E. Kneen, R. M. Sandstedt,* Arch. Biochem. *9,* 235 (1946).

[10] *D. E. Bowman,* Science *102,* 358 (1945).

[11] *A. Hernandez, W. G. Jaffé,* Acta Cient. Venez. *19,* 183 (1968); *W. G. Jaffé, R. Moreno, V. Wallis,* Nutr. Rep. Int. *7,* 169 (1973).

[12] *J. J. Marshall, C. M. Lauda,* J. Biol. Chem. *250,* 8030 (1975).

[13] *J. R. Powers, J. R. Whitaker,* J. Food Biochem. *1,* 217, 239 (1977).

[14] *K.-H. Pick, G. Wöber,* Z. Physiol. Chem. *359,* 1371, 1379 (1978); Prep. Biochem. *9,* 293 (1979).

[15] *M. N. Rao, K. S. Shurpalekar, O. E. Sundaravalli,* Indian J. Biochem. *4,* 185 (1967); *7,* 241 (1970).

[16] Reviews: a) *J. J. Marshall:* Physiological Effects of Food Carbohydrates in ACS Symp. Ser., Vol. 15, Am. Chem. Soc., Washington 1975, p. 244ff.; b) *V. Buonocore, T. Petrucci, V. Silano,* Phytochemistry *16,* 811 (1977); c) Proc. 3. Int. Congr. Obesity, Satellite Symp. No. 7, Siena (Italien), October 13.–15, 1980; Regulators of Intestinal Absorption in Obesity, Diabetes and Nutrition; d) *V. Buonocore, E. Poerio, V. Silano* in [16c], Vol. 1, p. 87; Abstract see: La Clinica Dietologica *7,* 429 (1980). Recent works: e) *P. E. Granum, J. R. Whitaker,* J. Food Biochem. *1,* 385 (1977); f) *P. E. Granum, ibid. 2,* 103 (1978); g) *M. Richardson, N. Kashlan* in [16c], Vol. 1, p. 103; h) *C. M. O'Connor, M. D. O'Donnell, K. F. McGeeney* in [16c], Vol. 2, p. 119; Abstract see: La Clinica Dietologica *7,* 443 (1980); i) *C. M. O'Connor, K. F. McGeeney,* Biochim. Biophys. Acta *658,* 387, 397 (1981).

[17] *D. D. Schmidt, W. Puls,* DOS 2003934 (1971) (German priority January 26, 1970), Bayer AG.

[18] *E. Truscheit, D. D. Schmidt, A. Arens, H. Lange, W. Wingender* in [16c], Vol. 2, p. 157; Abstract see: La Clinica Dietologica *7,* 451 (1980).

[19] *W. Puls, U. Keup,* Diabetologia *9,* 97 (1973).

[20] *W. Puls,* Habilitationsschrift, Universität Düsseldorf 1980.

[21] *W. Frommer, W. Puls, D. Schäfer, D. D. Schmidt,* DOS 2064092 (1972) (German priority December 28, 1970), Bayer AG.

[22] *W. Frommer, B. Junge, U. Keup, L. Müller, W. Puls, D. D. Schmidt,* DOS 2347782 (1975) (German priority September 22, 1973), Bayer AG.

[23] *D. D. Schmidt, W. Frommer, B. Junge, L. Müller, W. Wingender, E. Truscheit, D. Schäfer,* Naturwissenschaften *64,* 535 (1977).

[24] *H. Umezawa:* Enzyme Inhibitors of Microbial Origin, University Park Press, Baltimore 1972.

[25] *W. Frommer, B. Junge, L. Müller, D. D. Schmidt, E. Truscheit,* Planta Med. (J. Med. Plant Res.) *35,* 195 (1979).

[26] *W. Wingender* in [2], p. 548; *T. Aoyagi, H. Umezawa* in *E. Reich, D. B. Rifkin, E. Shaw:* Proteases and Biological Control, Cold Spring Harbor Conf. Cell Proliferation *2,* 429 (1975); *H. Umezawa, T. Takita, T. Shiba:* Bioactive Peptides Produced by Microorganisms, Wiley, New York 1978; *T. Aoyagi, H. Umezawa* in *Lj. Vitale, V. Simeon:* Industrial and Clinical Enzymology, FEBS Symp. *61,* 89 (1980).

[27] *W. J. Whelan,* Biochem. J. *122,* 609 (1971).

[28] *D. J. Manners,* Essays Biochem. *10,* 37 (1974).

[29] *J. J. Marshall,* Adv. Carbohydr. Chem. Biochem. *30,* 257 (1974).

[30] *Z. Gunja-Smith, J. J. Marshall, C. Mercier, E. E. Smith, W. J. Whelan,* FEBS Lett. *12,* 101 (1970).

[31] *J. W. Mayo, D. M. Carlson,* Arch. Biochem. Biophys. *163,* 498 (1974).

[32] *P. Cozzone, G. Marchis-Mouren,* Biochim. Biophys. Acta *257,* 222 (1972).

[33] *P. Bernfeld,* Methods Enzymol. *1,* 149 (1955).

[34] *R. Ruyssen, A. Lauwers:* Pharmaceutical Enzymes – Properties and Assay Methods, p. 66, Story-Scientia, Gent 1978.

[35] *K. Fossum, J. R. Whitaker,* J. Nutr. *104,* 930 (1974).

[36] *J. J. Marshall, C. M. Lauda,* Stärke *27,* 274 (1975).

[37] *G. Semenza,* Enzymes Biol. Membr. *3* (Membrane Transport), 349 (1976).

[38] *J. K. Kelly, D. H. Alpers,* Biochim. Biophys. Acta *315,* 113 (1973).

[39] *K. A. Conklin, K. M. Yamashiro, G. M. Gray,* J. Biol. Chem. *250,* 5735 (1975).

[40] *J. J. Marshall, C. M. Sturgeon, W. J. Whelan,* Anal. Biochem. *82,* 435 (1977).

[41] *G. Semenza,* Carbohydr. Metab. Its Disord., Vol. III, Academic Press, London 1981, in press.

[42] *A. Dahlqvist,* Enzymol. Biol. Clin. *11,* 52 (1970).

[43] a) *U. Brodbeck:* Enzyme Inhibitors (Proc. Meet., Basel, March 20–21, 1980), Verlag Chemie, Weinheim 1980; b) *L. Müller, B. Junge, W. Frommer, D. D. Schmidt, E. Truscheit* in [43a], p. 106.

[44] *D. D. Schmidt, W. Frommer, L. Müller, E. Truscheit,* Naturwissenschaften *66,* 584 (1979).

[45] *W. Puls, U. Keup, H. P. Krause, L. Müller, D. D. Schmidt, G. Thomas, E. Truscheit,* Front. Horm. Res. *7,* 235 (1980).

[46] *D. D. Schmidt, W. Frommer, B. Junge, L. Müller, E. Truscheit, W. Wingender* in [16c], Vol. 1, p. 203; Abstract see: La Clinica Dietologica *7,* 449 (1980).

[47] *S. Ueda, Y. Koba,* US-Pat. 3806421 (1974) (Jap. priority May 31, 1971), Hayashibara Biochemical Laboratories; Agric. Biol. Chem. *37,* 2025 (1973).

[48] *Y. Koba, M. Najima, S. Ueda,* Agric. Biol. Chem. *40,* 1167 (1976).

[49] *S. Ueda, Y. Koba, H. Chaen,* Carbohydr. Res. *61,* 253 (1978).

[50] *H. Chaen, S. Ueda,* Agric. Biol. Chem. *43,* 2265 (1979).

[51] *S. Murao,* US-Pat. 4010258 (1977) (Jap. priority March 15, 1974), Ajinomoto Co., Inc. und Eisai Co., Ltd.; *S. Murao, K. Ohyama,* Agric. Biol. Chem. *39,* 2271 (1975).

[52] *S. Murao, K. Ohyama, S. Ogura,* Agric. Biol. Chem. *41,* 919 (1977); *K. Ohyama, S. Murao,* ibid. *41,* 2221 (1977).

[53] *S. Murao, K. Ohyama,* Agric. Biol. Chem. *43,* 679 (1979).

[54] *H. Goto, T. Inukei, M. Amano,* Japanische Offenlegungsschrift 7577594 (1975) (Jap. priority November 20, 1973), Amano Pharmaceutical Co., Ltd.

[55] *W. Frommer, L. Müller, D. D. Schmidt, W. Puls, H. P. Krause, U. Heber,* DOS 2658563 (1978) (German priority December 23, 1976).

[56] *S. Inouye, T. Tsuruoka, T. Niida,* J. Antibiot. *19,* 288 (1966).

[57] *H. Paulsen, I. Sangster, K. Heyns,* Chem. Ber. *100,* 802 (1967).

[58] *S. Inouye, T. Tsuruoka, T. Ito, T. Niida,* Tetrahedron *24,* 2125 (1968).

[59] *T. Niwa, S. Inouye, T. Tsuruoka, Y. Koaze, T. Niida,* Agric. Biol. Chem. *34,* 966 (1970).

[60] *E. T. Reese, F. W. Parrish, M. Ettlinger,* Carbohydr. Res. *18,* 381 (1971).

[61] *H. Murai, K. Ohata, H. Enomoto, Y. Yoshikuni, T. Kono, M. Yagi,* DOS 2656602 (1977) (Jap. priority December 29, 1975), Nippon Shinyaku Co., Ltd.

[62] *S. Matsumura, H. Enomoto, Y. Aoyagi, Y. Ezure, Y. Yoshikuni, M. Yagi,* DOS 2850467 (1979) (Jap. priority November 21, 1977), Nippon Shinyaku Co., Ltd.

[63] *S. Murao, S. Miyata,* Agric. Biol. Chem. *44,* 219 (1980).

[64] *K. Ueda, S. Gochyo,* Japanische Offenlegungsschrift 51-54990 (1976) (Jap. priority November 5, 1974), Ajinomoto Co., Ltd.

[65] *A. Belloc, J. Florent, J. Lunel, D. Mancy, J.-C. Palla,* DOS 2702417 (1977) (French priority January 22, 1976), Rhône-Poulenc Industries.

[66] *V. Oeding, W. Pfaff, L. Vértesy, H.-L. Weidemüller,* DOS 2701890 (1978) (German priority January 19, 1977), Hoechst AG.

[67] a) *L. Vértesy, V. Oeding, R. Bender, G. Nesemann, D. Sukatsch, K. Zepf* in [16c], Vol. 2, p. 269; Abstract see: La Clinica Dietologica *7,* 452 (1980); b) *H. Aschauer, L. Vértesy, G. Braunitzer,* Z. Physiol. Chem. *362,* 465 (1981).

[68] *M. Otani, T. Saito, S. Satoi, J. Mizoguchi, N. Muto,* DOS 2855409 (1979) (Jap. priority December 28, 1977), Toyo Jozo Co., Ltd.

[69] *K. Kangouri, S. Namiki, T. Nagate, K. Sugita, S. Omura,* US-Pat. 4197292 (1980) (Jap. priority February 10, 1978), Taisho Pharmaceutical Co.

[70] *Y. Suhara, K. Yokose, K. Watanabe, K. Ogawa,* DOS 2905649 (1979) (Brit. priority February 14, 1978), Hoffmann-La Roche und Co. AG.

[71] *S. Murao, A. Goto, Y. Matsui, K. Ohyama,* Agric. Biol. Chem. *44,* 1679 (1980).

[72] a) *S. Murao, A. Goto, M. Arai,* Agric. Biol. Chem. *44,* 1683 (1980); b) *S. Omoto, J. Itoh, T. Niwa, T. Shomura, S. Niizato, S. Inouye,* DOS 3035193 A1 (1981) (Jap. priority September 19, 1979), Meiji Seika Kaisha Ltd.

[73] a) *B. Junge, H. Böshagen, J. Stoltefuß, L. Müller* in [43a], p. 123; b) *B. Junge, H. Böshagen, F. Heiker, L. Müller, J. Stoltefuss:* Lecture, Fall Meet. Am. Chem. Soc., New York 1981.

[74] *W. Puls, U. Keup, H. P. Krause, G. Thomas* in [16c], Vol. 1, p. 231; Abstract see: La Clinica Dietologica *7,* 458 (1980).

[75] *K. Schöffling, I. Hillebrand, P. Berchtold,* Front. Horm. Res. *7,* 248 (1980).

[76] *P. Berchtold, I. Hillebrand, K. Boehme, R. Aubell, L. Nagel, H. Schulz* in [16c], Vol. 1, p. 261; Abstract siehe: La Clinica Dietologica *7,* 426 (1980).

[77] *W. Puls, U. Keup, H. P. Krause, K. O'Dea, R. Sitt* in [16c], Vol. 1, p. 153; Abstract see: La Clinica Dietologica *7,* 458 (1980).

[78] *P. Berchtold, N. H. Kiesselbach* in [16c], Vol. 1, p. 181; Abstract see: La Clinica Dietologica *7,* 426 (1980).

[79] *W. Frommer, B. Junge, U. Keup, L. Müller, W. Puls, D. D. Schmidt,* DOS 2347798 (1975) (German priority September 22, 1973), Bayer AG.

[80] *W. Frommer, W. Puls, D. D. Schmidt,* DOS 2209832 (1973) (German priority March 1, 1972), Bayer AG.

[81] *S. Horii, T. Iwasa, E. Mizuta, Y. Kameda,* J. Antibiot. *24,* 59 (1971).

[82] Revidierte Struktur von Validamycin A: *T. Suami, S. Ogawa, N. Chida,* J. Antibiot. *33,* 98 (1980).

[83] *S. Horii, Y. Kameda,* J. Chem. Soc. Chem. Commun. *1972,* 747.

[84] a) *Y. Kameda, S. Horii,* J. Chem. Soc. Chem. Commun. *1972,* 746; b) *Y. Kameda, N. Asano, M. Yoshikawa, K. Matsui,* J. Antibiot. *33,* 1575 (1980).

[85] *W. Frommer, W. Puls, D. D. Schmidt,* DOS 2209833 (1973) (German priority March 1, 1972), Bayer AG.

[86] *W. Frommer, W. Puls, D. D. Schmidt,* DOS 2209834 (1973) (German priority March 1, 1972), Bayer AG.

[87] *H. Hidaka, T. Takaya, J. J. Marshall,* J. Jpn. Starch Sci. *27,* 114 (1980).

[88] *G. Hanozet, H.-P. Pircher, P. Vann, B. Oesch, G. Semenza,* J. Biol. Chem. *256,* 3703 (1981).

[89] *H. Sigrist, P. Ronner, G. Semenza,* Biochim. Biophys. Acta *406,* 433 (1975).

[90] *W. F. Caspary,* Lancet *1978,* 1231.

[91] *W. F. Caspary, S. Graf,* Res. Exp. Med. *175,* 1 (1979).

[92] *A. Cogoli, G. Semenza,* J. Biol. Chem. *250,* 7802 (1975).

[93] *G. Semenza, A.-K. von Balthazar,* Eur. J. Biochem. *41,* 149 (1974).

[94] *H. Braun, A. Cogoli, G. Semenza,* Eur. J. Biochem. *52,* 475 (1975).

[95] *A. Quaroni, E. Gershon, G. Semenza,* J. Biol. Chem. *249,* 6424 (1974).

[96] Nach Untersuchungen von *W. Gau,* Bayer AG, Wuppertal, persönliche Mitteilung.

[97] *A. K. Grover, R. J. Cusley,* Biochim. Biophys. Acta *482,* 109 (1977).

[98] *G. Legler, K.-R. Roeser, H.-K. Illig,* Eur. J. Biochem. *101,* 85 (1979).

[99] Ernährungsbericht 1976, Deutsche Gesellschaft für Ernährung, Frankfurt 1976.

[100] *W. Puls, U. Keup, H. P. Krause, G. Thomas, F. Hoffmeister,* Naturwissenschaften *64,* 536 (1977).

[101] *I. Hillebrand, P. Berchtold* in [43a], p. 153.

[102] *J. E. Mörmann, H. R. Mühlemann,* Lebensmittelwiss. Technol. *14,* 166 (1981).

# 4-Aryldihydropyridines, a New Class of Highly Active Calcium Antagonists

**By Friedrich Bossert, Horst Meyer, and Egbert Wehinger**[*]

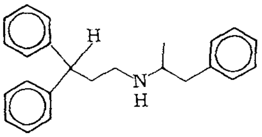
*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

The aryldihydropyridines first prepared by *Hantzsch* almost 100 years ago have recently been found to be highly effective calcium antagonists with suitable pharmacological profiles. An illustrative example is dimethyl-1,4-dihydro-2,6-dimethyl-4-(*o*-nitrophenyl)pyridine-3,5-dicarboxylate (Nifedipine) which is already employed therapeutically. This substance lowers the frequency of attack of angina pectoris and reduces blood pressure. The discovery of the therapeutic activity of this class of substances initiated renewed investigation of the Hantzsch condensation and the synthesis of numerous 4-aryldihydropyridines and related compounds. Qualitative and quantitative structure/activity relationships of these substances can be deduced from their biological data.

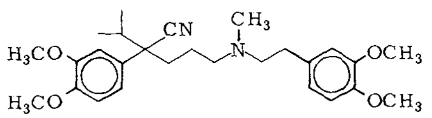
## 1. Introduction: What is a Calcium Antagonist?

"Calcium antagonists" are inhibitors of electromechanical coupling which cause a dose-dependent reduction of transmembranal $Ca^{2+}$ influx into the cells of the contractile system such that the $Ca^{2+}$-dependent myofibril-ATPase converts less phosphate-bound energy into mechanical work. Accordingly, the oxygen demand of the beating heart and the contractile tonus of the coronary and the peripheral resistance vessels are reduced. This mechanism of action results in three fundamental effects[1,2]:

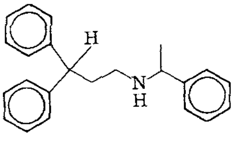
1) the direct damping of myocardial work-load metabolism,
2) an increase in blood supply to the coronary vessels,
3) a reduction in arterial flow resistance.



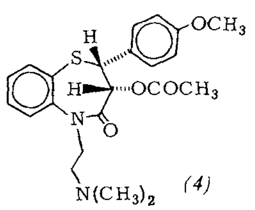
*(1)*



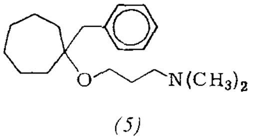
*(2)*



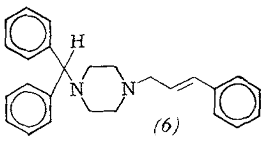
*(3)*



*(4)*



*(5)*



*(6)*

The vasodilating effect of calcium antagonists finds clinical application especially in the treatment of oxygen deficiency diseases of the heart such as angina pectoris. Since they reduce arterial flow resistance, calcium antagonists with suitable pharmacological profiles are also of interest in the treatment of hypertension[3,4,5].

"Specific" calcium antagonists, *i.e.* drugs in which the calcium antagonistic effect is the major one both qualitatively and quantitatively, are prenylamine *(1)*[6,7], verapamil *(2)*[6,7], fendiline *(3)*[8], diltiazem *(4)*[9], bencyclan *(5)*[10] and cinnarizine *(6)*[11].

From a chemist's point of view it is noticeable that all these drugs contain an aryl moiety with a basic alkyl or arylalkyl side chain as essential active structure[12].

## 2. Nifedipine, a Highly Active Calcium Antagonist with 4-Aryldihydropyridine Structure

A completely new, highly active, calcium antagonistic structure without the essential basic side chain was found in the form of the 4-aryldihydropyridines[13].

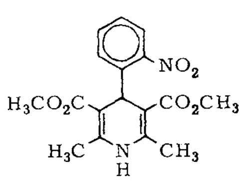
As a class of chemical compounds 1,4-dihydropyridine-3,5-dicarboxylates have been known since 1882 when *Hantzsch* discovered them as stable intermediates in the pyridine synthesis which bears his name[14,15]. In spite of their ready accessibility and the significance of dihydropyridines as coenzymes of numerous dehydrogenases, this class of compounds found little interest up until the mid-sixties[16]. Then, the vasodilating properties and hence the pharmacological qualities of numerous 4-aryldihydropyridine-3,5-dicarboxylates first became known and widely investigated as a result of work in our laboratories[13] and, independently, at the US pharmaceutical company Smith, Kline & French[17].

One member of this class of compounds, nifedipine *(7)* (Adalat®)[*,18,19] has already passed through clinical trials and is now in therapeutic use in many countries.

---

[*] Dr. F. Bossert, Dr. H. Meyer [+], Dr. E. Wehinger
Chemisch-wissenschaftliches Laboratorium Pharma der Bayer AG
Postfach 101709, D-5600 Wuppertal 1 (Germany)
[+] Author to whom correspondence should be addressed.

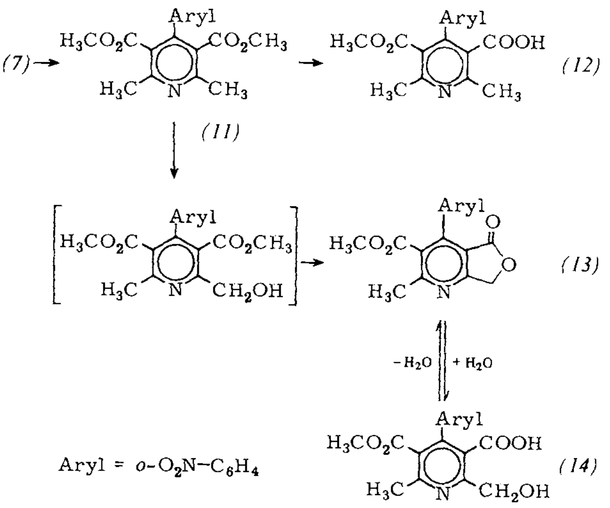
[*] Adalat® = Bayer AG trademark, Leverkusen, W. Germany.



Nifedipine *(7)*

*Fleckenstein et al.* showed that nifedipine is a highly active inhibitor of transmembranal calcium influx, which displays its calcium antagonistic effect in isolated vessels even at dilution levels of a billionth[20]. Clinical studies confirmed the results of animal experiments: well-tolerated by the patient, nifedipine reduces the frequency of attacks in angina pectoris in a highly significant manner at very low doses (individual dose 5—20 mg/person)[21,22]. Furthermore this drug can also be used in the treatment of hypertension[23].

The manufacturing process for nifedipine *(7)* starts with 2-nitrotoluene which, after reaction with diethyl oxalate and subsequent hydrolysis, yields (2-nitrophenyl)pyruvate *(8)*. This product *(8)* can be dihalogenated with technical sodium hyperchlorite and cleaved in a haloform reaction to give 2-nitrobenzal chloride *(9)* in one step. Hydrolysis of *(9)* in sulfuric acid yields 2-nitrobenzaldehyde *(10)*, which is otherwise difficultly accessible on a technical scale[24]. This aldehyde is then condensed with methyl acetoacetate and ammonia in methanol according to *Hantzsch* to give nifedipine *(7)*.

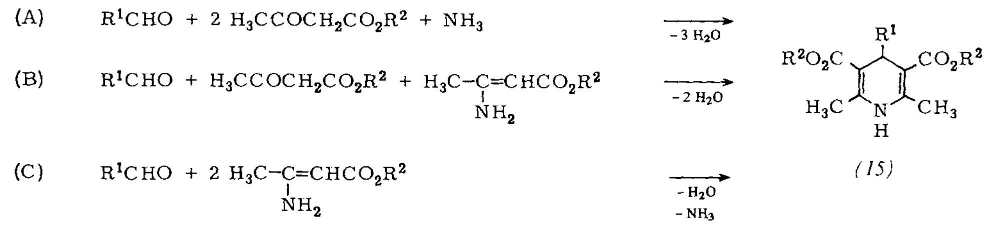


Aryl = $o$-$O_2N$–$C_6H_4$

## 3. Synthesis of 4-Aryl-1,4-dihydropyridines and Related Compounds

### 3.1. Variants of the Hantzsch Condensation

Apart from the classical Hantzsch synthesis, *i.e.* the one-pot condensation of aldehyde and β-ketoester (acetoacetate) in the molar ratio 1 : 2 with ammonia [eq. (A)], two further variations [eq. (B) and (C)] of the synthesis of 1,4-dihydropyridine-3,5-dicarboxylates *(15)* are known[27,28]. The standard conditions are heating under reflux for 6—20 h in a lower alcohol solvent.



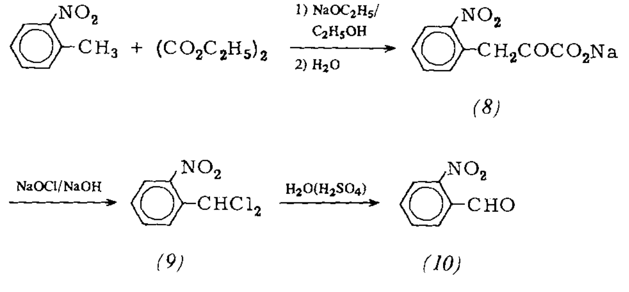
(A) $R^1CHO + 2\ H_3CCOCH_2CO_2R^2 + NH_3 \xrightarrow[-3\,H_2O]{}$

(B) $R^1CHO + H_3CCOCH_2CO_2R^2 + H_3C{-}\underset{NH_2}{C}{=}CHCO_2R^2 \xrightarrow[-2\,H_2O]{}$

(C) $R^1CHO + 2\ H_3C{-}\underset{NH_2}{C}{=}CHCO_2R^2 \xrightarrow[-H_2O,\ -NH_3]{}$

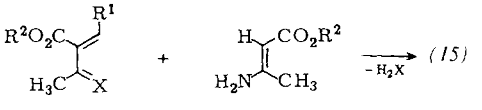
*(15)*

The hydroxycarboxylic acid *(14)*, in equilibrium with the corresponding lactone *(13)*[25], and the 2,6-dimethylpyridinecarboxylic acid *(12)*[26] have been characterized as end-products in the biotransformation of nifedipine. Oxidation to the pharmacologically inactive pyridine derivative *(11)* may be assumed to be the primary step in metabolic degradation.



$(10) + 2\ H_3CCOCH_2CO_2CH_3 + NH_3 \xrightarrow[-3\,H_2O]{} (7)$

The crucial step in all three variations is the cyclizing Michael addition of aminoisocrotonate *(17)* to the Knoevenagel condensation product *(16)*.

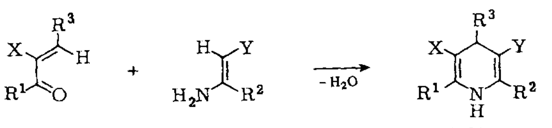


*(16)*, X = O, NH *(17)*

### 3.2. Controlled Cyclizing Michael Addition; Synthesis of Enantiomeric Dihydropyridines

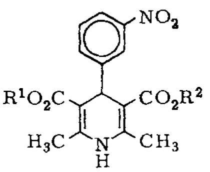
The intermediacy of *(16)* enables the synthesis of 1,4-dihydropyridines *(20)* with non-identical substituents in the 2,6- or 3,5-positions. Apart from the ester function other acceptor substituents such as oxo-, cyano-, sulfonyl-, or nitro-groups can stabilize the 1,4-dihydropyridine system.

The following products under clinical development are examples of 1,4-dihydropyridines with non-identical ester functions, which are accessible *via* cyclizing Michael reac-



(18) (19) (20)

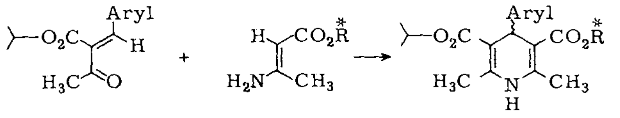
tions: nimodipine (21) (cerebral vasodilator)[29,30], nitrendipine (22) (antihypertensive)[31] and nicardipine (23) (cerebral vasodilator)[32]. Nicardipine is manufactured by the Japanese pharmaceutical company, Yamanouchi Pharm, which has been working intensively in the 1,4-dihydropyridine area since 1973[33].



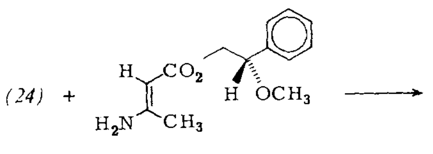
| | $R^1$ | $R^2$ |
|---|---|---|
| (21) | $CH(CH_3)_2$ | $(CH_2)_2OCH_3$ |
| (22) | $CH_3$ | $C_2H_5$ |
| (23) | $CH_3$ | $(CH_2)_2N(CH_3)CH_2C_6H_5$ x HCl |

1,4-Dihydropyridines of the type (21), (22) and (23) possess a chiral center at C-4 and thus can exist in enantiomeric forms. The synthesis of such antipodes will now be illustrated with the enantiomers of (21) as an example[34].

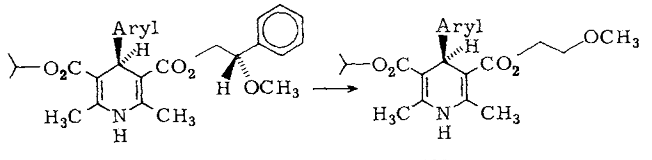
The most expedient route involves the synthesis of a 1,4-dihydropyridine derivative (26) with a chiral ester component. After separation of the two possible diastereomers the chiral ester group is converted into an achiral function



(24) (25) (26)



(27)

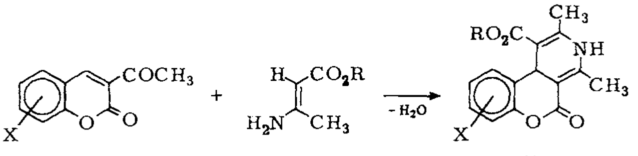


(28) (29)

Aryl = $m$-$O_2N$–$C_6H_4$

by solvolysis. If 2-methoxy-2-phenylethyl 3-aminoisocrotonate (27) is used, the ring-closure to the dihydropyridine occurs diastereoselectively to give the uniformly configurated derivative (28), which can be converted into the optically pure antipode of nimodipine (29) by selective alkanolysis of the chiral ester group. The other antipode of nimodipine is obtainable in an analogous way.

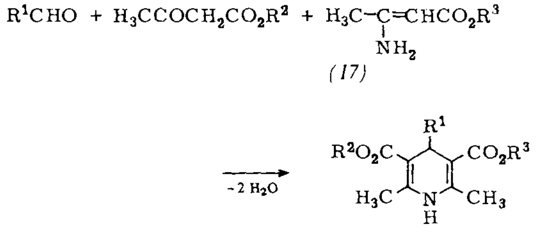
3-Acetylcoumarins (30), readily available from 2-hydroxybenzaldehydes and diketene, can also serve as substrates for the cyclizing Michael addition. They condense with the aminoesters (17) at 150°C without solvent to yield the tricycles (31)[35].



(30) (17) (31)

X = H, Alkyl, Alkoxy, Halogen

If an aldehyde is allowed to react analogously to eq. (B) with acetoacetate and amino esters (17) having non-identical ester functions, then the "mixed" 1,4-dihydropyridines (32) are obtained[36]. The symmetrically substituted dihydropyridines, which could be expected according to eq. (C), are only isolated as by-products in a few cases.

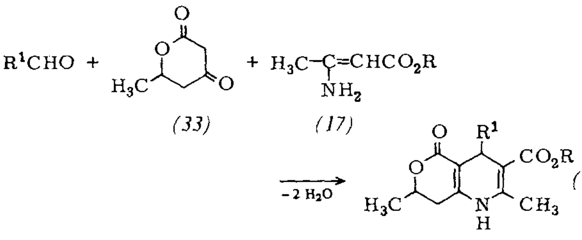


$$R^1CHO + H_3CCOCH_2CO_2R^2 + H_3C\text{–}\underset{NH_2}{C}{=}CHCO_2R^3$$

(17)

(32)

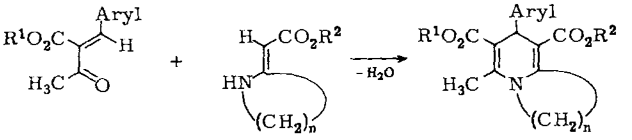
The condensation of aldehydes with β-ketolactones (33) and amino esters (17), which leads to the annelated 1,4-dihydropyridines (34) in high yields, is a further example of this three-component synthesis[37].



(33) (17) (34)

### 3.3. Synthesis of 1,4-Dihydropyridines with a Bridgehead Nitrogen Atom

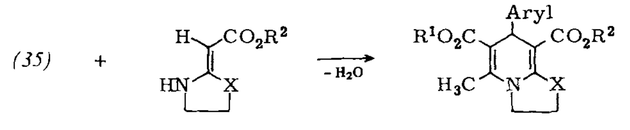
The cyclizing Michael addition of the alkylene bridged 3-aminoisocrotonate (36) to the arylalkylideneacetoacetate (35) yields the bicyclic 1,4-dihydropyridine-3,5-dicarboxylate (37) in high yield[38].



(35) (36) (37)

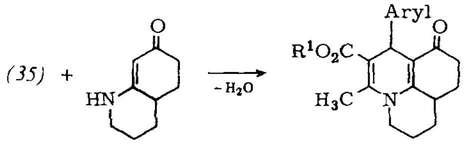
n = 3, 4, 5

We were able to extend this principle of bridgehead nitrogen heterocycle synthesis to the derivatives (38) which bear a further heteroatom in the 2-position. Oxygen, nitrogen and sulfur could be introduced[38].

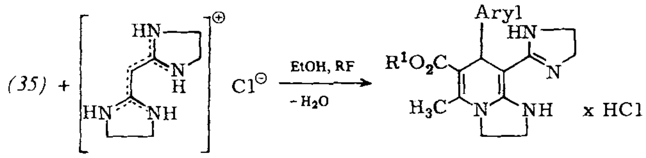

(38)

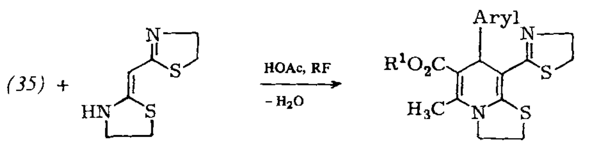
X = O, S, NH

*(35)* reacts with the bicyclic ketone *(39)* in refluxing glacial acetic acid to give the tricyclic dihydropyridines *(40)*[38].


(39) (40)

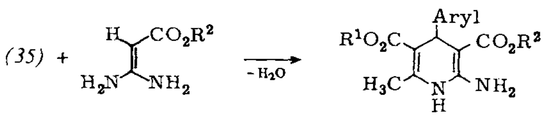
In the special case of the malonodiimide derivatives *(41)* and *(43)* the imino function is able to exercise both the "push" and the "pull" functions of a donor/acceptor-substituted olefin. The cyclizing Michael addition to *(35)* yields the dihydropyridine derivatives *(42)* and *(44)* bearing a heterocyclic substituent at C-3[39].


(41) (42)

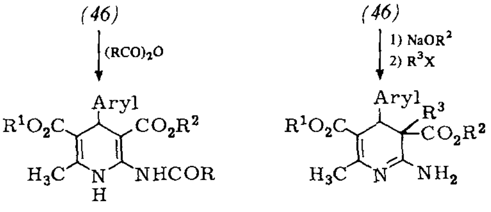

(43) (44)

### 3.4. Synthesis of 2-Amino Substituted Dihydropyridines and Their Reactions

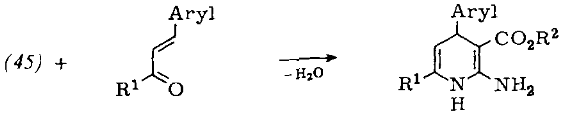
The synthetic potential in the dihydropyridine area can be greatly extended by the use of amidinoacetic esters as Michael addends. In their tautomeric enediaminocarbonyl form *(45)* they can be regarded formally as 3-aminocrotonates in which the methyl group has been replaced by an amino group. The cyclizing Michael addition of *(45)* to *(35)* yields the 2-amino-1,4-dihydropyridine-3,5-dicarboxylates *(46)*[40] in good yields, which, as polyfunctional molecules are available for numerous further reactions.

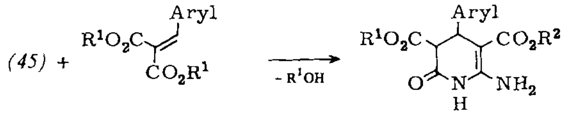

(45) (46)

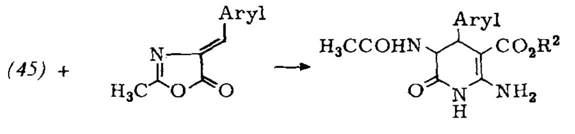
Only the acylation and alkylation of *(46)* will be mentioned here. Acylation with carboxylic anhydrides occurs, as would be expected, at the exocyclic nitrogen to give *(47)*. In contrast, alkylation occurs at C-3 after deprotonation to give the 3,4-dihydropyridines *(48)*[41]. The regioselectivity of the alkylation contrasts with the *N*-alkylation of 2,6-dialkyl-1,4-dihydropyridine-3,5-dicarboxylates *(15)* under similar conditions[42,43], but is in accordance with *Gompper*'s allopolarization principle which postulates alkylation at the carbon atom for donor substitution of the enamine anion in the 2-position[44].


(47) (48)

The amidinoacetic esters *(45)* are more reactive partners than 3-aminocrotonates *(17)* in the Michael addition. The condensation of *(45)* with simple α,β-unsaturated ketones *(49)* leads to the 1,4-dihydropyridinemonocarboxylates *(50)*[40], whereas addition to arylalkylidenemalonates *(51)* and 4-aralkylidene-2-methyloxazole-5(4*H*)-ones *(53)* yields the amino and diamino substituted dihydropyridones *(52)* and *(54)*, respectively[45].


(49) (50), $R^1$ = Alkyl, Aryl

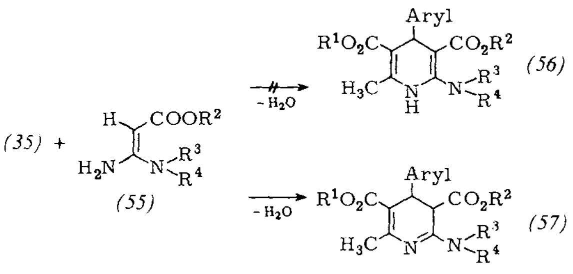

(51) (52)


(53) (54)

The *N,N*-dialkyl-substituted enediamines *(55)* do not react as expected with *(35)* to give *(56)*, but instead to give the 3,4-dihydropyridines *(57)*[40], as indicated by the $^1$H-NMR, $^{13}$C-NMR, and mass spectra[46].

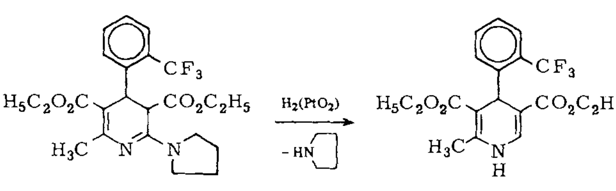
Apparently the highly substituted 1,4-dihydropyridine system switches to the less strained 3,4-dihydropyridine structure when highly hindered substituents are introduced.

Whereas the tautomeric conversion of *(57)* into *(56)* is not possible, the 3,4-dihydropyridines *(57)* can be converted by hydrogenolysis into 1,4-dihydropyridines unsubstituted in the 2-position, which are otherwise difficultly



$R^3$, $R^4$ = Alkyl; $R^3$ + $R^4$ = Alkylene

accessible. For example, the hydrogenation of *(58)* in glacial acetic acid over $PtO_2$ provides the 1,4-dihydropyridine *(59)* in good yield *via* an addition/elimination reaction[47].

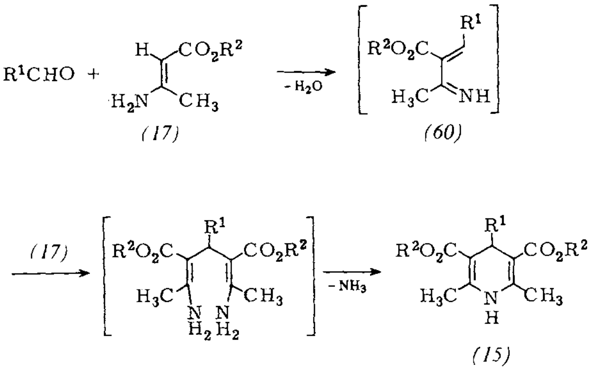


(58) (59)

### 3.5. Synthesis of 2,6-Heterosubstituted Dihydropyridines

In variant (C) of the Hantzsch condensation (see Section 3.1), an aldehyde is condensed with 3-aminoisocrotonate *(17)* in the molar ratio 1 : 2 with elimination of water and ammonia to give the dihydropyridine *(15)*[28].

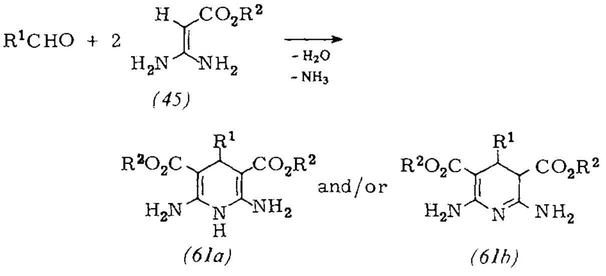
The non-isolable 2-arylalkylideno-3-iminobutanoate *(60)* resulting from a prior Knoevenagel condensation, may be postulated as intermediate in this reaction. The subsequent step would then be the Michael addition of *(17)* to *(60)* followed by the cyclizing condensation to *(15)*.



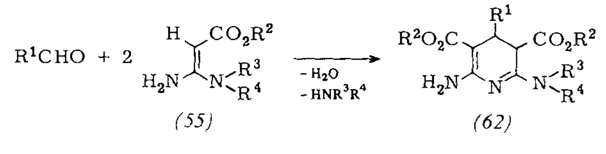
$R^1$ = Aryl, $R^2$ = Alkyl

Reaction of an aldehyde with double molar quantities of the amidinoacetic ester *(45)* in ethanol under reflux leads to the 2,6-diaminodihydropyridine-3,5-dicarboxylates *(61)* by an analogous mechanism[48].

Depending upon the substitution, the double bond isomers *(61a)* and/or *(61b)* are formed. Steric factors [cf. *(57)*] must exercise some influence on the isomer distribution, but are not the sole cause.

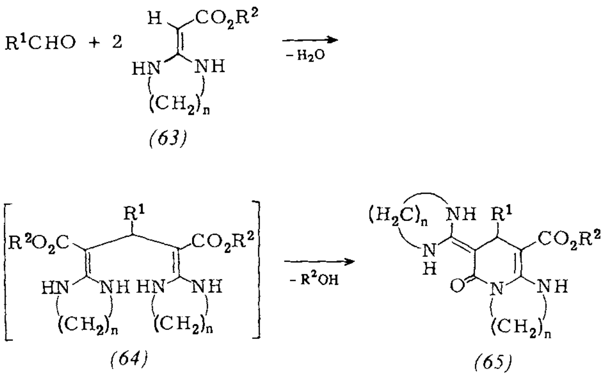


The condensation of aldehydes with the *N,N*-dialkyl-substituted amidinoacetic esters *(55)* to give the 3,4-dihydropyridine derivatives *(62)*[48] clearly shows the steric influence of the dialkylamino group. In this case the dialkylamine-elimination is favored over the alternative cleavage of ammonia.



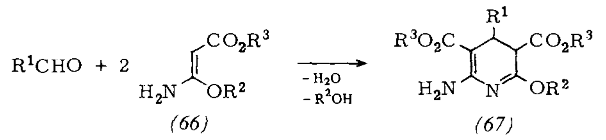
$R^3$, $R^4$ = Alkyl; $R^3$ + $R^4$ = Alkylene

In the analogous reaction of aldehydes with *N,N'*-bridged amidinoacetic esters *(63)* the Michael adducts *(64)* may be formulated as intermediates. Interestingly the amine components are not eliminated here. An alternative ring-closure takes place with the ester function to give the dihydropyridones *(65)*[48].



n = 2,3

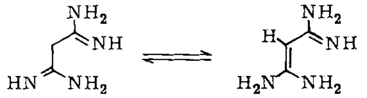
The formal replacement of the methyl group in 3-aminoisocrotonates *(17)* by an alkoxy function leads to the enamino form *(66)*, the imidate derived from cyanoacetate. The enamine form of such compounds postulated by *Cope* from the molar refraction[49] is confirmed by $^1H$-NMR spectroscopy. Condensation of *(66)* with an aldehyde in ethanol (reflux) affords the alkoxy derivatives *(67)*[50].



The structure of *(67)* is ascertained from IR, UV, NMR and mass spectral data, which exclude the alternative 1,4-dihydro form.

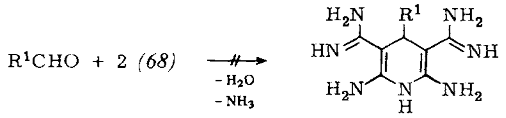
### 3.6. Special Cases of the Hantzsch Condensation

Malondiamidines such as the parent compound *(68)* can be regarded as special cases of an acceptor-substituted enamine. It has been shown that the methylene group in *(68)*



*(68)*

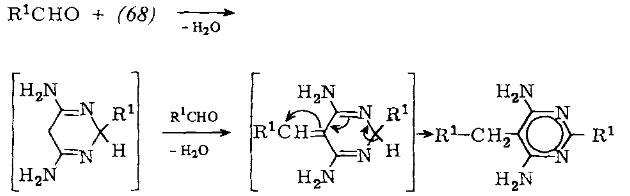
is capable of condensation with carbonyl compounds such as 1,3-diketones[51]. However, the condensation of *(68)* with aromatic aldehydes in the molar ratio 2 : 1 does not lead to the 3,5-diamidino-2,6-diamino-1,4-dihydropyridines *(69)* as would be expected in analogy to the synthesis of *(61a)*



*(69)*

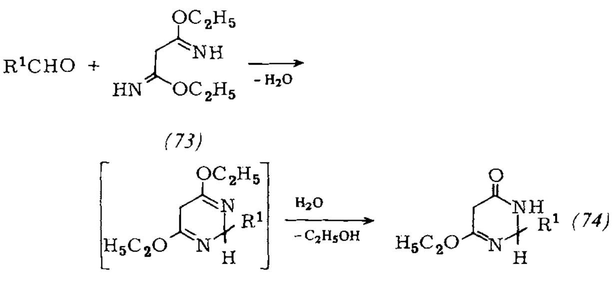
and/or *(61b)*; instead, products are isolated whose molecular weights correspond to the reversed mole ratio of the starting materials after elimination of 2 moles $H_2O$. In fact the condensation of aldehydes with *(68)* in the molar ratio 2 : 1 can be carried out in a widely variable synthesis such that 4,6-diaminopyrimidines *(72)* are formed in high yield[52].

This simple synthesis may be explained by the following multistep process.



*(70)* *(71)* *(72)*

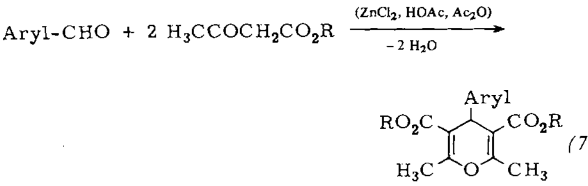
If among 3-iminoenamines such as *(68)* the possibility of a [5+1]-condensation (aminal formation) with aldehydes prevails, then this reaction is apparently favored over that of electrophilic attack at carbon. Aromatic aldehydes confirm to this hypothesis in that they condense with diethyl malonimidate *(73)* to give 6-ethoxy-4-oxo-2,3,4,5-tetrahydropyrimidines *(74)* after hydrolysis of a lactim ether function[53].



*(73)* *(74)*

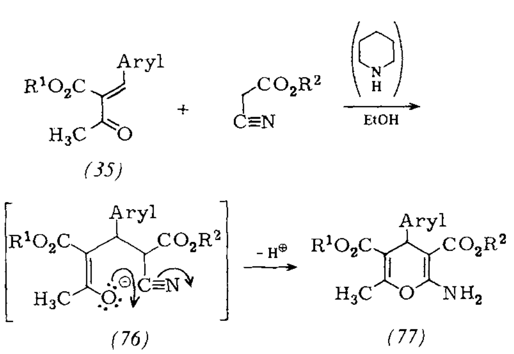
### 3.7. Synthesis of 4-Aryl-4*H*-pyrans, 4-Aryldihydropyridazines and Related Heterocycles

4*H*-Pyran derivatives *(75)* are oxa-analogues of 4-aryl-1,4-dihydropyridine-3,5-dicarboxylates. According to *Wolinsky* and *Hauer*[54] they are accessible by acid condensation of aromatic aldehydes with acetoacetates.



*(75)*

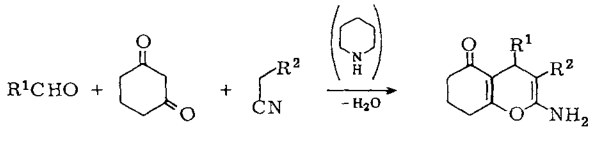
We obtained the corresponding 2-amino-4*H*-pyrans *(77)* by base catalyzed cyclizing Michael addition of cyanoacetates to the arylalkylideno-acetoacetates *(35)*[55].



*(35)* *(76)* *(77)*

The mechanism of this simple formation of the 4*H*-pyran system probably involves nucleophilic attack of the enolate anion of the Michael adduct *(76)* on the nitrile group.

The relationship of this pyran synthesis (cf. also [56]) with the Hantzsch dihydropyridine synthesis is clearly seen in the three-component reaction of aliphatic or aromatic aldehydes, 1,3-dicarbonyl compounds such as cyclohexan-1,3-dione and the nitriles *(78)* with an activated methylene group. 2-Amino-5-oxo-5,6,7,8-tetrahydro-4*H*-chromenes *(79)* are obtained in good yields from a piperidine-catalyzed reaction in ethanolic solution[57].

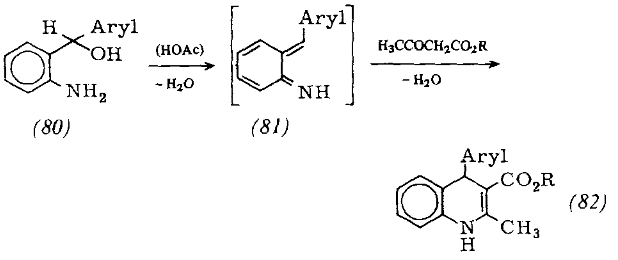


*(78)* *(79)*

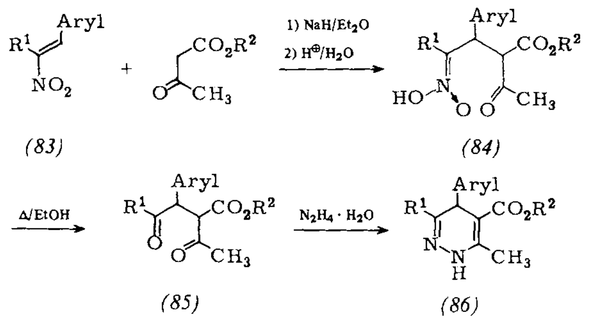
$R^2$ = CN, $CO_2R^3$

1,4-Dihydroquinoline-3-carboxylates *(82)*, are obtainable by condensation of 2-aminobenzyl alcohols *(80)* with β-dicarbonyl compounds in glacial acetic acid[58]. Here again a cyclizing Michael addition to the quinoneimine derivative *(81)* is to be formulated as the key step.

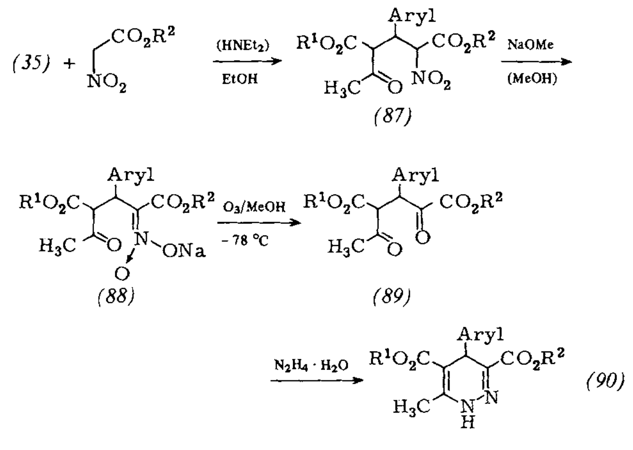
1,4-Dihydropyridazine-5-carboxylates *(86)* with alkyl or aryl substituents in the 3-position *(86)* are accessible by the following reaction sequence[59]. Addition of acetoacetate to



the nitrostyrene or nitrostilbene *(83)* furnishes the nitronic acid *(84)* after mild hydrolysis[60], which is converted into the 1,4-diketone *(85)* by a thermal Nef reaction[61]. A [4+2]-condensation with hydrazine hydrate results in the formation of *(86)*.

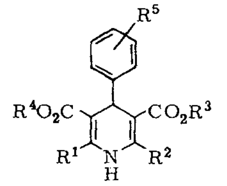


The 1,4-dihydropyridazine-3,5-dicarboxylates *(90)*, pyridazine analogues of the 1,4-dihydropyridines *(15)*, are obtained[59] by an interesting synthetic equivalent of the Nef reaction[62]. Michael addition of nitroacetic esters to the aralkylideno-acetoacetate *(35)* provides the adducts *(87)*, which are converted to the nitronates *(88)* by treatment with sodium methoxide. Low temperature ozonolysis of *(88)* permits the introduction of the carbonyl function in the α-position to give the diketodiester *(89)* which can then be condensed conventionally with hydrazine hydrate to give *(90)*.



## 4. Structure/Activity Relationships

Based on the biological data of a large number of 1,4-dihydropyridines with the general formula *(91)*, which have been synthesized in our laboratories, some qualitative structure/activity relationships can be deduced. Accordingly, an optimum in biological activity (vasodilation, reduction of blood pressure) is to be expected when the following structural parameters are met:



*(91)*

a) 1,4-Dihydropyridines unsubstituted at nitrogen.

b) Lower alkyl groups are optimal substituents ($R^1$, $R^2$) in the 2,6-positions. Replacement of one alkyl group by amino is tolerated.

c) Carboxylate groups are superior to other acceptor substituents such as CN, COR, $SO_2R$, $CONR_2$, $NO_2$ *etc.*, both in the 3- and the 5-position. The alcohol component of the ester group can be saturated, unsaturated, straight-chain or branched. The alkyl chain may be interrupted by heteroatoms or silicon[63,64]. 1,4-Dihydropyridines with non-identical ester groups ($R^3 \neq R^4$) are in many cases superior to the corresponding derivatives with identical substitution[31].

d) A phenyl substituent is superlative in the 4-position of the dihydropyridine even though its replacement by other monocyclic or polycyclic arenes or heteroarenes is possible within limits[17]. Monosubstitution of phenyl ($R^5$) by acceptor substituents such as $NO_2$, CN, $CF_3$ *etc.* in the *ortho-* or *meta*-position has a positive influence. *Para*-substitution, on the other hand, causes a marked reduction in, or even loss of activity.

With the aid of Hansch analysis[65] it was possible to establish a quantitative relationship between physicochemical substituent properties and the negative ionotropic activity[*] on the papillary muscle of the cat for a small selection of 1,4-dihydropyridine derivatives *(91)*[66].

## 5. Prospects

The discovery that intermediates in a named reaction familiar to chemists for almost 100 years have high pharmacological activity has recently awakened the interest of numerous companies and other institutions in the Hantzsch dihydropyridines as a class. The synthetic potential of the Hantzsch reaction thus revealed could also be of value for other branches of heterocyclic chemistry. The progress to date in the chemistry, pharmacology and clinical application of 1,4-dihydropyridines leads one to expect interesting results in the future.

*In conclusion we would like to thank numerous colleagues for the years of fruitful collaboration, in particular Drs. G. Franckowiak, S. Goldmann, H. Horstmann, B. Junge (chemical research), W. Vater, K. Stoepel, S. Kazda, R. To-*

---

[*] Negative monotropic activity is the reduction of the contractility of cardiac muscle.

*wart, A. Heise, K. Schlossmann (pharmacology), and J. Kurz, C. Wünsche (structural research).*

Received: December 2, 1980 [A 379 IE]
German version: Angew. Chem. *39*, 755 (1981)

---

[1] *F. W. Schildberg, A. Fleckenstein,* Pflügers Arch. Gesamte Physiol. Menschen Tiere *283*, 137 (1965).

[2] *A. Fleckenstein,* Med. Klin. *70*, 1665 (1975).

[3] *P. Meisel, M. Rohde, M. Rönfanz, H. Teichmann, R. Fermum,* Pharmazie *31*, 417 (1976).

[4] *H. U. Lehmann, H. Hochrein,* Med. Klin. *75*, 288 (1980).

[5] *R. G. Rahwan, M. E. Piascik, D. T. Witiak,* Can. J. Physiol. Pharmacol. *57*, 443 (1979).

[6] *Y. K. Byon, A. Fleckenstein,* Pflügers Arch. Ges. Physiol. Menschen Tiere *312*, R 8 (1969).

[7] *A. Fleckenstein, H. Kammermeier, H. J. Döring, H. J. Freund,* Z. Kreislaufforsch. *56*, 716; 839 (1967).

[8] *A. Fleckenstein, G. Fleckenstein-Grün, Y. K. Byon,* Arzneim.-Forsch. *27*, 562 (1977).

[9] *T. Nagao, T. Ikeo, M. Sato,* Jpn. J. Pharmacol. *27*, 330 (1977).

[10] *K. Landmark, H. Refsum,* Acta Pharmacol. Toxicol. *43*, Suppl. 1, 15 (1978).

[11] *T. Godfraind, A. Kaba, R. Rojas,* Brit. J. Pharmacol. *49*, 164 P (1973).

[12] *H. Meyer,* Lecture at the GdCh Specialist Group Symposium "Perspectives in Coronary Therapy", February 16, 1979, Frankfurt/Main (Germany).

[13] *F. Bossert, W. Vater,* Naturwissenschaften *58*, 578 (1971).

[14] *A. Hantzsch,* Justus Liebigs Ann. Chem. *215*, 1 (1882).

[15] *U. Eisner, J. Kuthan,* Chem. Rev. *72*, 1 (1972).

[16] *A. P. Phillips,* J. Am. Chem. Soc. *71*, 4003 (1949).

[17] *B. Loev, M. M. Goodman, K. M. Snader, R. Tedeschi, E. Macho,* J. Med. Chem. *17*, 956 (1974).

[18] *F. Bossert, W. Vater,* Südafr. Pat. 6801482 (1968), Bayer AG; Chem. Abstr. *70*, 96641 d (1969).

[19] *W. Vater, G. Kroneberg, F. Hoffmeister, H. Kaller, K. Meng, A. Oberdorf, W. Puls, K. Schlossmann, K. Stoepel,* Arzneim.-Forsch. *22*, 1 (1972).

[20] *G. Grün, A. Fleckenstein,* Arzneim.-Forsch. *22*, 334 (1973).

[21] *P. Lichtlen, H. J. Engel, R. Wolf,* Z. Kardiol. *1978*, Suppl. 5, 60.

[22] *H. Breithaupt, P. Walter,* Med. Welt *30*, 233 (1979).

[23] *I. Kuwayima, H. Nagura, M. Sakai, Y. Hada, C. Kamata, J.-I. Mifune, S. Miatsushita,* Jpn. Circ. J. *41*, 748 (1977).

[24] *H. Meyer,* DOS 2415062 (1975), Bayer AG; Chem. Abstr. *84*, 16962k (1976).

[25] *H. Medenwald, K. Schloßmann, C. Wünsche,* Arzneim.-Forsch. *22*, 53 (1972).

[26] *S. Kondo, A. Kuchiki, K. Tamamoto, K. Akimoto, K. Takahashi, N. Awata, I. Sugimoto,* Chem. Pharm. Bull. *28*, 1 (1980).

[27] *H. Fox, J. Lewis, W. Wenner,* J. Org. Chem. *16*, 1259 (1951).

[28] *A. H. Cook, I. M. Heilbronn, L. J. Steger,* J. Chem. Soc. *1943*, 413.

[29] *H. Meyer, F. Bossert, W. Vater, K. Stoepel,* DOS 2117571 (1972), Bayer AG; Chem. Abstr. *78*, 16038q (1973).

[30] *R. Towart, S. Kazda,* Brit. J. Pharmacol. *67*, 409 P (1979).

[31] *H. Meyer, F. Bossert, E. Wehinger, K. Stoepel, W. Vater,* Arzneim.-Forsch. *31*, 407 (1981).

[32] *T. Takenaka, S. Usuda, T. Nomura, H. Maeno, T. Sado,* Arzneim.-Forsch. *26*, 2172 (1976).

[33] *M. Iwanami, T. Shibanume, M. Fujimoto, R. Kawai, K. Tamazawa, T. Takenaka, K. Takahaski, M. Murakami,* Chem. Pharm. Bull. *27*, 1426 (1979).

[34] *E. Wehinger, H. Meyer, F. Bossert, W. Vater, R. Towart, K. Stoepel,* DOS 2935451 (1981), Bayer AG.

[35] *H. Meyer,* unpublished.

[36] *H. Meyer, F. Bossert,* DOS 2117573 (1972), Bayer AG; Chem. Abstr. *78*, 16042m (1973).

[37] *H. Meyer,* unpublished.

[38] *H. Meyer, F. Bossert, H. Horstmann,* Justus Liebigs Ann. Chem. *1977*, 1888.

[39] *H. Meyer,* Liebigs Ann. Chem. *1981*, in press.

[40] *H. Meyer, F. Bossert, H. Horstmann,* Justus Liebigs Ann. Chem. *1977*, 1895.

[41] *H. Meyer, F. Bossert, W. Vater, K. Stoepel,* DOS 2310747 (1974), Bayer AG.

[42] *P. J. Brignell, U. Eisner, P. G. Farrell,* J. Chem. Soc. *B 1966*, 1083.

[43] *J. F. Briellmann, H. J. Callot,* Tetrahedron *26*, 4799 (1970).

[44] *R. Gompper, H.-U. Wagner,* Angew. Chem. *88*, 389 (1976); Angew. Chem. Int. Ed. Engl. *15*, 321 (1976).

[45] *H. Meyer, F. Bossert, H. Horstmann,* Justus Liebigs Ann. Chem. *1978*, 1483.

[46] *E. L. Esmans, R. A. Domisse, F. C. Alderweireldt,* Org. Mass Spectrom. *1975*, 854.

[47] *H. Meyer,* unpublished.

[48] *H. Meyer, F. Bossert, H. Horstmann,* Justus Liebigs Ann. Chem. *1978*, 1476.

[49] *S. A. Glickmann, A. C. Cope,* J. Am. Chem. Soc. *67*, 1017 (1945).

[50] *H. Meyer, F. Bossert, H. Horstmann,* Justus Liebigs Ann. Chem. *1976*, 1762.

[51] *H. Meyer, J. Kurz,* Justus Liebigs Ann. Chem. *1978*, 1491.

[52] *H. Meyer,* Liebigs Ann. Chem. *1979*, 1291.

[53] *H. Meyer,* Liebigs Ann. Chem. *1980*, 673.

[54] *J. Wolinsky, H. S. Hauer,* J. Org. Chem. *34*, 3169 (1969).

[55] *H. Meyer, F. Bossert, W. Vater, K. Stoepel,* DOS 2235406 (1974), Bayer AG; Chem. Abstr. *80*, 120765 (1974).

[56] *M. Quinteiro, C. Seoane, J. L. Soto,* Tetrahedron Lett. *1977*, 1835.

[57] *H. Meyer,* unpublished.

[58] *H. Meyer, F. Bossert, W. Vater, K. Stoepel,* DOS 2310746 (1974), Bayer AG; Chem. Abstr. *82*, 4226u (1975).

[59] *G. Franckowiak,* Liebigs Ann. Chem. *1982*, in press.

[60] *F. Boberg, R. G. Schultze,* Chem. Ber. *88*, 74 (1955).

[61] *F. Boberg, R. G. Schultze,* Chem. Ber. *90*, 1215 (1957).

[62] *J. E. McMurry, J. Melton, H. Padgett,* J. Org. Chem. *39*, 259 (1974).

[63] *F. Bossert, H. Horstmann, H. Meyer, W. Vater,* Arzneim.-Forsch. *29*, 226 (1979).

[64] *R. Tacke, A. Bentlage, R. Towart, H. Meyer, F. Bossert, W. Vater, K. Stoepel,* Z. Naturforsch. *B 35*, 494 (1980).

[65] *C. Hansch* in *C. J. Cavallito:* Structure-Activity Relationships, Vol. 1, Pergamon Press, Oxford 1973, p. 75.

[66] *R. Rodenkirchen, R. Bayer, R. Steiner, F. Bossert, H. Meyer, E. Möller,* Naunyn-Schmiedebergs Arch. Pharmacol. *310*, 69 (1979).

## High Pressure Michael Addition Catalyzed by Fluoride Ions[**]

By *Kiyoshi Matsumoto*[*]

Michael addition and related reactions constitute the most generic synthetic means for the construction of quaternary C atoms[1]. Recently, we described the high pressure Michael addition of components which either do not react or at most react sluggishly at atmospheric pressure[2]. Recent developments in phase transfer[3] catalysis and 'naked' fluoride anion catalyzed reactions prompted us to investigate fluoride catalyzed Michael additions—specifically in homogeneous solution—since high pressures can easily be accomplished under these conditions. The previously reported[2] Michael additions took place in moderate to excellent yields under conditions of $n$Bu$_4$NF catalysis at normal pressure, as summarized in Table 1. However, the reaction of diethyl isopropylmalonate and diethyl phenylmalonate with chalcone was unsuccessful, even in the presence of 'naked' fluoride anions generated by a variety of different methods[4]. This probably arises from the increased steric hindrance caused by substituents in the vicinity of the Michael donor reaction center and concomitant difficulties in the deprotonation step. These problems were expeditiously circumvented *via* recourse to the combined use of $n$Bu$_4$NF catalysis and high pressure, although yields of products were only moderate; *(7)* and *(8)* were obtained in 20 and 28% yield, respectively.

The use of high pressures may be of value in Michael additions and related reactions where the use of 'naked' fluoride anion or strong bases is not appropriate due to side reactions such as elimination[1,5] or fragmentation[6], and where even 'naked' fluoride anion is not powerful enough to induce reaction because of energy barriers imposed by steric and electronic effects.

### *Procedure*

Reaction at normal pressure: Michael acceptor (3 mmol), donor (6 or 15 mmol), and 10 mL of a 1 M solution of $n$Bu$_4$NF in tetrahydrofuran (THF)[7] are mixed under nitrogen and stirred at room temperature (Table 1). The reaction mixture is diluted with 50 mL of benzene and extracted several times with water to remove the catalyst. The organic layer is dried over $MgSO_4$ and worked-up as previously described[2].

Reaction at high pressure: Michael acceptor (3 mmol) and donor (6 mmol) are diluted with a 1 M-THF solution of

Table 1. Fluoride catalyzed Michael addition.

| Acceptor | Donor | Product | | $t$ [d] | Isolated yield [%] |
|---|---|---|---|---|---|
| $PhCH{=}CHCO_2CH_3$ | $CH_3-\underset{NO_2}{\underset{\vert}{C}H}-CH_3$ | $\begin{array}{l}PhCHCH_2CO_2CH_3\\ \quad\vert\\ O_2N-C(CH_3)_2\end{array}$ | *(1)* | 5 | 88 [b] |
| $H_2C{=}\underset{CH_3}{\underset{\vert}{C}}CO_2CH_3$ | $\underset{NO_2}{\underset{\vert}{C}H_2}-CH_2-CH_3$ | $\begin{array}{l}CH_2CH(CH_3)CO_2CH_3\\ \quad\vert\\ O_2N-CHC_2H_5\end{array}$ | *(2)* | 5 | 87 |
| $CH_3CH{=}CHCO_2CH_3$ | $\underset{NO_2}{\underset{\vert}{C}H_2}-CH_2-CH_3$ | $\begin{array}{l}CH_3CHCH_2CO_2CH_3\\ \quad\vert\\ O_2N-CHC_2H_5\end{array}$ | *(3)* | 5 | 96 |
| $PhCH{=}CH-\underset{O}{\underset{\Vert}{C}}-Ph$ | $\begin{array}{l}C_2H_5\\ \vert\\ HC(CO_2C_2H_5)_2\end{array}$ | $\begin{array}{l}PhCHCH_2COPh\\ \quad\vert\\ C_2H_5-C(CO_2C_2H_5)_2\end{array}$ | *(5)* | 2 | 35 |
| $PhCH{=}CH-\underset{O}{\underset{\Vert}{C}}-Ph$ | $\begin{array}{l}n\mathrm{Bu}\\ \vert\\ HC(CO_2C_2H_5)_2\end{array}$ | $\begin{array}{l}PhCHCH_2COPh\\ \quad\vert\\ n\mathrm{Bu}-C(CO_2C_2H_5)_2\end{array}$ | *(6)* | 3 | 28<br>17 [c] |
| $PhCH{=}CH-\underset{O}{\underset{\Vert}{C}}-Ph$ | $\begin{array}{l}i\mathrm{Pr}\\ \vert\\ HC(CO_2C_2H_5)_2\end{array}$ | $\begin{array}{l}PhCHCH_2COPh\\ \quad\vert\\ i\mathrm{Pr}-C(CO_2C_2H_5)_2\end{array}$ | *(7)* | 5 | 0 [d] |
| $PhCH{=}CH-\underset{O}{\underset{\Vert}{C}}-Ph$ | $\begin{array}{l}Ph\\ \vert\\ HC(CO_2C_2H_5)_2\end{array}$ | $\begin{array}{l}PhCHCH_2COPh\\ \quad\vert\\ Ph-C(CO_2C_2H_5)_2\end{array}$ | *(8)* | 5 | 0 [d] |

[a] See [2] for the yields under high pressure as well as some physical data of the Michael adducts. [b] This reaction did not take place in boiling ethanol in the presence of KF: see *S. Kambe, H. Yasuda*, Bull. Chem. Soc. Jpn. *39*, 2549 (1966). [c] 1.5 mmol chalcone and 1.5 mmol diethyl $n$-butylmalonate in 5 mL of a 1M solution of $n$Bu$_4$NF-THF (12 h). [d] See [4].

---

[*] Prof. Dr. K. Matsumoto
College of Liberal Arts & Sciences, Kyoto University, Kyoto 606 (Japan)

[**] Synthesis of Organic Compounds under High Pressure, Part 3. This work was supported by Research Grants from the Ministry of Education (Grant-in-aid, No. 284021 and 554146). - Part 2: [2].

0570-0833/81/0909-0770 $ 02.50/0

Table 2. Selected physical data of Michael adducts *(7)* and *(8)* [a].

*(7)*: oil; IR (neat): $\nu = 1680, 1720\ \mathrm{cm}^{-1}$ (C=O); $^{13}$C-NMR: $\delta = 14.1$ (q, 2$CH_3$), 18.1 (q, $CH_3$), 19.7 (q, $CH_3$), 31.0 (d, $CH$), 42.8 (d, $CH$), 43.1 (t, $CH_2CO$), 60.9 (t, 2O$CH_2$), 66.0 (s, $C$), 127.1, 127.8, 128.0, 128.4, 129.5 (6 d, aromatic $CH$), 137.1, 139.3 (2s, aromatic $C$), 170.2 (s, 2$C$=O), 197.9 (s, Ph$C$=O) [b]

*(8)*: M.p. 98–99°C; IR (KBr): $\nu = 1670, 1730\ \mathrm{cm}^{-1}$ (C=O); $^{13}$C-NMR: $\delta = 13.5$ (q, 2$CH_3$), 48.2, 48.8 (d, $CH$), 56.6, 56.5 (t, $CH_2CO$), 60.6 (t, 2O$CH_2$), 61.2 (s, $C$), 127.1–138.7 (group of peaks due to aromatic carbons), 168.0, 171.9 (2s, $C$=O), 193.1, 194.0 (2s, Ph$C$=O) [b, c]

[a] Satisfactory elementary analyses were obtained. [b] Solvent: $CDCl_3$/TMS. [c] The pairs of signals are possibly due to the presence of conformational isomers.

$n$Bu$_4$NF[7] under $N_2$ in a 10 mL Teflon capsule which is stored for 5 d at 30 °C at 10 kbar, and worked-up as usual.

Received: February 23, 1981 [Z 823 IE]
German version: Angew. Chem. *93*, 803 (1981)

---

[1] *S. F. Martin*, Tetrahedron *36*, 419 (1980).

[2] *K. Matsumoto*, Angew. Chem. *82*, 1046 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1013 (1980).

[3] *E. V. Dehmlow, S. Dehmlow:* Phase Transfer Catalysis. Verlag Chemie, Weinheim 1980; *W. E. Keller:* Compendium of Phase Transfer Reactions and Related Synthetic Methods, Fluka AG, CH-9470 Buchs 1979.

[4] a) $n$Bu$_4$NF in THF (5 d); b) KF and 18-crown 6 in refluxing acetonitrile with stirring (2 h): *I. Belsky*, J. Chem. Soc. Chem. Commun. *1977*, 237; c) $n$Bu$_4$NCl and KF·2$H_2O$ in acetonitrile with stirring at room temperature (21 h): *L. A. Carpino, A. G. Sau*, J. Chem. Soc. Chem. Commun. *1979*, 514; d) CsF in refluxing acetonitrile with stirring (24 h): *D. N. Reinhout, F. de Jong, H. P. M. Tomassen*, Tetrahedron Lett. *1979*, 2067.

[5] Solvolytic fragmentation and E2 elimination have a negative volume of activation and therefore may be accelerated by pressure: *W. J. le Noble, H. Kelm*, Angew. Chem. *92*, 887 (1980); Angew. Chem. Int. Ed. Engl. *19*, 841 (1980).

[6] *L.-F. Tietze, U. Reichert*, Angew. Chem. *92*, 832 (1980); Angew. Chem. Int. Ed. Engl. *19*, 830 (1980).

[7] Aldrich Chemical Co. $n$Bu$_4$NF·3$H_2O$ in THF from Fluka AG was also effective.

---

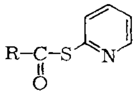
## 1-Phenyl-2-tetrazoline-5-thione, an Effective Reagent for the Synthesis of Macrocyclic Lactones[**]

By *Ulrich Schmidt* and *Manfred Dietsche*[*]

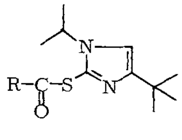
*Dedicated to Professor Arthur Lüttringhaus on the occasion of his 75th birthday*

Methods which have proven useful for the synthesis of macrocyclic lactones from hydroxy acids include the "double activation" method of *Corey* with 2-pyridinethiol esters *(1)*[1] and especially 2-imidazolethiols such as *(2)*[2], as well as the use of onium salts of azaarenes according to the method of *Mukaiyama*[3]. Substantial activation of *(1)* is possible with silver salts[4]. *(1)* and *(2)* are almost always prepared by oxidation-reduction condensation[5]. However, a very disturbing feature[6] is that the reaction products must be separated from pyridinethiol, triphenylphosphane oxide, dipyridyl sulfide, and, in the case of Ag-activation, from excess silver thiolate.

*(1)*

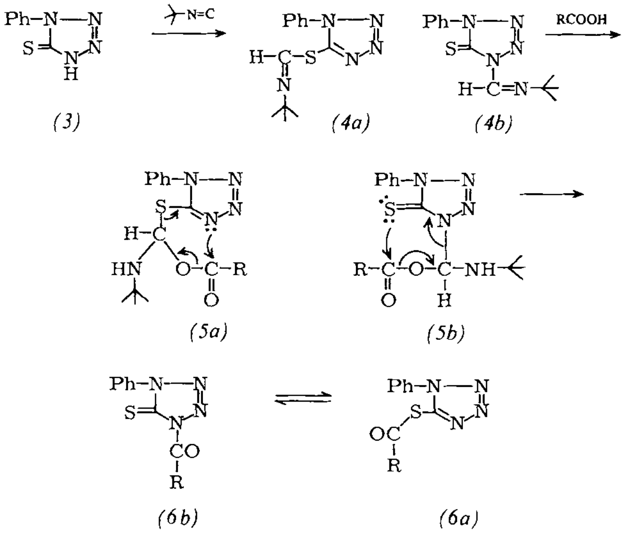


*(2)*

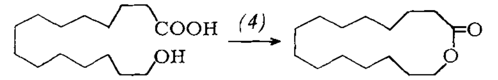


We have now found a very effective cyclization method for hydroxy acids. 1-Phenyl-2-tetrazoline-5-thione *(3)*, which is readily accessible from phenyl isothiocyanate and sodium azide[7], is allowed to react with *tert*-butyl isocyanide to give *(4a)* or *(4b)* which is reacted with the hydroxy acid.

*tert*-Butyl isocyanide reacts within a few minutes with *(3)*, suspended in toluene, to give a solution of the thioformimidate *(4a)* or the formamidine *(4b)*[8], which on treatment with carboxylic acids forms the mixture of the *S*- and *N*-acyl compounds *(6a)*+*(6b)* *via* the intermediates *(5a)* and *(5b)*, resp.[9]. The one rapidly rearranges to the other. The highly active acyl compounds can be used for *C*-acylation, for racemization-free peptide formation at −30 °C, and for ester formation.



The compounds *(6)*, R = ω-hydroxyalkyl, are such strong acylating agents that a silver ion catalyst is superfluous in the lactonization. The 16-, 17-, 18- and 20-membered lactones are formed in over 90% yield (determined gas-chromatographically) without extreme dilution in $3.5 \times 10^{-3}$ M solution in boiling toluene. The 13-membered ring was obtained in only 55% yield, probably because the larger activation energy for the formation of medium-sized rings requires prolonged heating of the thermolabile compounds *(6)*. Work-up is particularly easy when 1-(*m*-dimethylaminophenyl)-2-tetrazoline-5-thione is used for the activation. This reagent can be readily removed from the reaction product by dilute mineral acids.



### Procedure

Pentadecanolide (Exaltolide) *(8)*: To a mixture of *(3)* (124 mg, 1.2 mmol) and anhydrous toluene (5 mL) is added 100 mg (1.2 mmol) of *tert*-butyl isocyanide. After 5 minutes stirring at room temperature the now homogeneous solution is added to 258.5 mg (1.0 mmol) of ω-hydroxypenta-

---

[*] Prof. Dr. U. Schmidt, Dipl.-Chem. M. Dietsche
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] Carboxy Group Activation, Part 2. This work was supported by the Fonds der Chemischen Industrie and by BASF AG.—Part 1: *U. Schmidt, D. Heermann*, Angew. Chem. *91*, 330 (1979); Angew. Chem. Int. Ed. Engl. *18*, 308 (1979).

decanoic acid *(7)* and diluted with toluene to a total volume of 185 mL. The mixture is boiled under reflux for 30 min, cooled, evaporated down to *ca.* 5 mL in a vacuum, filtered through a short silica gel column (*ca.* 15 g silica gel S 0.063—0.1 mm) and eluted with benzene. After removal of solvent *in vacuo,* the residue is distilled in a Kugelrohr; *(8),* b.p. 110 °C (bath temp.)/0.1 torr, yield 193 mg (80%).

Received November 27, 1980 [Z 826 IE]
German version: Angew. Chem. *93,* 786 (1981)

---

[1] *E. J. Corey, K. C. Nicolaou,* J. Am. Chem. Soc. *96,* 5614 (1974).
[2] *E. J. Corey, D. J. Brunelle,* Tetrahedron Lett. *1976,* 3409.
[3] *T. Mukaiyama,* Angew. Chem. *91,* 798 (1979); Angew. Chem. Int. Ed. Engl. *18,* 707 (1979).
[4] *H. Gerlach, A. Thalmann,* Helv. Chim. Acta *57,* 2661 (1974).
[5] *T. Mukaiyama,* Angew. Chem. *88,* 111 (1976); Angew. Chem. Int. Ed. Engl. *15,* 94 (1976).
[6] *E. J. Corey, D. A. Clark,* Tetrahedron Lett. *1979,* 2875.
[7] *E. Lieber, J. Ramachandran,* Can. J. Chem. *37,* 101 (1959).
[8] $^1$H-NMR: $\delta = 1.42$ (s, 9 H), 7.6 (m, 3 H), 8.0 (m, 2 H), 8.78 (s, 1 H).
[9] $^1$H-NMR of the acetyl compounds *(6),* $R = CH_3$: $\delta = 2.39$ and 2.85 (both s, together 3 H in the ratio 3 : 2), 7.59 (m, 5H).

## Preparation and Structure of Iodocuprates(I) with Tetrahedral Face-to-Face Coupling

By *Hans Hartl* and *Farbod Mahdjour-Hassan-Abadi*[*]

Halometalates, like the oxometalates, exhibit an extremely wide variation in their structural chemistry. Particularly interesting in this respect are compounds with $d^{10}$-electron configuration at the metal, *e.g.* the halocuprates(I) and -argentates(I). These halometalates are, *inter alia,* also of industrial importance, since some of the compounds of this type show ionic conductivity in the solid state[1].

Halometalates $R_mM_nX_p$ (R = organic cation, M = metal, X = Cl, Br, I) are usually prepared by reaction of metal halides with the halides RX in solution or by solid state reactions. We have found that the direct reaction of the metals with triiodides $RI_3$, or with iodine in the presence of the iodide RI in organic solvents, often lead in a simple manner not only to well-known but also to new iodometalates. The composition and structure of the iodometalates isolable by precipitation in these reactions depend on the nature (size, form, charge distribution) of the cations R. Thus, reaction of Cu with $R^1I_3$ = tetramethylammonium triiodide or $R^2I_3$ = dimethyl(3-dimethylamino-2-aza-2-propenylidene)ammonium triiodide[2] led, *inter alia,* to compounds of the composition $R^1Cu_2I_3$ and $R^2Cu_2I_3$, respectively. The triiododicuprate(I) ion in these compounds has a structure which completely deviates from the known types of structure of $Cu_2X_3^-$ (X = Cl, Br, I)[3]: $CuI_4$-tetrahedra linked alternately *via* common edges and faces (!) into ${}^1_\infty(Cu_2I_3^-)$ single chains (Fig. 1). Examples of face to face coupling in tetrahedrally coordinated polyhedra have so far not been described in the literature[5].

$[(C_2H_5)_4N]Cu_2I_3$
$R^1Cu_2I_3$

$[(CH_3)_2N{=}CH{-}N{=}CH{-}N(CH_3)_2]Cu_2I_3$
$R^2Cu_2I_3$

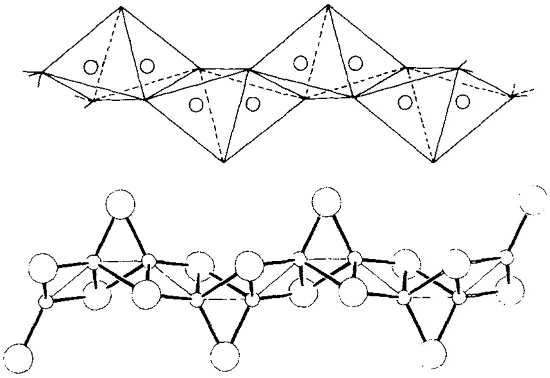


Fig. 1. Structure of the ${}^1_\infty(Cu_2I_3^-)$ anion in the iodocuprate(I)s $R^1Cu_2I_3$ and $R^2Cu_2I_3$. Top: polyhedral model of the chain (Cu: circles); bottom: spherical model of the chain (I: large circles; Cu: small circles).
$R^1Cu_2I_3$, orthorhombic, $Pna2_1$; $a = 842.0(2)$, $b = 1775.5(4)$, $c = 1073.6(2)$ pm. $Z = 4$. 1426 measured reflections, 1123 reflections with $I > 2\sigma(I)$, STOE diffractometer, $Cu_{K\alpha}$-radiation, $R = 0.056$. Symmetry of the ${}^1_\infty(Cu_2I_3^-)$ anion: glide plane. Cu—I 247.5(1)—296.1(1) pm, mean value 270.2 pm; Cu—Cu 250.7(1) and 267.9(1) pm (face- or edge linked); I—Cu—I 95.4(2)—121.4(3)°.
$R^2Cu_2I_3$, monoclinic, $C2/c$; $a = 1572(1)$, $b = 1227(1)$, $c = 850(1)$ pm, $\beta = 108.26(6)$, $Z = 4$. 1336 measured reflections, 985 reflections with $I > \sigma(I)$, SIEMENS diffractometer, $Mo_{K\alpha}$-radiation, $R = 0.034$. Symmetry of the ${}^1_\infty(Cu_2I_3^-)$ anion: twofold rotation axis/glide plane. Cu—I 253.1(2)—291.6(2) pm, mean value 270.2 pm; Cu—Cu 249.1(2) and 269.9(2) pm (face- and edge-linked, resp.); I—Cu—I 99.7(3)—123.1(3)°.

Moreover, the short distances of 249.1 pm and 250.7 pm between the Cu atoms bridged by the three iodine atoms in $R^2Cu_2I_3$ and $R^1Cu_2I_3$, respectively, are remarkable. They are the shortest Cu—Cu distances so far observed in copper-halogen compounds. Shorter distances could only be established in a few organo-copper compounds[6] (for comparison: Cu—Cu in the metal: 256 pm). To what extent the short Cu—Cu contacts are to be ascribed to metal-metal bonding or to the three bridging iodine atoms cannot be established by bond length considerations alone, since comparable values for compounds with analogous Cu—Cu coupling are not known. For the same reason the relationships between Cu—Cu distances and bond energies calculated by *Mehrotra* and *Hoffmann*[7] cannot be considered as evidence for metal-metal bonding in $R^2Cu_2I_3$ and $R^1Cu_2I_3$. The distances between the Cu atoms coupled *via* common edges of iodine tetrahedra (269.9 and 267.9 pm, respectively) are likewise relatively small. The low electrical conductivity of $3 \times 10^{-13}\ \Omega^{-1}\ cm^{-1}$ at 20 °C, measured on pellets of powdered $R^2Cu_2I_3$ would however discount an unambiguous one-dimensional conductivity *via* Cu—Cu—Cu bonds in the direction of the axis of the chain.

What type of relationships exist between the structure of the iodocuprate(I) ions and nature of the cations R cannot be decided on the basis of the present data. The form and charge distribution of the cations $R^1$ and $R^2$ are very different: $R^1$ is spherical with spherical charge distribution; $R^2$ is planar with delocalized π-electron system. Nevertheless, the same type of anion structure ${}^1_\infty(Cu_2I_3^-)$ with only slight differences in the bond lengths and angles is present in both cases (Fig. 1). If one chooses for R the cations *N*-methylpyridinium or methyltriphenylphosphonium, which are comparable with the cations $R^2$ and $R^1$, respectively, so far as type of structure is concerned, then iodocuprates(I) with a Cu : I ratio of 2 : 3 can indeed also be prepared, but the structure depicted in Figure 1 could not be detected[3].

*Procedure*

$R^2Cu_2I_3$: A mixture of $R^2I_3$ (2.55 g, 5 mmol) and Cu powder (1.28 g, 20 mmol) in anhydrous chloroform (40

---

[*] Prof. Dr. H. Hartl, Dipl.-Chem. F. Mahdjour-Hassan-Abadi
Institut für Anorganische und Analytische Chemie der Freien Universität
Fabeckstrasse 34/36, D-1000 Berlin 33 (Germany)

mL) is heated to boiling solution until the solution decolorizes (*ca.* 2 h). After cooling and filtering, the gray residue is rapidly dissolved in dimethylformamide. Addition of anhydrous benzene to the solution furnishes a white crystalline precipitate of m.p. 189—190 °C.

$R^1Cu_2I_3$: A mixture of $R^1I$ (1.26 g, 5 mmol) and Cu powder (1.27 g, 20 mmol) in acetone (100 mL) is heated together with $I_2$ (1.28 g, 5 mmol) under reflux until the solution turns yellow. On cooling the hot filtered solution, needle-like crystals separate out; m.p. 176—177 °C.

For the preparation of pure crystals it has proven advantageous to work with an excess of copper, since the separation of unreacted $RI_3$ causes difficulties, while unreacted Cu can be filtered off.—Both iodocuprates are readily soluble in dimethylformamide and pyridine but only sparingly soluble in acetone. They are insoluble in benzene, ether, petroleum ether, chloroform, and water.

Received: October 1979 [Z 828 IE]
revised: September 5, 1980
German version: Angew. Chem. *93*, 804 (1981)

---

[1] *H. Rickert*, Angew. Chem. *90*, 38 (1978); Angew. Chem. Int. Ed. Engl. *17*, 37 (1978); *L. Y. Y. Chan, S. Geller*, J. Solid State Chem. *25*, 85 (1978).

[2] *H. Hartl, H. Pritzkow, J. Jander*, Chem. Ber. *103*, 652 (1970); *H. Pritzkow, H. Hartl*, Acta Crystallogr. *B 29*, 1777 (1973).

[3] $CsCu_2Cl_3$ [4a], $C_6H_5N_2Cu_2Br_3$ [4b], and $C_6H_8NCu_2I_3$ [4c] contain infinite double series of $CuX_4$ tetrahedra, which are each bonded *via* three common edges ($C_6H_5N_2^+$ = phenyldiazonium, $C_6H_8N^+$ = *N*-methylpyridinium). In $[(C_6H_5)_3(CH_3)P]Cu_2I_3$ [4d] there are isolated $Cu_4I_6^{2-}$ moieties with tetrahedral $Cu_4$ clusters; the iodine atoms are situated above the edges of the tetrahedra.

[4] a) *C. Brink, N. F. Binnendijk, J. v. d. Linde*, Acta Crystallogr. *7*, 176 (1954); b) *C. Rømming, K. Waerstad*, Chem. Commun. *1965*, 299; c) *H. Hartl, F. Mahdjour-Hassan-Abadi*, unpublished results; d) *G. A. Bowmaker, G. R. Clark, D. K. P. Yuen*, J. Chem. Soc. Dalton Trans. *1976*, 2329.

[5] *A. F. Wells*: Structural Inorganic Chemistry, Clarendon Press, Oxford 1975, p. 158.

[6] *A. Camus, N. Marsich, G. Nardin, L. Randaccio*, Inorg. Chim. Acta *23*, 131 (1977).

[7] *P. K. Mehrotra, R. Hoffmann*, Inorg. Chem. *17*, 2187 (1978).

## Selective CH-Insertion Reactions of Free Arylhalocarbenes[***]

By *Karl Steinbeck* and *Joachim Klein*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Carbenes not only have the ability to form cyclopropanes on reaction with olefinic double bonds but also to react with CH-bonds with insertion. Such insertion reactions, however, usually proceed unspecifically or in very low yields[1]. In continuation of our investigations on the selectivity of reactions of electrophilic carbenes[2] we were able to show that CH-insertion of dichloro- and dibromocarbene (generated in the two-phase system 50% sodium hydroxide/haloform, in the presence of phase transfer catalysts[3]) can proceed selectively, in many cases even specifically, and in good to very good yields. In order to extend this obviously preparatively useful method to the synthesis of C—C bonds we have investigated the behavior of further electrophilic carbenes and report here on the first observed selective CH-insertion of arylhalocarbenes.

Attempts to generate arylhalocarbenes from arylidene halides *(1)* by α-elimination in the liquid-liquid two-phase system with 50% sodium hydroxide failed. According to *Moss et al.*[5] arylhalocarbenoids are formed on reaction of *(1)* with potassium *tert*-butoxide, while reaction with a crown ether such as [18]crown-6 leads to *free* arylhalocarbenes. We have found that only the free carbenes form the expected CH-insertion products. The arylhalocarbenes reacted about as selectively as the dihalocarbenes. Thus, we were able to carry out both the hydroalkylation of free chloro(phenyl)carbene (aryl = $C_6H_5$, X = Cl) with cumene and adamantane to give the 1-chloro-2-methyl-1,2-diphenylpropane *(2a)* and 1-(α-chlorobenzyl)adamantane *(3a)* as well as the hydroalkoxyalkylation with 2-methyltetrahydrofuran to 2-(α-chlorobenzyl)-2-methyltetrahydrofuran *(4a)* and, especially, also the capped hydroacylation with 4,4,5,5-tetramethyl-2-phenyl-1,3-dioxolane to 2-(α-chlorobenzyl)-4,4,5,5-tetramethyl-2-phenyl-1,3-dioxolane *(5a)*, R = $C_6H_5$ (see Table 1).

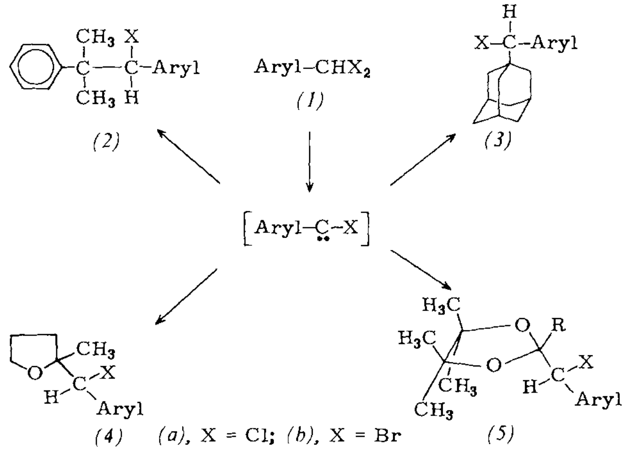


Table 1. Some data of the insertion products *(2a)*—*(5a)*, Aryl = $C_6H_5$, X = Cl.

| Cpd. | Yield [%] [a] | B.p. [°C/torr] | M.p. [°C] | $^1$H-NMR ($CDCl_3$, δ values) |
|---|---|---|---|---|
| *(2a)* | 21 | 115/0.005 | | 1.35 and 1.45 (2s, 6H), 5.03 (s, 1H), 7.0—7.2 (m, 10H) |
| *(3a)* | 10 | | 85 | 1.3—2.1 (m, 15H), 5.75 (s, 1H), 7.3 (m, 5H) |
| *(4a)* [b] | 19 | 95/0.5 | | 1.13 and 1.20 (2s, 3H), 1.40—2.32 (m, 4H), 3.45—3.92 (m, 2H), 4.80 (s, 1H), 7.07—7.40 (m, 5H) |
| *(5a)*, R = $C_6H_5$ | 44 | 130/0.05 | 77 | 0.90 and 0.96 (2s, 6H), 1.30 (s, 6H), 5.07 (s, 1H), 7.03—7.63 (m, 10H) |

[a] Referred to benzylidene chloride *(1a)*. [b] Diastereomeric pair.

*(1a)*, aryl = $C_6H_5$, X = Cl, and 1.5-fold excess of base were allowed to react in the presence of 5 mol-% [18]crown-6 at 80 °C with an excess of the respective substrate. *(2a)*—*(5a)* were the sole isolable products. Excess of unreacted educt could be removed by distillation. The structure of the insertion product is confirmed by NMR and mass spectra as well as by CH analysis.

---

[*] Priv.-Doz. Dr. K. Steinbeck [**], Dipl.-Chem. J. Klein
Institut für Organische Chemie der Technischen Hochschule
Prof.-Pirlet-Strasse 1, D-5100 Aachen (Germany)

[**] Present address: Bayer AG, FE-FWI Q 18, 5090 Leverkusen (Germany)

[***] Part 6 of the Series, Applications of Phase Transfer Catalysis.—Part 5: *K. Steinbeck*, J. Chem. Res. *1980*, (S) 95; (M) 1163.

These reactions can be applied to other arylhalocarbenes. Thus, reaction with free bromo(phenyl)carbene, from benzylidene bromide *(1b)*, aryl = $C_6H_5$, X = Br, leads to formation of the α-bromobenzyl insertion products *(2b)*, *(3b)*, *(4b)*, *(5b)*, R = $C_6H_5$. The use of aryl groups other than phenyl is usually not very favorable, since substituents either lower the acidity of *(1)* (first step of the α-elimination rendered difficult) or increase the stability of the carbanion (second step of the α-elimination difficult). Positive results were obtained with free chloro(*p*-toyl)carbene.

The methods described above enable selective coupling of an electrophilic carbene with reactive CH compounds and lead, in the case of halogen-containing carbenes and 2,4,4,5,5-pentasubstituted dioxolanes to ketals of α-haloketones [type *(5)*] with defined content and position of the halogen.—An example of the preparative application of the method to other electrophilic carbenes is the selective CH-insertion of the carbene 3-methyl-1,2-butadieneylidene (prepared by reaction of 3-chloro-3-methyl-1-butyne in a two-phase system with 50% NaOH[6]) into the $C^2$—H bond of 1,3-dioxolanes.

*Procedure*

A mixture of *(1a)* (20.5 g, 0.125 mol) and substrate (20 g) is added dropwise within 12 h into a mixture of potassium *tert*-butoxide (21 g, 0.19 mol), [18]crown-6 (1.6 g) and substrate (80 g) at 80 °C. After 48 hours stirring at 80 °C the reaction mixture is diluted with water and extracted with ether. Distillation of the organic phase affords the products *(2a)*-*(5a)* (see Table).

Received: September 7, 1979 [Z 829 IE]
supplemented: April 28, 1980
German version: Angew. Chem. *93*, 787 (1981)

---

[1] Cf. also: *W. Kirmse:* Carbene Chemistry, Academic Press, New York 1964, and references cited therein.

[2] *K. Steinbeck*, Habilitationsschrift, Technische Hochschule Aachen 1979; Tetrahedron Lett. *1978*, 1103; Chem. Ber. *112*, 2402 (1979).

[3] *E. V. Dehmlow*, Angew. Chem. *86*, 187 (1974); Angew. Chem. Int. Ed. Engl. *13*, 170 (1974); *M. Mąkosza*, Pure Appl. Chem. *43*, 439 (1975).

[4] *S. M. McElvain, P. L. Weyna*, J. Am. Chem. Soc. *81*, 2579 (1959); *R. A. Moss*, J. Org. Chem. *27*, 2683 (1962).

[5] *R. A. Moss, F. G. Pilkiewicz*, J. Am. Chem. Soc. *96*, 5632 (1974).

[6] *S. Julia, D. Michelot, G. Linstrumelle*, C. R. Acad. Sci. Ser. *C 278*, 1523 (1974).

---

## Synthesis and Reactions of Methylenecyclopropanes; Isolation of a [4+2]-Cycloadduct of Methylenecyclopropene[**]

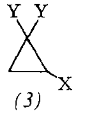
By *Andreas Weber* and *Markus Neuenschwander*[*]

Although numerous derivatives of methylenecyclopropene (triafulvene) *(1)* and cyclopropenylidenecyclopentadiene (pentatriafulvalene calicene) *(2)* have been described, the parent cyclic, crossed conjugated compounds are so far unknown[1]. The intermediary appearance of *(1)* has been implicated in studies on elimination reactions of 1,2-dichloro-1-methylcyclopropane[2], however, a cycloadduct of triafulvene *(1)* could not be isolated.

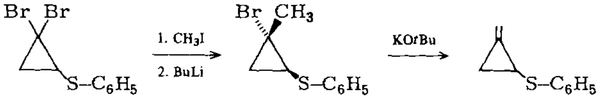
Trisubstituted cyclopropanes of type *(3)* are suitable precursors for *(1)* and *(2)*[3]: by analogy to other 1,1-dihalocyclopropanes[4] it should be possible to metalate and alkylate them[5]. After cleavage of HY, the substituent X could then be converted into a leaving group and be eliminated.


*(1)*

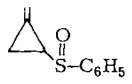

*(2)*



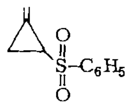
*(3)*



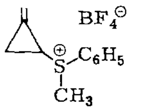
*(4)* *(5)* 93% *(6)* 70%



*(7)* 83%



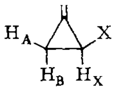
*(8)* 80%

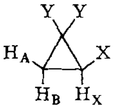


*(9)* ~95%

This synthetic plan[6] can be simply performed on 1,1-dibromo-2-phenylthiocyclopropane *(4)*[3]: reacting a solution of *(4)* (4 mmol) and methyl iodide (6 mmol) in THF (tetrahydrofuran) with butyllithium (4 mmol) at −95 °C results in the isolation in 93% yield of *trans*-1-bromo-1-methyl-2-phenylthiocyclopropane *(5)*, from which HBr can be eliminated by the action of potassium *tert*-butoxide to give the key intermediate *(6)*.

Table 1. $^1$H-NMR data (80 MHz, $CDCl_3$, δ-values rel. to TMS) of the cyclopropane derivatives *(4)*—*(11)*.





| Compound | $H_A$ ($J_{AB}$) | $H_B$ ($J_{BX}$) | $H_X$ ($J_{AX}$) | Further signals |
|---|---|---|---|---|
| *(4)* | 1.59<br>(7.9) | 2.11<br>(10.3) | 2.90<br>(7.2) | 7.4—7.05 (m, 5 H) |
| *(5)* [a] | 0.92<br>(7.0) | 1.67<br>(9.8) | 2.86<br>(5.9) | 7.35—7.05 (m, 5 H)<br>1.83 (s, 3 H) |
| *(6)* | 1.38<br>(9.5) | 1.82<br>(7.7) | 2.83<br>(4.2) | 7.28 (m, 5 H)<br>5.56 (m, 2 H) |
| *(7)* [b] | [b] | [b] | 2.84 | 7.7—7.2 (m, 5 H)<br>5.65—5.35 (m, 2 H) |
| *(8)* | 2.10<br>(10.0) | 1.77<br>(8.4) | 3.10<br>(4.4) | 8.1—7.25 (m, 5 H)<br>5.7—5.35 (m, 2 H) |
| *(9)* [b] | [b] | [b] | 3.68 | 8.15—7.5 (m, 5 H)<br>6.14—5.47 (4 m, 2 H)<br>3.45 + 3.25 (2 s, 3 H) |
| *(10)* | [c] | [c] | 3.64 | 5.62 (m, 1 H)<br>5.47 (m, 1 H)<br>1.27 (s, 9 H) |
| *(11)* | 1.20<br>(10.5) | 1.30<br>(6.6) | 3.62<br>(2.9) | 5.69 (m, 1 H)<br>5.45 (m, 1 H)<br>3.36 (s, 3 H) |

[a] *trans*-Compound. [b] Diastereomeric mixture. $H_A$ and $H_B$ form a complex multiplet between $\delta = 2.0$ and 1.3 in *(7)* and between 2.4 and 1.8 in *(9)*. [c] The multiplet from $H_A$ and $H_B$ ($\delta = 1.5$—1.1) is covered by the signal from the $Me_3C$—O group.

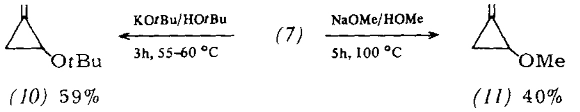
---

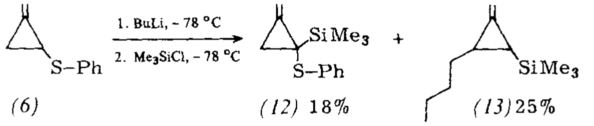
[*] Prof. M. Neuenschwander, Dr. A. Weber
Institut für Organische Chemie der Universität
Freiestrasse 3, CH-3012 Bern (Switzerland)

[**] Fulvenes, Fulvalenes, Part 32. Part 31 [5]. This work was supported by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project No. 2.621-0.80).

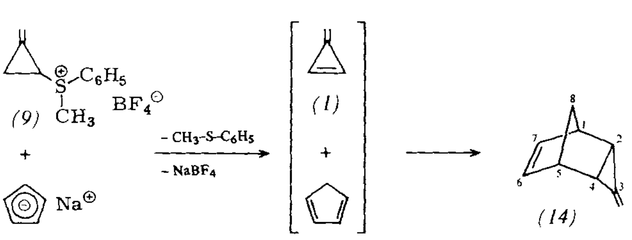
Oxidation with $NaIO_4$ in $CH_3OH/H_2O$ or with $H_2O_2$ in $CH_3COOH$ results in formation of the sulfoxide *(7)* and the sulfone *(8)* in high yield. Alkylation of *(6)* with trimethyloxonium tetrafluoroborate also proceeds almost quantitatively, however the oily diastereomeric mixture of *(9)* is not easily purified.—The structure of the compounds has been verified by analytical and spectroscopic data. The $^1H$-NMR spectra of *(4)* to *(9)* are characterized by the ABX- or AMX-systems of the three-membered ring protons (Table 1).

Both *(7)* and *(8)* react with strong bases, such as potassium *tert*-butoxide or lithium diisopropylamide in THF, between −20 and −78 °C. In this way, diphenyl disulfide (stemming from the initially formed sulfenic acid) is formed from the sulfoxide *(7)*, which indicates that the leaving group is cleaved; however, the expected three-membered-ring products could not be isolated or detected spectroscopically. If the basic elimination of HX from *(7)* is performed in the presence of high concentrations of a protonic trapping reagent, such as *tert*-butyl alcohol or methanol, 1-*tert*-butoxy-2-methylenecyclopropane *(10)*[2] or 1-methoxy-2-methylenecyclopropane *(11)* are isolated in high yield[7]. In addition to the expected product *(12)*, the silylation of *(6)* yields 1-butyl-2-methylene-3-trimethylsilylcyclopropane *(13)* (25%).





Since $S_N2$ reactions on substituted cyclopropanes are hardly possible, these results implicate the intermediate formation of methylenecyclopropene *(1)*. On the other hand, methyl phenyl sulfide can be cleaved off the sulfonium salt *(9)* under extremely mild conditions[8]; this also indicates that *(1)* could occur as an intermediate. Finally, a hydrocarbon with the empirical formula $C_9H_{10}$ is isolated in 13% yield[8] when *(9)* is reacted with an equivalent of sodium cyclopentadienide in furan/THF; the spectroscopic data indicate the structure shown in *(14)*: the number of lines in the $^1H$- and $^{13}C$-NMR spectra (Fig. 1) corresponds to the symmetry of the molecule.



The $^1H$-NMR signals at $\delta = 5.81$ (6-H/7-H) and 3.00 (1-H/5-H) are typical of norbornenes, while the multiplet at $\delta = 4.98$ (methylene groups on C-3) appears at almost the same chemical shift as the exocyclic $CH_2$-group of *(13)* (5.1). The assignment of the signals at $\delta = 1.93$ (2-H/4-H) and 1.84 (8-H/8'-H), as well as the *endo*-configuration of *(14)* follows from decoupling experiments.—In the $^{13}C$-NMR spectrum C-6/C-7 ($\delta = 133.4$) and C-1/C-5 (45.0) absorb in the typical norbornene region, while the signal from C-8 (63.7) is displaced to somewhat higher frequencies[9]; the characteristically low frequency (20.7) of the signals from C-2/C-4 reflects the ring strain of the three-membered ring, and the chemical shifts of the C-atoms of the exocyclic double bond (142.9, C-3 and 102.2, C-9) are also typical.

In summary, investigations of elimination- and trapping-reactions of methylenecyclopropanes, such as *(7)*—*(9)*, provide convincing evidence that the reactive methylenecyclopropene *(1)* occurs as an intermediary.

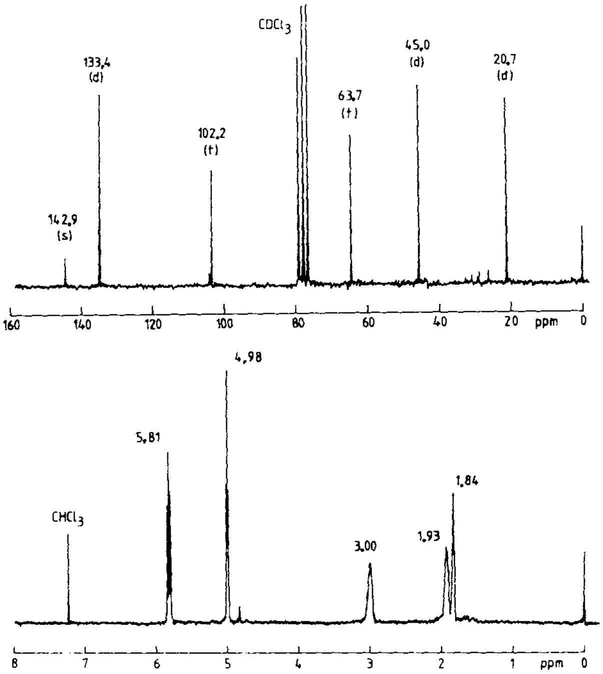


Fig. 1. NMR-spectra of *(14)*. Bottom: $^1H$-NMR ($CDCl_3$, 100 MHz). Top: $^{13}C$-NMR ($CDCl_3$, 25 MHz).

### *Procedure*

*(9)*: A solution of *(6)*[3] (2 mmol) in 2 mL anhydrous $CH_3NO_2$ is dropped into a solution of trimethyloxonium tetrafluoroborate (2 mmol) in 3 mL anhydrous $CH_3NO_2$ under $N_2$ at 0 °C. After stirring for 2 h at 0 °C, the yellow-brown solution is concentrated at 5 torr/20 °C, the residue washed with pentane (3 × 5 mL) and dried under high vacuum at 20 °C: brown oil, yield according to $^1H$-NMR *ca.* 95%.

*(14)*: Sodium cyclopentadienide (3 mmol) in 2 mL anhydrous THF is dropped, within a period of 40 min, into a suspension of *(9)* (2 mmol) in 10 mL anhydrous furan under $N_2$ at room temperature. The initial lemon-yellow, subsequently red-brown reaction mixture (with cloudy precipitate) is stirred for 4 h, and then held for 14 h at 0 °C. Following addition of 10 mL water, the mixture is extracted with pentane (3 × 15 mL); the organic phase is dried over $MgSO_4$ and concentrated at 200 torr/0—20 °C. Chromatography with pentane on 10 g silica gel [*(14)* elutes with the solvent front] and preparative gas chromatography on 10% Carbowax at 60 °C gives analytically pure *(14)*. Yield 13%.

Received: January 9, 1981 [Z 830 IE]
German version: Angew. Chem. *93*, 788 (1981)

[1] Attempts to synthesize *(1)* and *(2)*: *F. Fisher, D. E. Applequist*, J. Org. Chem. *30*, 2089 (1965); *M. Oda, R. Breslow, J. Pecoraro*, Tetrahedron Lett. *1972*, 4419; *M. Neuenschwander, W. K. Schenk*, Chimia *29*, 217 (1975).

[2] *W. E. Billups, A. J. Blakenay, N. T. Chamberlain*, J. Org. Chem. *41*, 3771 (1976).

[3] *A. Weber, G. Sabbioni, R. Galli, M. Neuenschwander*, Chimia *35*, 57 (1981). *(4)* is accessible from bromoform and phenyl vinyl sulfide in 49% yield by treatment with NaOH *via* phase transfer catalysis.

[4] a) *K. G. Taylor, J. Chaney*, J. Am. Chem. Soc. *94*, 8924 (1972); *C. A. Stein, T. H. Morton*, Tetrahedron Lett. *1973*, 4939; b) *K. Kitatani, T. Hiyama, H. Nozaki*, J. Am. Chem. Soc. *97*, 949 (1975); Bull. Chem. Soc. Jpn. *50*, 3288 (1977).

[5] While methylation of lithium cyclopropylcarbenoids is easy, their reaction with electrophilic cyclopentadienes causes serious problems. Cyclopentenone can be reacted with lithium cyclopropylcarbenoids bearing groups X of low steric requirement. *G. Sabbioni, A. Weber, R. Galli, M. Neuenschwander*, Chimia *35*, 95 (1981).

[6] *A. Weber*, Dissertation, Universität Bern 1978.

[7] Similar yields of *(10)* and *(11)* were obtained by reaction of the sulfone *(8)* with potassium *tert*-butoxide in *tert*-butyl alcohol as well as with sodium methoxide in methanol.

[8] Use of bases having nucleophilic properties reduces the yields of the trapped products of type *(10)* and *(11)*.

[9] This chemical shift is typical of C-8 in tricyclo[3.2.1.0$^{2,4}$]oct-6-enes with an *endo*-orientated three-membered ring. Cf. *e.g. H. Günther, W. Herrig, H. Seel, S. Tobias*, J. Org. Chem. *45*, 4329 (1980).

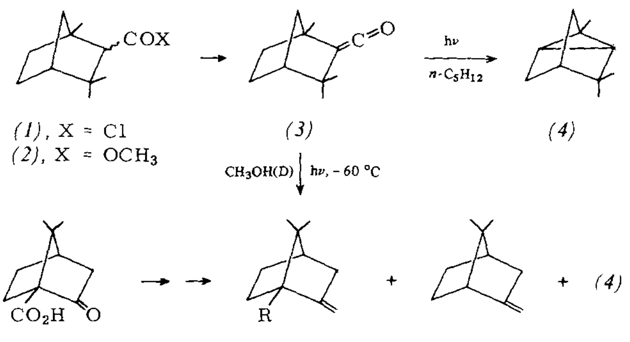
---

## Photoreactions of Sterically Hindered Ketenes

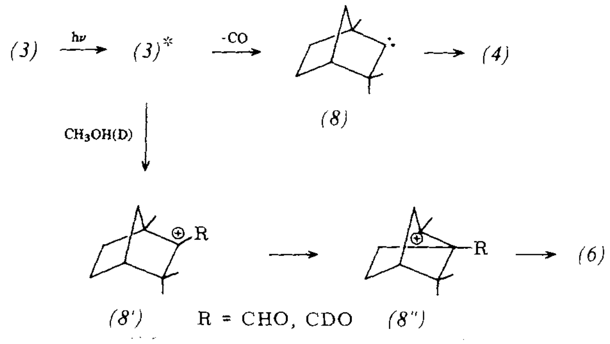
By *Wolfgang Kirmse* and *Walter Spaleck*[*]

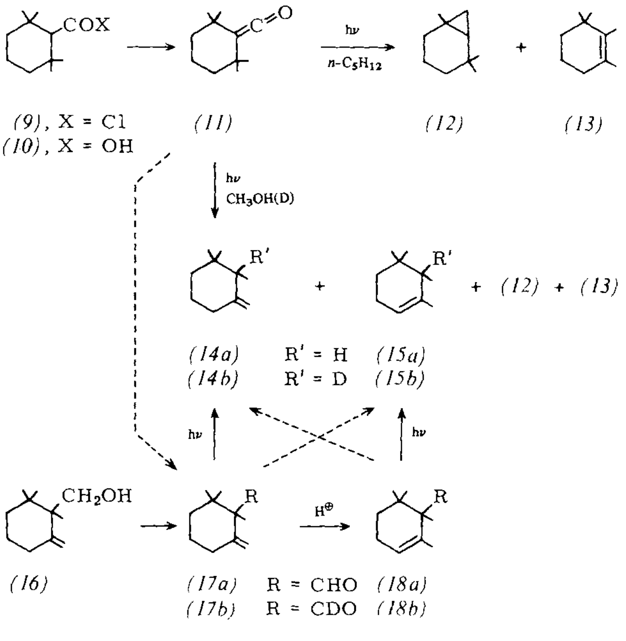
The formation of methylene by gas phase photolysis of ketene has been thoroughly investigated[1]. Ketenes are rarely used in solution as carbene-sources, since they rapidly dimerize and react with nucleophiles. We have found, however, that sterically hindered dialkylketenes, in addition to forming carbenes, undergo novel photoreactions, which indicates an "umpolung" of the excited state.

The acid chlorides *(1)*[2], *(9)*[3] and *(19)*[4], upon treatment with triethylamine (benzene, 130—140 °C, sealed tube), yielded the ketenes *(3)* (19%), *(11)* (30%) and *(20)* (45%) (yields after purification by preparative gas chromatography). Irradiation of a solution of *(3)* in pentane (high pressure Hg lamp, quartz, $N_2$) led to cyclofenchene *(4)*, the typical C—H-insertion product of carbene *(8)*. *(3)* reacts rapidly with methanol at room temperature to give a mixture of the esters *(2)* (*exo* : *endo* = 1 : 10). Photolysis of *(3)* competes with addition of methanol at −60 °C. Hereby, *(4)* and *(6a)* are initially formed in the ratio 1 : 1; at longer periods of irradiation, photodecarbonylation of *(6a)* occurs leading to formation of α-fenchene *(7)*.



The constitution of the surprising photoproduct *(6a)* was verified by independent synthesis from ketopinic acid *(5)*[5] (1. $CH_2N_2$, 2. $Ph_3P{=}CH_2$, 3. $LiAlH_4$, 4. dicyclohexylcarbodiimide/$H_3PO_4$/dimethyl sulfoxide (DMSO), total yield 34%). Formally, *(6a)* is formed from *(3)* by hydrogen transfer from the 1-methyl group to the ketene carbon atom. This does not, however, occur *via* an intramolecular reaction since irradiation of *(3)* in $CH_3OD$ produced *(6b)*. We formulate the novel photoisomerization as a protonation of the excited ketene *(3)** to give the carbenium ion *(8')*, which yields *(8'')* *via* a Wagner-Meerwein rearrangement; finally, deprotonation of *(8'')* leads to the aldehydes *(6a)* or *(6b)*. According to quantum mechanical calculations, the carbonyl carbon of the ketene carries a positive charge in the ground state and a partial negative charge in the excited state ($^3A_2$ and $^1A_2$)[6]. The reaction *(3)**→*(6)* provides experimental verification of this.





Irradiation of ketene *(11)* in pentane yielded *(12)* and *(13)* in the ratio 30 : 1. This result is typical of β-branched carbenes, insertion into the γ-C—H bonds being preferred to alkyl group migration[7]. *(11)* reacts with methanol in the dark only after several days. Photolysis of *(11)* in methanol yields the alkenes *(14a)* (34%) and *(15a)* (15%), in addition to *(12)* (30%) and *(13)* (6%). The aldehyde *(17a)* could—even at −60 °C—only be detected in small amounts (1—2%) after short periods of irradiation. For purposes of comparison, the aldehyde *(17a)* was prepared from *(16)*[8]

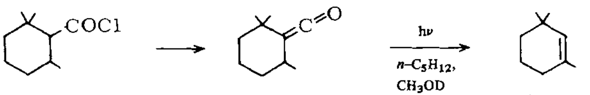
---

[*] Prof. Dr. W. Kirmse, Dr. W. Spaleck
Abteilung für Chemie der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)

(dicyclohexylcarbodiimide/$H_3PO_4$/DMSO, 65%) and isomerized to *(18a)* with 4-toluenesulfonic acid (benzene, 80 °C, 44%). Irradiation of *(17a)* in methanol gave predominantly *(14a)* (70—75%), in addition to *(13)* and *(15a)*; from *(18a)*, predominantly *(15a)* (80—85%), in addition to *(13)* and *(14a)*, were formed. Both aldehydes reacted more rapidly than ketene *(11)* and hence could not be enriched by photolysis. Irradiation of *(11)* in $CH_3OD$ led to *(14b)* with 0.96 D/mol and to *(15b)* with 0.94 D/mol, while *(12)* contained only 0.11 D/mol. These results indicate that a photoprotonation, with concomitant rearrangement, is also probable for *(11)*, *i.e.* formation of *(14)* and *(15)* on the reaction path

$$(11)^* \rightarrow (17) + (18) \rightarrow (14) + (15).$$

In contrast, the irradiation of *(20)* in pentane and methanol resulted, exclusively, in formation of 1,3,3-trimethylcyclohexene *(21)*, the β-C—H shift product of the carbene formed by decarbonylation[7]; *(21)* is formed in $CH_3OD$, without significant deuterium incorporation. Apparently,



*(19)* *(20)* *(21)*

CO cleavage from *(20)** occurs considerably more rapidly than the reaction with methanol.

Received: February 16, 1981 [Z 831 IE]
German version: Angew. Chem. *93*, 791 (1981)

CAS Registry numbers:
*(1)*, 76275-39-3; *endo-2*, 78672-57-8; *exo-2*, 78672-58-9; *(3)*, 78672-59-0; *(4)*, 488-97-1; *(5)*, 464-78-8; *(6a)*, 78672-60-3; *(9)*, 54439-96-2; *(11)*, 73683-20-2; *(12)*, 78672-61-4; *(13)*, 3949-35-7; *(14a)*, 1846-45-3; *(15a)*, 3757-05-9; *(16)*, 78672-62-5; *(17a)*, 78672-63-6; *(18a)*, 78672-64-7; *(19)*, 78737-55-0; *(20)*, 78672-65-8; *(21)*, 503-47-9.

---

[1] Review: *W. Kirmse:* Carbene Chemistry, Academic Press, New York 1971, p. 9—14.
[2] *L. Carlsen, H. Egsgaard, E. Schaumann, H. Mrotzek, W.-R. Klein,* J. Chem. Soc. Perkin Trans. II *1980*, 1557. Only mass spectroscopic evidence for *(3)* is described in this work: *(3)* was not isolated.
[3] Preparation of carboxylic acid *(10)*: *M. de Botton*, Bull. Soc. Chim. Fr. *1966*, 2212.
[4] *D. Shive, J. Horeczy, G. Wash, H. L. Lochte*, J. Am. Chem. Soc. *64*, 385 (1942).
[5] *P. D. Bartlett, L. H. Knox*, J. Am. Chem. Soc. *69*, 3189 (1939).
[6] a) *J. L. Del Bene*, J. Am. Chem. Soc. *94*, 3713 (1974); b) *L. B. Harding, W. A. Goddard III, ibid. 98*, 6093 (1976).
[7] See [1], p. 236—241.
[8] *H. R. Vogt, H. Schinz*, Helv. Chim. Acta *37*, 1779 (1954).

## Photometry with Laser Diodes: Determination of $D_2O$ and Compounds with OH Groups

By *Martin Wenzel*[*]

Ordinary spectrophotometers deal with the UV/VIS-region up to 800 nm. Only a few spectrometers can, in addition, analyze the near infrared ($\lambda = 800-2500$ nm). Furthermore, this region is also not accessible by conventional IR spectrometers. The near infrared, however, offers interesting analytical possibilities[1], in particular for the determination of compounds with OH- or NH-groups. Compounds having OH-groups show, for example, in addition to a strong absorption in the region of the fundamental vibrations at 2700—2800 nm, harmonics in the near IR in the 1300—1400 nm region[2].

In the following, a new method of analyzing compounds with OH- or NH-groups at 1350 nm is described using an apparatus which neither recquires a monochromator nor a filter for these wavelengths. As light source, the apparatus uses a laser diode ($In_{1-x}Ga_xAs_{1-y}P_y$)[3] which emits light of 1350 nm wavelength and which is normally used for the transmission of information in glass fibers. The laser beam is modulated, passes through the measuring cuvette and is subsequently recorded by a frequency-specific photodetector. Finally, the signal is transformed in the usual way to an extinction value. Since the light emitted from semiconductor lasers is rigorously monochromatic, measurements can be performed on absorption edges without the problems which arise with broadband light sources.

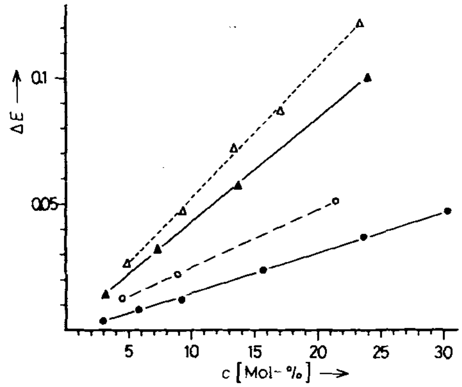


Fig. 1. Concentration dependence of the extinction difference with water and alcohols. (●—●) $C_2H_5OH$ in cyclohexane; (○---○) $CH_3OH$ in acetone; (▲—▲) $H_2O$ in dioxane; (△---△) $H_2O$ in acetone. Measurements made with a laser diode ($\lambda = 1350$ nm); path length: 1 cm; 25 °C; reference cuvette; pure solvent.

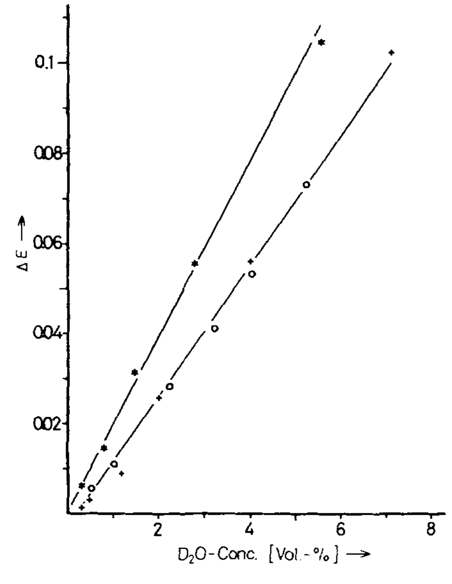


Fig. 2. Concentration dependence of the extinction difference of aqueous samples with different $D_2O$ concentration. (+---+) serum; (○—○) water; (*---*) urine. The serum and urine were treated with the same volume of $H_2O$ (reference cuvette) and $D_2O$ (sample cuvette). All further particulars are as in Fig. 1.

The concentration of compounds with OH-groups can be measured directly using a photometer constructed on this principle with tempered cuvette holders. Figure 1 shows the calibration curves obtained for four mixtures:

---

[*] Prof. Dr. M. Wenzel
Institut für Pharmazie, Biologisch-chemische Abteilung (FB 22, WE 1) der Freien Universität
Königin-Luise-Strasse 2—4, D-1000 Berlin 33 (Germany)

ethanol and cyclohexane, methanol and acetone, water and dioxane, as well as water and acetone. These curves are linear up to relatively high fractions of the OH-containing compound. Similar calibration curves were obtained with glycine and albumin in water (harmonic of the NH-vibrational frequency).

The $D_2O$ content of water can also be measured, since deuterium oxide only shows a small IR absorption at 1350 nm[4]. The applications for this method in the fields of medicine and biochemistry are particularly interesting, since the $D_2O$ content of native serum or urine can be determined directly. Calibration curves are reproduced in Figure 2. For biological samples it is therefore unneccessary to separate the aqueous component from the constituents *e.g.* by freeze-sublimination.

Received: December 1, 1980 [Z 832 IE]
German version: Angew. Chem. *93*, 793 (1981)

---

[1] *H. Volkmann:* Handbuch der Infrarot-Spektroskopie, Verlag Chemie, Weinheim 1972; *F. S. Parker:* Application of Infrared Spectroscopy in Biochemistry, Biology and Medicine, Adam Hilger 1971.

[2] *W. Kaye*, Spectrochim. Acta *6*, 257 (1954).

[3] Mitsubishi Electric ML 7201-X.

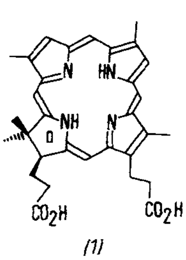
[4] *R. Keil*, Z. Anal. Chem. *249*, 289 (1970).

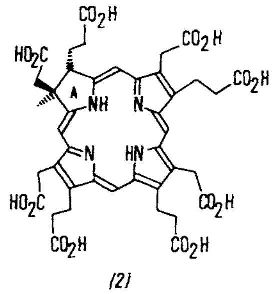
[5] *M. Wenzel*, J. Klin. Chem. Klin. Biochem. *14*, 185 (1976); *M. Wenzel, B. Hölscher, T. Günther, H. J. Merker, ibid. 17*, 123 (1979); *J. H. Fischer, Ch. Asmuth, M. Wenzel*, Experientia *37*, 263 (1981).

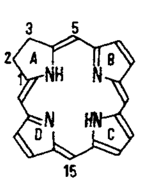
## A Directed Synthesis of the Chlorin System[**]

By *Franz-Peter Montforts*[*]

Bonellin *(1)* and the so-called Factor I *(2)* are structurally novel, porphinoid pigments of the chlorin type *(3)*. This fundamental skeletal structure was hitherto known only from its occurrence in the chlorophylls. Bonellin *(1)*, the sex-differentiating pheromone of *Bonellia viridis*, a sea animal of the Echiuroid family and widely distributed in the Mediterranean, has attracted the attention of biologists and chemists because of its unusual physiological properties[1]. In 1978, *Pelter et al.*[1h] were able to establish the constitution of the natural product, already isolated in pure form in 1939[1d], by X-ray structure analysis; however, the absolute configuration of the single center of chirality remained an open question.

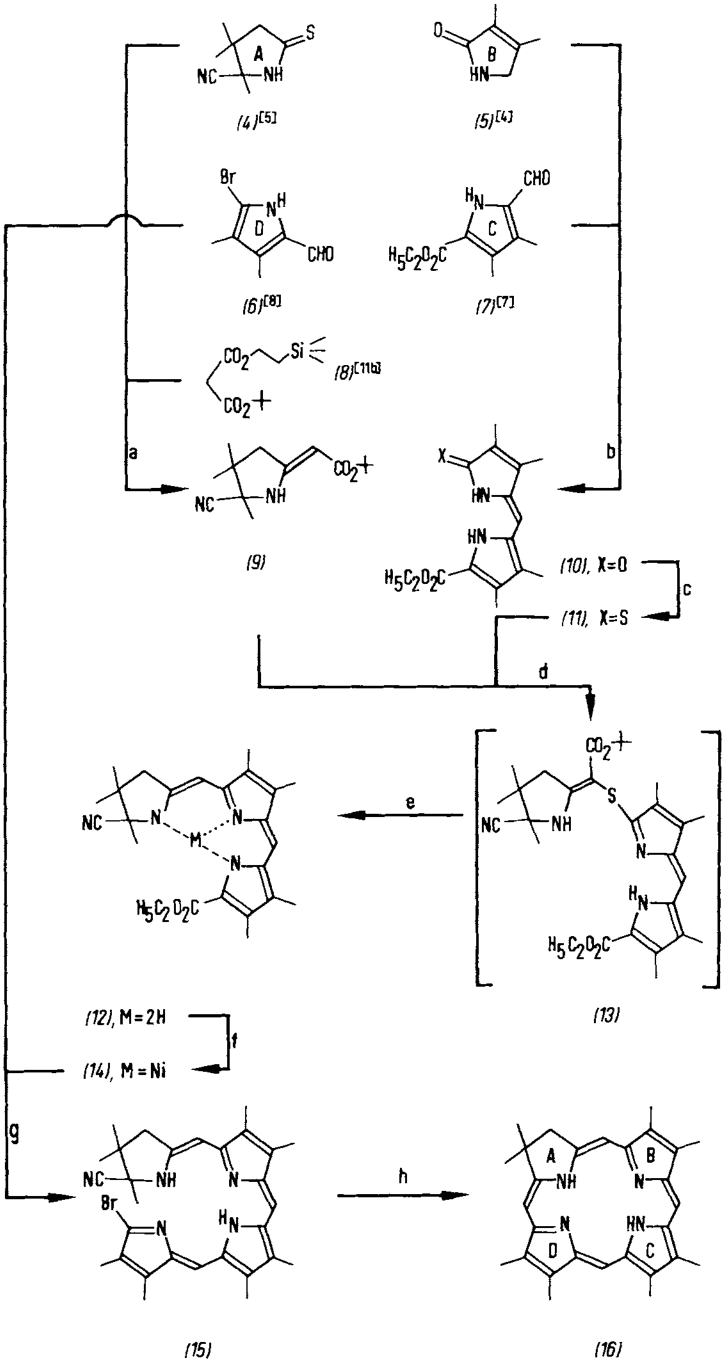

*(1)*


*(2)*


*(3)*

The Factor I *(2)* was found in vitamin $B_{12}$-producing microorganisms by *Müller et al.* and *Arigoni et al.*[2] and the reduced form was demonstrated to be a biosynthetic precursor of the sirohydrochlorins and of vitamin $B_{12}$.

Although chlorin syntheses are known[3], selective routes which would provide access to the characteristic structural unit containing the geminal dialkyl groups of the partially



Scheme 1. Reaction conditions: a: 1) *(4)*+ 1.2 equiv *(8)*/1.1 $(C_6H_5CO_2)_2$/3.7 $K_2CO_3$ in $CH_3CN$, 0°C→room temperature (RT), crude work-up. 2) 80°C in $P(OC_2H_5)_3$, crude work-up. 3) 1.07 $(n\text{-}C_4H_9)_4NF$ in tetrahydrofuran, reflux, *(4)*, 2 N $HCl/CH_2Cl_2$, extraction, separation by preparative HPLC (47% cryst.). b: 2-diazabicycloundecene (DBU)/molecular sieve 3 Å in THF, reflux (67% cryst.). c: 1 $P_2S_5$/6 $NaHCO_3$ in THF, RT (85% cryst.). d: 1) *(9)*+1 *N*-bromosuccinimide in $CH_2Cl_2$, RT. 2) 0.95 *(11)*/4 DBU in $CH_3CN$, RT (85% TLC pure). e: 8 $P(CH_2CH_2CN)_3/CF_3CO_2H$—$CHCl_3$ (1:10), reflux (41% cryst) referred to *(11)*, 49% referred to *(13)*. f: 2.6 $Ni(CH_3CO_2)_2 \cdot 4H_2O$/50 $CH_3CO_2Na$ in $CH_3OH$—THF (2:1), RT (86% cryst.). g: 1) *(14)* in THF+100 KOH in $CH_3OH$—$H_2O$ (9:1), reflux under argon (hydrolysis of the ethyl ester), crude work-up. 2) + 2*(6)*/6 *p*-toluenesulfonic acid in $CHCl_3$, reflux, under argon (63% cryst.) h: 1) 4 $Zn(CH_3CO)_2 \cdot 2H_2O$/90 KO*t*Bu in *tert*-butyl alcohol (degassed) 70°C, under argon. 2) 25% $HCl/CH_2Cl_2$, extraction, (72% TLC pure, 57% cryst.). With the exception of *(13)*, all compounds of *(4)*–*(16)* were characterized by elemental analysis and UV/VIS, IR, $^1H$-NMR, and mass spectra.

---

[*] Dr. F. P. Montforts
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt/Main 50 (Germany)

[**] This work was supported by the Verband der Chemischen Industrie by a Liebig stipend. I wish to thank Prof. Dr. *A. Eschenmoser* and Prof. Dr. *G. Quinkert* for valuable discussions, and for supplying the necessary substances.

saturated rings D and A in the natural products *(1)* and *(2)* are still lacking.

Paramount in our synthesis is the 2-pyrrolinone *(5)*[4] whose lactam function can be coupled with a geminal dimethylated building block A *(4)*[5] by methods adopted from corrin chemistry, while condensation with the pyrrolaldehyde *(7)*[7] in the 5-position is possible according to the principles of bile-pigment synthesis[6]. Incorporation of the ring D *(6)*[8] is achieved *via* the classical routes of porphin chemistry.

The pyrrolinone *(5)* and the aldehyde *(7)* undergo a base-catalyzed reaction to give the bicyclic lactam *(10)*, which is converted with $P_2S_5/NaHCO_3$[9] into its thio-analogue *(11)*[10].

The thiolactam *(4)* is converted by reaction with the selectively cleavable malonic ester *(8)*[11] *via* sulfide contraction (oxidative variant)[5] into the vinylogous urethane *(9)*.

Coupling of *(9)* and *(11)* *via* a brominating agent[5b] affords the tricyclic sulfide *(13)*, which is converted by a variant of the sulfide contraction, developed by *Rasetti*[11c] for an isobacteriochlorin synthesis, into the CC coupled tricycle *(12)*. Direct hydrolysis of the ester function in *(12)* was of little preparative use, since considerable decyanidation also occurs. Circumvention of this problem was achieved *via* the readily accessible intermediary nickel complex *(14)*, in which the metal atom activates the ester function by participation in the complexation[12], such that a rapid, selective hydrolysis is possible.

The crude product of ester hydrolysis undergoes direct acid-catalyzed condensation with decarboxylation and decomplexation with the bromopyrrolaldehyde *(6)* to give the tetracycle *(15)*. Reaction with potassium *tert*-butyl alkoxide in the presence of zinc(II)[13], which exercises a template effect and can be readily removed acidolytically from the ligand system that is formed, finally leads to cyclization of the tetracycle *(15)* to the chlorin *(16)*[14].

Received: April 27, 1981 [Z 833 IE]
German version: Angew. Chem. *93*, 795 (1981)

---

[1] a) *F. Baltzer*, Handb. Zool. *2*, 62 (1931); b) *R. F. Nigrelli, M. F. Stempien, G. D. Ruggieri, V. R. Liguori, J. T. Cecil*, Fed. Proc. Fed. Am. Soc. Exp. Biol. *26*, 1197 (1967); c) *L. Cariello, M. DeNicola Giudici, L. Zanetti, G. Prota*, Experientia *34*, 1427 (1978); d) *E. Lederer*, C. R. Acad. Sci. *209*, 528 (1939); e) *A. Pelter, J. A. Ballantine, V. Ferrito, V. Jaccarini, A. F. Psaila, P. J. Schembri*, J. Chem. Soc. Chem. Commun. *1976*, 999; f) *L. Agius, J. A. Ballantine, V. Ferrito, V. Jaccarini, P. Murray-Rust, A. Pelter, A. F. Psaila, P. J. Schembri*, Pure Appl. Chem. *51*, 1847 (1979); g) *J. I. Mathews, S. E. Braslavsky, P. Camilleri*, Photochem. Photobiol. *32*, 733 (1980); h) *J. A. Ballantine, A. F. Psaila, A. Pelter, P. Murray-Rust, V. Ferrito, P. Schembri, V. Jaccarini*, J. Chem. Soc. Perkin Trans. I *1980*, 1080.

[2] a) *R. Deeg, H.-P. Kriemler, K.-H. Bergmann, G. Müller*, Z. Physiol. Chem. *358*, 339 (1977); b) *G. Müller, R. Deeg, K. D. Gneuss, G. Gunzer* in *B. Zagalak, W. Friedrich:* Vitamin $B_{12}$ and Intrinsic Factor; Proc. 3rd Eur. Symp. Zürich, de Gruyter, Berlin 1979, p. 279; c) *M. Imfeld, D. Arigoni, ibid.*, p. 315.

[3] a) *H. Fischer, H. Helberger*, Justus Liebigs Ann. Chem. *471*, 295 (1929); b) *U. Eisner, A. Lichtarowicz, R. P. Linstead*, J. Chem. Soc. *1957*, 733; c) *H. H. Inhoffen, J. W. Buchler, R. Thomas*, Tetrahedron Lett. *1969*, 1141; d) *H. W. Whitlock Jr., R. Hanauer, M. Y. Oester, R. K. Bower*, J. Am. Chem. Soc. *91*, 7485 (1969); e) *R. Bonnett, M. J. Dimsdale, G. F. Stephenson*, J. Chem. Soc. *C 1969*, 564; f) An exception is Woodward's chlorophyll synthesis; cf. *R. B. Woodward*, Angew. Chem. *72*, 651 (1960).

[4] *J. H. Atkinson, R. S. Atkinson, A. W. Johnson*, J. Chem. Soc. *1964*, 5999.

[5] a) *Y. Yamada, D. Miljkovic, P. Wehrli, B. Golding, P. Löliger, R. Keese, K. Müller, A. Eschenmoser*, Angew. Chem. *81*, 301 (1969); Angew. Chem. Int. Ed. Engl. *8*, 343 (1969); b) *E. Götschi, W. Hunkeler, H. J. Wild, P. Schneider, W. Fuhrer, J. Gleason, A. Eschenmoser, ibid. 85*, 950 (1973) and *12*, 910 (1973).

[6] Cf. *e.g. H. Plieninger, J. Ruppert*, Justus Liebigs Ann. Chem. *736*, 43 (1970).

[7] *D. Dolphin, R. L. N. Harris, J. L. Huppatz, A. W. Johnson, I. T. Kay*, J. Chem. Soc. *C 1966*, 30.

[8] *P. S. Clezy, A. J. Liepa*, Aust. J. Chem. *24*, 1933 (1971); *H. Fischer, M. Hoefelmann*, Justus Liebigs Ann. Chem. *533*, 216 (1938).

[9] *J. W. Scheeren, P. H. J. Ooms, R. J. F. Nivard*, Synthesis *1973*, 149. $NaHCO_3$ addition was decisive for the success of the reaction.

[10] Similar thiolactams have been obtained by acid thiolysis of α-bromodipyrromethenes Cf. [11b].

[11] a) *H. Gerlach*, Helv. Chim. Acta *60*, 3039 (1977); b) *S. Ofner, V. Rasetti, D. B. Zehnder, A. Eschenmoser, ibid.*, in press; c) *V. Rasetti*, Diss. ETH Zürich No. 6462, Juris Verlag, Zürich 1979.

[12] Complexation of the ester function in *(14)* is revealed in the IR spectrum. The carbonyl absorption of the free ligand *(12)* observed at 1675 $cm^{-1}$ is absent in the spectrum of the nickel complex *(14)*.

[13] *F. P. Montforts, S. Ofner, V. Rasetti, A. Eschenmoser, W. D. Woggon, K. Jones, A. R. Battersby*, Angew. Chem. *91*, 752 (1979); Angew. Chem. Int. Ed. Engl. *18*, 675 (1979).

[14] Note added in proof: After this work had been completed, two novel chlorin syntheses were reported which produced yields of 7.4 and 6.8% in the last step: *R. J. Snow, C. J. R. Fookes, A. R. Battersby*, J. Chem. Soc. Chem. Commun. *1981*, 524.

---

## 4,4-Disubstituted 1,4-Dihydropyridines by Intramolecular Addition of Carbanions to Pyridines

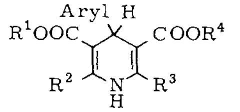
By *Siegfried Goldmann*[*]

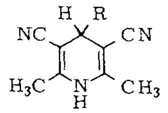
*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

1,4-Dihydropyridines exhibit analgetic[1a] and, above all, coronary dilating and hypertensive activity[1b,c].

Only 1,4-dihydropyridines such as *(1)* and *(2)*, monosubstituted in the 4-position, were previously accessible[1c]—by Hantzsch synthesis or by addition of carbanions to pyridines[2]. All attempts[3] to prepare 4,4-disubstituted derivatives have so far been unsuccessful: Neither the Hantzsch synthesis with ketones[4a] nor preparation *via* the addition of nucleophiles to 4-substituted pyridines[4b] proved useful in this respect.

*(1)*





*(2)*

We have now succeeded, however, in methylating the 4-aryl-substituted pyridine derivative *(3)* exclusively in the 4-position. An alternative route *via* a carbanion attached intramolecularly to the pyridine ring was chosen for this[5].

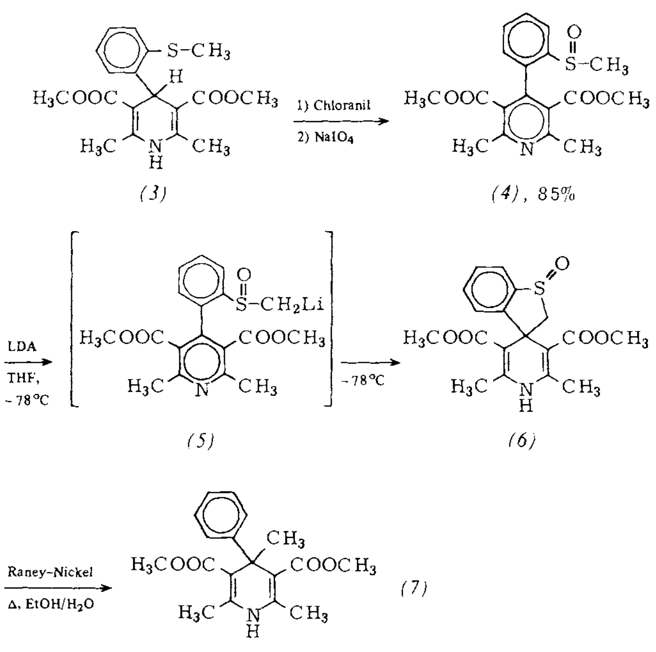
The dihydropyridine *(3)*, which is readily accessible by the Hantzsch synthesis, was oxidized with chloranil[6] to the pyridine and then with periodate[7] to the sulfoxide *(4)*. Metalation with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −78 °C affords the carbanion *(5)*, which spontaneously stabilizes as *(6)* at −78 °C. Removal of the "handle" with Raney nickel leads to the 4,4-disubstituted 1,4-dihydropyridine *(7)* in 74% yield.

### Procedure

*(6)*: A solution of diisopropylamine (25.2 mL, 0.25 mol) in anhydrous THF (200 mL) was prepared under $N_2$ and treated with butyllithium (0.25 mol; 15% in hexane) at 0 °C. This solution was then added to a solution of *(4)* (36 g, 0.1 mol) in THF (400 mL) cooled to −78 °C. It was immediately protonated at −78 °C with $CH_3OH$ and

---

[*] Dr. S. Goldmann
Chemisch-Wissenschaftliches Labor Pharma der Bayer AG
Postfach 10 17 09, D-5600 Wuppertal 1 (Germany)



NH$_4$Cl/H$_2$O; after addition of 500 mL of H$_2$O the resulting precipitate was filtered off by suction, washed with water, and dried at 100 °C. Yield 29 g (80%) *(6)*; m.p. 286–289 °C (dec.). $^1$H-NMR (CDCl$_3$/CD$_3$OD): $\delta=2.15$ (s, 3H), 2.2 (s, 3H), 3.2 (s, 3H), 3.3 (s, 3H), 3.4 (d, $J=13$ Hz, 1H), 4.2 (d, $J=13$ Hz, 1H), 7.2–7.5 (m, 3H), 7.6–7.8 (m, 1H).

*(7)*: A solution of *(6)* (12 g, 33 mmol) in aqueous 75% ethanol (600 mL) was treated with Raney nickel (100 g, aqueous suspension) and the mixture boiled under reflux for 5 h. After cooling, the mixture was filtered by suction, the filtrate concentrated in a rotary evaporator, and the residue recrystallized from ethyl acetate. Yield 7.6 g (74%) *(7)*; m.p. 148–150 °C. $^1$H-NMR (CDCl$_3$): $\delta=1.9$ (s, 3H), 2.1 (s, 6H), 3.2 (s, 6H), 5.6 (s, broad, NH), 6.9–7.5 (m, 5H). – $^{13}$C-NMR (CDCl$_3$): $\delta=19.4$, 25.8, 43.5, 50.3, 110.2, 125.0, 127.1, 127.9, 139.8, 150.9, 163.7.

Received: January 26, 1981 [Z 836 IE]
German version: Angew. Chem. 93, 798 (1981)

---

[1] a) *A. P. Phillips*, J. Am. Chem. Soc. *71*, 4003 (1949); *A. P. Phillips, L. O. Randall*, US-Pat. 2359329 (1944), Burroughs Wellcome; b) *F. Bossert, W. Vater*, Belg. Pat. 689377 (1967), Bayer AG; *F. Bossert, W. Vater*, Naturwissenschaften *58*, 578 (1971); *B. Loev, S. J. Ehrreich, R. E. Tedeschi*, J. Pharm. Pharmacol. *24*, 917 (1972); *B. Loev, M. M. Goodman, K. M. Snader, R. Tedeschi, E. Macko*, J. Med. Chem. *17*, 956 (1974); c) *F. Bossert, H. Meyer, E. Wehinger*, Angew. Chem. *93*, 755 (1981); Angew. Chem. Int. Ed. Engl. *20*, 762 (1981).

[2] Review: *U. Eisner, J. Kuthan*, Chem. Rev. *72*, 1 (1972); *T. Taguchi, M. Nishi, K. Watanabe, T. Mukaiyama*, Chem. Lett. *1973*, 1307; *A. E. Hauck, C.-S. Giam*, J. Chem. Soc. Perkin Trans. I *1980*, 2070.

[3] Exception: 4,4-disubstituted 3,5-dicyano-1,4-dihydropyridines can be prepared in small yields. Cf. US-Pat. 3973025 (1976), (John Wyeth and Brother Ltd.).

[4] a) *B. Loev, K. M. Snader*, J. Org. Chem. *30*, 1914 (1965); b) *R. Lukeš, J. Kuthan*, Collect. Czech. Chem. Commun. *26*, 1422 (1961).

[5] Cf. also: *G. Vanags, E. I. Stankevich*, Zh. Obshch. Khim *30*, 3287 (1960), Chem. Abstr. *55*, 21119 (1961); *L. Leitis, G. Duburs, M. Simanska, G. Vanags*, Chem. Abstr. *59*, 12182 (1963); *G. Duburs, G. Vanags*, Dokl. Akad. Nauk, SSSR *134*, 1356 (1960), Chem. Abstr. *55*, 10438 (1961); *G. Adembri, S. Chimichi, R. Nesi, M. Scotton*, Gazz. Chim. Ital. *109*, 117 (1979); *T. Naito, O. Miyata, I. Ninomiya*, J. Chem. Soc. Chem. Commun. *1979*, 517.

[6] *R. C. Fuson, J. J. Miller*, J. Am. Chem. Soc. *79*, 3477 (1957).

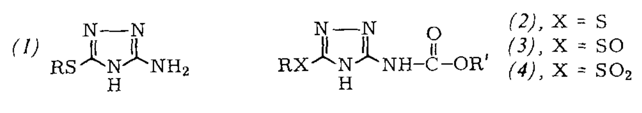
[7] *N. J. Leonard, C. R. Johnson*, J. Org. Chem. *27*, 282 (1962); *H. E. Baumgarten*, Org. Synth., Coll. Vol. V, Wiley, New York 1973, p. 791.

# Carboxylic Acid Derivatives of 3-Alkylthio-5-amino- and 3-Alkylsulfonyl-5-amino-1,2,4-triazoles

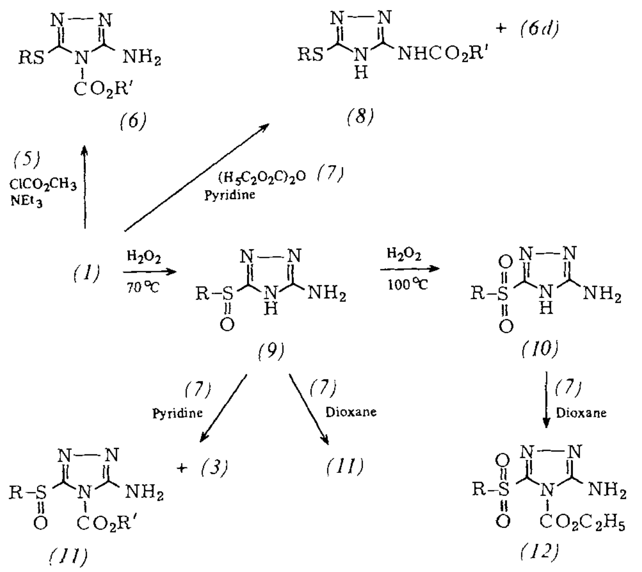
By *Klaus Sasse* and *Harald Niedrig*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Carbamate esters of type *(2)* are of interest from the point of view of biological investigations. We therefore initially studied the acylation of 3-alkylthio-5-amino-1,2,4-triazoles *(1)*, which are readily accessible in good yields *via* the method of *Heitke* and *McCarty*[1]. In α-amino-N-heterocycles the ring N atom[2] is acylated first and only somewhat drastic conditions lead to acylation of the *exo*-orientated amino group. In some cases a thermal rearrangement of the ring *N*-acyl- into the more thermodynamically stable *exo-NH*-acyl-compound occurs.



We found that methyl chloroformate *(5)* reacts with *(1a)* and *(1b, d)* in the presence of triethylamine to give exclusively the 4-methoxycarbonyl derivatives *(6a)*–*(6c)*. Thermal rearrangement of the acyl groups did not occur; only symmetrical urea derivatives were formed upon heating to 150 °C in phenol.



Reaction of *(1a)* with diethyl dicarbonate *(7)* in pyridine produces the isomers *(6d)* and *(8)* (30 : 70), whose structures were assigned by $^1$H-NMR spectroscopy; their separation is straightforward, due to the considerably lower solubility of *(8)* in toluene. Oxidation of the 3-amino-5-propylthio-triazole *(1c)* by H$_2$O$_2$ at 70 °C gave the sulfoxide *(9)* and at 100 °C the sulfone *(10)*. Treatment of the latter species with *(7)* in boiling dioxane produces, exclusively, the ring-acylated compounds *(11)* and *(12)*, respectively; in contrast, both acyl derivatives *(3c)* and *(11)* are formed from *(9)* upon treatment with *(7)* in pyridine (Table 1).

---

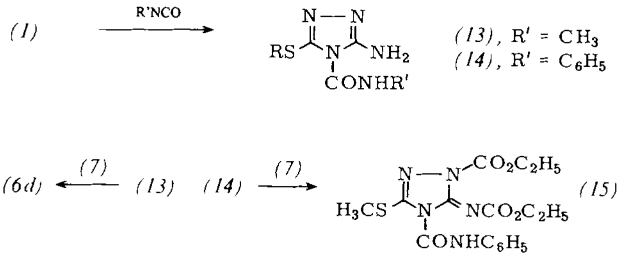
[*] Dr. K. Sasse, Dr. H. Niedrig
Zentralbereich Forschung und Entwicklung der Bayer AG
Bayerwerk, D-5090 Leverkusen 1 (Germany)

Table 1. Yields, melting points and selected spectroscopic data of the compounds prepared [a].

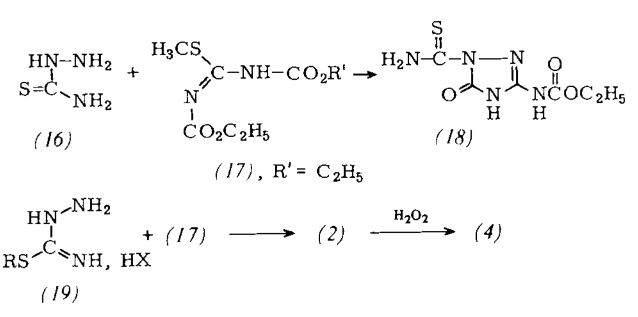
| Compd. | R | R′ | Yield [%] | M.p. [°C] | IR (KBr) νCO [cm⁻¹] |
|---|---|---|---|---|---|
| *(1a)* | $CH_3$ | — | 91 | 136 [b] | — |
| *(1b)* | $C_2H_5$ | — | 87 | 65—66 [c] | — |
| *(1c)* | $n$-$C_3H_7$ | — | 90 | 64—65 [c] | — |
| *(1d)* | $n$-$C_4H_9$ | — | 68 | 62—63 [d] | — |
| *(2a)* [e] | $CH_3$ | $CH_3$ | 57 | 220—222 [f] | 1734 |
| *(2b)* | $C_2H_5$ | $n$-$C_3H_7$ | 43 | 198—200 (P) [g] | — |
| *(2c)* | $n$-$C_3H_7$ | $C_2H_5$ | 52 | 200 [h] | — |
| *(2d)* | $i$-$C_3H_7$ | $CH_3$ | 46 | 153—154 [i] | — |
| *(2e)* | $n$-$C_4H_9$ | $n$-$C_3H_7$ | 39 | 186 [j] | — |
| *(2f)* | $C_6H_5CH_2$ | $C_2H_5$ | 52 | 191—192 [f] | — |
| *(3)* | $n$-$C_3H_7$ | $C_2H_5$ | 24 | 107—108 | 1710 |
| *(4a)* [k] | $CH_3$ | $CH_3$ | 93 | 260 (dec.) [i] | 1733 |
| *(4b)* | $C_2H_5$ | $n$-$C_3H_7$ | 47 | 123—124 [c] | — |
| *(4c)* | $n$-$C_3H_7$ | $C_2H_5$ | 72 | 167—168 [l] | — |
| *(4d)* | $i$-$C_3H_7$ | $CH_3$ | 51 | 160 [m] | — |
| *(4e)* | $n$-$C_4H_9$ | $n$-$C_3H_7$ | 48 | 125—126 [g] | — |
| *(4f)* | $C_6H_5CH_2$ | $C_2H_5$ | 66 | 203—204 [l] | — |
| *(6a)* [n] | $CH_3$ | $CH_3$ | 75 | 150—151 [c] | 1746 |
| *(6b)* | $C_2H_5$ | $CH_3$ | 83 | 153—154 [c] | — |
| *(6c)* | $n$-$C_4H_9$ | $CH_3$ | 71 | 134—135 [c] | — |
| *(6d)* [p] | $CH_3$ | $C_2H_5$ | 32 | 135—136 | 1733 |
| *(8)* [o] | $CH_3$ | $C_2H_5$ | 14 | 210 | 1714 |
| *(9)* | $n$-$C_3H_7$ | — | 63 | 146—147 | — |
| *(10)* | $n$-$C_3H_7$ | — | 47 | 171 | — |
| *(11)* | $n$-$C_3H_7$ | $C_2H_5$ | 69 | 116—117 | 1745 |
| *(12)* | $n$-$C_3H_7$ | $C_2H_5$ | 69 | 111—112 | — |
| *(13a)* [q] | $CH_3$ | $CH_3$ | 67 | 118 [r] | 1695 |
| *(13b)* | $C_2H_5$ | $CH_3$ | 73 | 99 [r] | — |
| *(13c)* | $n$-$C_4H_9$ | $CH_3$ | 74 | 99 [r] | — |
| *(14a)* | $CH_3$ | $C_6H_5$ | 53 | 163 [r] | — |
| *(14b)* | $n$-$C_3H_7$ | $C_6H_5$ | 62 | 112 [s] | — |
| *(14c)* | $n$-$C_4H_9$ | $C_6H_5$ | 88 | 103 [s] | — |

[a] All compounds gave satisfactory $^1H$-NMR-, IR- and mass-spectra. [b] From acetonitrile. [c] From ethyl acetate. [d] From ethyl acetate/ligroin. [e] $^1H$-NMR ($(CD_3)_2SO$): $\delta = 2.48$ (s, $SCH_3$), 3.68 (s, $OCH_3$), 10.5—11.5 (br., NH), 12.5—13.5 (br., NH). [f] From dimethyl formamide (DMF)/methanol. [g] From $n$-propanol. [h] From DMF/ethanol. [i] From methanol. [j] From DMF/propanol. [k] IR (KBr): 1338, 1158 $cm^{-1}$ ($\nu SO_2$); $^1H$-NMR ($(CD_3)_2SO$): $\delta = 3.22$ (s, $SO_2CH_3$), 3.74 (s, $OCH_3$), 11.5 (s, NH), 13.5—14.5 (br., NH). [l] From methanol. [m] From methanol/water (1:1). [n] $^1H$-NMR ($CDCl_3$): $\delta = 2.56$ (s, $SCH_3$), 4.04 (s, $OCH_3$), 6.91 (s, $NH_2$). [p] $^1H$-NMR ($(CD_3)_2SO$): $\delta = 1.31$ (t, $CCH_3$), 2.43 (s, $SCH_3$), 4.34 (q, $OCH_2$), 7.10 (s, $NH_2$). [o] $^1H$-NMR ($(CD_3)_2SO$): $\delta = 1.23$ (t, $CCH_3$), 2.48 (s, $SCH_3$), 4.12 (q, $OCH_2$), 10.5—11.5 (br., NH), 12.5—13.5 (br., NH). [q] $^1H$-NMR ($(CD_3)_2SO$): $\delta = 2.48$ (s, $SCH_3$), 2.75 (d, N—$CH_3$), 7.03 (s, $NH_2$), 7.35—8.0 (br., NH). [r] From toluene. [s] From petroleum ether (85—100 °C).

The selective acylation of the $NH_2$-function after the ring-NH group is previously blocked by a carbamoyl moiety, as in *(13)*, was unsuccessful; the $N$-carbamoyltriazoles *(13)* and *(14)* could be prepared, *via* 1,4-diazabicyclo[2.2.2]octane (DABCO) catalysis, from *(1)* and isocyanates. *(13)* does not react with *(5)*; with *(7)* in boiling dioxane, the carbamoyl groups were exchanged for the ethoxycarbonyl moiety resulting in formation of *(6d)*. Only the thermally stable phenylcarbamoyl compound *(14)* reacted with *(7)* *via* a double acylation procedure to give *(15)*.



We now attempted to introduce the carbamate ester moiety at the triazole synthesis stage: only the triazolinone *(18)* was formed from condensation of the thiosemicarbazide *(16)* with $N,N'$-bisethoxycarbonyl-$S$-methylisothiourea *(17)* in acetic acid. If instead of the thiosemicarbazide its $S$-alkyl derivative *(19)* is used, however, the desired 3-alkoxycarbonylamino-5-alkylthio-1,2,4-triazoles *(2)* are formed, whose oxidation to the sulfones *(4)* with $H_2O_2$ proceedes smoothly (Table 1).



R = $CH_3$, $C_2H_5$, $n$-$C_3H_7$, $n$-$C_4H_9$, $CH_2C_6H_5$;
R′ = $CH_3$, $C_2H_5$, $n$-$C_3H_7$; X = Halogen

## *Procedure*

Yields, melting points and spectroscopic data are given in Table 1.

*(6a)—(6c)*: *(5)* (9.5 g, 0.1 mol) is dropped into a solution of *(1)* (0.1 mol) and triethylamine (10.1 g, 0.1 mol) in 100 mL dioxane at 10—15 °C; the mixture is stirred for 2 h at room temperature, diluted with water, and filtered off.

*(6d)/(8)*: A mixture of *(1a)* (13.0 g, 0.1 mol) in 100 mL dioxane and 25 mL pyridine is heated to boiling with *(7)* (50 g) for 5 h. Insoluble material is filtered off and the filtrate concentrated under reduced pressure. The residue is refluxed in 100 mL toluene and the insoluble material filtered off while still hot. Combined insoluble fractions: 2.8 g *(8)* (14%). The toluene solution is cooled in ice, treated with the same volume of ligroin, recooled, and filtered off. Yield: 6.5 g *(6d)* (32%).

*(9)*: A solution of *(1c)* (15.9 g, 0.1 mol) in 200 mL $H_2O$ and 5 mL $CH_3CO_2H$ at 70 °C is treated, dropwise, with 15 g (0.15 mol) 35% $H_2O_2$, stirred for 2 h at 70 °C and filtered. The filtrate is concentrated under reduced pressure to 1/3 of its original volume and cooled for 24 h on ice. The precipitate is filtered off and recrystallized from a little water. Yield 11 g (63%).

*(10)*: A solution of *(9)* (17.4 g, 0.1 mol) in 120 mL 50% acetic acid at 100 °C is treated dropwise with 15 g (0.15 mol) 35% $H_2O_2$. The mixture is stirred for 3 h at 100 °C, 100 mL water added and cooled for 24 h on ice, before being filtered-off. Yield: 9 g (47%).

*(11)* and *(12)*: 0.1 mol *(9)* or *(10)*, respectively, in 150 mL dioxane is heated to boiling for 5 h with 50 g *(7)* and the solution concentrated under reduced pressure. *(11)*: residue stirred with ether, cooled on ice and filtered-off. Recrystallization from ethyl acetate. Yield: 17 g (69%). *(12)*: Residue recrystallizes from ethanol. Yield: 18 g (69%).

*(3a)*: *(9)* (17.4 g, 0.1 mol) is reacted as described in the preparation of *(6d)/(8)*; the reaction solution is concentrated under reduced pressure. The oily residue dissolves in water and is made weakly alkaline by addition of dilute sodium hydroxide. Pyridine is distilled out using steam; the residue is acidified with dilute hydrochloric acid and concentrated under reduced pressure. The resulting resi-

due is purified by column chromatography on silica gel (eluent: ethyl acetate). Yield: 6 g (24%).

*(13)/(14):* A solution of *(1)* (0.1 mol) in 100 mL dioxane, in the presence of 0.1 g DABCO, is treated with 0.1 mol methyl or phenyl isocyanate; the mixture is stirred for 2 h at room temperature and for 3 h at 40–50 °C; the whole is then cooled, filtered off or concentrated under reduced pressure and recrystallized.

*(18):* A solution of *(17)* (23.4 g, 0.1 mol) and *(16)* (9.1 g, 0.1 mol) in 100 mL acetic acid is gradually heated to boiling. The mixture is refluxed for 4 h, allowed to cool and the crystallizate filtered off. Recrystallization from butanol yields 11.3 g (48.7%) *(18)*, m.p. >250 °C.

*(2):* A solution of 0.1 mol *(17)* and 0.1 mol *(19)* in 100 mL acetic acid is refluxed for 5 h. The cooled reaction mixture is then poured into 400 mL ice-water and the crystallizate filtered off and dried.

*(4):* $H_2O_2$ (21.4 g, 0.22 mol, 35%) is added dropwise to a solution of *(2)* (0.1 mol) in 150 mL acetic acid at 90 °C. After cooling, excess $H_2O_2$ is reduced with conc. $NaHSO_3$ solution. The reaction mixture is concentrated under reduced pressure, and the residue stirred with water, filtered off, and dried.

Received: May 29, 1981 [Z 840 IE]
German version: Angew. Chem. *93*, 835 (1981)

---

[1] *B. T. Heitke, C. G. McCarty*, J. Org. Chem. *39*, 1522 (1974).

[2] a) *K. H. Mayer, D. Lauerer, H. Heitzer*, Synthesis *1975*, 673; b) *ibid. 1977*, 804.

---

# [2+2]-Cycloaddition of *N,N*-Dimethyl-*N*(2-methyl-1-propenylidene)ammonium ("Tetramethylketeniminium") Ion to α,β-Unsaturated Carbonyl Compounds

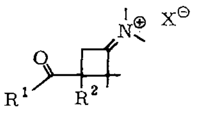
By *Hans-Georg Heine* and *Willy Hartmann*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

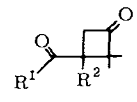
Salts containing the *N,N*-dimethyl-*N*(2-methyl-1-propenylidene)ammonium ion ("keteniminium salts") *(1)* are very reactive compounds owing to an energetically exceptionally low-lying unoccupied molecular orbital of the ammonium ion[1a]. For example, they considerably surpass the ketenes[2] in their readiness to undergo [2+2]-cycloadditions[1b] to simple alkenes and alkynes. Thus, dimethylketene only shows sufficient reactivity with 2-butene above 100 °C[2b], whereas *(1)* ($X = BF_4$) already undergoes smooth reaction at room temperature. We have now found that *(1)* ($X = ZnCl_3$) even adds to α,β-unsaturated carbonyl compounds, thus clearly demonstrating once again the difference in reactivity in comparison with ketenes, [2+2]-cycloadditions of which to relatively electron-poor double bonds are not known[3].

Reaction of *(1)* and methyl acrylate in boiling dichloromethane and subsequent hydrolysis of the primary product *(2a)* affords 3-methoxycarbonyl-2,2-dimethylcyclobutanone *(3a)* in good yields[4]. Its structure is confirmed by the product of the Baeyer-Villiger oxidation—methyl terebinate. The corresponding addition of methyl acrylate to *(1)* leads to *(3b)*, a degradation product of α-pinene[5]. *(1)* reacts even better with methyl methacrylate, giving the cyclobutanone *(3c)*. On the other hand, *(1)* does not react with *trans*-methyl crotonate or with methyl 3-methyl-2-butenoate under the same conditions, not even after 48-60 h. Dimethylamides of acrylic and methacrylic acid are suitable reactants. However, in the addition of *(1)* to methacrylic dimethylamide besides the main product *(3e)*, *ca.* 10% of the regioisomer *(4e)* is formed. Vinyl and isopropenyl methyl ketone behave similarly to the two acrylamides on reaction with *(1)*. Methyl vinyl ketone furnishes exclusively *(3f)*, whose structure is confirmed by degradation to terebic acid, whereas isopropenyl methyl ketone affords *(3g)* and *(4g)* in the ratio 80:20.

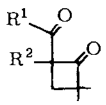
*(1)*



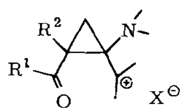
*(2)*



*(3)*



*(4)*



*(5)*

Table 1. Cyclobutanones *(3)* from *(1)* ($X = ZnCl_3$) and α,β-unsaturated carbonyl compounds.

| *(3)* | $R^1$ | $R^2$ | B.p. [°C/torr] | $n_D^{20}$ | Yield [a] [%] |
|---|---|---|---|---|---|
| *(a)* | $OCH_3$ | H | 87–88/12 | 1.4391 | 57 |
| *(b)* | $OC_2H_5$ | H | 93–96/14 | 1.4384 | 60 |
| *(c)* | $OCH_3$ | $CH_3$ | 89–92/12 | 1.4433 | 71 |
| *(d)* | $N(CH_3)_2$ | H | 86–91/0.08 | 1.4750 | 65 |
| *(e)* | $N(CH_3)_2$ | $CH_3$ | 50–51 [b] | – | 20 |
| *(f)* | $CH_3$ | H | 91–92.5/12 | 1.4481 | 48 |
| *(g)* | $CH_3$ | $CH_3$ | 97–103/13 [c] | 1.4548 | 34 |

[a] Polymerization of the α,β-unsaturated carbonyl compounds competes to varying extents with the cycloaddition. [b] M.p. [°C] (ligroin); the 90:10 mixture of *(3e)* and *(4e)* boils at 83–87 °C/0.15 torr, $n_D^{20} = 1.4770$. [c] Isomeric mixture of *(3g)* and *(4g)* (80:20).

The orientation of the substituents in the cycloadducts *(2)* and *(3)*, which does not correspond to the polarity of the components, is remarkable[6]. On reaction with α,β-unsaturated carbonyl compounds *(1)* possibly reacts like a carbene as a 1,1-pull-push reagent[1a]; in a [1+2]-cycloaddition, primarily the cyclopropyldimethylcarbenium ion *(5)* is formed; such intermediates are formulated for the proton-catalyzed rearrangement of *N*-phenylazaspiropentanes to phenylimino-substituted cyclobutanes[7]. Exclusive or preferred migration of the substituted alkyl group then leads to *(2)*.

## *Procedure*

A solution of 1-chloro-1-dimethylamino-2-methyl-1-propene (150.0 g, 1.1 mol) in anhydrous $CH_2Cl_2$ (250 mL) is added dropwise within 30 min to a stirred mixture of methyl acrylate (86.0 g, 1.0 mol) and anhydrous $ZnCl_2$ (165.0 g, 1.2 mol) in anhydrous $CH_2Cl_2$ (200 mL). After 14 hours heating under reflux the reaction mixture is treated with 1000 mL of water, stirred overnight, the phases separated, and the aqueous phase extracted exhaustively with ether in a Kutscher-Steudel apparatus. Subsequent work-up of the organic extract and fractional distillation afford 89.6 g

---

[*] Dr. H.-G. Heine and Dr. W. Hartmann
Zentralbereich Forschung und Entwicklung,
Wissenschaftliches Hauptlaboratorium der Bayer AG,
Postfach 166, D-4150 Krefeld 11 (Germany)

(57%) *(3a)*, (98.6% pure); IR ($CCl_4$): $\nu = 1755$ (ester carbonyl) and 1805 (four-membered ring carbonyl) $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 1.11$ (s, $CH_3$), 1.32 (s, $CH_3$), 2.80–3.50 (m, $CHCH_2$) and 3.76 (s, $OCH_3$).

Received: May 22, 1981 [Z 838 IE]
German version: Angew. Chem. *93*, 805 (1981)

---

[1] a) *L. Ghosez, M. J. O'Donnel* in *A. P. Marchand, R. E. Lehr*: Pericyclic Reactions, Vol. 2, Academic Press, New York 1977, p. 79ff.; b) *J. Marchand-Brynaert, L. Ghosez,* J. Am. Chem. Soc. *94*, 2870 (1972); *C. Hornaert, A. M. Hesbain-Frisque, L. Ghosez,* Angew. Chem. *87*, 552 (1975); Angew. Chem. Int. Ed. Engl. *14*, 569 (1975).

[2] a) *L. Ghosez, J. Marchand-Brynaert,* Adv. Org. Chem. *9*, 421 (1976); b) *N. S. Isaacs, P. Stanbury,* J. Chem. Soc. *1973*, 166.

[3] For example, diphenylketene does not react with acrylates or acrylonitrile even over several weeks at 90—100°C: *R. Huisgen, L. A. Feiler,* Chem. Ber. *102*, 3391 (1969).

[4] All new compounds gave appropriate spectroscopic data.

[5] *K. P. Sivaramakrishnan, L. H. Brannigan, C. S. Marvel,* J. Org. Chem. *37*, 4206 (1972).

[6] According to perturbation theoretical MO calculations the cyclobutanone with the methoxycarbonyl group in position-2 was to be expected on cycloaddition of the dimethylketene with methyl acrylates: *R. Sustmann, A. Ansmann, F. Vahrenholt,* J. Am. Chem. Soc. *94*, 8099 (1972).

[7] *J. K. Crandall, W. W. Conover,* J. Org. Chem. *39*, 63 (1974).

[8] *B. Haveaux, A. Dekoker, M. Rens, A. R. Sidani, J. Toye, L. Ghosez,* Org. Synth. *59*, 26 (1980).

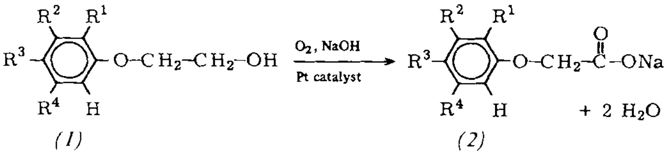
## Activation of Oxidations with Oxygen on Platinum Metals Using the Example of the Conversion of 2-Phenoxyethanols to Phenoxyacetic Acids

By *Helmut Fiege* and *Karlfried Wedemeyer*[*]

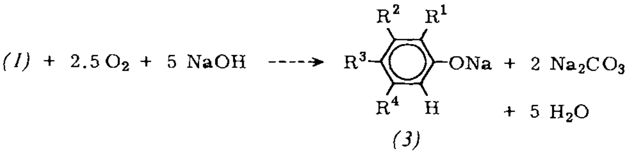
*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Phenoxyacetic acids are valuable organic intermediates and of considerable economic importance as growth-regulating herbicides[1]. They are mainly prepared industrially by heating the corresponding phenols with monochloroacetic acid in aqueous sodium hydroxide[2].

Since alcohols in aqueous alkaline media can often be selectively oxidized by $O_2$ (air) on platinum catalysts to carboxylic acids[3] 2-phenoxyethanols *(1)*, readily accessible from the reaction of phenols with ethylene oxide, could be converted into phenoxyacetic acids *(2)*.



Oxidations of this type have already been intensively investigated[4], however, the efficiency of the catalysts, the reaction conditions required, as well as the yields, were highly unsatisfactory. The transformation of *(1)* into *(2)* was accompanied by an undesired oxidative degradation of the hydroxyethyl group, which led to formation of the phenol *(3)* and $CO_2(Na_2CO_3)$[4b].



We have now found that the reaction can be vastly improved if small amounts of bismuth or lead as activators, and if necessary cadmium as coactivator, are added[5]. By this means, *at normal pressure and at short reaction times, almost quantitative yields* are possible using relatively small amounts of catalyst. The 2-phenoxyethanol concentration can be considerably increased above the levels previously achieved and the catalyst can be used several times without marked reduction in yield[6].

Table 1. Influence of lead-, bismuth- and cadmium-charges on the oxidation of 2-phenoxyethanol (0.1 mol) to phenoxyacetic acid in sodium hydroxide (5 N, 100 mL) on a platinum/active charcoal catalyst (0.65 g with 1% platinum) at 70 °C with $O_2$ at atmospheric pressure.

| Activator [a] | Coactivator [b] | $O_2$-uptake [mol] | t [h] | Yield [c] [%] |
|---|---|---|---|---|
| without | without | 0.0 | 6 | 0 [d] |
| Pb | without | 0.1 | 6 | 34 |
| Bi | without | 0.1 | 6 | 35 |
| Pb | Cd | 0.1 | 3.5 | 98 [e] [f] |
| Bi | Cd | 0.1 | 6 | 53 |
| without | Cd | 0.0 | 6 | 0 [d] |

[a] $5 \times 10^{-4}$ mol lead(II) or bismuth(III) nitrate. [b] $1 \times 10^{-4}$ mol cadmium(II) nitrate. [c] The fraction of $O_2$ not used for phenoxyacetic acid degrades a corresponding amount of 2-phenoxyethanol to phenol. [d] Unchanged 2-phenoxyethanol recovered. [e] M.p. = 98.5—99 °C. [f] Yield at 50 or 60 °C = 100%.

The influence of lead, bismuth and cadmium charges on the oxidation of 2-phenoxyethanol on active charcoal containing plantinum is shown in Table 1. Practically no oxidation occurs at the 1% platinum level. Oxidation first occurs upon addition of lead or bismuth. A further improvement occurs if cadmium, *e.g.* as $Cd(NO_3)_2$, is also added to the reaction mixture. The action of this coactivator in combination with lead is particularly marked. This system almost completely stops the oxidative degradation of the educt and in addition increases the rate of oxidation. The oxidation ceases after uptake of the stoichiometric amount of oxygen required for formation of phenoxyacetic acid.

Table 2. Influence of lead- and bismuth-charges on the oxidation of 2-phenoxyethanol (0.1 mol) to phenoxyacetic acid in sodium hydroxide (1.1 N; 100 mL) on a palladium/medical charcoal catalyst (0.65 g with 5% palladium) at 90 °C with $O_2$ at atmospheric pressure.

| Activator [a] | 0.1 mol $O_2$-uptake in [h] | Yield [%] |
|---|---|---|
| without | 10 [b] | 40 [d] |
| Pb | 1.75 [c] | 93 |
| Bi | 1.5 [c] | 100 |

[a] $5 \times 10^{-4}$ mol lead(II) nitrate or $5 \times 10^{-5}$ mol bismuth(III) nitrate. [b] $O_2$-uptake does not cease after this time. [c] End of $O_2$-uptake. [d] See Table 1, footnote [c].

In the presence of lead or bismuth as activator, an almost quantitative conversion *(1)*→*(2)* can be achieved on palladium—charcoal catalysts without additional dosing with cadmium. In the absence of lead or bismuth the reaction time is considerably longer and the yield poor (Table 2); moreover, the reaction does not stop after uptake of the stoichiometric amount of oxygen required for phenoxyacetic acid formation. Considerable amounts of phenol are formed as by-product.

---

[*] Dr. H. Fiege [+], Dr. K. Wedemeyer
Bayer AG, OC-Forschung 2
D-5090 Leverkusen 1 (Germany)
[+] Author to whom correspondence should be addressed.

Table 3. Substituted phenoxyacetic acids obtained by oxidation of substituted 2-phenoxyethanols (0.05 mol) in sodium hydroxide (1.3 N; 100 mL) with $O_2$ at atmospheric pressure at 90 °C on 0.65 g medical charcoal with 10% palladium in the presence of $5 \times 10^{-5}$ mol bismuth(III) nitrate as activator.

| $R^1$ | $R^2$ | $R^3$ | $R^4$ | 0.05 mol $O_2$ taken up in h | Yield [a] [%] | M. p. [b] [°C] |
|---|---|---|---|---|---|---|
| H | H | H | H | 1.0 | 100 | 98.5—99 |
| H | H | $CH_3$ | H | 0.75 | 99 | 137—138 |
| H | $CH_3$ | $CH_3$ | H | 1.0 | 95 | 161—162 |
| H | H | $C(CH_3)_3$ | H | 0.75 | 98 | 81—92 |
| H | H | Cl | H | 1.25 | 94 | 153—156 |
| $CH_3$ | H | Cl | H | 2.0 | 98 | 117—118 |
| H | $CH_3$ | Cl | $CH_3$ | 1.0 | 92 | 144—147 |
| Cl | H | Cl | H | 1.5 | 95 | 126—136 [c] |
| Cl | H | Cl | Cl | 1.5 | 95 | 147—152 |
| H | H | $OCH_3$ | H | 1.0 | 97 | 111—112 |

[a] After acidification to pH = 1, extracted with ether and determined acidimetrically in the extract. [b] Uncorrected M.p. of the extract (crude acid). The compounds gave satisfactory elemental analyses and conclusive IR- and NMR-spectra. [c] Contaminated with 2,6-dichlorophenoxyacetic acid.

The reaction also proceeds in excellent yield with some substituted 2-phenoxyethanols[7], although the conditions have not yet been optimized (Table 3).

### *Procedure*[5]

0.65 g powdered medical charcoal (10%, Pd content), 25 mg $Bi(NO_3)_3 \cdot 5H_2O$, 100 mL 1.3 N sodium hydroxide and 0.05 mol 2-phenoxyethanol are placed in a cylindrical glass vessel (250 mL, 5—6 cm inner diameter), fitted with stirrer, internal thermometer and $O_2$-inlet, which is thermostated by an outer mantel (Table 3).

After air is displaced from the flask by $O_2$, the stirrer (*ca.* 1500 rpm) is switched on, the mixture is heated to 90°C, and $O_2$ is passed in (from a calibrated burette with manostat) at atmospheric pressure until uptake ceases; in general, 0.05 mol $O_2$ are taken up.

After the catalyst has been filtered off from the still warm solution and washed with water, the filtrate is acidified to pH = 1 with 20% sulfuric acid and extracted five times with 50 mL ether. The resulting solution is dried over $Na_2SO_4$ and concentrated, leaving phenoxyacetic acid as residue (Table 3).

Received: April 27, 1981 [Z 841 IE]
German version: Angew. Chem. *93*, 812 (1981)

CAS Registry numbers:
*(1)*, $R_1 = R_2 = R_3 = R_4 = H$, 122-99-6; *(1)*, $R_1 = R_2 = R_4 = H$, $R_3 = CH_3$, 15149-10-7; *(1)*, $R_1 = R_4 = H$, $R_2 = R_3 = CH_3$, 34221-43-7; *(1)*, $R_1 = R_2 = R_4 = H$, $R_3 = C(CH)_3$, 713-46-2; *(1)*, $R_1 = R_2 = R_4 = H$, $R_3 = Cl$, 1892-43-9; *(1)*, $R_1 = CH_3$, $R_2 = R_4 = H$, $R_3 = Cl$, 36220-29-8; *(1)*, $R_1 = H$, $R_2 = R_4 = CH_3$, $R_3 = Cl$, 5825-79-6; *(1)*, $R_1 = R_3 = Cl$, $R_2 = R_4 = H$, 120-67-2; *(1)*, $R_1 = R_3 = R_4 = Cl$, $R_2 = H$, 2122-77-2; *(1)*, $R_1 = R_2 = R_4 = H$, $R_3 = OCH_3$, 5394-57-0; Pt, 7440-06-1; Pd, 7440-05-3; Pb, 7439-92-1; Bi, 7440-69-9; Cd, 7440-43-9; $O_2$, 7782-44-7.

---

[1] a) *R. Wegler, L. Eue* in *R. Wegler:* Chemie der Pflanzenschutz- und Schädlingsbekämpfungsmittel, Springer, Berlin 1977, Vol. 5, p. 180 pp; b) *G. Jäger* in *K. H. Büchel:* Pflanzenschutz und Schädlingsbekämpfung, Thieme, Stuttgart 1977, p. 133 pp.

[2] *H. Arold* in Ullmanns Encyklopädie der technischen Chemie, 4th edition, Verlag Chemie, Weinheim 1975, Vol. 9, p. 578 pp. This process is also unsatisfactory because sodium chloride is ultimately formed from the total chlorine required for the preparation of chloroacetic acid and a considerable excess of chloroacetic acid must be used to achieve the complete conversion of phenol; its hydrolysis product, glycolic acid, causes problems in waste water treatment.

[3] *K. Heyns, H. Paulsen* in *W. Foerst:* Neuere Methoden der präparativen organischen Chemie, Verlag Chemie, Weinheim 1960, Vol. 2, p. 208 pp; *K. Heyns, H. Paulsen, G. Rüdiger, J. Weyer*, Fortschr. Chem. Forsch. *11*, 285 (1969).

[4] a) *I. I. Ioffe, Yu. T. Nikolaev, M. S. Brodskii*, Kinet. Katal. *1*, 112 (1960); *I. I. Ioffe, Yu. T. Nikolaev, ibid. 2*, 145 (1961); b) *I. I. Ioffe, Yu. T. Nikolaev, G. A. Sukhareva*, Russ. J. Phys. Chem. *42*, 142 (1968).

[5] *H. Fiege, K. Wedemeyer*, DOS 2851788 (1978), Bayer AG.

[6] In terms of its activity as an activator, it is immaterial which oxidation state, or what type, of bismuth, cadmium or lead compound is added. The activators can be introduced with the catalyst or added directly to the liquid reaction mixture.

[7] Dr. *M. Dietrich*, Bayer AG, Dormagen, is thanked for samples of 2-(4-chloro-2-methylphenoxy)ethanol and 2-(2,4-dichlorophenoxy)ethanol. We prepared the other 2-phenoxyethanols using a method based on that of *E. Becker* and *E. Barthel* (Monatsh. Chem. *77*, 80 (1947)).

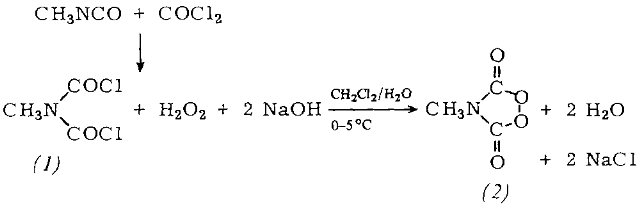
# 4-Methyl-1,2,4-dioxazolidine-3,5-dione, a Cyclic Imidodiacyl Peroxide

By *Hermann Hagemann*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

The easily accessible open-chain diacyl peroxides have long since acquired industrial significance as free radical initiators in polymerizations; cyclic diacyl peroxides are, however, less well known[1].

It has now been found that *N*-methylazamalonyl peroxide *(2)*, the first example of the previously unknown 1,2,4-dioxazolidine-3,5-dione can be particularly easily prepared. The educt *N*-methyliminodicarbonyl dichloride *(1)* was originally synthesized by chlorinating 4-methyl-1,2,4-dithiazolidine-3,5-dione but is now more readily obtainable by addition of phosgene to methyl isocyanate[2].



Solutions of *(1)* in dichloromethane react with 35% $H_2O_2$ and 10% sodium hydroxide at *ca.* 0—5 °C in a smooth cyclization step to the colorless, crystalline product *(2)*, m.p. = 89 °C.

The new cyclic diacyl peroxide *(2)* has an intense, characteristic smell and—as expected—behaves as a powerful oxidizing agent. The crystals are readily soluble in organic solvents *e.g.* $CH_2Cl_2$ or $CHCl_3$ and begin to sublime at *ca.* 50 °C at atmospheric pressure. The constitution of *(2)* has been confirmed from the C=O vibrational frequency at 1785 $cm^{-1}$, elemental analysis, and mass spectrum.

Received: May 29, 1981 [Z 842 IE]
German version: Angew. Chem. *93*, 813 (1981)

CAS Registry numbers:
*(1)*, 23197-35-5; *(2)*, 78715-73-8.

---

[1] *H. Kleinfeller, K. Rastädter*, Angew. Chem. *65*, 543 (1953); *W. Adam, R. Rucktäschel*, J. Am. Chem. Soc. *93*, 557 (1971).

[2] *G. Zumach, E. Kühle*, Synthesis *1970*, 542; *H. Hagemann, K. Ley*, DBP 1932830 (1971), Bayer AG.

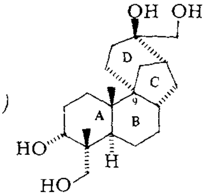
---

[*] Dr. H. Hagemann
Bayer AG, ZB-FE
D-5090 Leverkusen (Germany)

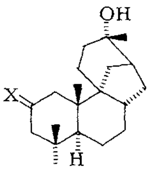
## An Expeditious and Efficient Entry into the Aphidicolin and Related Natural Products Ring Skeleton[**]

By *K. C. Nicolaou* and *Robert E. Zipkin*[*]

The potent antiviral and antimitotic properties of aphidicolin *(1)*[1], coupled with its novel and highly unusual molecular framework present a formidable and important challenge. Of particular interest to the synthetic chemist is the arrangement of the rings B, C, and D. The diterpenes stemodinone *(2)*[2] and stemodin *(3)*[2] are structurally related to aphidicolin *(1)* but differ from it in the stereochemistry of rings C and D. After considerable effort, total syntheses of all three natural products have recently been reported[3]. Although elegant, these syntheses suffer from poor yields and/or because they are multi-step routes, whereby the construction of the C/D ring system was especially problematical.

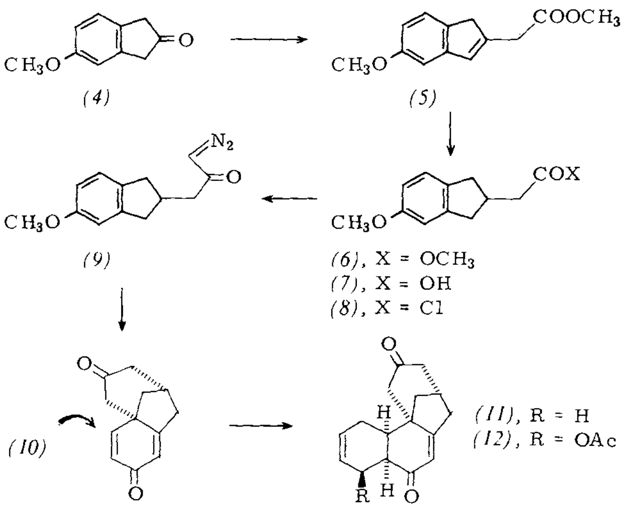


*(1)*



*(2)*, X = O
*(3)*, X = α-OH, H

We report here an expeditious, stereocontrolled and highly efficient construction of the ring structures of compounds *(1)*–*(3)* which is, furthermore, conceptually different from previous methods. The strategy for this new entry into the aphidicolin *(1)* and related structures depends on two key operations; firstly a diazoketone acid-induced cyclization[4] and secondly a regio- and stereocontrolled Lewis acid-catalyzed Diels-Alder reaction.



5-Methoxy-2-indanone *(4)*[5] reacted with $(MeO)_2P(O)CH_2CO_2Me/NaH$ in tetrahydrofuran (THF) (−50 °C→25 °C) to afford a mixture of the unsaturated ester *(5)*, (60–70%, mixture of (*E*)- and (*Z*)- α,β- and β,γ-unsaturated isomers; in the formula scheme only the latter is shown!) which was subjected to catalytic hydrogenation ($Pd/C-CH_3OH$, 25 °C) to afford the methyl ester *(6)* in quantitative yield. Base hydrolysis (LiOH, $H_2O$, $CH_3OH$, 25 °C) of *(6)* led to the acid *(7)* (100%), which was converted to the acid chloride *(8)* (oxalyl chloride-pyridine, $CH_2Cl_2$, 0 °C, 100%), which reacted further ($CH_2N_2$, ether, −20 °C) to give *(9)* (90%). *(9)* reacted with $CF_3COOH$ to give the crystalline dienone *(10)*[6] in 80% yield; this species not only contains the correct BCD ring system of *(1)*, *(2)*, and *(3)*, but also carries appropriate functionality for building on the A ring, *via* a Diels-Alder reaction. Dreiding molecular models clearly suggested a regio- and stereocontrolled approach of a diene component from the "left-side" and from the "top" (arrow). Indeed, it was found that brief exposure of *(10)* to butadiene in $CH_2Cl_2$ at 0 °C in the presence at $SnCl_4$ resulted in a single crystalline product the tetracycle *(11)* (97%). The selectivity of this Diels-Alder reaction was demonstrated by reacting the dienone *(10)* with 1-acetoxybutadiene under whereby the crystalline adduct *(12)* was formed in 90% yield (accompanied by a small amount of an as yet unknown stereoisomer). *(11)* and *(12)* were characterized by spectroscopic and X-ray crystallographic[7] measurements (Table 1 and Fig. 1).

Table 1. Selected physical properties of compounds *(10)*–*(12)*.

*(10)*: m.p. 97.5–98 °C; $^1$H-NMR ($CDCl_3$, 250 MHz): $\delta$ = 1.90–2.20 (m, 3 H), 2.45–2.95 (m, 6 H), 6.15 (d, $J$ = 1 Hz, 1 H), 6.27 (dd, $J$ = 10, 1 Hz, 1 H), 7.06 (d, $J$ = 10 Hz, 1 H); IR ($CCl_4$): $\nu$ = 1725, 1670, 1645 cm$^{-1}$.

*(11)*: m.p. 172–172.5 °C; $^1$H-NMR ($CDCl_3$, 250 MHz): $\delta$ = 1.70–3.10 (m, 15 H), 5.58 (m, 1 H), 5.70 (m, 1 H), 5.87 (s, 1 H); IR ($CCl_4$): $\nu$ = 1725, 1678 cm$^{-1}$.

*(12)*: m.p. 183–184 °C; $^1$H-NMR ($CDCl_3$, 250 MHz): $\delta$ = 1.78–2.80 (m, 11 H), 2.12 (s, 3 H), 3.08 (d, $J$ = 16 Hz, 1 H), 3.45 (t, $J$ = 4 Hz, 1 H), 5.45 (m, 1 H), 5.65 (m, 1 H), 5.77 (s, 1 H), 5.78 (m, 1 H); IR ($CCl_4$): $\nu$ = 1740, 1725, 1670 cm$^{-1}$.

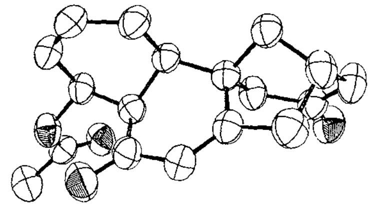


Fig. 1. X-ray crystallographic structure of *(12)*.

These observations clearly qualify this pathway as a rapid and highly efficient entry into the polycyclic ring framework of the natural products *(1)*–*(3)*.

### *Procedure*

*(10)*: A solution of *(9)* (230 mg, 1.0 mmol) in anhydrous $CH_2Cl_2$ (12.5 mL) was added dropwise to a stirred solution of $CF_3COOH$ (25 mL) in dry $CH_2Cl_2$ (12.5 mL) at −20 °C under an argon atmosphere. After 5 min the reaction mixture was diluted with $CH_2Cl_2$ (200 ml) and washed successively with $H_2O$ (3 × 50 mL), saturated $NaHCO_3$ solution (2 × 50 ml) and dried over $MgSO_4$. After evaporation of the solvent and preparative thin layer chromatography (silica gel, 2.5% $CH_3OH$ in ether) *(10)* was obtained as colorless crystals (150 mg, 80%) and was recrystallized from ether/pentane.

*(11)*: *(10)* (188 mg, 1.0 mmol) was dissolved in anhydrous $CH_2Cl_2$ (2 mL), cooled to 0 °C and the solution saturated

---

[*] Prof. Dr. K. C. Nicolaou, R. E. Zipkin
Department of Chemistry, University of Pennsylvania
Philadelphia, PA 19104 (USA)

[**] This work was supported by Grünenthal Chemie (Germany) and ICI Americas (USA). K. C. Nicolaou is a Fellow of the A. P. Sloan Foundation (1979–1983) and a Camille and Henry Dreyfus Teacher-Scholar (1980–1985).

with butadiene $SnCl_4$ (390 mg, 1.5 mmol) in dry $CH_2Cl_2$ (6 mL) was added dropwise and the reaction mixture was stirred for 2 h while being allowed to warm up to room temperature. Ice (10 g) and ether (200 mL) were added and the organic phase was separated and washed with $H_2O$ (20 mL), saturated $NaHCO_3$ solution (20 mL), and saturated sodium chloride solution (20 mL). Drying over $MgSO_4$, followed by evaporation afforded *(11)* which was recrystallized from chloroform/ether furnishing colorless crystals (235 mg, 97%).

*(12):* A stirred solution of *(10)* (188 mg, 1.0 mmol) and 1-acetoxylbutadiene (224 mg, 2.0 mmol) in anhydrous $CH_2Cl_2$ (6 mL) were cooled to 0 °C and treated under an argon atmosphere with a solution of $SnCl_4$ (260 mg, 1.0 mmol) in anhydrous $CH_2Cl_2$ (4 mL). After 30 min at 0 °C the reaction was quenched with ice (10 g) and ether (200 mL) and the organic phase separated and washed with $H_2O$ (20 mL), saturated $NaHCO_3$ solution (20 mL), and saturated sodium chloride solution (20 ml). Followed by evaporation, preparative thin-layer chromatography (silica gel, 10% acetone in $CH_2Cl_2$, and recrystallization from ether/petroleum ether afforded *(12)* as colorless crystals (269 mg, 90%).

Received: March 5, 1981 [Z 844 IE]
German version: Angew. Chem. *93*, 811 (1981)

---

[1] *W. Dalziel, B. Hesp, K. M. Stevenson, J. A. J. Jarvis,* J. Chem. Soc. Perkin Trans. 1 *1973*, 2841.

[2] *P. S. Manchand, J. D. White, H. Wright, J. Clardy,* J. Am. Chem. Soc. *95*, 2705 (1973).

[3] Aphidicolin: (a) *E. J. Corey, M. A. Tius, J. Das,* J. Am. Chem. Soc. *102*, 1744 (1980); *J. E. McMurry, A. Andrus, G. M. Visander, J. H. Musser, M. A. Johnson, ibid. 101*, 1331 (1979); *B. M. Trost, Y. Nishimura, K. Yamamoto, ibid. 101*, 1328 (1979); b) Stemodinone and Stemodin: *E. J. Corey, M. A. Tius, J. Das, ibid. 102*, 7612 (1980).

[4] An elegant application of this type of reaction in the total synthesis of gibberellins has recently been reported: *L. Lombardo, L. N. Mander, J. V. Turner,* J. Am. Chem. Soc. *102*, 6626 (1980).

[5] *D. J. Beames, L. N. Mander,* Aust. J. Chem. *27*, 1257 (1974).

[6] Structure *(10)* represents the isomer corresponding to the aphidicolin *(1)* skeleton. The other enantiomer which was also obtained in this reaction corresponds to the skeleton of stemodinone *(2)* and stemodin *(3)*.

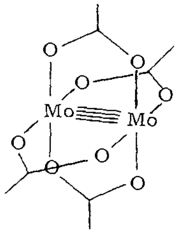
[7] We are indebted to Dr. *Patrick Carroll* (Department of Chemistry, University of Pennsylvania) for his assistance in solving the X-ray crystallographic structure of *(12)*.

---

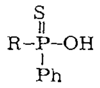
## Determination of the Absolute Configuration of Alkyl(phenyl)thiophosphinic *O*-Acids and of *O*-Alkyl Alkylthiophosphonates from the Circular Dichroism of Their Complexes with $[Mo_2(O_2CCH_3)_4]$[**]

By *Jan Omelańczuk* and *Günther Snatzke*[*]

*In situ* complexes of optically active carboxylic acids with the readily accessible and stable "parent complex" $[Mo_2(O_2CCH_3)_4]$ *(1)* exhibit several Cotton effects between 800 and 300 nm in dimethyl sulfoxide (DMSO); the signs of the two CD bands between 450 and 300 mn could be empirically correlated with the absolute configurations of the acids, which act as bidentate ligands. The sector rule could also be derived non-empirically for the Cotton effect at about 420 nm using qualitative MO theory[1].

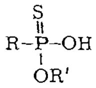


*(1)*



$$R-\overset{\overset{S}{\|}}{\underset{\underset{Ph}{|}}{P}}-OH$$

*(2a)*, R = Me
*(2b)*, R = Et
*(2c)*, R = *t*Bu



$$R-\overset{\overset{S}{\|}}{\underset{\underset{OR'}{|}}{P}}-OH$$

*(3a)*, R = R' = Me
*(3b)*, R = R' = Et
*(3c)*, R = Me, R' = *i*-$C_3H_7$

Of the alkyl(phenyl)thiophosphinic *O*-acids *(2)*, only *(2c)* gave CD bands in DMSO in the presence of *(1)*; surprisingly, however, we were able to observe two or three strong Cotton effects for *(2a—c)* in trifluoroacetic acid. Thus, despite the enormous excess of achiral, potential $F_3CCO_2^-$ ligands, the thiophosphinic acids complex sufficiently enough to yield easily measurable CD curves which retain their shape and magnitude over sufficiently long periods. *(2)* possibly does not occur as bidentate ligand, but as an additional axial substituent at one or both ends of the $Mo_2$ dumbbell. In crystals of $[Mo_2(O_2CR)_4]$-complexes, this position is usually occupied by an oxygen atom[2] of a neighboring molecule. This is also evidenced by the fact that practically no CD could be measured with acids such as phenylalanine in $CF_3CO_2H$.

All (+)-(*R*)-acids give a negative Cotton effect at about 490 nm, a further one about two to three times more positive at about 400 nm, and, at higher concentration, an additional slightly positive Cotton effect can be observed at about 540 nm (Fig. 1). The seleno-analogue behaves in exactly the same way. In the case of the (−)-(*S*)-enantiomers the CD curves are enantiomorphic. Similar Cotton effects are obtained in acetic acid, but they are not so intense.

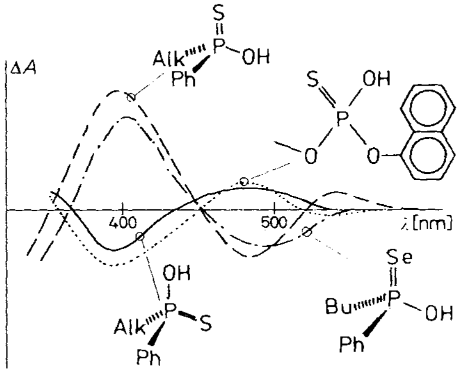


Fig. 1. CD spectra of alkyl(phenyl)thiophosphinic acids [(*R*)- and (*S*)-form] of (*R*)-*tert*-butyl(phenyl)selenophosphinic acid and of methyl α-naphthyl thiophosphate in $CF_3CO_2H$.

In pyridine the Cotton effects were recognizable, but much smaller; they rapidly changed their shape and became weaker. Nevertheless, these CD curves are also characteristic and can be used for the determination of the absolute configuration of *(2)*: the (+)-(*R*)-forms give three broad positive Cotton effects at about 590 nm (weak), 450 nm (strong) and 360 nm (medium). It is well-known that

---

[*] Prof. Dr. G. Snatzke, Dr. J. Omelańczuk [+]
Lehrstuhl für Strukturchemie der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)

[+] Alexander-von-Humboldt fellow, present address:
Institute for Molecular and Macromolecular Research
of the Polish Academy of Sciences
Boczna 5, PL 90-362 Łódź (Poland)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and an Alexander-von-Humboldt fellowship grant.

pyridine is incorporated in the complex as additional axial ligand[3].

Optically active *O*-alkyl alkylthiophosphonates *(3)* likewise give Cotton effects with *(1)* in pyridine or trifluoroacetic acid, but not in DMSO. However, in $CF_3CO_2H$ they are also very much smaller and rapidly disappear, probably due to hydrolysis of the ester group. Interestingly, however, we did obtain a clear CD with the (+)-methyl-α-naphthyl diester of monothiophosphoric acid under these conditions (Fig. 1). In pyridine in the presence of *(1)* the (+)-(*R*)-acids give a strong, broad, negative Cotton effect at about 480 nm and a likewise negative but weaker one at about 400 nm; the appearance of a further, positive Cotton effect is recognizable at shorter wavelengths (Fig. 2). *In situ* complexes of the (−)-(*S*)-compounds gave the corresponding enantiomorphic CD curves.

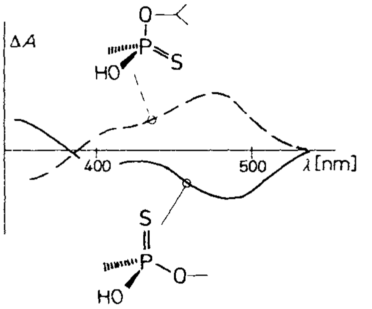


Fig. 2. CD spectra of (+)-(*R*)-*(3a)* and (−)-(*S*)-*(3c)* in pyridine.

*In situ* complexes with *(1)* are not only suitable for the determination of the absolute configuration of optically active carboxylic acids[1], glycols[1] and amino alcohols[4], but also of substituted thiophosphinic acids *(2)* and of esters of the thiophosphonic acid *(3)*. They are even more suitable than direct CD measurements[5], since the Cotton effects lie in a much more conveniently accessible wavelength region and there is no interference by bands of the ligands.

## *Procedure*

The acid[9] (0.5 to 1.5 mg) was dissolved in a solution of *(1)* in $CF_3CO_2H$ or pyridine (about 3 to 5 mM). The CD was immediately measured thereafter in cuvettes of layer thickness 2.00 to 0.10 nm using an ISA-Jobin-Yvon Mark III dichrograph.

Received: January 26, 1981 [Z 846 IE]
German version: Angew. Chem. 93, 815 (1981)

CAS Registry numbers:
*(1)*, 14221-06-8; *(R)-2a*, 38607-73-7; *(S)-2b*, 38607-74-8; *(R)-2c*, 54100-47-9; *(S)-2c*, 55705-77-6; *(R)-3a*, 38315-71-8; *(S)-3b*, 5152-74-9; *(S)-3c*, 38315-77-4; *(R)-tert*-butyl(phenyl)selenophosphinic acid, 51584-27-1; *(+)-O*-methyl-O-α-naphthylthiophosphoric acid, 48154-37-6.

---

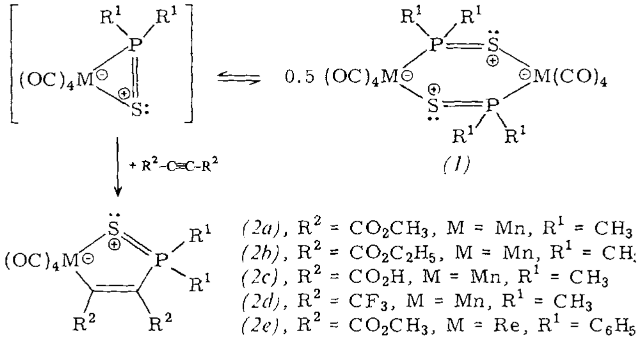
[1] *G. Snatzke, U. Wagner, H. P. Wolff*, Tetrahedron *37*, 349 (1981).
[2] *F. A. Cotton, M. Extine, L. D. Gage*, Inorg. Chem. *17*, 172 (1978).
[3] *F. A. Cotton, J. G. Norman Jr.*, J. Am. Chem. Soc. *94*, 5697 (1972).
[4] *J. Engel, G. Snatzke*, Chem. Ztg. *105*, 85 (1981).
[5] *M. Mikołajczyk, M. Para, J. Omelańczuk, M. Kajtár, G. Snatzke*, Tetrahedron *28*, 4357 (1972).
[6] Review: *M. Mikołajczyk, M. Leitloff*, Russ. Chem. Rev. *44*, 670 (1975).
[7] *B. Krawiecka, Z. Skrzypczyński, J. Michalski*, Phosphorus *3*, 177 (1973).
[8] *J. Omelańczuk, P. Kielbasiński, J. Michalski, J. Mikołajczak, M. Mikołajczyk, A. Skowrońska*, Tetrahedron *31*, 2809 (1975).
[9] Acids used: (+)-(*R*)-*(2a)* [6], (−)-(*S*)-*(2b)* [6], (+)-(*R*)-*(2c)* [6], (−)-(*S*)-*(2c)* [6], (+)-(*R*)-*tert*-butyl(phenyl)selenophosphinic acid [7], (+)-*(R)*-*(3a)* [6], (−)-(*S*)-*(3b)* [6], (−)-*(S)*-*(3c)* [6], (+)-*O*-methyl-*O*-α-naphthyl thiophosphate [8].

---

# Thiaphosphametallacyclopentadienes as Intermediates in the Cyclotrimerization of Alkynes with their Phosphorus-Sulfur Analogues[**]

By *Ekkehard Lindner, Axel Rau*, and *Sigurd Hoehne*[*]

Metallacyclopentadienes and $\eta^2$-metallabicyclohept dienes occur as reactive intermediates in the catalytic c clotrimerization and cyclocotrimerization of alkyne These compounds can also be synthesized in a directe manner and their catalytic activity tested[1]. We have no successfully obtained the P═S analogous intermediat products *(2)* by trapping the unstable thiaphosphametalla cyclopropene, which exists in equilibrium with *(1)*[2], wit electron-poor alkynes.



*(1)*

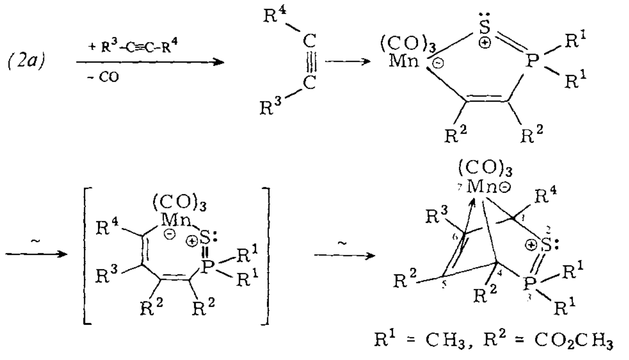
*(2a)*, $R^2 = CO_2CH_3$, M = Mn, $R^1 = CH_3$
*(2b)*, $R^2 = CO_2C_2H_5$, M = Mn, $R^1 = CH$
*(2c)*, $R^2 = CO_2H$, M = Mn, $R^1 = CH_3$
*(2d)*, $R^2 = CF_3$, M = Mn, $R^1 = CH_3$
*(2e)*, $R^2 = CO_2CH_3$, M = Re, $R^1 = C_6H_5$

The yellow (M = Mn) or colorless (M = Re) thiaphosphametallacyclopentadienes *(2)* are highly soluble in polar solvents and thermally stable. They were characterized by complete elemental analysis, mass-, IR-, and NMR-spectra (Table 1); *(2a)* was in addition characterized by crystal structure analysis[3] (Fig. 1). The molecular ions of *(2a)*, *(2b)*, *(2d)*, and *(2e)* were observed in the mass spectra.

Table 1. IR- and NMR-Data of *(2a)* (δ-values, *J* in Hz).

| IR [cm$^{-1}$] | $^1$H- [d] | $^{31}$P{$^1$H}- [e]<br>NMR | $^{13}$C{$^1$H}- [d] |
|---|---|---|---|
| ν(CO) [a] 2087 m-s,<br>2012 vs, 2008 sh,<br>1963 s-vs;<br>ν(C═O) [b] 1527 m;<br>ν(P═S) [c] 555 w | 2.03 (d,<br>*J* = 13.7, $PMe_2$),<br>3.76, 3.86<br>(both s, OMe) | 75.1 (s) | 128.29 (s,<br>S—Mn—C═),<br>159.20 (d,<br>*J* = 27.4, P—C═) |

[a] In $CCl_4$. [b] In KBr. [c] In Polyethylene. [d] $CDCl_3$ rel. TMS. [e] $CH_2Cl_2$ rel. 85% $H_3PO_4$ ext.



$R^1 = CH_3$, $R^2 = CO_2CH_3$
*(3a)*, $R^3 = R^4 = CO_2C_2H_5$
*(3b)*, $R^3 = H$, $R^4 = CO_2CH_3$

---

[*] Prof. Dr. E. Lindner, Dipl.-Chem. A. Rau, Dr. S. Hoehne
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

[**] Preparation and Properties of and Reactions with Metal-Containing Heterocycles, Part 14. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 13: *E. Lindner, G. Funk, S. Hoehne*, Chem. Ber. *114*, 2465 (1981).

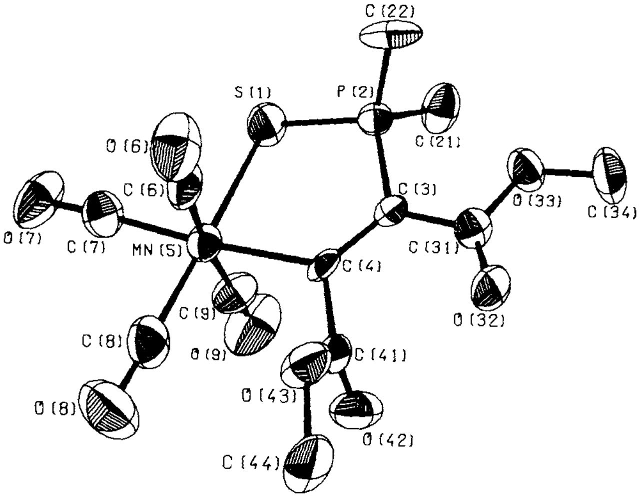


Fig. 1. ORTEP-representation of *(2a)* in the crystal (vibrational ellipsoids with 50% probability).

| Bord lengths | [pm] | Angle [°] | |
|---|---|---|---|
| S1—P2 | 199.6(4) | Mn5—S1—P2 | 99.9(2) |
| P2—C3 | 178.8(9) | S1—P2—C3 | 107.7(3) |
| C3—C4 | 135.6(12) | P2—C3—C4 | 116.9(6) |
| C4—Mn5 | 204.9(8) | C3—C4—Mn5 | 126.3(6) |
| Mn5—S1 | 240.6(4) | C4—Mn5—S1 | 87.4(3) |

The five-membered ring in *(2a)* is almost planar (sum of the internal ring angles 538°). The S1—P2 and C3—C4 bonds (199.6 and 135.6 pm) have considerable π-character. The Mn5—S1 distance is clearly longer than the sum of the covalent radii, and the coordination octahedron at manganese is only slightly distorted.

*(2a)* is kinetically labile and reacts with other alkynes *via* elimination of CO and insertion into the Mn—C σ-bond to produce a metallacycloheptatriene with vacant coordination sites[4], which immediately rearranges *via* reductive C—S-coupling to the λ$^4$-thia-λ$^5$-phospha-η$^2$-manganabicyclo[2.2.1]heptadiene *(3)*. This structural type is already known[5].

With the P═S analogues, the course of the cyclotrimerization of alkynes shows, among other things, that the triply bonded C atoms of the newly incorporated alkyne occupy positions C1 and C6 in *(3)*. In the case of *(3b)*, regiospecific insertion results with exclusive formation of the isomer with R$^3$ at C6. Due to the similar covalent radii and electronegativity of P and S, P═S behaves like a C═C-group. The yellow compounds *(3)*, which are readily soluble in polar solvents, decompose above 130 °C. They were characterized by complete elemental analysis, IR-, mass-, and $^1$H-NMR-spectra[6].

### *Procedure*

*(2a)*: A mixture of 0.58 mol *(1)* and 2.28 mol acetylenedicarboxylic acid dimethyl ester in 100 mL tetrahydrofuran (THF) is heated, under CO atmosphere, to 60 °C for 20 min. The reaction is monitored by thin layer chromatography and is interrupted after *ca.* 15 min by removal of the solvent. Purification is carried out by medium pressure chromatography on silica gel using $CH_2Cl_2$; yield 52%.

*(3b)*: 1.07 mol *(2a)* and 2.12 mol methyl propiolate in 100 mL THF are heated to 66 °C. The solvent is removed after 10 min and the residue chromatographed on silica gel using medium pressure chromatography ($CCl_4$/$CHCl_3$ 2 : 1); yield 64%.

Received: December 5, 1980 [Z 849a IE]
German version: Angew. Chem. 93, 821 (1981)

[1] *H. Suzuki, K. Itoh, Y. Ishii, K. Simon, J. A. Ibers*, J. Am. Chem. Soc. *98*, 8494 (1976); *L. D. Brown, K. Itoh, H. Suzuki, K. Hirai, J. A. Ibers, ibid. 100*, 8232 (1978); *P. Caddy, M. Green, E. O'Brien, L. E. Smart, P. Woodward*, J. Chem. Soc. Dalton Trans. *1980*, 962.

[2] *E. Lindner, B. Schilling*, Chem. Ber. *110*, 3889 (1977).

[3] Monoclinic crystals of *(2a)* from dichloromethane/*n*-hexane; space group C2/c, $a = 2434.9(6)$, $b = 1438.4(4)$, $c = 1032.1(9)$ pm, $\beta = 108.99(4)°$, $Z = 8$, $\rho_{calc.} = 1.56$ g·cm$^{-3}$. The structure was solved by direct methods and Fourier-difference syntheses and anisotropically refined for 2264 independent reflections ($\theta = 3-25°$) to $R = 0.093$ using the SHEL-76 program (except for H).

[4] *Y. Wakatsuki, K. Aoki, H. Yamazaki*, J. Am. Chem. Soc. *101*, 1123 (1979).

[5] *E. Lindner, A. Rau, S. Hoehne*, Angew. Chem. *91*, 568 (1979); Angew. Chem. Int. Ed. Engl. *18*, 534 (1979).

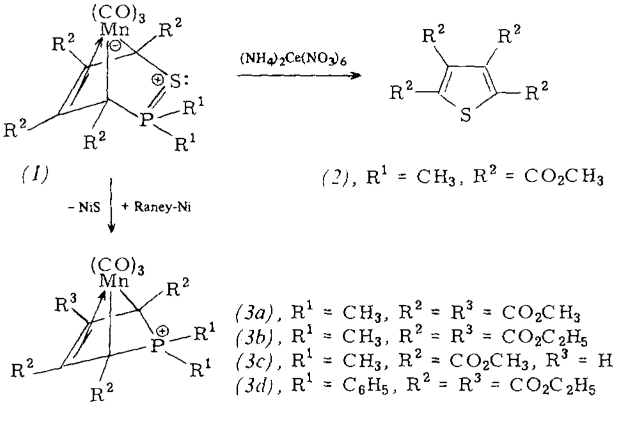
[6] IR: *(3a), (3b)* (in $CCl_4$): 2026 vs, 1954 s, 1944 s; 2020 vs, 1940 cm$^{-1}$ s (CO); MS: *m/z*: *(3a)* 544 ($M^+$), *(3b)* 458 ($M^+$); $^1$H-NMR: *(3b)* ($CDCl_3$, rel. TMS): $\delta = 3.73, 3.79, 3.86$ (s, $OCH_3$), 6.30 (d, $J = 2.9$ Hz, H-6).

## Syntheses with λ$^4$-Thia-λ$^5$-phospha-η$^2$-manganabicyclo[2.2.1]heptadiene[**]

By *Ekkehard Lindner, Axel Rau*, and *Sigurd Hoehne*[*]

Only a few syntheses of heterocycles using metal catalysis have been described. One of the few examples is the preparation of pyridine derivatives by the action of nitriles and alkynes on cobalt complexes, whereby cobaltacyclopentadienes appear as reactive intermediates[1]. As in the catalytic cyclotrimerization of alkynes, the removal of the metal group from aza-η$^2$-cobaltabicyclo[2.2.1]heptadiene should be the last step in the catalytic cycle.

In the course of investigations on the cyclotrimerization of alkynes with their phosphorus-sulfur analogues[2] we obtained the thiaphosphamanganabicyclo[2.2.1]heptadiene *(1)* which with CO[2b] or Ce(IV) salts[3] underwent cleavage, not only of the Mn(CO)$_3$- but also of the P(CH$_3$)$_2$-group, with almost quantitative formation of the thiophene derivative *(2)*.



*(1)*

*(2)*, R$^1$ = CH$_3$, R$^2$ = CO$_2$CH$_3$

*(3a)*, R$^1$ = CH$_3$, R$^2$ = R$^3$ = CO$_2$CH$_3$
*(3b)*, R$^1$ = CH$_3$, R$^2$ = R$^3$ = CO$_2$C$_2$H$_5$
*(3c)*, R$^1$ = CH$_3$, R$^2$ = CO$_2$CH$_3$, R$^3$ = H
*(3d)*, R$^1$ = C$_6$H$_5$, R$^2$ = R$^3$ = CO$_2$C$_2$H$_5$

Under catalytic hydrogenation conditions with Raney nickel, ring contraction *via* selective sulfur extrusion to the novel λ$^4$-phospha-η$^2$-manganabicyclo[2.2.1]hexene *(3)* occurs.

---

[*] Prof. Dr. E. Lindner, Dipl.-Chem. A. Rau, Dr. S. Hoehne
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

[**] Preparation and Properties of and Reactions with Metal-Containing Heterocycles, Part 15. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. - Part 14: [2a].

0570-0833/81/0909-0788 $ 02.50/0

The yellow, thermally stable compounds *(3)* are readily soluble in polar solvents and can also formally be considered as $\eta^4$-phosphole complexes. They were identified by total elemental analysis, mass- ($M^+$), IR- and NMR-spectra (Table 1), and *(3a)*, additionally, by an X-ray structure analysis[4] (Fig. 1).

Table 1. IR- and NMR-data for *(3a)* ($\delta$-values, $J$ in Hz).

| IR [a] $\nu$(CO) [cm$^{-1}$] | $^1$H- [b] | $^{31}$P{$^1$H}- [c] NMR | $^{13}$C{$^1$H}- [b] |
|---|---|---|---|
| 2028 vs, 1958 s, 1946 s | 1.51, 2.36 (both d, $J$=11.7, 14.1, PMe$_2$), 3.68, 3.89 (both s, OMe) | 51.6 (s) | 29.83 (d, $J$=83.2, Mn—C—P), 96.26 (d, $J$=16.0, C=C) |

[a] In $CCl_4$. [b] $CDCl_3$ rel. TMS. [c] $CH_2Cl_2$ rel. 85% $H_3PO_4$ ext.

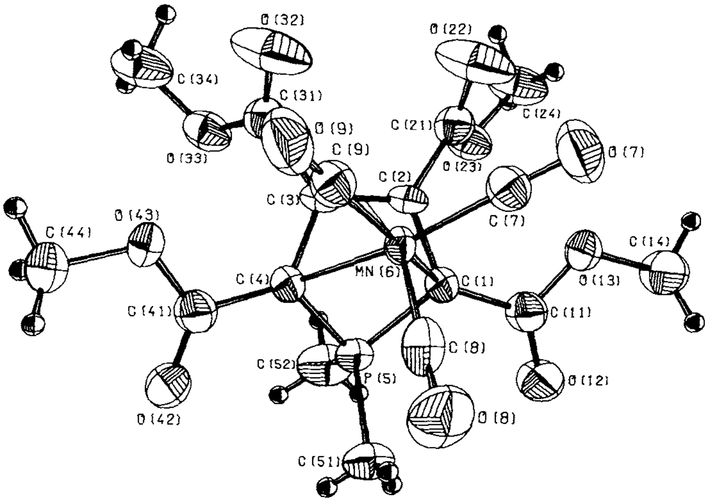


Fig. 1. ORTEP-representation of *(3a)* in the crystal (vibrational ellipsoids with 50% residence probability).

| Bond lengths [pm] | | Angles [°] | |
|---|---|---|---|
| C1—C2 | 144.7(9) | P5—C1—C2 | 108.3(5) |
| C2—C3 | 140.6(13) | C1—C2—C3 | 111.4(6) |
| C3—C4 | 144.7(9) | C2—C3—C4 | 111.4(6) |
| C4—P5 | 176.9(7) | C3—C4—P5 | 108.3(5) |
| P5—C1 | 176.9(7) | C4—P5—C1 | 88.4(5) |
| C1—Mn6 | 215.8(8) | C1—Mn6—C4 | 69.7(2) |
| Mn6—C4 | 215.8(8) | Mn6—C1—C2 | 65.9(4) |
| C2—Mn6 | 205.0(7) | Mn6—C1—P5 | 91.6(3) |
| Mn6—C3 | 205.0(7) | Mn6—C4—C3 | 65.9(4) |
| | | Mn6—C4—P5 | 91.6(3) |

*(3a)* possesses a crystallographic reflection plane in which Mn6 with one of the three CO, as well as phosphorus with the two methyl-groups, lie. The atoms C1 to C4 (bond length sequence, long-short-long) and P5 form a five-membered ring having an envelope conformation, in which the phosphorus is separated by *ca.* 67 pm from the plane formed by C1—C4. The interplanar angle amounts to 32°. The unusually small value of 88.4° for the C1—P5—C4 angle is due to steric effects. The ester groups on C1 and C4 are only 1.0°, and those on C2 and C3 *ca.* 5.6° rotated out of the plane. Until now only corresponding phosphole complexes with three- or five-bonded phosphorus have been known[5]. The complexes *(3)* are potential educts for the synthesis of difficultly accessible phosphole derivatives.

*Procedure*

*(2):* A solution of 0.38 mmol *(1)* and 0.45 mmol $(NH_4)_2Ce(NO_3)_6$ in 30 mL methanol/tetrahydrofuran (1 : 1) is stirred for 30 min. After removal of the solvent the residue is extracted three times with benzene and filtered. Chromatographic purification on silica gel using ethyl acetate follows; yield 95%.

*(3a, b, d):* 0.38 mmol *(1)* and 19.0 mmol Raney-nickel in 100 mL methanol are stirred. After 24 h the mixture is centrifuged and the solvent removed. Purification using medium pressure chromatography on silica gel with $CHCl_3$ follows: yields 92—98%.

Received: December 5, 1980 [Z 849b IE]
German version: Angew. Chem. *93*, 822 (1981)

---

[1] *H. Bönnemann*, Angew. Chem. *90*, 517 (1978); Angew. Chem. Int. Ed. Engl. *17*, 505 (1978); *Y. Wakatsuki, H. Yamazaki*, J. Chem. Soc. Dalton Trans. *1978*, 1278.

[2] a) *E. Lindner, A. Rau, S. Hoehne*, Angew. Chem. *93*, 821 (1981); Angew. Chem. Int. Ed. Engl. *20*, 787 (1981); b) *ibid. 91*, 568 (1979) or *18*, 534 (1979).

[3] *Y. Wakatsuki, H. Yamazaki*, J. Organomet. Chem. *139*, 169 (1977).

[4] Monoclinic crystals of *(3a)* from methanol (space group $P2_1/m$), $a=842.6(2)$, $b=1622.1(4)$, $c=864.8(2)$ pm, $\beta=116.62(2)°$, $Z=2$, $\rho_{calc}=1.523$ g/cm$^3$. The structure was solved with Patterson and Fourier-difference syntheses and anisotropically refined to $R=0.127$ and $R_w=0.081$ for 1546 independent reflections using the SHEL-76 program (except for H).

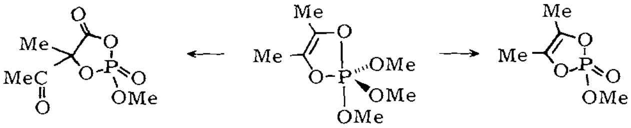
[5] *E. H. Braye, W. Hübel, I. Caplier*, J. Am. Chem. Soc. *83*, 4406 (1961); *J. L. Davidson, D. W. A. Sharp*, J. Fluorine Chem. *7*, 145 (1976).

## Synthesis of Highly Reactive Cyclic Enediol Phosphates and Cyclic Acyl Phosphates by Direct Phosphorylating Ring Closure

By *Reiner Schwarz* and *Ivar Ugi*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Oxyphosphorane derivatives such as *(1)* are stabilized by a five-membered ring with O—P—O partial structure, whereas ring strain occurs in analogous cyclic phosphates[1]. Such phosphates react with nucleophiles up to $10^7$ times more rapidly than their open-chain analogues[2] and, moreover, are selective phosphorylating agents[3]. This was observed, in particular, in the case of the cyclic enediol phosphate *(2a)*, the cyclic acyl phosphate *(3)*, and some derivatives obtainable therefrom. Compounds of this type with sp$^2$-hybridized C-atoms in the ring were hitherto accessible only *via* oxyphosphorane derivatives such as *(1)*.



*(3)* *(1)* *(2a)*

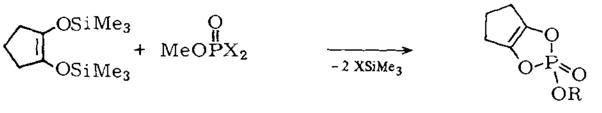
We were able to synthesize such cyclic phosphates by direct phosphorylating ring closure.—The results of the reac-

---

[*] Prof. Dr. I. Ugi
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)
Dr. R. Schwarz
Institut für Allgemeine Chemie und Biochemie
der Technischen Universität München, Freising-Weihenstephan (Germany)

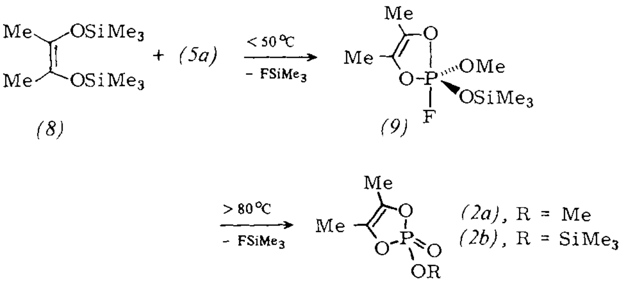
[**] This work was supported by the Deutsche Forschungsgemeinschaft.

tions of *O*-, *N*- and *S*-silylated compounds with phosphorus halides like PF$_5$[4] stimulated further investigations into whether *O*-trimethylsilylated enediols such as *(4)*[5a] react with methyldihalophosphates *(5)* to give cyclic enediol phosphates. Both on reaction with *(5a)* as well as with *(5b)* we obtained the enediol phosphate *(6)*, in 89 and in 83% yields, respectively. In the case of *(5b)*, 8% of *(7)* was also formed.



*(4)* *(5a)*, X = F *(6)*, R = Me
*(5b)*, X = Cl *(7)*, R = SiMe$_3$

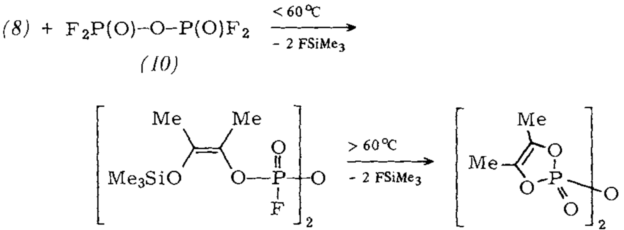
For the analogous synthesis of *(2a)* from acetoin, 3-trimethylsiloxy-2-butanone is first prepared and then deprotonated with LiN*i*Pr$_2$ at room temperature and finally trimethylsilylated. On reaction of the favored product, the *cis*-compound *(8)*, with *(5a)* below 50 °C, *(9)* could be detected by $^{31}$P- and $^{19}$F-NMR spectroscopy. Above 80 °C, *(2a)* is formed in 90% yield. Reaction of *(8)* and *(5b)* at 75 °C affords a mixture of *(2a)* and *(2b)*[2d].



*(8)* *(9)*

*(2a)*, R = Me
*(2b)*, R = SiMe$_3$

When *(8)* is allowed to react with tetrafluorodiphosphate *(10)* below 60 °C, *(11)* can be detected, whereas reaction at higher temperatures leads to formation of *(12)*[5c].

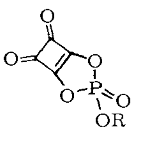


*(10)*

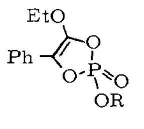
*(11)* *(12)*

Bis(trimethylsilyl) squarate reacts with *(5a)* analogously to *(8)*→*(9)*→*(2a)* at 50 °C *via* a fluorophosphorane as detectable intermediate, whereas *(13a)* is formed at 80 °C. Reaction with *(5b)* affords both *(13a)* (62%) and *(13b)* (29%).

The β-ethoxy-α,β-bis(trimethylsiloxy)styrene, accessible from ethyl mandelate, reacts with *(5a)* to give exclusively *(14a)* (74%)[6] and with *(5b)* to give, aside from *(14a)* (11%) and *(14b)* (8%), mainly unidentifiable products.

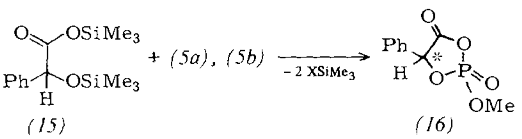


*(13a)*, R = Me
*(13b)*, R = SiMe$_3$

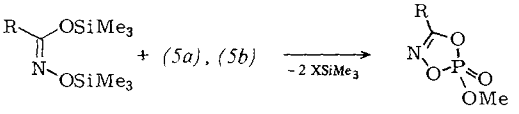


*(14a)*, R = Me
*(14b)*, R = SiMe$_3$

Trimethylsilylated (+)-mandelic acid *(15)* reacts with *(5a)* or *(5b)* to give the cyclic acyl phosphate *(16)* in yields of up to 48%.



*(15)* *(16)*



*(17a)*, R = CF$_3$ *(18a)*, R = CF$_3$
*(17b)*, R = *p*-NO$_2$–C$_6$H$_4$ *(18b)*, R = *p*-NO$_2$–C$_6$H$_4$

The hydroximic acid derivatives *(17a)* and *(17b)*[7], accessible from hydroxamic acids, furnish the 1,3,4,2λ$^5$-dioxazaphosphole derivatives[8] *(18a)* (68%) and *(18b)* (64%), respectively, on reaction with *(5a)* and *(5b)*.—Some NMR data of the products are collected in Table 1.

Table 1. Some NMR data (δ-values) of the synthesized compounds [a].

| | |
|---|---|
| *(2a)*: | $^1$H: 1.89 (s, 6 H), 3.83 (d, 3 H, $^3J_{PH}=11.0$); $^{31}$P{$^1$H}: 11.8 |
| *(2b)*: | $^1$H: 0.28 (s, 9 H), 1.85 (s, 6 H); $^{13}$C{$^1$H}: 0.79 (s, SiC), 11.0 (s, CH$_3$), 133.2 (s, C=C); $^{31}$P{$^1$H}: 3.1 |
| *(6)*: | $^1$H: 1.82 (m, 2 H), 2.20 (m, 4 H), 3.54 (d, 3 H, $^3J_{PH}=13.7$); $^{31}$P{$^1$H}: 5.4 |
| *(7)*: | $^1$H: 0.23 (s, 9 H), 1.80 (m, 2 H), 2.20 (m, 4 H); $^{31}$P{$^1$H}: 4.3 |
| *(8)*: | $^1$H: 0.09 (s, 18 H), 1.63 (s, 6 H) $^{13}$C{$^1$H}: 0.78 (s, SiC), 17.7 (s, CH$_3$), 129.1 (C=C) |
| *(8)*: | EtO and Ph instead of 2Me: $^1$H: 0.11 (s, 9 H), 0.21 (s, 9 H), 1.83 (t, 3 H, $^3J_{HH}=7.2$), 3.76 (q, 2 H, $^3J_{HH}=7.2$), 7.38 (m, 5 H) |
| *(9)*: | $^{19}$F: 18.1 (d, $^1J_{PF}=976$); $^{31}$P{$^1$H}: −47.4 (d, $^1J_{PF}=976$) |
| *(9)*: | —CO—CO— instead of 2Me: $^{19}$F: 5.8 (d, $^1J_{PF}=922$); $^{31}$P{$^1$H}: −32.0 (d, $^1J_{PF}=920$) |
| *(11)*: | $^{31}$P: −7.9 (d, $^1J_{PF}=957$) |
| *(12)*: | $^1$H: 1.93 (s, 6 H); $^{31}$P: −1.3 (d, $^2J_{POP}=17.3$) |
| *(13a)*: | $^1$H: 3.79 (d, 3 H, $^3J_{PH}=13.8$); $^{31}$P{$^1$H}: 5.5 |
| *(13b)*: | $^1$H: 0.25 (s, 9 H); $^{31}$P: 2.0 (s) |
| *(14a)*: | $^1$H: 1.92 (t, 3 H, CH$_3$, $^3J_{HH}=6.9$), 3.84 (q, 2 H, $^3J_{HH}=6.9$), 4.01 (d, 3 H, OCH$_3$, $^3J_{PH}=11.3$), 7.42 (m, 5 H); $^{13}$C{$^1$H}: 133.2, 136.0 (s, C=C); $^{31}$P{$^1$H}: 9.8 |
| *(14b)*: | $^1$H: 0.23 (s, 9 H), 1.89 (t, 3 H, $^3J_{HH}=6.4$), 3.80 (q, 2 H, $^3J_{HH}=6.4$), 7.38 (m, 5 H); $^{13}$C{$^1$H}: 134.1, 138.5 (s, C=C); $^{31}$P{$^1$H}: 6.4 |
| *(16)*[b]: | $^1$H: 3.60 (d, 3 H, $^3J_{PH}=11.6$), 5.47, 5.50 (d, 1 H, $^3J_{PH}=14.3$), 7.18–7.40 (m, 5 H); $^{31}$P{$^1$H}: 5.9, 6.3 |
| *(17a)*: | $^1$H: 0.24 (s, 9 H), 0.30 (s, 9 H); $^{19}$F: 3.08 (s) |
| *(17b)*: | $^1$H: 0.19 (s, 9 H), 0.22 (s, 9 H), 8.31 (m, 4 H) |
| *(18a)*: | $^1$H: 4.12 (d, 3 H, $^3J_{PH}=11.7$); $^{19}$F: 8.35 (s); $^{31}$P: 15.8 (q, $^3J_{PH}=11.5$) |
| *(18b)*: | $^1$H: 4.08 (d, 3 H, $^3J_{PH}=9.7$), 8.38 (m, 4 H); $^{31}$P: 16.9 (q, $^3J_{PH}=9.5$) |

[a] Correct elemental analyses were obtained for all isolated compounds. $^1$H- and $^{13}$C-NMR: TMS intern., CDCl$_3$; $^{19}$F-NMR: CF$_3$COOH extern., CDCl$_3$; $^{31}$P-NMR: H$_3$PO$_4$ extern., C$_6$D$_6$. *J* in Hz. [b] Diastereomers.

## *Procedure*

*(8)*: A solution of 3-trimethylsiloxy-2-butanone[9] (32.0 g, 0.20 mol) in dimethylformamide (DMF) (50 mL) is slowly added dropwise to 0.21 mol of LiN*i*Pr$_2$ at room temperature such that the internal temperature of the reaction mixture does not exceed 40 °C. A solution of ClSiMe$_3$ (60.4 g, 0.40 mol) in DMF (25 mL) is then added dropwise to the warm mixture, which is finally stirred for 1 h at 40 °C, filtered, and the separated precipitate is washed three times

with 10 mL of tetrahydrofuran. The combined filtrates are distilled and the crude product is fractionated twice at 60—65 °C/15 torr in a spinning band column. *(8)* [38.6 g (83%)] is obtained as an opalescent liquid, b. p. 64 °C/12 torr.

*(2a):* A solution of *(5a)* (5.57 g, 0.048 mol) in toluene (15 mL) is added dropwise to a solution of *(8)* (11.5 g, 0.048 mol) in toluene (15 mL) at 85 °C. The mixture is then stirred for 30 min at 80 °C, cooled to 60 °C, and distilled in a high vacuum. 7.09 g (90%) of *(2a)* is obtained; b.p. 64—65 °C/0.2 torr).—The other cyclic phosphates are prepared analogously.

Received: January 21, 1981 [Z 850 IE]
German version: Angew. Chem. *93*, 836 (1981)

---

[1] *D. Marquarding, F. Ramirez, I. Ugi, P. Gillespie*, Angew. Chem. *85*, 99 (1973); Angew. Chem. Int. Ed. Engl. *12*, 91 (1973).

[2] a) *F. Westheimer*, Acc. Chem. Res. *1*, 70 (1968); b) *P. C. Haake, F. Westheimer*, J. Am. Chem. Soc. *83*, 1102 (1961); c) *F. Ramirez, J. F. Marecek, I. Ugi*, Synthesis *1975*, 99; d) J. Am. Chem. Soc. *97*, 3809 (1975); e) *I. Ugi, P. Lemmen, F. Ramirez*, Chem. Ber. *109*, 3738 (1976).

[3] *F. Ramirez, S. L. Glaser, P. Stern, P. Gillespie, I. Ugi*, Angew. Chem. *85*, 39 (1973); Angew. Chem. Int. Ed. Engl. *12*, 66 (1973); *F. Ramirez, J. F. Marecek, H. Tsolis, H. Okasaki*, J. Org. Chem. *42*, 771 (1977).

[4] *G. O. Doak, R. Schmutzler*, J. Chem. Soc. *A 1971*, 1295; *L. B. Littlefield, G. O. Doak*, Phosphorus Sulfur *3*, 35 (1977).

[5] a) *K. Rühlmann*, Synthesis *1971*, 236; b) cf. *H. O. House, R. A. Auerbach, M. Gall*, J. Org. Chem. *38*, 514 (1973); c) *F. Ramirez, H. Okasaki, J. F. Marecek*, Synthesis *1975*, 637.

[6] For an analogous compound from lactic acid and $PCl_5$, see *P. Lemmea*, Tetrahedron Lett. *1979*, 4461.

[7] *J. Rigaudy, E. Lytwyn, P. Wallach, N. K. Cuong*, Tetrahedron Lett. *1980*, 3367.

[8] *E. von Hinrichs, I. Ugi*, J. Chem. Res. *1978*, 3973; see also *E. Fluck, M. Vargas*, Z. Anorg. Allg. Chem. *437*, 53 (1977).

[9] *H. Teichmann, V. Prey*, Justus Liebigs Ann. Chem. *732*, 121 (1970).

## Crystallochemical Correlate to the Anomaly of Hydrofluoric Acid

By *Dietrich Mootz*[*]

The low acid strength of dilute hydrofluoric acid relative to the other hydrohalides and its increasing dissociation with increasing concentration constitute an anomaly in inorganic chemistry, which has been the subject of numerous investigations and discussions. A recent explanation is based on an ion-pair $H_3O^+ \cdot F^-$, indicated by IR-spectroscopy. The ion-pair is held together by an especially strong hydrogen bond, and increasingly dissociates according to $[H_3O^+ \cdot F^-] + HF \rightleftharpoons H_3O^+ + HF_2^-$ only at higher HF concentrations[1].

Results of X-ray structure analyses, which were carried out on compounds $H_2O \cdot HF$, $H_2O \cdot 2HF$, and $H_2O \cdot 4HF$ in the solid-state (melting points between −36 and −100 °C), together with a new determination of the $H_2O$—HF phase diagram[2] now correlate with the anomaly and especially with this explanation. All three structures prove to be those of oxonium salts—$H_3OF$, $H_3OHF_2$ and $H_3OH_3F_4$—with three very strong hydrogen bonds per oxonium ion and with average O···F distances of 2.467, 2.502 and 2.536 Å respectively, appear less tightly bound as the HF content increases.

Received: March 2, 1981 [Z 851 a IE]
German version: Angew. Chem. *93*, 823 (1981)

CAS Registry numbers:
HF, 7664-39-3.

---

[*] Prof. Dr. D. Mootz
Institut für Anorganische Chemie und Strukturchemie der Universität
Universitätsstr. 1, D-4000 Düsseldorf (Germany)

[1] *P. A. Giguère, S. Turrell*, J. Am. Chem. Soc. *102*, 5473 (1980).

[2] *D. Mootz, U. Ohms, W. Poll*, Z. Anorg. Allg. Chem., in press; *D. Mootz, W. Poll, ibid.*, in press.

## Triethanolamine: Dimerization *via* a Ring of Six Hydrogen Bonds

By *Dieter Brodalla* and *Dietrich Mootz*[*]

A special type of dimerization—*via* a ring of six hydrogen bonds to give a cage—was found on analysis of the crystal structure of tris(2-hydroxyethyl)amine.

Growth of a single crystal directly on the diffractometer in a sealed glass capillary in a stream of cold gas was achieved by means of a miniature zone refining method using focussed radiation[1]. The measurements were carried out at 140 K; trigonal rhombohedral crystal system, space group $R\bar{3}$, lattice constants hexagonal $a = b = 1149.1(1)$, $c = 1070.0(1)$ pm and $Z = 6$ molecules in the unit cell[2].

Two triethanolamine molecules facing each other form a cage-like dimer with $C_{3i}$-$\bar{3}$ symmetry (Fig. 1), in which the 2-hydroxyethyl groups enclose the free electron pairs on the nitrogen atoms[3], and the oxygen atoms are bound by six homodromic[4] symmetry-equivalent hydrogen bonds [O···O 270.1(1), O—H 84(1), H···O 186(1) pm, $\sphericalangle$O—H···O 172(1)°], to give a six-membered ring in chair form.

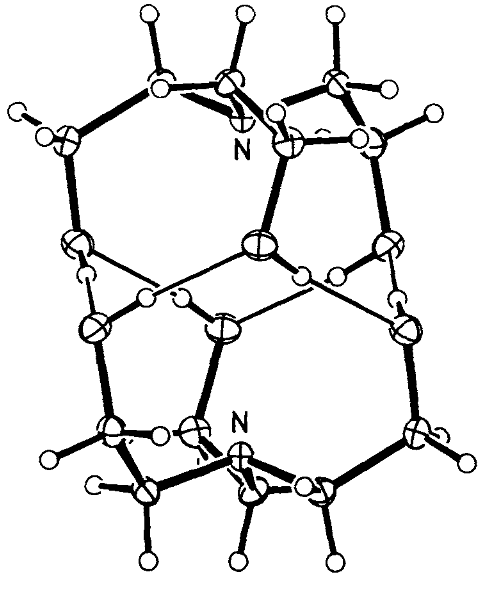


Fig. 1. The cage-shaped dimer of $N(CH_2CH_2OH)_3$ with the ring of six hydrogen bonds (center), ORTEP diagram [5].

The dimeric units in the crystal are arranged according to the principle of cubic close packing. The crystal structures, determined in the same way on mono- and diethanolamine, show cross-linking to give higher associates in which the N-atom also participates in the hydrogen bonding.

Received: March 11, 1981 [Z 851 b IE]
German version: Angew. Chem. *93*, 824 (1981)

CAS Registry numbers:
Triethanolamine, 102-71-6.

---

[*] Prof. Dr. D. Mootz, Dipl.-Chem. D. Brodalla
Institut für Anorganische Chemie und Strukturchemie der Universität
Universitätsstr. 1, D-4000 Düsseldorf (Germany)

[1] *D. Brodalla, D. Mootz*, poster at the Symposium des Arbeitskreises KSAM der GDCh-Fachgruppe „Analytische Chemie“ in Martinsried (Germany), March *1981*.
[2] Syntex P2$_1$ four-circle diffractometer with modified LT-1 cooling unit, Mo$_{K_\alpha}$, ω-scan, $2\Theta_{max}=60°$, 762 reflections, of which 722 observed ($F_0 \geq 3\sigma_F$), program system EXTL, $R_1=0.026$.
[3] The crystal structure of $[(HOC_2H_4)_3NH]^+SH^-$ (unpublished) shows the same geometry for the singly protonated molecule.
[4] *W. Saenger*, Nature *279*, 343 (1979).
[5] *C. K. Johnson*, ORTEP II, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tenn. (1976).

## Non-Ergodic Behavior of Excited Radical Cations in the Gas Phase[**]

By *Gisbert Depke, Chava Lifshitz, Helmut Schwarz,* and *Eva Tzidony*[*]

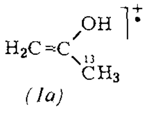
*Dedicated to Professor Hans D. Beckey on the occasion of his 60th birthday*

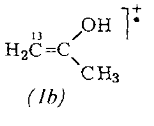
One of the central questions in reaction dynamics today is whether highly excited molecules behave ergodically[1], *i.e.* whether unimolecular dissociations are slower than intramolecular vibrational energy redistribution. It has been shown for neutral molecules[2] that energy randomization is completed within a few picoseconds and that molecules behave non-ergodically only under special conditions[2a]. If similar non-ergodic behavior were found in ionic systems, then one of the basic assumptions of the quasi-equilibrium theory (QET) of mass spectra[3] would be violated.

Evidence for the non-statistical behavior of the enol radical cation of acetone *(1)*, through measurements of kinetic energy release distributions *T* of the dissociation fragments, has recently appeared[4]. In that study and in previous ones[5], [$^2$H]-labeled isotopomers of *(1)* were employed and there was the ever present possibility of kinetic isotope effects. In order to circumvent this problem, we have now prepared the [$^{13}$C]-labeled isotopomers *(1a)* and *(1b)*. We report here on the unimolecular dissociation of this radical cation in the gas phase and present evidence indicating that this system is characterized by non-ergodic behavior.

The study of [$^2$H]-labeled ions *(1)*, strengthened by thermochemical arguments[4,5], has shown that the CH$_3$-cleavage from metastable ions *(1)* (lifetimes $\approx 10^{-5}$ s) does not take place by direct α-cleavage ($(1) \nrightarrow (3) + CH_3$), but by dissociation to ion *(5)* following a rate determining [1,3]-H-shift ($(1) \rightarrow (4) \rightarrow (2)$) (Fig. 1). A highly excited intermediate acetone radical cation *(2)** is formed, whose lifetime has been estimated to be $5\times10^{-13}$ s[4].

If *(2)** were to behave ergodically, one would expect, on the basis of the chemical equivalence of the two methyl groups, that the two specifically [$^{13}$C]-labeled ions *(1a)* and *(1b)* would eliminate the radicals $^{13}CH_3^{\cdot}$ and $^{12}CH_3^{\cdot}$ in equal (1 : 1) proportions. Furthermore, the kinetic energy release, *T*, for the $^{13}$CH$_3$- and $^{12}$CH$_3$-eliminations, would be expected to be closely similar. If, however, the internal energy of *(2)** is distributed non-statistically prior to dissociation (*i.e.* the behavior is non-ergodic), then—despite the equivalence of both methyl group—the two $^{13}$CH$_3$ and $^{12}$CH$_3$ radicals would be expected to cleave-off at different rates. Previous data[4,5a] indicate that discrimination against the CH$_3$ group, which is originally present in *(1)*, is to be expected[4,5c] and that the *T*-value for the elimination of this group should be smaller than for the alternative process in which the methyl radical is formed from the original CH$_2$ group and the hydrogen atom of the OH group.


*(1a)*


*(1b)*

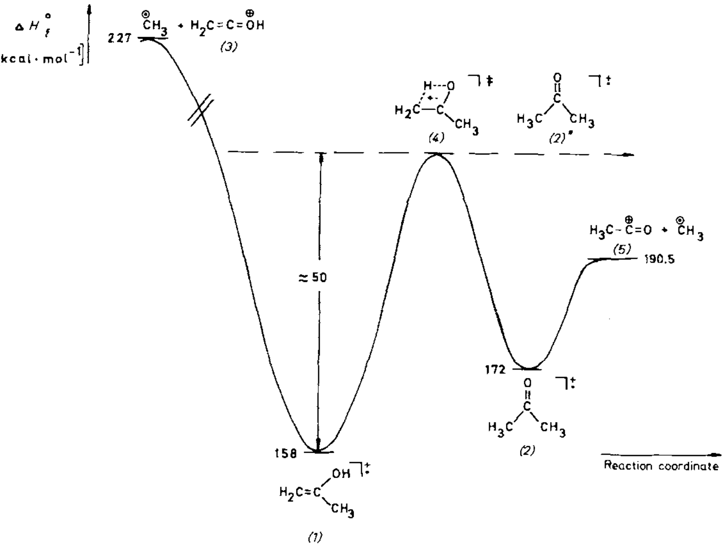


Fig. 1. Energy profile for the isomerization and dissociation of the enol radical cation of acetone *(1)*. The reaction coordinate is complex; it involves a [1.3]-H-shift (*(1)*→*(2*)*), followed by a C—C-cleavage leading to formation of the acyl ion *(5)*.

Table 1. $^{13}$CH$_3$- *versus* $^{12}$CH$_3$-elimination from the radical cations *(1a)* and *(1b)*. The relative intensities were obtained from MIKE-spectra and the translational energy values (calculated from the widths at half-height of the metastable peaks) were obtained from high voltage scans (MAT 311 mass spectrometer at 70 eV ionizing energy; 3 kV acceleration potential, 300 μA emission current) [a].

| Ion | rel. intensity [%] | | *T* [meV] | |
|---|---|---|---|---|
| | $^{13}$CH$_3$ | $^{12}$CH$_3$ | $^{13}$CH$_3$ | $^{12}$CH$_3$ |
| *(1a)* | 42.3 ± 2.5 | 57.7 ± 2.5 | 59.4 | 71.5 |
| *(1b)* | 53.5 ± 1.6 | 46.5 ± 1.6 | 74 | 62.2 |

[a] Details concerning the methodology may be found in [5]. The ions *(1a)* and *(1b)* were produced from the [$^{13}$C]-labelled ketones, [1-$^{13}$C]-2-hexanone and [3-$^{13}$C]-2-hexanone, respectively, *via* McLafferty rearrangements.

The data presented in Table 1 (different loss of $^{13}$CH$_3$ and $^{12}$CH$_3$; $T_{^{13}CH_3} \neq T_{^{12}CH_3}$) demonstrate quite convincingly that the electron impact-induced unimolecular methyl eliminations from the enol radical cation of acetone *(1)* do not behave statistically. Hence, a fundamental assumption of the quasi-equilibrium theory, namely that the distribution of internal energy between the vibrational states is statistical, is apparently violated by *(1)*.

Received: February 24, 1981 [Z 852 IE]
German version: Angew. Chem. *93*, 824 (1981)

CAS Registry numbers:
*(1a)*, 78790-65-5; *(1b)*, 78790-66-6.

---

[*] Prof. Dr. H. Schwarz, Dipl.-Chem. G. Depke
Institut für Organische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)
Prof. Dr. C. Lifshitz, E. Tzidony, M. Sc.
Department of Physical Chemistry, Hebrew University
Jerusalem 91904 (Israel)

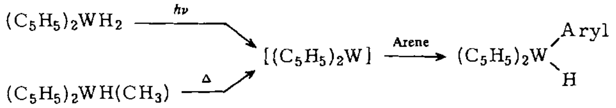
[**] This work has been supported by the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft and the Technische Universität Berlin (Exchange Program TUB/HUJ).

[1] *I. Oref, B. S. Rabinovitch*, Acc. Chem. Res. *12*, 166 (1979).
[2] a) *J. D. Rynbrandt, B. S. Rabinovitch*, J. Phys. Chem. *74*, 4175 (1970); *ibid. 75*, 2164 (1971); J. Chem. Phys. *54*, 2275 (1971); b) *R. A. Coveleskie, D. A. Dolson, C. S. Parmenter*, J. Chem. Phys. *72*, 5774 (1980).
[3] *H. M. Rosenstock, M. B. Wallenstein, A. L. Wahrhaftig, H. Eyring*, Proc. Natl. Acad. Sci. USA *38*, 667 (1952); *C. Lifshitz*, Adv. Mass Spectrom. *7A*, 3 (1977).
[4] *C. Lifshitz, E. Tzidony*, Int. J. Mass Spectrom. Ion Phys. *39*, 181 (1981).
[5] a) *F. W. McLafferty, D. J. McAdoo, J. S. Smith, R. Kornfeld*, J. Am. Chem. Soc. *93*, 3720 (1971); b) *J. H. Beynon, R. M. Caprioli, R. G. Cooks*, Org. Mass Spectrom. *9*, 1 (1974); c) *C. Lifshitz, E. Tzidony, D. T. Terwilliger, C. E. Hudson*, Adv. Mass Spectrom. *8*, 859 (1980).
[6] *R. G. Cooks, J. H. Beynon, R. M. Caprioli, R. G. Lester:* Metastable Ions, Elsevier, Amsterdam, 1973.

## Synthesis of Hydrido(phenyl)osmium(II)- from Benzeneosmium(0)-Complexes: Intramolecular Insertion of a Lewis Basic Metal Atom into an $sp^2$-C—H Bond[1]

By *Rainer Werner* and *Helmut Werner*[*]

In recent years, considerable interest has been shown in the problem of activating C—H bonds by transition metals. *Green et al.*[2] found that *e.g.* bis(cyclopentadienyl)tungsten ("tungstenocene"), prepared *in situ* by photolysis of $(C_5H_5)_2WH_2$ or thermolysis of $(C_5H_5)_2WH(CH_3)$, can react with arenes by insertion into an $sp^2$-C—H bond.



We recently reported the synthesis of a series of benzeneosmium(0) complexes of the type $C_6H_6OsLL'$[3]. If tertiary phosphanes or phosphites are selected as the ligands L and L′, the compounds obtained, as shown in eq. (a), are thermolabile; they decompose even during attempts to separate off the naphthalene formed as by-product.

$$[C_6H_6OsLL'I]PF_6 + 2\,NaC_{10}H_8 \xrightarrow{THF} C_6H_6OsLL' + C_{10}H_8 + NaI + NaPF_6 \qquad (a)$$

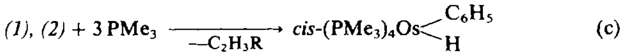
$L = L' = PPh_3,\ P(OMe)_3$

The alkene(trimethylphosphane) complexes $C_6H_6Os(PMe_3)C_2H_3R$ are considerably more stable and are obtained in an analogous way to that shown in eq. (a). They can be isolated in pure form by reaction of the hydrido cations $[C_6H_6OsH(PMe)_3C_2H_3R]^\oplus$ with NaH[3].

$$C_6H_6Os(PMe_3)C_2H_3R \underset{H^\ominus}{\overset{H^\oplus}{\rightleftharpoons}} [C_6H_6OsH(PMe_3)C_2H_3R]^\oplus \qquad (b)$$

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

Our attempt to synthesize the bis(trimethylphosphane) complex $C_6H_6Os(PMe_3)_2$, which should be an even stronger Lewis base than the homologous $C_6H_6Ru(PMe_3)_2$[4], by exchange of the coordinated alkene in *(1)* or *(2)* for $PMe_3$ was unsuccessful. At room temperature both *(1)* and *(2)* react very slowly with trimethylphosphane; after 24 h only a slight reduction in the concentration of the alkene complex is detected as indicated by NMR spectroscopy. Upon warming the solution ($C_6H_6$) to 70 °C [for *(1)* after 20 h, for *(2)* after 5 h] compound *(3)* is formed practically quantitatively. Instead of the expected exclusive displacement of the alkene, insertion of the osmium into a C—H bond of the benzene also occurs.



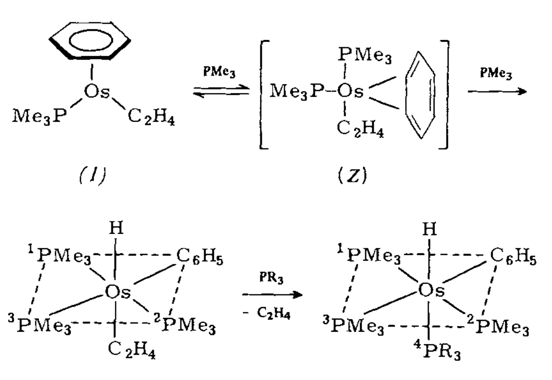
$$(1), (2) + 3\,PMe_3 \xrightarrow[-C_2H_3R]{} cis\text{-}(PMe_3)_4Os{<}^{C_6H_5}_{H} \qquad (c)$$

*(3)*

Repetition of the reaction in $C_6D_6$ indicates that an *intra*molecular oxidative addition has occured; only *(3)*, and no complex containing the $Os(C_6D_5)D$ grouping, is formed. Hence, the insertion of the metal does not proceed *via* a benzene/phosphane exchange.

The changes in the $^1H$-NMR spectrum provide information on the course of the reaction. While no intermediate product is observed in the formation of *(3)* from *(2)*, such a species can be unequivocally detected in the reaction of *(1)* with $PMe_3$. Its spectroscopic data (Table 1) confirm the structure $(C_2H_4)(PMe_3)_3Os(C_6H_5)H$ *(4)*. When the reaction of *(1)* with $PMe_3$ (molar ratio 1 : 4) in benzene is interrupted after 2 h, a mixture of 80% *(4)*, 10% *(1)*, and 10% *(3)* is obtained. Almost pure *(4)* was obtained by recrystallization and this was characterized by mass spectroscopy. In the presence of excess trimethylphosphane, *(4)* reacts completely to give *(3)*. An ethylosmium complex cannot be detected, *i.e.* no insertion of the coordinated ethylene into the Os—H bond occurs. Furthermore, a reductive elimination of benzene from *(3)* in the presence of trimethylphosphane cannot be observed.

In order to clarify the stereochemistry of the final step in the synthesis of *(3)* from *(1)*, *(4)* was reacted with $PMe_2Ph$. The ethylene coordinated in the *trans*-position to the hydride ligand is quantitatively exchanged after 7 h ($C_6H_6$, 70 °C). In a reaction which proceeds with rigorous stereospecificity, the phosphane occupies the alkene-site, which was verified by selective decoupling experiments. The formation of *(3)* and $(PMe_3)_3(PMe_2Ph)Os(C_6H_5)H$ *(5)* from *(1)* can therefore be formulated as follows:



*(3)*, $R_3$ = $Me_3$, *(5)*, $R_3$ = $Me_2Ph$

In the intermediate product *(Z)*, we postulate a $\eta^4$-coordination of the benzene, which is not without precedent in the chemistry of areneruthenium(0) and osmium(0) complexes[5]. The question of whether the hydrido(olefin) compound *(4)* is formed from *(Z)* *via* a one-step reaction or

---

[*] Prof. Dr. H. Werner, Dipl.-Chem. R. Werner
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

Table 1. $^1$H-NMR and $^{31}$P-NMR data for *(3)—(5)*, in $C_6D_6$ [$\delta$-values, TMS int. ($^1$H) or 85% $H_3PO_4$ ext. ($^{31}$P); $J$ and $N$ in H; for assignments see formula scheme].

| Complex | $^1PMe_3$, $^2PMe_3$ | $^3PMe_3$ | $^4PR_3$ | $OsC_6H_5$ | $OsH$ | $^1PMe_3$, $^2PMe_3$ | $^3PMe_3$ | $^4PR_3$ |
|---|---|---|---|---|---|---|---|---|
| *(3)* | 1.22 vt<br>$N = 6.0$ | 1.39 d [a]<br>$J_{PH} = 5.5$ | 1.37 d [a]<br>$J_{PH} = 6.0$ | 7.16 m | −9.80 d × q<br>$J_{^{1,2,3}PH} = 23$<br>$J_{^4PH} = 73$ | −47.42 t<br>$J_{^{1,2}P^{3,4}P} = 17.1$ | −58.51 m | −58.51 m |
| *(4)*<br>[b] | 1.14 vt<br>$N = 6.8$ | 1.09 d<br>$J_{PH} = 6.2$ | | 7.32 m | −7.10 d × t<br>$J_{^{1,2}PH} = 17$<br>$J_{^3PH} = 25$ | −43.93 d<br>$J_{^{1,2}P^3P} = 15.2$ | −58.74 t<br>$J_{^{1,2}P^3P} = 15.2$ | |
| *(5)* | 1.17 vt<br>$N = 6.0$ | 1.37 d<br>$J_{PH} = 6.2$ | 1.73 d<br>$J_{PH} = 5.2$<br>7.23 m | [c] | −9.90 d × q<br>$J_{^{1,2,3}PH} = 22$<br>$J_{^4PH} = 74$ | −48.07 d × d<br>$J_{^{1,2}P^3P} = 15.6$<br>$J_{^{1,2}P^4P} = 17.7$ | −60.01 d × t<br>$J_{^{1,2}P^3P} = 15.6$<br>$J_{^3P^4P} = 10.2$ | −42.32 d × t<br>$J_{^{1,2}P^4P} = 17.7$<br>$J_{^3P^4P} = 10.2$ |

[a] Exact assignment of both signals to the $PMe_3$ groups in the 3- and 4-positions is not possible. [b] Signals of the $C_2H_4$-protons at $\delta = 1.88$ d × t, $J_{^{1,2}PH} = 3.0$, $J_{^3PH} = 4.5$. [c] Signal lies under the signal of the $PMe_2Ph$ protons.

whether another intermediate species is involved, remains open; the insertion of the metal must result from this.

The activation of C—H bonds has fundamental significance for the comprehension of numerous reactions catalyzed by metal complexes. The cleavage of an sp$^2$-C—H bond by a Lewis basic metal was first described by *Chatt et al.*[6], who obtained the compounds $(dmpe)_2Ru(C_6H_5)H$ and $(dmpe)_2Ru(C_{10}H_7)H$ (dmpe = $Me_2PC_2H_4PMe_2$) by reduction of $(dmpe)_2RuCl_2$ with sodium or potassium in the presence of benzene or naphthalene. The compound $(dmpe)_2Ru(C_{10}H_7)H$ exists in equilibrium with $(dmpe)_2Ru(C_{10}H_8)$[6].

To the best of our knowledge the synthesis of *(3)* from *(1)* or *(2)* is the first proof that the metal atom of a stable $\eta^6$-arene metal complex, after successive addition of further donor ligands, can undergo insertion into an sp$^2$-C—H bond without prior dissociation of the ($\eta^6$-$C_6H_6$) metal bond. An extension to the preparation of other aryl(hydrido) metal compounds appears to be possible.

Received: January 8, 1981 [Z 854 IE]
German version: Angew. Chem. *93*, 826 (1981)

---

[1] Basic Metals, Part 32. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and by BASF AG, Ludwigshafen and DEGUSSA, Hanau. Part 31: *W. Hofmann, H. Werner*, Chem. Ber., in press.

[2] *N. J. Cooper, M. L. H. Green, R. Mahtab*, J. Chem. Soc. Dalton Trans. *1979*, 1557; *M. Berry, K. Elmitt, M. L. H. Green, ibid. 1979*, 1950.

[3] *H. Werner, R. Werner*, J. Organomet. Chem. *194*, C 7 (1980).

[4] *H. Werner, R. Werner*, Angew. Chem. *90*, 721 (1978); Angew. Chem. Int. Ed. Engl. *17*, 683 (1978).

[5] *G. Huttner, S. Lange, E. O. Fischer*, Angew. Chem. *83*, 579 (1971); Angew. Chem. Int. Ed. Engl. *10*, 556 (1971).

[6] *J. Chatt, J. M. Davidson*, J. Chem. Soc. *1965*, 843.

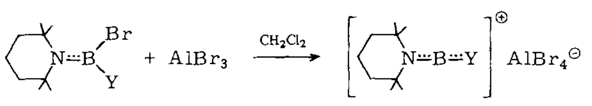
## Boron Cations with a Dicoordinate B Atom

By *Heinrich Nöth* and *Rudolf Staudigl*[*]

Cations of boron with the coordination number 4 are formed on aminolysis of suitable boron halides, on nucleophilic halide-displacement from amine-borohalide adducts with bases, and on electrophilic hydride-exchange in amine-boranes with halogen in the presence of bases[1]; the composition of these salts can be represented by the general formulas $[R_2BLL']X$, $[RXBLL']X$, $[RBL_3]X_2$, and $[BL_4]X_3$ (R = H, Hal; L, L′ = $NH_3$, $NH_2R$, $NR_3$, pyridine; X = Cl, Br, I). Compounds containing triply coordinated cations $[X_2BL]Y$, on the other hand, have so far rarely been described in the literature[2], while dicoordinated cations $[XBX]^{\oplus}$ were hitherto unknown[3]. The latter species formally contain one B atom with an electron quartet; it should therefore be very electrophilic and could correspond to a "superelectrophile".

It is well known that the electron-deficiency in boron compounds can be compensated considerably by $\pi$-back-bonding. Exploiting this principle we have now succeeded in synthesizing salts whose cations contain boron with coordination number 2[4].

Reaction of anhydrous aluminum bromide with a series of 2,2,6,6-tetramethylpiperidinoboron bromides in dichloromethane leads to specific displacement of bromide, which is trapped as tetrabromoaluminate. By formation of this less nucleophilic anion, and owing to the steric and electronic shielding of the B atom by the bulky 2,2,6,6-tetramethylpiperidino-moiety (tmp), dicoordinated boron cations are generated.



| Y = | $N(CH_3)_2$ | $N(C_2H_5)_2$ | $C_6H_5$ | $CH_3$ |
|---|---|---|---|---|
| Salt | *(1)* | *(2)* | *(3)* | *(4)* |
| $\delta(^{11}B)$ | 36.7 | 37.6 | 56.0 | 59.6 |
| $\delta(^{27}Al)$ | 80.7 | 80.7 | 81 | 80.7 |
| $\Delta\nu_{1/2}(^{27}Al)$ | 20 | 20 | 80 | 48 |
| M.p. [°C] | 114 | 90—95 | dec. | dec. |

$^{27}$Al-NMR spectra confirm exclusive formation of the $AlBr_4^{\ominus}$ anion, which, compared to $Al_2Br_6$, is characterized by its substantially sharper signal; the linewidth of $\Delta\nu_{1/2} \approx 20$ Hz observed in *(1)* and *(2)* corresponds to an undistorted tetrahedral $AlBr_4^{\ominus}$. The $^{11}$B-NMR signals of *(1)—(4)* are shifted 6—18 ppm downfield relative to those of the starting compounds tmpB(Br)Y; their linewidths, which are greater by a factor of about 5, are consistent with a *linear* heteroallene structure (for *(1)—(3)*). Also consistent with such a structure are the isotopically split IR bands at

---

[*] Prof. Dr. H. Nöth, Dr. R. Staudigl
Institut für Anorganische Chemie der Universität
Meiserstr. 1, D-8000 München 2 (Germany)

1850—1900 cm$^{-1}$, which we assign to an antisymmetric $BN_2$ vibration in *(1)* and *(2)*.

The heteroallene structure of *(1)* was confirmed by X-ray structure analysis. The projection onto the *a/c* plane of the monoclinically crystallizing compound (Fig. 1) shows a linear NBN framework ($\sphericalangle$NBN 176(3)°) and orthogonal orientation of the $C_2N$ planes (88°). One of the two BN distances was found to be 130(4) pm. This is the shortest so far recorded[5].

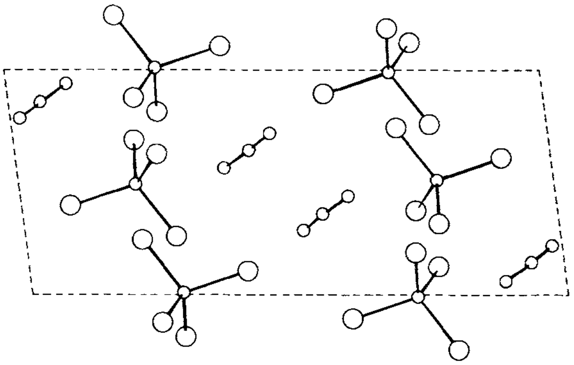


Fig. 1. ORTEP diagram of the unit cell of *(1)*, projection on the *a/c* plane, with omission of the C-skeletal atoms of the tetramethylpiperidino- and dimethylamino-ligands on the boron cation. The shortest Br...B distance is 412 pm. Hence there is no interaction between B and Br atoms.

The B atom of the cation of salt *(4)* can formally be considered as having, at most, an electron sextet. Compared to *(1)* and *(2)* this compound is thermally less stable. The crystals rapidly decompose at room temperature; in $CH_2Cl_2$, decomposition at room temperature is slow enough to enable a definite NMR spectra to be recorded. Less sterically demanding nucleophiles such as $Br^{\ominus}$ (from $[(C_4H_9)_4N]Br$) react with the new boron cations, *e.g.* of *(1)*, to give the educt[6].

The stabilization of these cations of boron by steric and electronic factors is obviously more effective than in the monomeric boron imide $C_6F_5$—B$\equiv$N—$t$C$_4$H$_9$, which also contains a dicoordinated B atom[7] and, in contrast to *(1)—(4)*, undergoes dimerization.

### *Procedure*

Diethylamino(2,2,6,6-tetramethylpiperidino)boron(1+) tetrabromoaluminate *(3)*: A stirred solution of tmp($Et_2N$)Br (2.24 g) in $CH_2Cl_2$ (12 mL) is treated portionwise at −20 °C with 1.92 g of $AlBr_3$. The clear solution is first warmed to room temperature. Subsequent slow cooling to −78 °C affords crystalline *(3)*, while rapid cooling furnishes not quite pure *(3)* as a colorless oil. Yield 3.7 g (90%), m.p. 90—95 °C, rapid decomposition at 130 °C. The equivalent conductivity of a 1.415 M solution in $CH_2Cl_2$ at 20 °C was found to be 31.1 $\Omega^{-1}$ cm$^2$. *(3)* is only slightly sensitive to hydrolysis[8].

Received: August 7, 1980 [Z 855 IE]
revised: May 18, 1981
German version: Angew. Chem. *93*, 830 (1981)

---

[1] Gmelins Handbuch der Anorganischen Chemie, Supplement to 8th edition, Band 37, Borverbindungen, Teil 10 (1976); references cited therein.

[2] *A. T. Balaban, A. Arsene, I. Bally, A. Barabas, M. Paraschiv,* Tetrahedron Lett. *1965*, 3925; *H. Nöth, P. Fritz,* Z. Anorg. Allg. Chem. *322*, 297 (1963).

[3] *J. M. Davidson, C. M. French,* J. Chem. Soc. *1958*, 114; *D. Armstrong, P. J. Perkins, ibid. A 1966*, 1026.

[4] *J. Higashi, A. D. Eastman, R. W. Parry* shall report on the characterization of bis(diisopropylamino)boron tetrachloroaluminate: *R. W. Parry*, private communication.

[5] Space group $P2_1/n$, $a=767.8(4)$, $b=1456(1)$, $c=1791(1)$ pm, $\beta=97.25(4)°$, $Z=4$. Refinement to $R_1=0.104$. The rather poor structure determination is attributed in part to the low quality of the single crystals prepared so far. Hence a discussion of the bond lengths cannot be meaningful at present. But the crystal structure analysis affords unambiguous information about the constitution and geometry. In particular it confirms the findings derived from spectroscopic data. Fractional coordinates and parameters of the temperature factors are available on request from the Cambridge Crystallographic Data Center.

[6] A detailed description of our results will appear in Inorg. Chem. together with the results of *Parry et al.* [4].

[7] *P. I. Paetzold, A. Richter, T. Thijssen, S. Würtenberg,* Chem. Ber. *112*, 3811 (1979).

[8] All compounds *(1)—(4)* were characterized by elemental analysis and NMR spectroscopy ($^1$H, $^{11}$B, $^{13}$C, $^{27}$Al).

## Synthesis of Enantiomerically Pure (*R*)- and (*S*)-α-Hydroxyketones and Vicinal Diols; Asymmetric Nucleophilic Carbamoylation[**]

By *Dieter Enders* and *Hermann Lotter*[*]

*Dedicated to Professor Rolf Appel on the occasion of his 60th birthday*

The use of masked nucleophilic acylation agents is part of the repertoire of organic synthesis[1]. Reagents which bring about direct nucleophilic acylation are also increasing in importance[2]. While enzymatic variants of the cyanohydrin synthesis and the acyloin addition have to a degree been successfully used[3], generally applicable methods for asymmetric CC-coupling using chiral carbonyl-d$^1$-reagents[4] are not yet available[5].

The α-hydroxyamides *(3)* can be obtained in good yield *via* asymmetric nucleophilic carbamoylation by addition of lithium tetramethylpiperidide (Li-TMP) to a mixture of the ketone *(1)* and the chiral formamide *(2)* in tetrahydrofuran (THF), ether, and *n*-pentane (4:4:1) at −100 °C. The chiral carbamoyllithium compounds of type *(4)* ($R=CH_3$) formed as intermediates are highly reactive and the diastereomeric excess of hydroxyamides *(3)* is low (de = 5—20%)[6]. The hydroxyamides can, however, be readily separated into the pure diastereomers *(SS)—(3)* and *(SR)—(3)* by simple column chromatography or, more rapidly, by preparative high pressure liquid chromatography (HPLC). Subsequent reaction with methyllithium permits the preparation of both enantiomers of the α-hydroxyketones *(5)* and the vicinal diols *(6)* in enantiomerically pure form (see Table 1).

In all cases, methyllithium cleavage of the amides *(3)* proceeds to completion; depending on the reaction conditions, either more hydroxyketone *(5)* or more diol *(6)* can be obtained[7]. *(5)* and *(6)* are separated by column chromatography.

Since the diols *(6)* are crystalline, ee-values of >90% can be achieved after two recrystallizations (*n*-pentane), even when the diastereomeric separation step is omitted.

---

[*] Prof. Dr. D. Enders, Dipl.-Chem. H. Lotter
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Straße 1, D-5300 Bonn 1 (Germany)

[**] This work (part of the planned dissertation of *H. L.*) was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and Degussa, Hanau. Presented, in part, in 1980 (among others, Chemiedozententagung, Erlangen, ACS-Meeting, Las Vegas and Arbeitsgruppe, Organische Chemie, Bad Nauheim).

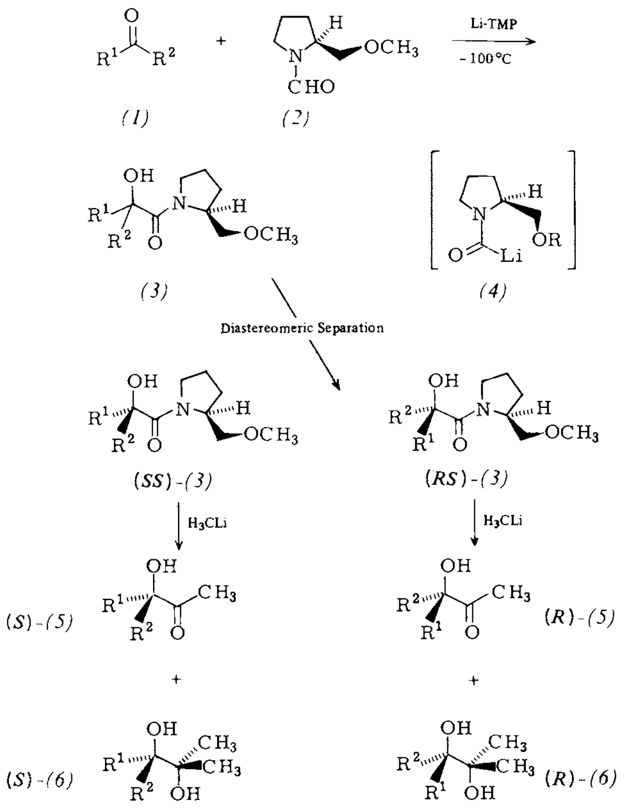


Table 1. Hydroxyamides *(3)*, prepared by a combination of asymmetric CC-coupling/chromatographic separation of diastereomers, as well as enantiomerically pure [a] α-hydroxyketones *(5)* and vicinal diols *(6)*.

| | $R^1$ | $R^2$ | *(3)* Yield [%] [b] | *(RS)-/(SS)-(3)* M.p. [°C] B.p. [°C/torr] [c] | *(RS)-/(SS)-(3)* $[\alpha]_D^{20}$ (*c*, $C_6H_6$) | *(R)-/(S)-(5)* B.p. [°C/torr] [c] | *(R)-/(S)-(5)* $[\alpha]_D^{20}$ (*c*, EtOH) | *(R)-/(S)-(6)* M.p. [°C) | *(R)-/(S)-(6)* $[\alpha]_D^{20}$ (*c*, EtOH) |
|---|---|---|---|---|---|---|---|---|---|
| *(a)* | *t*-$C_4H_9$ | $CH_3$ | 80 (90) | 90—91 | − 47.8 (1.8) | 81—82/15 | − 49.9 (1.8) | 48.5—49.5 | −13.3 (2.5) |
| | | | | 113/0.1 | + 22.5 (1.5) | 89/25 | + 51.0 (1.7) | 48.0—48.5 | +13.1 (1.8) |
| *(b)* [d] | $C_6H_5$ | $CH_3$ | 71 (84) | 108.5—109 | −103.2 (2.2) | 99—102/5 | +152.1 (2.0) | 60.5—61.5 | −19.8 (2.8) |
| | | | | 82—83 | − 15.5 (2.3) | 103—105/5 | −150.6 (2.1) | 60.0—61.0 | +19.6 (1.7) [e] |
| *(c)* | $C_6H_5$ | *i*-$C_3H_7$ | 77 (80) | 84.5—85 | − 82.5 (2.3) | 94—95/2 | −298.7 (1.8) [f] | 75.0—76.0 | −44.8 (2.4) |
| | | | | 80.5—81 | − 30.1 (2.3) | 96—98/2 | +302.2 (1.9) [f] | 75.0—75.5 | +44.7 (2.4) |

[a] Checked by NMR spectroscopy using the chiral shift reagent tris[3-(heptafluoro-1-hydroxybutylidene)-(+)-campherato]europium(III) (ee≥97%). [b] Values in brackets crude yields. [c] Oven temperature during Kugelrohr distillation. [d] The assignment of the absolute configuration follows from an X-ray structure analysis of the hydroxyamide and comparison with literature data [e] [upper line: *(RS)-(3)*, *(R)-(5)* and *(R)-(6)*; lower line: *(SS)-(3)*, *(S)-(5)* and *(S)-(6)*]. [e] *D. J. Cram, L. K. Gaston, H. Jaeger*, J. Am. Chem. Soc. *83*, 2183 (1961): $[\alpha]_D^{25} = +20.34$ ($c=3.2$, EtOH), *(S)*-configuration. [f] In benzene; *(5c)* exhibits mutarotation in ethanol.

Hydrolysis of the amides *(3)* to the acids can only be performed using somewhat drastic conditions (boiling with conc. HCl); *e.g.* 2-hydroxy-2-methyl-3-phenylpropionic acid was obtained in 67% yield from *(3)*, $R^1=C_6H_5CH_2$, $R^2=CH_3$.

The variant described here—CC-coupling, followed by chromatographic separation of the diastereomers—permits the asymmetric nucleophilic acylation or hydroxyalkylation of ketones and is of particular interest if pure samples of both enantiomers have to be prepared.

The optimization of the diastereoselectivity of the asymmetric carbamoylation is current being investigated. For example, use of the lithium compounds *(4)*, $R=CH_2OCH_2CH_2OCH_3$, already doubles the diastereomeric excess (de≈30%)[8].

## *Procedure*

*(SS)- and (RS)-(3):* A solution of 22 mmol Li-TMP in 50 mL THF [prepared from 3.74 mL (22 mmol) 2,2,6,6-tetramethylpiperidine and 13.8 mL 1.59 N *n*-butyllithium solution in *n*-hexane] is cooled to −70 °C and dropped, over 20—60 min, into a solution of 20 mmol *(1)* and 20 mmol *(2)* in 135 mL THF:ether:*n*-pentane=4:4:1 under inert gas atmosphere at −100 °C. The mixture is stirred for 3—5 h at this temperature, allowed to warm up to 0 °C and after acidification of the aqueous phase with dilute HCl, worked-up in the usual way with ether/saturated NaCl solution. The crude diastereomeric mixtures are separated into the pure diastereomers *(SS)*- and *(RS)-(3)* by column chromatography [silica gel, *n*-pentane/THF (5:1, *(3a)*) or ethyl acetate/*n*-pentane (0.5—10:1)] or by preparative HPLC [prep. HPLC-system 830, DuPont, Bad Nauheim, Zorbax SIL-column, 2.4×25 cm, *n*-pentane/THF (5:1), 60 bar *(3a)* or *n*-pentane/ethyl acetate (4—6:1), 60—120 bar], separation factors α=1.5—2.0.

*(S)- or (R)-(5) and (S)- or (R)-(6):* 5 mmol *(SS)*- or *(RS)-(3)*, dissolved in 5 mL THF, is added over 5—10 min to a stirred solution of 22.5 mmol methyllithium (13.6 mL of a 1.65 N solution in ether) in 22.5 mL THF at −10 °C under inert gas atmosphere. The cleavage is complete after 24 h at 20 °C (TLC control). After work-up in the usual way with ether/saturated NaCl solution, the mixture is separated by column chromatography (silica gel, *n*-pentane/ether).

Received: February 18, 1981 [Z 857 IE]
German version: Angew. Chem. *93*, 831 (1981)

---

[1] Reviews: *D. Seebach*, Synthesis *1969*, 17; Angew. Chem. *81*, 690 (1969); Angew. Chem. Int. Ed. Engl. *8*, 639 (1969); *D. Seebach, M. Kolb*, Chem. Ind. (London) *1974*, 687; *O. W. Lever*, Tetrahedron *32*, 1943 (1976); *B.-T. Gröbel, D. Seebach*, Synthesis *1977*, 357.

[2] *D. Seebach, W. Lubosch, D. Enders*, Chem. Ber. *109*, 1309 (1976), and references cited therein; *U. Schöllkopf, H. Beckhaus*, Angew. Chem. *88*, 296 (1976); Angew. Chem. Int. Ed. Engl. *15*, 293 (1976); *A. S. Fletcher, K. Smith, K. Swaminathan*, J. Chem. Soc. Perkin Trans. I *1977*, 1881; *V. Rautenstrauch, M. Joyeux*, Angew. Chem. *91*, 72, 73 (1979); Angew. Chem. Int. Ed. Engl. *18*, 83, 85 (1979); *V. Rautenstrauch, F. Delay, ibid. 92*, 764 (1980) *19*, 726 (1980); *T. Tsuda, M. Miwa, T. Saegusa*, J. Org. Chem. *44*, 3734 (1979).

[3] *J. D. Morrison, H. S. Mosher:* Asymmetric Organic Reactions, Prentice-Hall, Englewood Cliffs, N. J., 1971, and references cited therein; *J. Mathieu, J. Weill-Raynal*, Bull. Soc. Chim. Fr. *1968*, 1211, and references cited therein.

[4] For d/a-nomenclature, see: *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979).

[5] For a first promising test see: *L. Colombo, C. Gennari, C. Scolastico, G. Guanti, E. Narisano*, J. Chem. Soc. Chem. Commun. *1979*, 591; see also: *N. Hirowatari, H. M. Walborsky*, J. Org. Chem. *39*, 604 (1974); *E. L. Eliel et al.*, J. Am. Chem. Soc. *100*, 1614 (1978); J. Org. Chem. *44*, 3598 (1979).

[6] By analogy to the internationally adopted abreviation ee, we use de for *d*iastereomeric *e*xcess.

[7] For example *(RS)-(3b)*→*(R)-(5b)/(R)-(6b)*: a) 4.5 equiv. $H_3CLi$, 24 h, 20 °C, *(5)*:*(6)*=29:71; b) 3 equiv. $H_3CLi$, 16 h, 0 °C, *(5)*:*(6)*=65:35.

[8] The reaction *(1b)*+*(2)*→*(3b)* (43%, de=10%) was performed independently in Göttingen: *E. Krauthausen*, Dissertation Universität Göttingen 1978; *U. Schöllkopf*, personal communication.

# A Facile Electrosynthesis of 1,2,4-Triazoline-3,5-diones[**]

By *Heinrich Wamhoff* and *Gerhard Kunz*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

1,2,4-Triazoline-3,5-diones *(2a—c)* ("4-R-TAD") are, as extremely reactive dienophiles[1], versatile synthetic building blocks[2]; they can, in general, be prepared by oxidation of the urazoles *(1a—c)* with *tert*-butyl hypochlorite[3a], trichloroacetyl isocyanate[3b], dinitrogen tetroxide[3c] and, particularly easily, with *N*-bromosuccinimide[3d]. While separation from by-products can cause problems in these synthetic methods, the preparative electrolysis of *(1a—c)* at a Pt electrode offers a surprisingly simple and unequivocal route to the triazolinediones *(2a—c)*. In addition, bis(triazolinediones) linked by bridging groups[4] *e.g.* *(4)* are readily prepared in this way (Table 1).

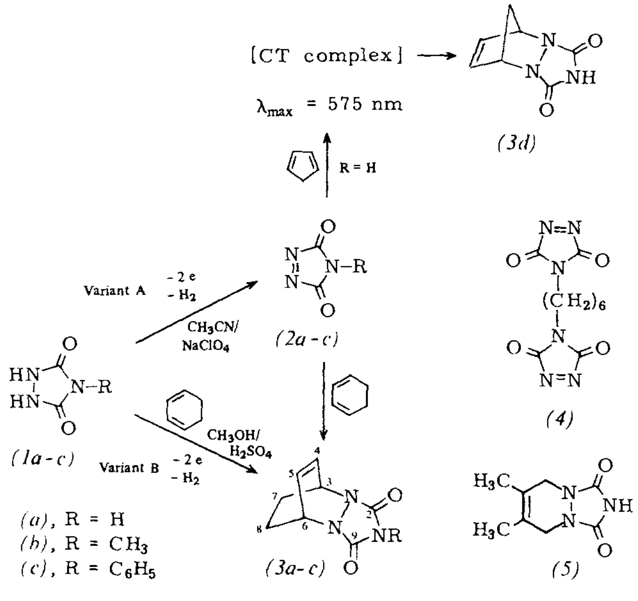


Table 1. Selected properties of the compounds synthesized.

| Compound | Yield [%] A | Yield [%] B [a] | M.p. [°C] | Spectral data |
|---|---|---|---|---|
| *(2a)* | 29 | | | IR($CH_2Cl_2$): 3175, 3070, 2980, 2300, 2250, 1750, 1710, 1375 $cm^{-1}$; UV($CH_2Cl_2$): $\lambda_{max} = 563$, 540, 520, 504 sh nm [b] |
| *(3a)* | 50 | 75 | 202—204 | IR(KBr): 3160, 3060, 2740, 1750, 1700, 1400 $cm^{-1}$; $^{13}C$-NMR($CH_2Cl_2$): $\delta = 157.38$ (C-2, 9), 130.46 (C-4, 5), 49.78 (C-3, 6), 21.90 (C-7, 8) |
| *(3d)* | 35 | | 214—215 [c] | |
| *(4)* | 12 | | 145 [d] | |
| *(5)* | | 62 | 215—216 [e] | |

[a] Variants A and B. [b] Ref. [6a]: $\lambda_{max} = 562$, 539, 518, 500 sh, nm. [c] Ref. [6b]: 214—216 °C. [d] *K. B. Wagener, S. R. Turner, G. B. Butler*, J. Polym. Sci. Polym. Lett. Ed. *1972*, 805. [e] Ref. [6b]: 216—217 °C.

Variant A of this electrochemical method is particularly well suited to the synthesis of the parent compound *(2a)*, which had already been postulated by *Stollé*[5] in 1912 but because of its low stability[6] ("elusive"[6a]) has remained incompletely characterized. Dilute solutions of *(2a)* can be stored for several months at low temperatures[7]. A further advantage with variant B is that *e.g.* Diels-Alder reactions can be carried out, even during the electrooxidation, as titrimetric trapping reactions of the triazolinedione *(2)*, *e.g.* reaction with cyclohexadiene gives *(3a)* and *(3b)* and with dimethylbutadiene *(5)* is produced.

A further simple preparative route to adducts of *(2a)* proceeds *via* metal complexes[8].

## *Procedure*

*Variant A (divided H-cell according to Lund*[9]*)*: *(1a—c)* (2 mmol) are suspended in an electrolyte consisting of 100 mL acetonitrile, 6.1 g sodium perchlorate and a drop of perchloric acid. Electrolysis proceeds at a Pt anode at 0 °C with a current density of 20 mA/$cm^2$ under an inert gas atmosphere. As soon as the color of the solution changes from deep pink to brown, 3 g sodium sulfate are added and after addition of a large amount of $CH_2Cl_2$, all the acetonitrile is removed *in vacuo*. The salts are removed from the red $CH_2Cl_2$ solution, which is then ready for further use; *(2a)*, *(3a)*, *(3d)*, *(4)* see Table 1.

*Variant B (non-divided reaction vessel for simultaneous cycloaddition)*: The conditions used are those described in variant A, however an open beaker is used and the electrolyte consists of 2% methanolic sulfuric acid; two Pt electrodes are used with a current density of 0.3 A/$cm^2$ in the presence of 1,3-cyclohexadiene or dimethylbutadiene. The mixture is worked-up by concentrating to a half of the original volume, the container filled-up with water, the mixture neutralized with sodium carbonate, and then concentrated to a tenth of its volume; the residue is extracted with $CH_2Cl_2$. After drying over magnesium sulfate, the solution is evaporated to dryness; *(3a)* and *(5)*, see Table 1. *(3b)* and *(3)*, R = 4-$ClC_6H_4$ or 3,4-$Cl_2C_6H_3$, are synthesized in an analogous manner.

Received: July 2, 1981 [Z 858 IE]
German version: Angew. Chem. *93*, 832 (1981)

CAS Registry numbers:
*(1a)*, 3232-84-6; *(1b)*, 16312-79-1; *(1c)*, 15988-11-1; *(2a)*, 4019-43-6; *(2b)*, 13274-43-6; *(2c)*, 4233-33-4; *(3a)*, 28144-78-7; *(3b)*, 78790-57-5; *(3d)*, 6248-69-7; *(3)*, R = 4-$ClC_6H_4$, 52568-44-2; *(3)*, R = 3,4-$Cl_2C_6H_3$, 52568-47-5; *(4)*, 38727-98-9; *(5)*, 28193-87-5; Cyclohexadiene, 592-57-4; Cyclopentadiene, 542-92-7.

---

[*] Prof. Dr. H. Wamhoff, Dipl.-Chem. G. Kunz
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Straße 1, D-5300 Bonn 1 (Germany)

[**] This work was supported by the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen and from Bayer AG.

---

[1] *C. Temple Jr., J. A. Montgomery* in *A. Weissberger, E. C. Taylor:* Heterocyclic Compounds, Vol. 37, Wiley, New York 1981, p. 526. Cf. *H. Wollweber:* Diels-Alder-Reaktion, Thieme, Stuttgart 1972, p. 62, 191 pp, and references cited therein.

[2] Vgl. *W. Adam, O. De Lucchi*, Angew. Chem. *92*, 815 (1980); Angew. Chem. Int. Ed. Engl. *19*, 762 (1980); *Th. Wagner-Jauregg*, Synthesis *1980*, 165, 769, and references cited therein.

[3] a) *R. C. Cookson, S. S. Gupte, J. D. R. Stevens, C. T. Watts*, Org. Synth. *51*, 121 (1971); b) *J. A. Moore, R. Muth, R. Sorace*, J. Org. Chem. *39*, 3799 (1974); c) *J. C. Stickler, W. H. Pirkle, ibid. 31*, 3144 (1966); d) *H. Wamhoff, K. M. Wald*, Org. Prep. Proced. Int. *7*, 251 (1975); cf. also *M. Fieser, L. F. Fieser:* Reagents for Organic Synthesis, Vol. 6, Wiley-Interscience, New York 1977, p. 75 pp.

[4] *K. M. Wald, H. Wamhoff*, Chem. Ber. *111*, 3519 (1978); *P. Ashkenazi, R. D. Macfarlane, W. A. Oertling, H. Wamhoff, K. M. Wald, D. Ginsburg*, Angew. Chem. *92*, 970, 972 (1980); Angew. Chem. Int. Ed. Engl. *19*, 933, 936 (1980).

[5] *R. Stollé*, Ber. Dtsch. Chem. Ges. *45*, 273 (1912).

[6] *J. E. Herweh, R. M. Fantazier*, Tetrahedron Lett. *1973*, 2101; J. Am. Chem. Soc. *96*, 1187 (1974); b) *M. G. de Amezúa, M. Lora-Tamayo, J. L. Soto*, Tetrahedron Lett. *1970*, 2407.
[7] Even a 2.5 month "old" $CH_2Cl_2$ solution of *(2a)*, which had been stored in the refrigerator, underwent a smooth reaction with cyclopentadiene to the adduct *(3d)*.
[8] *H. Wamhoff, G. Kunz*, unpublished results.
[9] *H. Lund*, Adv. Heterocycl. Chem. *12*, 233 (1970).

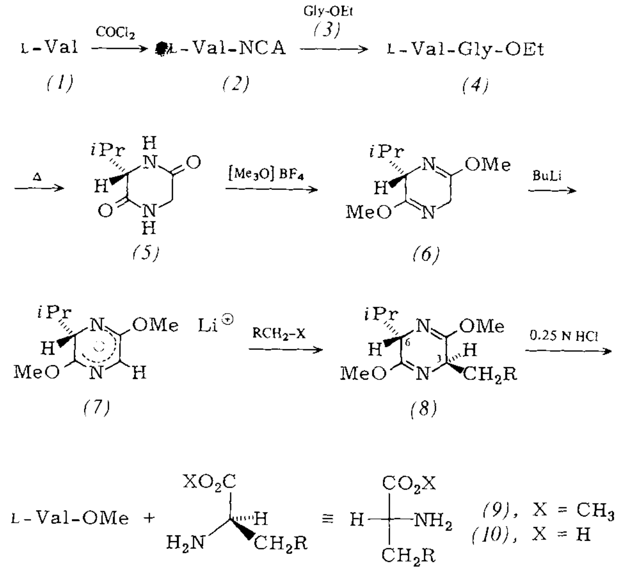
# Enantioselective Synthesis of *(R)*-Amino Acids Using L-Valine as Chiral Agent[**]

By *Ulrich Schöllkopf, Ulrich Groth*, and *Chuanzheng Deng*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

Optically active, non-proteinogenic amino acids are gaining increasing importance in research and application *e.g.* as enzyme inhibitors or pharmaceuticals.

We recently reported the enantioselective[1] synthesis of α-methylamino acids by reaction of the lithiated bislactim ether of *cyclo*-(L-Ala-L-Ala) with electrophiles[2]. We have now found that α-H amino acids [type *(10)*] can also be obtained by the "bislactim-ether method", *e.g.* starting from the mixed bislactim ethers *(6)*, which we obtained from *cyclo*-(L-Val-Gly) *(5)*. *(6)* is metalated regiospecifically in the glycine moiety by butyllithium. The lithium compound (7) (an ion pair) reacts with alkyl halides with, in part, >95% diastereoselectivity to give the adducts *(8)*. The alkyl residue enters *trans* to the isopropyl group on C-6, *i.e.* the (*R*)-configuration is induced at C-3. Hydrolysis liberates the (*R*)-amino acid methyl ester *(9)* as well as the chiral agent, methyl L-valinate. The two esters are separable by distillation. The enantiomeric excess (e.e. in Table 1) of esters *(9)* is determined ¹H-NMR spectroscopically with $Eu(hfc)_3$ on the signal of the ester methyl group. The (*R*)-configuration followed, either from the rotation of the esters *(9)* or of the amino acids *(10)*—insofar as these are configuratively known[3]—and/or from the ¹H-NMR spectrum of the adducts *(8)*.



Scheme 1. NCA = N-carboxyanhydride.

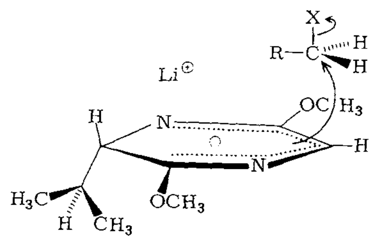
Table 1. Dihydropyrazines *(8)* and methyl (*R*)-α-aminoalkanoates *(9)* prepared from *(6)*.

| | $CH_2R$ | X' | *(8)* Yield [%] | (*R*)-*(9)* Yield [%] [a] | (*R*)-*(9)* e.e. [%] | $[\alpha]_D^{20}$ (EtOH) [b] |
|---|---|---|---|---|---|---|
| *(a)* | $CH_2—C_6H_5$ | Br | 81 | 73 | 91–95 [c] | −24.2 (*c* = 2.2) |
| *(b)* | $CH_2—3,4—(OCH_3)_2C_6H_3$ | Br | 91 | 78 | 85 | −15.0 (*c* = 0.9) |
| *(c)* | $CH_2—CH{=}CH—C_6H_5$ | Br | 90 | 89 | >95 | −18.7 (*c* = 0.9) |
| *(d)* | $CH_2—C{\equiv}C—C_6H_5$ | Br | 92 | 86 | >95 | + 3.3 (*c* = 1.0) |
| *(e)* | $CH_2—C{\equiv}CH$ | Br | 88 | 52 | 60–65 [c] | [d] |
| *(f)* | $CH_2—(CH_2)_5—CH_3$ | Br | 62 | 75 | 75–80 [c] | −19.0 (*c* = 1.1) |
| *(g)* | 2-naphthylmethyl | Br | 89 | 78 | 92 [c] | −15.6 (*c* = 0.9) |

[a] Referred to *(8)*. [b] For the given e.e. values. [c] Rotation of (*R*)- and (*S*)-*(10)* known [3]. [d] Since separation of *(9e)*/Val-$OCH_3$ by distillation is difficult, both esters were hydrolyzed with conc. HCl (1 h); *(10e)* was separated from sparingly soluble *(1)* by crystallization from water. *(10e)* [3]: $[\alpha]_D^{20}$ ($H_2O$) = +18.8 (*c* = 2.4).

We synthesized (*R*)-α-methylphenylalanine in >95% enantiomeric excess in an analogous way, starting from benzyl bromide and the bislactim ether of *cyclo*-(L-Val-L-Ala).

To explain the induction we assume that the lithium compound *(7)* contains a planar dihydropyrazine anion, one diastereotopic side of which is strongly shielded by the comparatively large isopropyl group. *(11)* is the formula proposed for the more favorable of the two transition states which leads to the (3*R*)-configuration of *(8)*. We postulate the "folded" conformation for the transition state, in which R is situated above the heterocyclic anion and thus closely approaches the center of induction. This conformation is stabilized either by a HOMO(anion)-LUMO(R) interaction or by van der Waals attraction.



*(11)*

We were also able to prepare other mixed bislactim ethers, *e.g.* those of *cyclo*-(L-Ala-Gly), *cyclo*-(L-Val-L-Ala), *cyclo*-(L-Val-L-Phe), *cyclo*-(L-Leu-Gly), *cyclo*-(L-*O,O*-dimethyl-α-methyldopa-Gly or -Ala) and *cyclo*-(α-methylphe-Gly) according to the method outlined in Scheme 1.

---

[*] Prof. Dr. U. Schöllkopf, Dipl.-Chem. U. Groth, C. Deng
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] Asymmetric Syntheses *via* Heterocyclic Intermediates, Part 6.—Part 5: [2c].

*0570-0833/81/0909-0798 $ 02.50/0*

*Procedure*

*(2):* A powerful stream of phosgene was passed into the suspension of *(1)* (46.8 g, 0.4 mol) in tetrahydrofuran (THF) (600 mL) at 40 °C until *(1)* was in solution (*ca.* 30 min). After 1 hours purging with anhydrous $N_2$ the solvent was removed *in vacuo*, the residue taken up in a little THF, and the solvent once again removed by distillation *in vacuo* (removal of hydrogen chloride!). *(2)* was dried for 30 min at 40 °C *in vacuo*; the yield was quantitative.

*(5):* The solution of *(2)* (*ca.* 0.4 mol) in THF (400 ml) was added dropwise to a vigorously stirred mixture of *(3* · HCl) (55.8 g, 0.4 mol), triethylamine (90.9 g, 0.9 mol) and $CHCl_3$ (500 mL) (2L three-necked flask) at −70 to −60 °C. After 3 hours stirring at −70 °C and 30 min at room temperature the triethylamine hydrochloride was separated off by suction, the solvent removed from the solution by distillation *in vacuo* (40 °C bath temperature), and the residue was taken up in 1700 mL toluene. The resulting solution and then suspension was heated for 12 h under reflux with (efficient mechanical) stirring and then cooled to 0 °C; *(5)* was recovered by suction, washed several times with ether, and then dried at 100 °C *in vacuo*. Yield 57 g (91%). For purification, *(5)* can be recrystallized from water. M.p. 254 °C, $[\alpha]_D^{20}=20.2$ ($c=0.9$, $H_2O$).

*(6):* The mixture of *(5)* (9.4 g, 60 mmol; dried for 3 d at 100 °C in a vacuum), $[Me_3O]BF_4$ (22.2 g, 150 mmol) and $CH_2Cl_2$ (200 mL) was stirred for a total of 3d at room temperature (after about 24 h a further 8.9 g (60 mmol) of $[Me_3O]BF_4$ was added[4]. After addition of a solution of $NaH_2PO_4 \cdot 2H_2O$ (28,1 g, 0.18 mol) and $Na_2HPO_4 \cdot 2H_2O$ (106.8 g, 0.6 mol) in water (500 mL), the organic phase was separated-off and the aqueous phase was extracted three times with $CH_2Cl_2$. The combined organic phases were dried over $MgSO_4$, the solvent drawn off *in vacuo*, and the residue distilled; yield 91 g (82%), b.p. 88 °C/8—12 torr, $[\alpha]_D^{20}=106.3$ ($c=1.0$, EtOH).

*(8c): n*-Butyllithium (2 mL of a 1.55 N solution in hexane, *i.e.* 3 mmol) was added (injection syringe) to a stirred solution of *(6)* (0.53 g, 2.9 mmol) in THF (7 mL) at −70 °C. The mixture was stirred for 10 min at this temperature and then treated dropwise with the solution of cinnamyl bromide (0.57 g, 2.9 mmol) in THF (6 mL). After 5 h the temperature of the mixture was allowed to rise to room temperature, the solvent removed in a vacuum, and the residue taken up in ether and extracted with water. The ethereal phase was dried over $MgSO_4$, the ether removed in a vacuum, and the residue distilled (Kugelrohr); yield 0.78 g (90%), b.p. 170—180 °C/0.5 torr.

*(9c):* A suspension of *(8c)* (0.18 g, 0.6 mmol) in 0.25 N HCl (4.8 mL, 1.2 mmol) was stirred for 10 h at room temperature. The mixture was extracted once with ether, which was rejected; the solvent was then removed *in vacuo* and the residue dissolved in a little water, covered with ether, and vigorously shaken with conc. ammonia solution until pH = 8—10. The ether phase was then separated off, the aqueous phase extracted twice with ether, and the combined ether phases dried over $MgSO_4$. The ether was removed in a vacuum and the residue distilled (Kugelrohr); yield 0.11 g (89%), b.p. 90—100 °C/0.1 torr, $[\alpha]_D^{20}=-18.7$ ($c=0.9$, EtOH), e.e. >95%[5]. Only one $OCH_3$ signal was recognizable in the $^1$H-NMR spectrum after addition of $Eu(hfc)_3$.

Received: January 20, 1981 [Z 815 IE]
German version: Angew. Chem. *93*, 793 (1981)

CAS Registry numbers:
*(1)*, 7004-03-7; *(2)*, 78342-41-3; *(3)* HCl, 623-33-6; *(5)*, 16944-60-8; *(6)*, 78342-42-4; *(8a)*, 78342-43-5; *(8b)*, 78342-44-6; *(8c)*, 78354-69-5; *(8d)*, 78342-45-7; *(8e)*, 78342-46-8; *(8f)*, 78342-47-9; *(9a)*, 21685-51-8; *(9b)*, 78392-35-5; *(9c)*, 78342-48-0; *(9d)*, 78342-49-1; *(9e)*, 78342-50-4; *(9f)*, 78342-51-5.

---

[1] Definition: We use the expression "enantioselective" when an excess of one enantiomer remains at the end of a reaction sequence after separation of the chiral agent.—(*R*)-Amino acids belong to the D-series.

[2] a) *U. Schöllkopf, W. Hartwig, U. Groth,* Angew. Chem. *91*, 922 (1979); Angew. Chem. Int. Ed. Engl. *18*, 863 (1979); b) *ibid. 92*, 205 (1980) and *19*, 212 (1980); c) *U. Schöllkopf, W. Hartwig, U. Groth, K. O. Westphalen,* Liebigs Ann. Chem. *1981*, 696.

[3] *(10e): A. C. A. Jansen, R. J. M. Weustink, K. E. T. Kerling, E. Havinga,* Recl. Trav. Chim. Pays-Bas *88*, 819 (1969); *O. Leukart, M. Caviezel, A. Eberle, E. Escher, A. Tun-kyi, R. Schwyzer,* Helv. Chim. Acta *59*, 2181 (1976); *(10f): S. M. Birnbaum, S. J. Fu, J. P. Greenstein,* J. Biol. Chem. *203*, 333 (1953); *(10g): L. Ghosez,* private communcation.

[4] $[Et_3O]BF_4$ is less expensive than $[Me_3O]BF_4$, and, moreover, it reacts more rapidly because it is soluble in $CH_2Cl_2$. On using the method we recommend the bisethoxylactim ether *(6)*, OEt instead of OMe. We used the bismethoxylactim ether *(6)* because the $^1$H-NMR spectra of the products are simpler. The quality of commercial reagents should be checked before use.

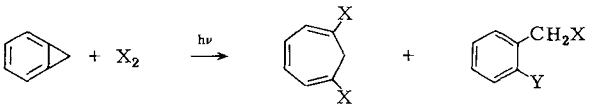
[5] We assume >95% d.e. or e.e. if only one diastereomer is recognizable in the $^1$H-NMR spectrum.

---

## Synthesis of 1,6-Disubstituted Cycloheptatriene Derivatives from Benzocyclopropene

By *Renji Okazaki, Masaharu O-oka, Norihiro Tokitoh, Yoko Shishido,* and *Naoki Inamoto*[*]

1,6-Disubstituted cycloheptatriene derivatives[1] are important both for the study of the cycloheptatriene-norcaradiene equilibrium[2a] and for the preparation of bridged aromatic heterocycles[2b]. Benzocyclopropene *(1)*[3], which until now has rarely been used as a synthetic building block, proved to be a suitable educt for the preparation of 1,6-dithiocyanato- and 1,6-diiodocycloheptatriene *(2a)* and *(2b)*, respectively, both of which are versatile, useful synthons.



*(1)*
$X_2 = (SCN)_2,\ I_2$

*(2a)*, X = SCN
*(2b)*, X = I

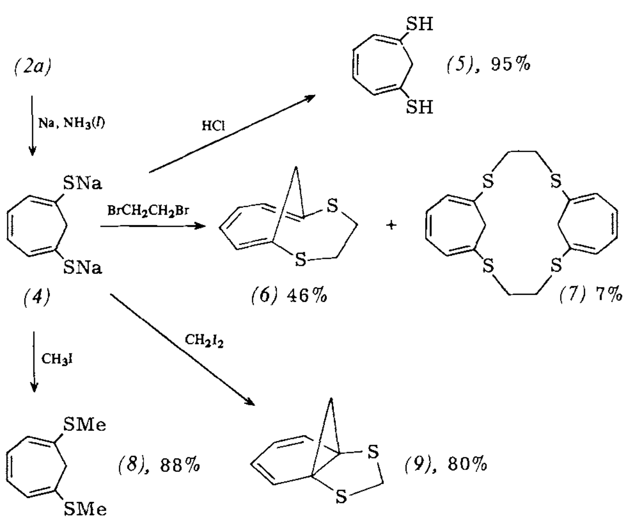
*(3a)*, X = Y = SCN
*(3b)*, X = NCS,
Y = SCN
*(3c)*, X = Y = I

Irradiation of a solution of *(1)* and thiocyanogen in benzene leads to formation of 61% *(2a)*, in addition to 27% *o*-thiocyanatobenzyl thiocyanate *(3a)* and 2% of the isomeric isothiocyanate *(3b)* (Table 1); when the reaction is performed in the dark, but otherwise under the same conditions, only 14% *(3a)* and 9% *(3b)* are formed. The photochemical reaction is inhibited by oxygen and 2,6-di-*tert*-butyl-4-methylphenol, both of which indicate a radical chain mechanism—similar to the reaction of olefins with $(SCN)_2$[4]. The addition of iodine to benzocyclopropene *(1)* also proceeds photochemically; hereby the two diiodides

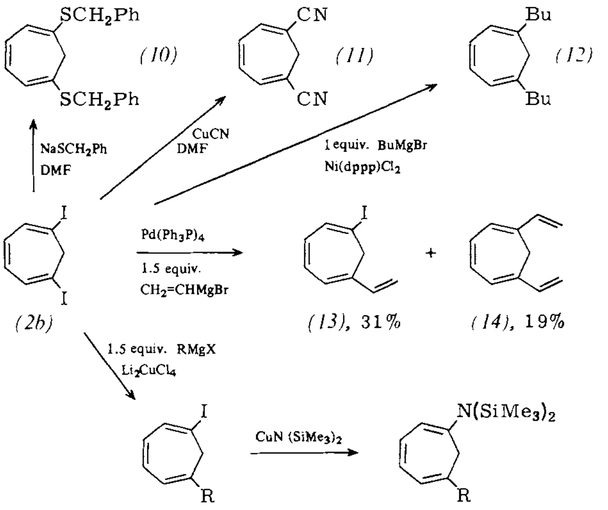
---

[*] Prof. Dr. R. Okazaki [+], Dipl.-Chem. M. O-oka,
Dipl.-Chem. N. Tokitoh, Dipl.-Chem. Y. Shishido, Prof. Dr. N. Inamoto,
Department of Chemistry, Faculty of Science
The University of Tokyo
Hongo 7-3-1, Bunkyoku, Tokyo 113 (Japan)
[+] Author to whom correspondence should be addressed.

*(2b)* and *(3c)* are formed in 67 and 4% yield, respectively[5].



The dithiocyanate *(2a)* can be reduced by treatment with sodium in liquid ammonia to the disodium salt *(4)* which, after acidification, yielded the dithiol *(5)* in 95% yield. *(4)* could be alkylated with iodomethane, diiodomethane and 1,2-dibromoethane, to produce the sulfide *(8)*, the [4.3.1]propellane *(9)* or the bicycle *(6)*, and the phane-like tricycle *(7)*, respectively (Table 1).



*(15a)*, R = $(CH_2)_2CH(OMe)_2$, 62% *(16a)*, R = $(CH_2)_2CH(OMe)_2$, 37%
*(15b)*, R = *n*Bu, 51%
*(15c)*, R = $CH=CH_2$, 71% *(16b)*, R = *n*Bu, 27%

Scheme 1. dppp = $Ph_2PCH_2CH_2CH_2PPh_2$.

Table 1. Some spectroscopic data of the new compounds [a].

*(2a)*: $^1$H-NMR: $\delta=3.03$ (s, 2H), 6.66 (s, 4H); IR (KBr): 2150 cm$^{-1}$.
*(3a)*: $^1$H-NMR: $\delta=4.27$ (s, 2H), 7.30—7.85 (m, 4H); IR: 2150 cm$^{-1}$.
*(3b)*: $^1$H-NMR: $\delta=4.88$ (s, 2H), 7.05—7.84 (m, 4H); IR: 2160, 2095 cm$^{-1}$.
*(5)*: $^1$H-NMR: $\delta=2.69$ (s, 2H), 3.36 (s, 2H, disappeared upon $D_2O$ exchange), 6.05—6.45 (m, 4H).
*(6)*: $^1$H-NMR: $\delta=2.03$ (d, $J=12$ Hz, 1H), 3.25 (d, $J=12$ Hz, 1H), 2.43—2.88 (m, 2H), 3.12—3.62 (m, 2H), 6.22—6.75 (m, 4H); $^{13}$C-NMR: $\delta=131.2$, 127.6, 118.6, 42.9, 33.7; MS: $m/z=182$ ($M^\oplus$), 167, 154, 153.
*(7)*: $^1$H-NMR: $\delta=2.55$ (s, 4H), 2.94 (s, 8H), 5.95—6.45 (m, 8H); MS: $m/z=364$ ($M^\oplus$), 207, 155, 154, 153, 121, 91.
*(8)*: $^1$H-NMR: $\delta=2.32$ (s, 6H), 2.60 (s, 2H), 5.76—6.46 (m, 4H).
*(9)*: $^1$H-NMR: $\delta=0.51$ (d, $J=6$ Hz, 1H), 2.25 (d, $J=6$ Hz, 1H), 3.68 (d, $J=12$ Hz, 1H), 4.20 (d, $J=12$ Hz, 1H), 5.90—6.70 (m, 4H); $^{13}$C-NMR: $\delta=127.2$, 120.5, 52.9, 37.3, 26.1.
*(10)*: $^1$H-NMR: $\delta=2.62$ (s, 2H), 4.00 (s, 4H), 6.0—6.5 (m, 4H), 7.29 (s, 10H).
*(11)*: $^1$H-NMR: $\delta=2.81$ (s, 2H), 6.85—7.00 (m, 4H).
*(12)*: $^1$H-NMR: $\delta=0.6$—2.6 (m, 18H), 2.25 (s, 2H), 5.7—6.4 (m, 4H) [b].
*(15a)*: $^1$H-NMR: $\delta=1.50$—1.96 (m, 2H), 2.06—2.46 (m, 2H), 2.90 (s, 2H), 3.16 (s, 6H), 4.23 (t, $J=5$ Hz, 1H), 5.73—6.63 (m, 4H) [b].
*(15b)*: $^1$H-NMR: $\delta=0.7$—1.9 (m, 9H), 2.90 (s, 2H), 5.80—6.80 (m, 4H) [b].
*(15c)*: $^1$H-NMR: $\delta=3.10$ (s, 2H), 5.18 (d, $J=10$ Hz, 1H), 5.52 (d, $J=17$ Hz, 1H), 6.0—6.9 (m, 5H) [b].
*(16a)*: $^1$H-NMR: $\delta=0.10$ (s, 18H), 1.48—2.44 (m, 4H), 2.24 (s, 2H), 3.24 (s, 6H), 4.32 (t, $J=5$ Hz, 1H), 5.48—6.38 (m, 4H) [b].
*(16b)*: $^1$H-NMR: $\delta=0.10$ (s, 18H), 0.6—1.6 (m, 9H), 2.20 (s, 2H), 5.3—6.2 (m, 4H) [b].

[a] $^1$H-NMR spectra were recorded in $CDCl_3$/TMS. [b] In $CCl_4$/TMS.

A series of reactions showed that the diiodide *(2b)* is also of synthetic interest as an intermediate (Scheme 1). Under nickel(II) catalysis[6a], *(2b)* reacts with one equivalent of *n*-butylmagnesium bromide to give exclusively 1,6-di-*n*-butylcycloheptatriene *(12)*, while under palladium(0) catalysis[6b] with 1.5 equivalents of vinylmagnesium bromide, the mono- and the divinylcycloheptatrienes *(13)* and *(14)*, respectively are formed[7]. Under conditions of copper catalysis[8], *(2b)* reacts with Grignard reagents to give the monosubstituted compounds *(15a)*—*(15c)* in good yield, from which *(15a, b)* were transformed into the amines *(16a, b)*[9] by treatment with copper bis(trimethylsilyl)amide. In addition, the dinitrile *(11)* and the sulfide *(10)*[10] were prepared by nucleophilic substitution in dimethylformamide (DMF).

The method described here is thus a general route for the synthesis of 1,6-disubstituted cycloheptatriene derivatives having halogen, sulfur, nitrogen, and carbon substituents.

## *Procedure*

*(2a)*: A solution of *(1)* (511 mg, 5.7 mmol) and 10 mmol $(SCN)_2$ (from $Pb(SCN)_2$ and $Br_2$) in 100 mL benzene was irradiated for 30 min using an Hg high-pressure lamp. The reaction mixture was chromatographed over silica gel (hexane/ether 2:1) whereupon 715 mg *(2a)* (61%, m.p. 76—77 °C), 316 mg *(3a)* (27%, oil) and 19 mg *(3b)* (2%, oil) were isolated. The reaction proceeded similarly on the 30 mmol scale.

*(5)*—*(9)*: Sodium (98 mg, 4.3 mmol) was added to a solution of *(2a)* (206 mg, 1.02 mmol) in 25 mL liquid ammonia at −78 °C, until a blue color persisted. After evaporation of the $NH_3$, the residue was treated with dilute hydrochloric acid and ether, and after removal of the solvent the ethereal solution yielded 149 mg *(5)* (95%). To synthesize *(6)*—*(9)*, the residue obtained after evaporation of the $NH_3$ was dissolved in 10 mL tetrahydrofuran and 0.5 mL hexamethylphosphoric triamide, and treated with the corresponding alkyl halide.

*(2b)*: A solution of $I_2$ (318 mg, 1.25 mmol) in 100 mL heptane was added over 1 h to an ice cold solution of *(1)* (103 mg, 1.55 mmol) in 80 mL heptane, which was simultaneously irradiated (Hg high-pressure lamp, filter: 0.1% aqueous $K_2CrO_4$ solution 10 °C). After addition of $I_2$ was complete, the solution was irradiated for a further 3 h. 265 mg *(2b)*[5a] (67%) and 16 mg *(3c)*[11] (4%) were isolated from the reaction mixture by chromatography (silica gel, pentane). The reaction can also be carried out on the 40 mmol scale, however, the yield of *(2b)* was reduced to 50—60%.

Received: October 24, 1979 [Z 824 IE]
German version: Angew. Chem. 93, 833 (1981)

---

[1] Some general synthetic routes to 1,6-disubstituted cycloheptatrienes: *R. Darms, T. Threlfall, M. Pesarom, A. Eschenmoser,* Helv. Chim. Acta *46,*

2893 (1963); *E. Vogel, R. Feldmann, H. Düwel,* Tetrahedron Lett. *1970,* 1941; *E. Vogel, W. Wiedemann, H. D. Roth,* Justus Liebigs Ann. Chem. *759,* 1 (1972).

[2] a) *G. Maier,* Angew. Chem. *79,* 446 (1967); Angew. Chem. Int. Ed. Engl. *6,* 402 (1967); *T. Toda,* Yuki Gosei Kagaku Kyokaishi *30,* 412 (1972); b) *M. Schäfer-Ridder, A. Wagner, M. Schwamborn, H. Schreiner, E. Devrout, E. Vogel,* Angew. Chem. *90,* 894 (1978); Angew. Chem. Int. Ed. Engl. *17,* 853 (1978).

[3] a) *B. Halton,* Chem. Rev. *73,* 113 (1973); *W. E. Billups,* Acc. Chem. Res. *11,* 245 (1978); b) *W. E. Billups, A. J. Blakeney, W. Y. Chow,* Org. Synth. *55,* 12 (1976).

[4] *R. G. Guy, J. J. Thompson,* Tetrahedron *34,* 541 (1978).

[5] a) Earlier *Vogel et al.,* synthesized 1,6-diiodocycloheptatriene *(2b)* from *(1)* and $I_2$ in $CCl_4$; the yield was, however, small and *(3c)* was the major product: *E. Vogel, W. Grimme, S. Korte,* Tetrahedron Lett. *1965,* 3625; b) when the reaction was conducted in normal sunlight, never more than 2% *(2b)* was obtained.

[6] a) *K. Tamao, K. Sumitani, Y. Kiso, M. Zenbayashi, A. Fujioka, S. Kodama, I. Nakajima, A. Minato, M. Kumada,* Bull. Chem. Soc. Jpn. *49,* 1958 (1976); b) *M. Yamamura, I. Moritani, S. Murahashi,* J. Organomet. Chem. *91,* C39 (1975).

[7] *H. Günther, H. Schmickler, U. H. Brinker, K. Nachtkamp, J. Wassen, E. Vogel,* Angew. Chem. *85,* 762 (1973); Angew. Chem. Int. Ed. Engl. *12,* 760 (1973).

[8] *J.-F. Normant, A. Commerçon, G. Cahiez, J. Villiéras,* C. R. Acad. Sci., Ser. *C 278,* 967 (1974).

[9] *F. D. King, D. R. M. Walton,* J. Chem. Soc. Chem. Commun. *1974,* 256.

[10] *J. R. Campbell,* J. Org. Chem. *29,* 1830 (1964).

[11] *R. N. Castle, J. L. Riebsomer,* J. Org. Chem. *21,* 142 (1956).

## Complexes of Iridium with Terminal $PF_2$-Ligands[**]

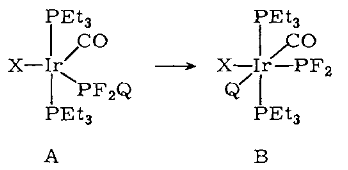
By *E. A. V. Ebsworth, Neil T. McManus,*
*David W. H. Rankin,* and *John D. Whitelock*[*]

Attempts to prepare complexes containing a metal bound to tricoordinated phosphorus have usually produced bridged species. Some derivatives of chromium and tungsten are known in which terminal $PCl_2$-groups are bound to the metal[1], but attempts to prepare $PF_2$-complexes of platinum have led to the production of dinuclear diplatinum complexes[2]. Here we report the synthesis and characterization of some complexes of iridium(III) containing terminal $PF_2$-ligands; these compounds should be suitable for use in the controlled synthesis of mixed-metal bridged complexes.

Reaction of a solution of $PF_2H$ and *trans*-$Ir(CO)I(PEt_3)_2$ at 233 K in toluene leads to the formation of a $PF_2H$-complex of pentacoordinated iridium (type A in Scheme 1). Two signals are observed in the $^{31}P\{H\}$-NMR spectrum (Table 1); a doublet at $\delta = -7$ ($^2J(PP) = 38$ Hz) arising from $PEt_3$, and a wide triplet from the $PF_2$-group at $\delta = 142$ ($^1J(PF) = 1103$ Hz) each line of which is further split into a narrow triplet because of coupling with the P atoms of the two $Et_3P$-groups. In the non-decoupled spectrum, each line of the $PF_2$-signal shows an additional doublet splitting of 415 Hz, a typical value for $^1J(PH)$ in tetracoordinated phosphorus compounds. The $^1H$-NMR spectrum shows a resonance at $\delta = 8.4$ with a doublet splitting of 415 Hz; each line is further split into a triplet [due to $^2J(FH)$] of triplets [due to $^3J(PH)$].

When the solution was allowed to warm to room temperature, the spectra changed. The P resonance of the $PF_2$-group shifts from $\delta = 142$ to $\delta = 378$; this implies a significant alteration in the environment of the $PF_2$-group. Moreover, the magnitude of $^2J(PP)$ becomes smaller and $J(HPF_2)$ drops from 415 Hz to 7.5 Hz. In the $^1H$-NMR spectrum, the resonance at $\delta = 8.4$ disappears and is replaced by a complex multiplet at $\delta = -16$ that must be due to H bound to Ir. It follows that the pentacoordinated iridium complex *(1)* (type A) formed initially has rearranged to give a new complex *(5)* of hexacoordinated iridium(III) (type B in Scheme 1) by oxidative addition of PH, leaving H and a terminal $PF_2$-group bound to the metal.

*trans*-$Ir(CO)(PEt_3)_2X + PF_2Q \longrightarrow$



| X | Q | Type A | Type B |
|---|---|---|---|
| I | H | *(1)* | *(5)* |
| Cl | Cl | *(2)* | *(6)* |
| Br | Br | *(3)* | *(7)* |
| I | I | *(4)* | *(8)* |

Scheme 1.

Similar reactions occur between $PF_2X$ and *trans*-$Ir(CO)X(PEt_3)_2$, X = Cl, Br or I. When X = Cl, the $^{19}F$- and $^{31}P$-NMR spectra show peaks with the multiplet structures expected for a complex of type A; the $PF_2$-chemical shift ($\delta = 97$) is in the same region as that of $PF_2Cl$-complexes. When the solution is allowed to warm to room temperature, the $PF_2$-resonance shifts to $\delta = 364.8$ *i.e.* the signal for *(6)* is similar to that for *(5)*. When X = Br, the concentration of the complex *(3)* (type A) at 193 K is small, and the assignment of the $PF_2$-resonance is doubtful; when X = I, we were unable to identify any of the signals expected for complex *(4)*. In each case, however, there are resonances due to complexes *(7)* or *(8)* (type B); in keeping with the assigned structure, all the $PF_2$-chemical shifts are very similar (Table 1).

Table 1. NMR data for the complexes of types A and B recorded in $[D_8]$toluene at 233 K [*(1)*–*(5)*] and at 298 K [*(6)*–*(8)*]; precision. ±1 to the last figure quoted ($J$ in Hz).

| Complex | Type | $\delta(PEt_3)$ | $\delta(PF_2)$ | $\delta(F)$ | $^1J(PF)$ | $^2J(PP)$ | $^3J(PF)$ |
|---|---|---|---|---|---|---|---|
| *(1)* [a] | A | −7.2 | 142 | −60.8 | 1103 | 38 | [c] |
| *(2)* | A | −6.9 | 97 | 4.9 | 1333 | 42 | 9 |
| *(3)* | A | 0.3 | 110 | 6.2 | 1341 | 45 | [c] |
| *(4)* | A | resonances not observed | | | | | |
| *(5)* [b] | B | −10.8 | 376.7 | −61.5 | 1111 | 25.9 | 17.1 |
| *(6)* | B | −9.3 | 364.8 | −68.3 | 1106 | 9.2 | 11.6 |
| *(7)* | B | −18.1 | 363.1 | −64.8 | 1108 | 8.5 | 11.1 |
| *(8)* | B | −31.9 | 364.8 | −61.0 | 1112 | 8.3 | 10.6 |

[a] $\delta(H) = 8.72$. [b] $\delta(H) = -16.0$; $^2J[HP(Et)] = 10$, $^2J[HP(F)] = 7.5$, $^3J(HF) = 11.5$ Hz. [c] Not resolved.

Complex *(5)* decomposes slowly in solution at room temperature, but complexes *(6)*—*(8)* are stable at room temperature and have been isolated and characterized by elemental analysis, IR-, and NMR-spectroscopy. Addition of $B_2H_6$ to a solution of *(8)* in $C_7H_8$ leads to a shift in the $PF_2$-resonance in the $^{31}P\{^1H\}$-NMR spectrum to $\delta = 250$,

---

[*] Prof. Dr. E. A. V. Ebsworth, N. T. McManus, Dr. D. W. H. Rankin, Dr. J. D. Whitelock,
Department of Chemistry, University of Edinburgh,
Edinburgh EH9 3JJ (Scotland)

[**] This work was supported by Messrs Johnson Matthey and the Science Research Council

together with a marked broadening of the lines. We interpret these observations as evidence that a bridged complex containing the grouping Ir—$PF_2$—$BH_3$ has been formed; in confirmation of this view, the $^{19}$F-NMR spectrum consists of a broad doublet, due to $^1J$(PF), each line of which is split into a 1 : 3 : 3 : 1 quartet by F—H coupling.

Received: August 18, 1980 [Z 825 IE]
German version: Angew. Chem. *93*, 785 (1981)

---

[1] *W. Malisch, R. Alsmann,* Angew. Chem. *88*, 809 (1976); Angew. Chem. Int. Ed. Engl. *15*, 769 (1976).

[2] *E. A. V. Ebsworth, D. W. H. Rankin, J. D. Whitelock,* unpublished results.

---

## Cobalt Mediated [2 + 2 + 2]-Cycloadditions: Stereospecific Intramolecular Reactions of Enediynes to Tricyclic Dienes Bearing Angular Methyl Groups[**]

By *Thomas R. Gadek* and *K. Peter C. Vollhardt*[*]

We recently reported on the inter- and intramolecular [2 + 2 + 2]cycloaddition of linear achiral enediynes containing terminal double bonds, using $CpCo(CO)_2$, to give polycyclic diene complexes (cp = cyclopentadienyl)[1]. We now describe similar stereospecific reactions of enediynes which may even be used to incorporate trisubstituted double bonds, producing tricyclic dienes with angular methyl groups. The molecules synthesized constitute good model systems for a variety of polycyclic natural products, particularly vitamin D precursors.

The educts *(1)* were prepared by Wittig reaction of the terminal acetylenic aldehydes or ketones with the appropriate acetylenic ylides[2]. The aldehydes or ketones generally originated from internal propargyl alcohols *via* the "acetylene-zipper" reaction[3], followed by standard structural manipulations. *Cis-* and *trans-(1)* were interconvertible by irradiation in the presence of sensitizer[4] and, if necessary, separated by preparative gas chromatography.

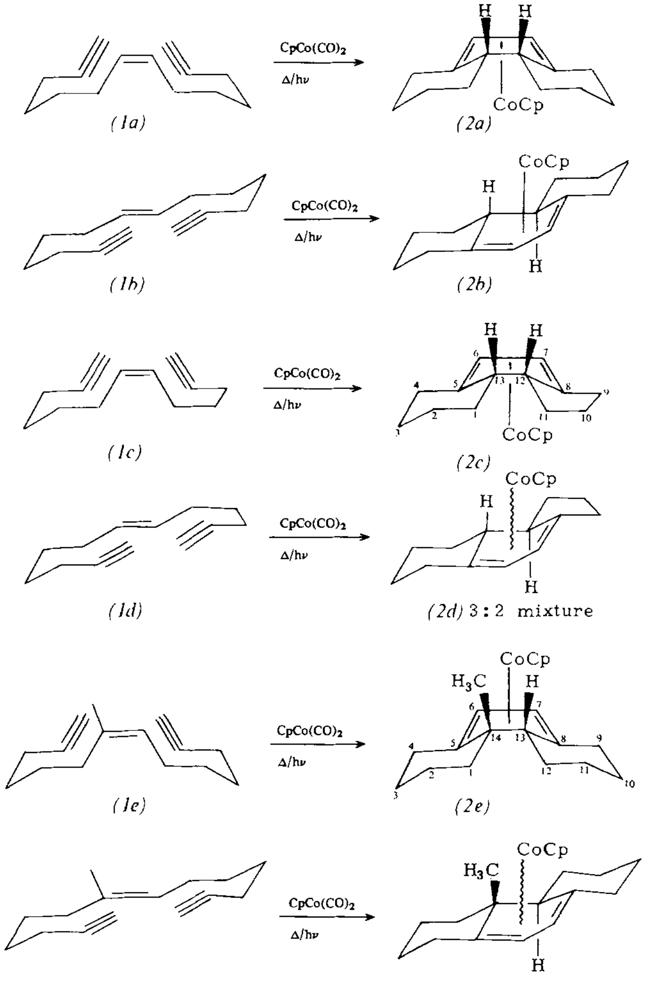
In a typical experiment, a solution of *(1)* and $CpCo(CO)_2$ in boiling *m*-xylene was irradiated to give the red-brown complexes *(2)* (Table 1) in fairly good yield, after chromatography on alumina. Stereochemical and spectral assignments were carried out by comparison with model compounds, utilizing the effect of the anisotropy of cobalt on the NMR spectra[1], symmetry considerations [cf. *(2a)* with *(2b)*], and off-center resonance proton decoupled $^{13}$C-NMR spectroscopy.

Three points of particular interest are:

1. The [2 + 2 + 2]-cycloaddition proceeds with retention of stereochemistry at the original double bond and also with remarkable stereoselectivity with respect to cobalt [cf. *(2a), (2b), (2c), (2e)*]; this might be valuable in asymmetric syntheses with an optically active metal compound.

2. The cyclopentadienylcobalt not only fulfills the function of the mediator of the cyclization but also serves to protect the diene unit from rearrangement and polymerization.

3. The ligands in *(2)*, all of which were either previously unknown - *(2a—d)* - or incompletely characterized - *(2e, f)*[5] - may be liberated as colorless oils in high yield by oxidative demetalation[6] (Table 1). Decomplexation of the mixtures *(2d)* and *(2f)* gave only one product, corroborating the structural assignment of the minor component.



*(2d)* 3 : 2 mixture

*(2f)* 3 : 1 - *endo-/exo*-$CH_3$

The origin of the stereoselectivity observed in the above reactions is not clear at present. It should be noted that trimethylsilylation of the alkyne moieties is detrimental to the successful outcome of the reaction.

Hydrogenated benz[*e*]indanes and phenanthrenes of the type synthesized here are frequent structural features in natural products. The ligands in *(2e)* and *(2f)* are of particular interest since they may be regarded as constituting the ABC-portion of steroids, which function as precursors to vitamin D and valuable steroid hormones. The cobalt mediated [2 + 2 + 2]-cycloaddition approach should provide a simple and effective route to these classes of compounds.

### *Procedure*

A degassed solution of *(1)* (1 mmol) and $CpCo(CO)_2$ (1.1 mmol) in *m*-xylene (50 mL) was refluxed and irradiated (visible light, GE-ENH, 250 W). After 1 h, the solvent was removed *in vacuo* (0.05 torr) and the residue chromato-

---

[*] Professor Dr. K. P. C. Vollhardt, T. R. Gadek
Department of Chemistry, University of California, Berkeley
Materials and Molecular Research Division,
Lawrence Berkeley Laboratory
Berkeley, California 94720 (USA)

[**] This work was supported by the National Science Foundation (CHE 79-03954) and the National Institutes of Health (GM 22479). *K.P.C.V.* is a Camille and Henry Dreyfus Teacher Scholar (1978—1983).

Table 1. Physical data of the diene complexes *(2)* and their free ligands. All new compounds gave satisfactory analytical and/or high resolution mass spectroscopic values. $^{1}$H-NMR (at 250 MHz unless otherwise stated) and $^{13}$C-NMR (63 MHz): $\delta$-values ($C_6D_6$); for numbering see *(2c)* and *(2e)*; *exo* and *endo* refer to the position of the proton relative to the metal.

*(2a)*: 63%; m.p. 43 °C; $^{1}$H-NMR (600 MHz): 4.50 (s, 2H, H$^{6,7}$), 4.45 (s, 5H, Cp), 1.91 (d, $J$=11.5 Hz, 2H), 1.67 (dd, $J$=9, 8 Hz, 4H), 1.63 (dd, $J$=12, 11 Hz, 4H), 1.35 (d, $J$=11.5 Hz, 4H), 1.23 (AA'm, 4H), 0.62 (dd, $J$=17, 11 Hz, 2H, H$_{13,14}$); $^{13}$C-NMR: 80.7 (Cp), 75.5 (C$^{6}$), 72.5 (C$^{5}$), 47.0 (C$^{13}$), 41.1, 32.7, 30.7, 28.0

*(2b)*: 63%; oil; $^{1}$H-NMR: 4.60 (d, $J$=4 Hz, 1H, H$^{6}$ or H$^{7}$), 4.55 (s, 5H, Cp), 4.47 (d, $J$=4 Hz, 1H, H$^{6}$ or H$^{7}$), 1.8—1.0 (m, 16H), 0.87 (dd, $J$=6.5, 7 Hz, 2H), 0.63 (dddd, $J$=12.5, 12.5, 12.5, 3.5 Hz, 1H), 0.16 (m, 1H, H$^{13exo}$); $^{13}$C-NMR: 80.1 (Cp), 75.6, 75.4, 71.7, 68.4, 52.9 (C$^{13endo}$), 42.9 (C$^{14exo}$), 40.6, 36.4, 35.7, 35.0, 30.0, 27.9, 26.8, 26.3

*(2c)*: 65%; oil; $^{1}$H-NMR (600 MHz): 4.51 (s, 5H, Cp), 4.47 (d, $J$=4.5 Hz, 1H, H$^{6}$ or H$^{7}$), 4.43 (d, $J$=4.5 Hz, H$^{6}$ or H$^{7}$), 2.56—1.20 (m, 14H), 0.90 (m, 2H, H$^{12,13}$); $^{13}$C-NMR: 80.0 (Cp), 75.3, 73.2, 50.8, 50.4, 41.5, 33.3, 33.1, 30.8, 28.2, 26.0, 22.3 [a]

*(2d)*: 63%; oil; $^{1}$H-NMR: 5.05 (d, $J$=4.3 Hz, 1H, H$^{6}$ or H$^{7}$), 4.52 (s, 5H, Cp), 4.46 (d, $J$=4.3 Hz, 1H, H$^{6}$ or H$^{7}$), 2.9—0.6 (m), 0.24 (m, 1H, H$^{12}$ or H$^{13exo}$); this spectrum also contains signals assigned to a second isomer (ratio 3:2) at 4.65 (s, Cp), 4.71 (d, $J$=5 Hz, H$^{6}$ or H$^{7}$), 4.47 (d, $J$=5 Hz, H$^{6}$ or H$^{7}$), 0.05 (m, H$^{12}$ or H$^{13exo}$); $^{13}$C-NMR: 81.2 (Cp), 79.8 (Cp), 74.5, 71.4, 56.2, 53.2, 48.3, 40.8, 36.9, 36.5, 35.7, 35.2, 34.2, 33.3, 29.9, 29.1, 27.6, 26.5 (2C), 26.4, 24.3, 23.3 [a]

*(2e)*: 74%; oil; $^{1}$H-NMR: 4.57 (d, $J$=4 Hz, 1H, H$^{6}$ or H$^{7}$), 4.49 (s, 5H, Cp), 4.43 (d, $J$=4 Hz, 1H, H$^{6}$ or H$^{7}$), 1.93 (ddd, $J$=13, 13, 4 Hz, 1H), 1.80—1.50 (m, 5H), 1.5—1.1 (m, 11H), 1.34 (s, 3H, CH$_3$), 0.98 (ddd, $J$=10.5, 4.5, 2 Hz, 1H), 0.85 (ddd, $J$=13, 13, 4.5 Hz, 1H), 0.62 (dddd, $J$=12, 12, 12, 4 Hz, 1H, H$^{12exo}$); $^{13}$C-NMR: 80.4 (Cp), 76.7 (2C), 75.8, 72.3, 55.9 (C$^{13}$), 42.3 (C$^{14}$), 41.1, 37.5, 35.9, 32.3, 31.2, 30.9, 29.8 (CH$_3$), 28.3, 22.8

*(2f)*: 76%; oil; $^{1}$H-NMR: 4.72 (d, $J$=4 Hz, 1H, H$^{6}$ or H$^{7}$), 4.53 (s, 5H, $C_5H_5$), 4.47 (d, $J$=4 Hz, 1H, H$^{6}$ or H$^{7}$), 1.88 (ddd, $J$=13, 13, 4 Hz, 1H), 1.78—1.42 (m, 8H), 1.41—1.2 (m, 6H), 1.28 (s, 3H, CH$_3$), 0.86 (dddd, $J$=12, 12, 12, 4 Hz, 1H), 0.17 (dd, $J$=12, 0.8 Hz, 1H, H$^{13}$); this spectrum also contains signals assigned to a second isomer (ratio 3:1): 4.53 (s, $C_5H_5$), 4.50 (d, $J$=4 Hz, H$^{6}$ or H$^{7}$), 4.41 (d, $J$=4 Hz, H$^{6}$ or H$^{7}$), 0.65 (s, 3H, CH$_3$); $^{13}$C-NMR major isomer: 79.9, 77.7, 77.6 (2C), 75.0, 48.3 (C$^{13}$), 44.5 (C$^{14}$), 37.1, 36.0, 30.6, 26.5, 25.7, 22.8, 21.8 (CH$_3$); minor isomer: 80.8, 76.1, 75.0, 57.2 (C$^{13}$), 42.6, 42.0, 41.5, 33.5, 32.5, 28.0, 27.9, 22.6

*cis*-1,2,3,4,4a,4b,5,6,7,8-decahydrophenanthrene [from *(2a)*]: 93%; $^{1}$H-NMR: 5.42 (s, 2H), 2.43 (m, 2H), 2.28 (m, 2H), 2.02 (bdd, $J$=12, 12 Hz, 2H), 1.80 (m, 6H), 1.27 (m, 6H); $^{13}$C-NMR: 115.5, 40.5, 35.2, 29.0, 28.5, 27.0 [b]

*trans*-1,2,3,4,4a,4b,5,6,7,8-decahydrophenanthrene [from *(2b)*]: 96%; $^{1}$H-NMR: 5.38 (s, 2H), 2.22 (bd, $J$=13 Hz, 2H), 2.1—1.7 (m, 10H), 1.45—1.15 (m, 6H); $^{13}$C-NMR: 115.1, 44.1, 37.1, 34.8, 28.6, 27.0 [b]

*cis*-1-*H*-2,3,6,7,8,9,9a,9b-octahydrobenz[e]indene [from *(2c)*]: 86%; $^{1}$H-NMR: 5.56 (bs, 2H), 2.93—2.56 (m, 2H), 2.5—1.1 (m, 14H); $^{13}$C-NMR: 115.5, 113.2, 43.1, 42.6, 36.5, 31.6, 30.1, 28.9, 27.7., 27.2, 24.9 [b]

*trans*-1-*H*-2,3,6,7,8,9,9a,9b-octahydrobenz[e]indene [from *(2d)*]: 89%; $^{1}$H-NMR: 5.61 (bs, 2H), 2.6—1.0 (m, 16H); $^{13}$C-NMR: 119.2, 114.2, 48.4, 42.0, 34.7, 33.2, 32.7, 30.2, 26.2, 25.8, 24.8 [b]

*cis*-1,2,3,4,4a,4b,5,6,7,8-decahydro-4a-methylphenanthrene [from *(2e)*]: 84%; $^{1}$H-NMR: 5.46 (d, $J$=6 Hz, 1H), 5.37 (dd, $J$=6, 2 Hz, 1H), 2.27 (m, 3H), 2.01 (ddd, $J$=12, 12, 4 Hz, 1H), 1.94—1.45 (m, 8H), 1.45—1.10 (m, 5H), 1.02 (s, 3H, CH$_3$); $^{13}$C-NMR: 116.3, 113.9, 52.2, 51.9, 37.1, 31.4, 31.2, 30.1, 27.8, 26.3, 25.5, 25.2, 22.4 [b]

*trans*-1,2,3,4,4a,4b,5,6,7,8-decahydro-4a-methylphenanthrene [from *(2f)*]: 92%; $^{1}$H-NMR: 5.46 (bs, 2H), 2.46—2.0 (m, 5H), 1.92—1.57 (m, 6H), 1.46 (ddddd, $J$=13, 13, 13, 3, 3 Hz, 1H), 1.40—1.14 (m, 5H), 0.87 (s, 3H, CH$_3$); $^{13}$C-NMR: 117.6, 117.5, 48.2, 48.0, 40.5, 32.8, 31.3, 30.0, 26.4, 25.5, 23.9, 16.4, 16.0 [b]

[a] Quaternary C atoms not detected. [b] Quaternary vinyl C-atoms not detected.

graphed on alumina (activity 2, under $N_2$) with pentane. The diene complex is eluted as a single red-brown band.

Received: February 11, 1981 [Z 827 IE]
German version: Angew. Chem. *93*, 801 (1981)

---

[1] *E. D. Sternberg, K. P. C. Vollhardt*, J. Am. Chem. Soc. *102*, 4839 (1980); *C. Chang, J. A. King, Jr., K. P. C. Vollhardt*, J. Chem. Soc., Chem. Commun. *1981*, 53.

[2] *C. Chang, C. G. Francisco, T. R. Gadek, J. A. King, Jr., E. D. Sternberg, K. P. C. Vollhardt*, in *B. M. Trost, C. R. Hutchinson*: Organic Synthesis Today and Tomorrow, Pergamon, New York 1981, p. 71.

[3] *J. C. Lindhoudt, G. L. van Mourik, H. J. J. Pabon*, Tetrahedron Lett. *1976*, 2565; *C. A. Brown, A. Yamashita*, J. Chem. Soc. Chem. Commun. *1976*, 959.

[4] *C. Moussebois, J. Dale*, J. Chem. Soc. C *1966*, 260.

[5] *W. Huber*, Ber. Dtsch. Chem. Ges. *71B* (1938) 725; *K. Dimroth, E. Dietzel, E. Stockstrom*, Justus Liebigs Ann. Chem. *549*, 256 (1941); *H. B. Charmbury, C. C. Wright*, J. Am. Chem. Soc. *66*, 526 (1944); *E. A. Braude, O. H. Wheeler*, J. Chem. Soc. *1955*, 329.

[6] *E. R. F. Gesing, J. P. Tane, K. P. C. Vollhardt*, Angew. Chem. *92*, 1057 (1980); Angew. Chem., Int. Ed. Engl. *19*, 1023 (1980).

# $[(\eta^5\text{-}CH_3C_5H_4)Mn(CO)_2Hg]_4$, a Compound with an $Mn_4Hg_4$ Eight-Membered Ring and Additional Hg—Hg Bonds

By *Wolfgang Gäde* and *Erwin Weiss*[*]

Numerous examples of mercury-transition metal compounds having linear M—Hg—M bridges are known. We wish to report here on the reaction of $K[\eta^5\text{-}CH_3C_5H_4)Mn(CO)_2GeH_3]$[1] with $Hg^{2+}$ ions in aqueous media, which yields the unexpected Ge-free compound $[(\eta^5\text{-}CH_3C_5H_4)Mn(CO)_2Hg]_4$ *(1)* (55%); in addition, the Hg-free compound $[(\eta^5\text{-}CH_3C_5H_4)Mn(CO)_2]_3Ge$ *(2)* (1%) is formed, which contains a GeMn double bond as well as two GeMn single bonds[2]. The course of the reaction is still unknown; the observed elimination of mercury indicates an oxidative action of the $Hg^{2+}$ ions.

An X-ray structure analysis[3] shows a novel ring system with an $Mn_4Hg_4$ eight-membered ring in the Hg-containing compound *(1)*. The molecule possesses a four-fold alternating axis. The four Hg atoms have an almost coplanar

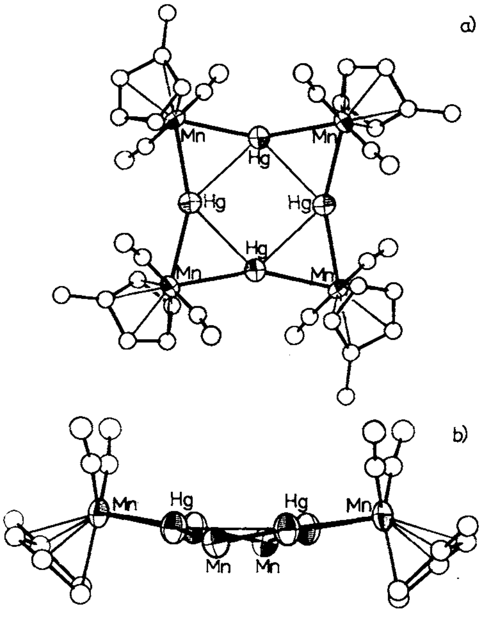


Fig. 1. a) Structure of *(1)* in the crystal, ORTEP-drawing. Mn—Hg 264.0(7), Hg—Hg 288.8(2), Mn—C(CO) 176(7) and 179(8), Mn—C(Cp) 209(9) to 218(5), average 212.4 pm; Mn—Hg—Mn 157.2, Hg—Mn—Hg 66.2(2), Hg—Mn—C(CO) 74(2) and 118(2), C(CO)—Mn—C(CO) 87(3)°. Crystal data: tetragonal space group $I\bar{4}$, $a$=1595.9(2), $c$=768.3(1) pm, $V$=1956.8×10$^{6}$ pm$^{3}$, $Z$=2, $\rho$(calc.) 2.64 g cm$^{-3}$. Mo$_{K\alpha}$-radiation, 986 independent reflections (up to $\Theta$=30°), $R$=0.099 (Mn and Hg anisotropic, C and O isotropic). b) Projection of *(1)* at right angles to the plane of the molecule, two of the Mn atoms shown without ligands.

---

[*] Prof. Dr. E. Weiss, Dr. W. Gäde
Institut für Anorganische und Angewandte Chemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

arrangement (deviation from planarity 0.4 pm), while in contrast the Mn atoms exhibit larger deviations (35.9 pm) (Fig. 1).

A similar eight-membered ring system is found in $[CdFe(CO)_4]_4 \cdot 2$acetone[4]; however, in this case a strongly distorted eight-membered ring is present, since two of the four Cd atoms are coordinated by acetone molecules. In contrast to this, metal-metal interaction in the $Hg_4$-ring of *(1)* must be assumed from the short Hg—Hg bond lengths (288.8 pm). For comparison: Hg—Hg bond lengths in $Hg_2X_2$ ($X = F$, Cl, Br, I, $NO_3$) 243—269 pm, in Hg metal 299 (α-form at 78 K), 282.5 and 316 pm (β-form at 77 K)[5]. The nonlinearity of the Mn—Hg—Mn groups, with a markedly small angle at the Hg atom, (157.2°) also indicates metal-metal interaction. The Mn—Hg bond length (264.0 pm) is only slightly longer than in $Hg[Mn(CO)_5]_2$ (261.0 pm)[6] and corresponds to a single bond.

A planar $Hg_4$-ring has also been observed in the alloy $Na_3Hg_2$[7]. Here, the $Hg_4$-unit possesses $D_{2h}$ symmetry; the Hg—Hg bond lengths are 296 and 301 pm. According to a bonding theory treatment due to *Corbett*[8], the actual negative charge is smaller than in the formal $Hg_4^{6-}$ representation.

### *Procedure*

All operations were performed in the absence of air. A solution of $HgCl_2$ (5.4 g, 20 mmol) in 100 mL water is dropped, with constant stirring, into a solution of $K[(\eta\text{-}CH_3C_5H_4)Mn(CO)_2GeH_3]$ (2.4 g, 7.9 mmol) in 50 mL water. After 30 min the gray suspension is extracted several times with ether, the red ether phase dried over $Na_2SO_4$, and concentrated under reduced pressure. The red oily residue is taken up in a little $CH_2Cl_2$. Dark red needles of *(1)* crystallize at *ca.* −25 °C (1.7 g, 1.1 mmol, 55% analytically pure). M.p. > 160 °C (decomp.) IR spectrum: $\nu(CO) = 1905$, 1863 $cm^{-1}$ (in $CH_2Cl_2$). Dark red *(2)* can also be obtained from the mother liquor following subsequent concentration and cooling (50 mg, 0.08 mmol, 1%).

Received: January 6, 1981 [Z 834 IE]
German version: Angew. Chem. *93*, 796 (1981)

---

[1] *W. Gäde, E. Weiss,* Chem. Ber. *114*, 2399 (1981).
[2] *W. Gäde, E. Weiss,* J. Organomet. Chem. *213*, 451 (1981).
[3] Dr. *Kopf* is thanked for performing the X-ray measurements.
[4] *R. D. Ernst, T. J. Marks, J. A. Ibers,* J. Am. Chem. Soc. *99*, 2090 (1977).
[5] *R. W. G. Wyckoff:* Crystal Structures, Vol. 1, Wiley-Interscience, New York 1965.
[6] *M. L. Katcher, G. L. Simon,* Inorg. Chem. *11*, 1651 (1972).
[7] *J. W. Nielsen, N. C. Baenziger,* Acta Crystallogr. *7*, 277 (1954); *E. J. Dewell, N. C. Baenziger, ibid. 8*, 705 (1955).
[8] *J. D. Corbett,* Inorg. Nucl. Chem. Lett. *5*, 81 (1969).

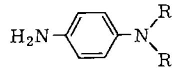
---

## Colored, Unsymmetric and Light-Sensitive Vesicle Membranes[**]

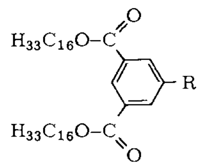
By *Jürgen-Hinrich Fuhrhop, Herbert Bartsch,* and *Detlev Fritsch*[*]

*Dedicated to Professor Hans Herloff Inhoffen on the occasion of his 75th birthday*

Vesicles facilitate the localization of three reaction components in aqueous solution: in the hydrophobic membrane interior and in the two water volumes inside and outside the cells[1]. If amphiphiles with reactive head groups are used, then these three reaction spaces can be supplemented by two further reaction centers on the membrane surfaces. First examples of this were monolayer, redox-active bipyridinium membranes[2]. We report here for the first time on bilayer vesicle membranes with phenylenediamine and benzenediazonium head groups, whose exterior surface can be multivariously modified by coupling reactions (color development in color photography; diazotype).



*(1a)*, R = $n\text{-}C_{14}H_{29}$
*(1b)*, R = $n\text{-}C_{16}H_{33}$



*(2a)*, R = $NH_2$
*(2b)*, R = $N^{\oplus}(CH_3)_3\ I^{\ominus}$
*(2c)*, R = $N_2^{\oplus}\ BF_4^{\ominus}$

The phenylenediamine derivatives *(1a)* and *(1b)* were obtained by dialkylation of *p*-aminoacetanilide with *n*-bromotetradecane and *n*-bromohexadecane, respectively, in dimethylformamide and subsequent acid hydrolysis (yield 70%). *(2a)* was accessible from dimethyl 5-aminoisophthalate by transesterification with *n*-hexadecanol in the presence of titanium(IV) butoxide (yield 35%). The free amino group was either permethylated with methyl iodide in dimethyl sulfoxide in the presence of tridodecylamine to *(2b)* (yield 40%) or diazotized in a $CH_2Cl_2/H_2O$ two-phase system with $HBF_4/NaNO_2$ to *(2c)* (yield 50%).

The products *(1a,b)* and *(2a—c)* were sparingly soluble in water, but aqueous suspensions became clear on ultrasonication (Ultrasonics sonicator W 220F, steps 3—4). The solutions of *(1a,b)* rapidly turned red (radical formation) during sonication in air, so they were therefore prepared under inert gas at pH = 3—5. The aqueous solutions of the diazonium compound *(2c)* were unstable above pH = 2; evolution of $N_2$ was accompanied by precipitation of a solid. Surprisingly, at pH = 1—2 no hydrolysis of the ester groups occurred; on the contrary, the vesicles from *(2c)* were now stable for days. The vesicles formed from *(2b)* could also be stored for several days, both in acid as well as in neutral media. Electron micrographs of the suspensions of *(1a,b)* and *(2a—c)* after sonification showed spherical structures of 200—1000 Å diameter. The vesicle interior was also stained on addition of uranyl acetate during the sonification of solutions of vesicles from *(1b)*. The layer thickness of the uncolored membrane was estimated as 50—100 Å. Interestingly, in addition to photographs showing the usual statistical size distribution of the vesicles (Fig. 1, top) (Ø = 250—1000 Å) others were also obtained which showed only microvesicles (Ø = 250—300 Å) (Fig. 1, center). In solutions of *(1a)* we also observed "large" vesicles with cracked surfaces, from which microvesicles were released (Fig. 1, bottom). These photographs are reminiscent of those taken under the optical microscope by *Fox* showing "buds" of microspheres[3], which serve as a model of biological cell division.

If the aqueous solution of *(1)* is treated with iodine and phenol the blue indoaniline dye is formed on the outer surface of the membrane within seconds, while the phenylene diamine residues situated on the interior surface hardly

---

[*] Prof. Dr. J.-H. Fuhrhop, Dipl.-Chem. H. Bartsch, D. Fritsch
Institut für Organische Chemie der Freien Universität
Takustr. 3, D-1000 Berlin 33 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

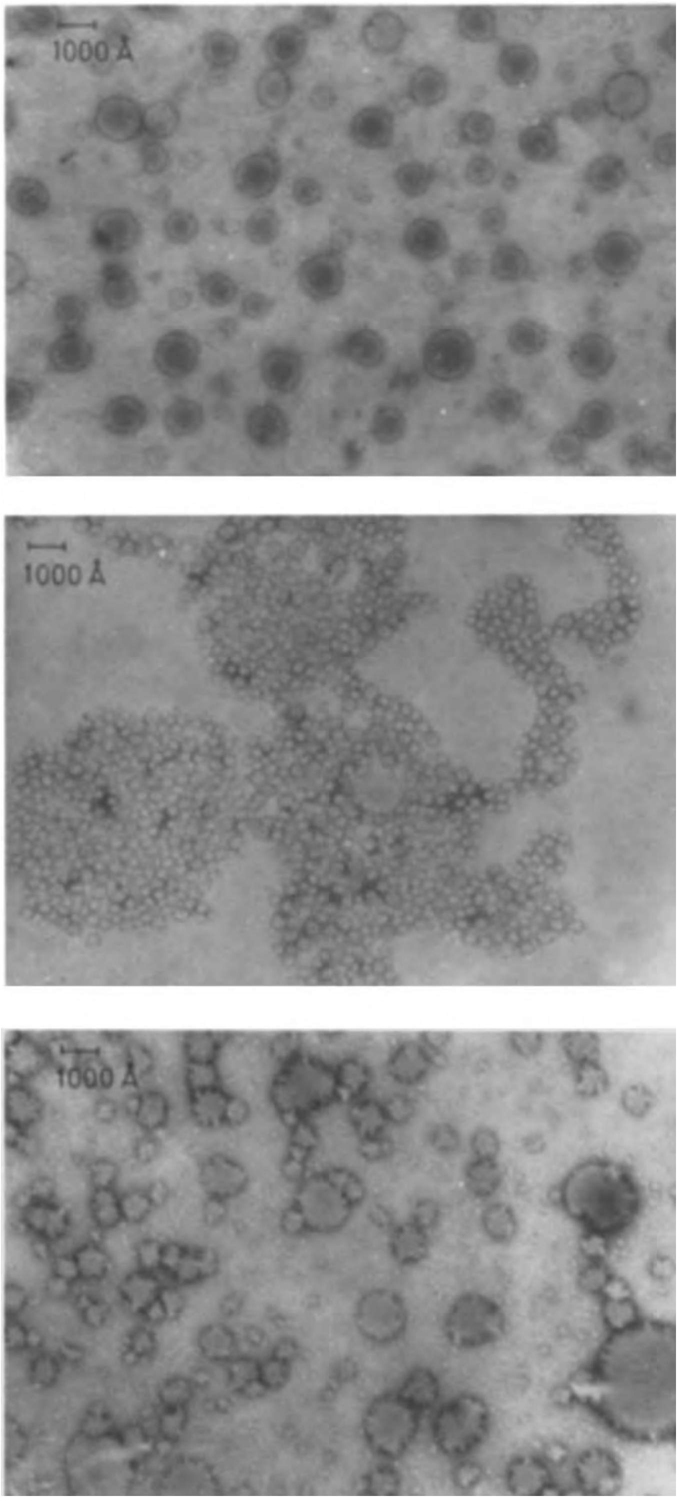


Fig. 1. Various forms of vesicles (see text) from *(1b)* (above and center) and *(1a)* (below). Magnification 40000 × ; stained with uranyl acetate.

react, even within 2 h[4]. In this way, stable soluble vesicles are accessible having an oxidized, colored external surface and an interior surface still in the reduced state. To our knowledge these are the first non-biological cells having an unsymmetrical bilayer membrane (BLM). Benzenediazonium vesicles from *(2c)* could be reacted in the same way with 7-amino-1-naphthol-3-sulfonic acid on the outer surface; the colored vesicles precipitated, though at only 5% conversion they remained in solution.

Finally, the benzenediazonium vesicles could also be decomposed and precipitated with visible light. When traces (*ca.* $10^{-7}$ M) of 5,10,15,20-porphinetetrakis(9-decenesulfonic acid)[5] were added as sensitizer to the vesicular solution of *(2c)* (*ca.* $10^{-4}$ M) the vesicles quantitatively precipitated within 10 min on irradiation with a 60W tungsten lamp; the diazonium salts are converted into chlorobenzene derivatives. The same solution decomposes only slowly (15%/d) in the dark.

Received: January 26, 1981 [Z 835 IE]
German version: Angew. Chem. *93*, 797 (1981)

---

[1] *J.-H. Fuhrhop*, Nachr. Chem., Tech. Lab. *28*, 792 (1980).

[2] *E. Baumgartner, J.-H. Fuhrhop*, Angew. Chem. *92*, 564 (1980); Angew. Chem. Int. Ed. Engl. *19*, 550 (1980).

[3] *S. W. Fox*, Naturwissenschaften *56*, 1 (1969).

[4] The selective reactivity of the outer membrane surfaces was demonstrated by measurements of the difference spectra of the completely reacted compounds in organic solvents [ethanol/water = 20 : 1 for *(1a, b)*, chloroform/methanol = 4 : 9 for *(2c)*] and in vesicular aqueous solution. Several independent measurements gave good reproducibility of these spectra.

[5] *J.-H. Fuhrhop, M. Baccouche*, Justus Liebigs Ann. Chem. *1976*, 2058.

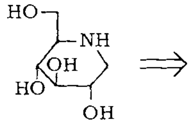
## A Four-Step Synthesis of 1-Deoxynojirimycin with a Biotransformation as Cardinal Reaction Step

By *Günther Kinast* and *Michael Schedel*[*]

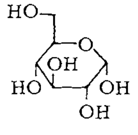
*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Inhibitors of intestinal α-glucosidases have proven to be pharmacologically and clinically effective in the treatment of carbohydrate-dependent metabolic disorders like diabetes mellitus[1]. We were, therefore, interested in the natural product 1-deoxynojirimycin *(1)*.

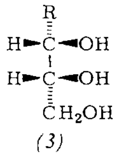
The previously reported methods for the synthesis of 1-deoxynojirimycin[2] involve many steps and necessitate resort to tedious protecting-group techniques; we report here on a short, combined chemical-microbiological synthesis[3] involving reductive conversion of glucose *(2)* into 1-amino-1-deoxy-D-sorbitol *(4a)*[4], which is subsequently transformed by bacteria of the genus *Gluconobacter*, which selectively oxidize the central of the three OH-groups in D-erythro-configurated compounds such as *(3)*[5] into 6-amino-6-deoxy-L-sorbose *(5a)*. Subsequent intramolecular reductive amination of *(5a)* according to the method of *Paulsen* then furnishes *(1)*.



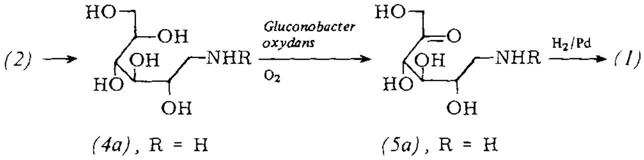
*(1)*



*(2)*



*(3)*



*(4a)*, R = H
*(4b)*, R = $CO_2CH_2Ph$

*(5a)*, R = H
*(5b)*, R = $CO_2CH_2Ph$

---

[*] Dr. G. Kinast, Dr. M. Schedel
Chemisch-wissenschaftliches Labor Pharma und Institut für Biochemie der Bayer AG
Postfach 101709, D-5600 Wuppertal 1 (Germany)

The direct biotransformation of *(4a)* into *(5a)*, however, proceeded in only low yields owing to the instability of the aminoketone *(5a)*, the amino group being free. Protection of the amino function by a benzyloxycarbonyl group proved especially favorable, since both *(4b)* as well as *(5b)* crystallize particularly well and deblocking of *(5b)* can be achieved in one step with ring-closure to give the 1-deoxynojirimycin *(1)*.

Reaction of *(4a)* with benzyloxycarbonyl chloride in water at pH = 8—10 afforded *(4b)*, which could be quantitatively oxidized with *Gluconobacter oxydans* to *(5b)*. The yield was more than 90%, for a conversion of 60—80 g per liter of culture medium. The hydrogenation of *(5b)* in methanol/water led stereoselectively[6], with removal of the protecting group and ring-closure, to 1-deoxynojirimycin *(1)*.

Using the same synthetic sequence, we were also able to prepare some *N*-alkyl-1-deoxynojirimycin derivatives[3] and—starting from D-mannose—the *manno*-isomer of *(1)*, 1,5-dideoxy-1,5-imino-D-mannitol[7] (yield 14%).

### *Procedure*

*(5b)*: 7 L of nutrient medium ($H_2O$, 5% sorbitol, 2% Ohly yeast extract, 0.4% $K_2HPO_4$, pH = 6.5 with KOH) is autoclaved in a 10 L fermenter for 45 min at 121 °C, inocculated with *Gluconobacter oxydans*[8] (250 mL pre-culture, same medium), and incubated for 24 h at 30 °C, 10 L air/min, 500 rpm. The culture is treated 5 times at intervals of 24 h with a hot (80—90 °C) solution of 100 g *(4b)* (m.p. 142—144 °C, from water) in 750 mL of water. After 2d *(5b)* begins to crystallize out, after 6d the fermentation is finished. The precipitate is filtered off by suction, dissolved in 6 L of methanol and the cell residues separated; the solvent is removed in a rotary evaporator and the residue recrystallized from 2-propanol. Yield 455 g (92%), m.p. 107—111 °C.

*(1)*: *(5b)* (50 g) is dissolved with gentle heating in methanol (500 mL) and the solution added to a suspension of palladium/carbon (10 g, 5%) in $H_2O$ (1000 mL) and immediately hydrogenated under a pressure of *ca.* 80 bar: 1 h at 40—50 °C, and finally 2 h at 60 °C. After removal of the catalyst by suction filtration the filtrate is evaporated down in a rotary evaporator and the residue recrystallized from 100 mL of ethanol/water (10 : 1). Yield 19.5 g (75%), m.p. 198—202 °C.

Received: March 31, 1981 [Z 837a IE]
German version: Angew. Chem. *93*, 799 (1981)

CAS Registry numbers:
*(1)*, 19130-96-2; *(2)*, 492-62-6; *(4a)*, 488-43-7; *(4b)*, 78672-49-8; *(5a)*, 74004-39-0; *(5b)*, 75016-28-3.

---

[1] *E. Truscheit, W. Frommer, B. Junge, L. Müller, D. D. Schmidt, W. Wingender,* Angew. Chem. *93,* 738 (1981); Angew. Chem. Int. Ed. Engl. *20,* 744 (1981).

[2] a) *H. Paulsen, I. Sangster, K. Heyns,* Chem. Ber. *100,* 802 (1967); b) *H. Paulsen, K. Todt,* Adv. Carbohydr. Chem. *23,* 115 (1968); c) *S. Inounye, T. Tsuruoka, T. Itoh, T. Niida,* Tetrahedron *24,* 2125 (1968); d) *H. Saeki, E. Ohki,* Chem. Pharm. Bull. *16,* 2477 (1968); e) Japanese Patent applns. J 55105-666 (1979) and J 55105-667 (1979), Nippon Shinyaku.

[3] *G. Kinast, M. Schedel,* DOS 2834122 (1978) und DOS 2853573 (1978), Bayer AG.

[4] *J. W. Long, G. N. Bollenback,* Meth. Carbohydr. Chem. *2,* 79 (1963).

[5] Review: *J. F. T. Spencer, P. A. J. Gorin,* Prog. Ind. Microbiol. *7,* 178 (1968).

[6] Hydrogenation in methanol on Raney-nickel leads predominantly to the 1,5-dideoxy-1,5-imino-L-iditol.

[7] *G. Kinast, M. Schedel,* unpublished results.

[8] *Gluconobacter oxydans* DSM 2003 obtained from the Deutsche Sammlung von Mikroorganismen in Göttingen.

---

## Reaction of 1-α-Cyano-1-deoxynojirimycin with Grignard Compounds—Complete Exchange of the CN— Group

By *Horst Böshagen, Walter Geiger,* and *Bodo Junge*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

In the reaction of α-aminonitriles with Grignard reagents replacement of the CN group by the organic moiety of the Grignard reagent was observed in some cases alongside the normal addition to the CN bond[1]. This reaction, the mechanism of which was elucidated by *Yoshimura, Ohgo* and *Sato*[2], occurs if the amino group is dialkylated or carries a phenyl- or benzyl-moiety[1b].

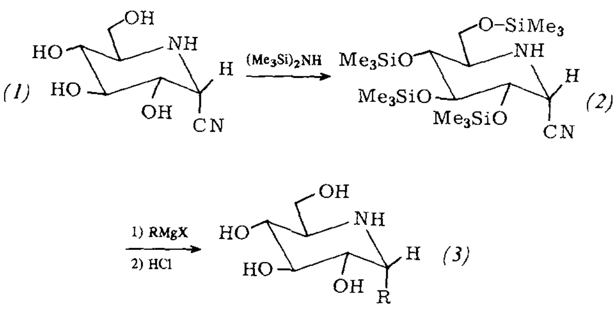


Table 1. Yields, melting points, and some spectroscopic data of the α-isomers of compounds *(3a)*—*(3h)* [a].

| Cpd. | R | Yield [%] | M.p. [°C] [b] | $^{13}$C-NMR (15.04 MHz, δ-values) |
|---|---|---|---|---|
| *(3a)* | $CH_3$ | 51 | 172 ($CH_3OH$) | — |
| *(3b)* | $C_2H_5$ | 58 | 160 ($CH_3OH$) | — |
| *(3c)* [c] | $n$-$C_4H_9$ | 45 | 147 ($i$-$C_3H_7OH$) | ($D_2O$, TSP-$d_4$-Na [g]) 56.4, 58.0 (C-1,5), 74.9, 75.2 (C-2,4), 76.8 (C-3), 64.6 (C-6); – 16.1 (C-4′), 24.6 (C-3′), 30.3 (C-2′), 26.1 (C-1′) |
| *(3d)* | $n$-$C_7H_{15}$ | 77 | 144 ($C_2H_5OH$) | — |
| *(3e)* [d] | $n$-$C_8H_{17}$ | 42 | 122 ($CH_3OH$) | (($(CD_3)_2SO$, TMS) 54.9, 55.6 (C-1,5), 72.9 (C-2,4), 74.6 (C-3), 62.2 (C-6); – 13.9 (C-8′), 22.0 (C-7′), 31.2 (C-6′), 28.6, 29.0, 29.1 (C-5′,4′,3′), 25.8 (C-2′), 24.0 (C-1′) |
| *(3f)* | $C_6H_5$ | 55 [e] | 278 [e] ($CH_3OH$) | (($(CD_3)_2SO$, TMS) 55.4, 57.2 (C-1,5), 67.2, 70.7 (C-2,4), 71.7 (C-3), 58.8 (C-6); – 128.0 (C-2′,4′,6′), 129.1 (C-3′,5′), 134.1 (C′-1) [e] |
| *(3g)* | $CH_2$—$C_6H_5$ | 47 | 145 ($CH_3OH$) | — |
| *(3h)* | $C_4H_3S$ [f] | 65 | 169 ($CH_3OH$) | — |

[a] Correct elemental analyses were obtained for all compounds. [b] In brackets: solvent used for recrystallization. [c] β-isomer of *(3c)*: $^{13}$C-NMR ($D_2O$, [g]) δ = 61.2, 62.9 (C-1,5), 74.2, 77.3 (C-2,4), 80.9 (C-3), 64.3 (C-6); 16.0 (C-4′), 24.9 (C-3′), 29.7 (C-2′), 33.2 (C-1′). [d] β-Isomer of *(3e)*: $^{13}$C-NMR ($(CD_3)_2SO$, TMS) δ = 59.1, 61.2 (C-1,5), 72.3, 75.1 (C-2,4), 79.2 (C-3), 62.2 (C-6), – 13.9 (C-8′), 22.0 (C-7′), 25.3 (C-2′), 31.8 (C-1′). [e] Yield and melting point for the hydrochloride; the $^{13}$C-NMR spectrum was measured on the hydrobromide. [f] $C_4H_3S$ = 2-thienyl. [g] [$D_4$] Sodium 3-(trimethylsilyl)propionate.

---

[*] Dr. H. Böshagen, Dr. W. Geiger, Dr. B. Junge
Wissenschaftliches Laboratorium V Werk Wuppertal-Elberfeld der Bayer AG
Postfach 101709, D-5600 Wuppertal 1 (Germany)

1-Deoxynojirimycin *(3)*, R=H[3], is a highly reactive α-glucosidase inhibitor[4], so our interest was attracted to the synthesis of derivatives substituted in the 1-position.

We therefore prepared from 1-deoxynojirimycin-1-sulfonic acid[5] the 1-α-cyano-1-deoxynojirimycin *(1)*, which was then silylated and subsequently allowed to react with Grignard compounds. This resulted in exclusive replacement of the CN group. As main product we obtained the α-compounds *(3)* as colorless crystals along with small amounts (< 5%) of the non-crystalline β-isomers. Departure of the cyanide and entry of the residue R take place on the same side of the molecule, in agreement with the findings of *Lednicer* and *Babcock*[1d].

α- and β-Isomers of *(3)* differ in the position of their $^{13}$C-NMR resonance signals. Compared to the β-isomers, the α-isomers show $\delta$-values about 3—6 ppm lower for the ring atoms C-1 and C-5 and about 7—8 ppm lower for the methylene α-coupled to the aliphatic moiety R.

### *Procedure*

*(1):* 1-Deoxynojirimycin-1-sulfonic acid (12.2 g, 50 mmol) is transferred to a stirred suspension of $Ba(OH)_2\cdot 8H_2O$ (15.8 g, 50 mmol) in water (50 mL). After addition of NaCN (3.3 g, 75 mmol) the mixture is treated dropwise and slowly at room temperature with 10 mL of 7.5 N hydrochloric acid. After 3 hours stirring the mixture is filtered by suction and the filtrate is concentrated under reduced pressure. The hot syrup is agitated with 100 mL of $CH_3CN/CH_3OH$ (1 : 1). After cooling, the salt is filtered off and the filtrate evaporated to dryness. The crude product is taken up in methanol and re-precipitated by addition of 300 mL of ethanol. Yield 8.75 g (80%) colorless prisms, m.p. 158 °C; IR (KBr): $\nu = 2240\ \text{cm}^{-1}$ (CN).

*(2):* A suspension of *(1)* (3.6 g, 20 mmol) in hexamethyldisilazane (40 mL) is treated with imidazole (0.6 g) and stirred at 60 °C until essentially all is in solution (*ca.* 2.5 h). The mixture is then filtered by suction and the filtrate evaporated to dryness under reduced pressure. The crude product (long prisms) can be used further without purification. Yield 8.5 g (89%); prisms (ligroin), m.p. 105 °C; $^{13}$C-NMR (15.04 MHz, $CDCl_3$): $\delta = -0.55$, 0.32, 1.00, 1.26 ($Si(CH_3)_3$), 52.6 (C-1), 58.1 (C-5), 64.0 (C-6), 71.9, 73.8 (C-2,4), 77.2 (C-3), 117.9 (CN).

Reaction of *(2)* with Grignard compounds: A solution of *(2)* (20 mmol) in anhydrous tetrahydrofuran (100 mL) is treated dropwise with a solution of the Grignard reagent (60 mmol) in anhydrous ether (75—100 mL). The mixture is stirred for 5 h at room temperature. It is then treated with conc. hydrochloric acid (10 mL) and water (200 mL) and stirred for a further 2 h. The aqueous phase is separated off, rendered neutral (pH=7) with 1 N NaOH solution, and evaporated to dryness under reduced pressure. The residue is taken up in methanol, insoluble salts are filtered off, and the filtrate is re-evaporated to dryness. The crude product is dissolved in water (50 mL), transferred to a Dowex 50 WX4 ion-exchange column (*ca.* 300 g exchanger), washed with water (1 L), and fractionally eluted with a 0.25% ammonia solution. The first fraction containing small amounts (< 5%) of β-isomer is followed by the main fraction consisting of pure α-isomer. Yield 40—60% (Table 1). Detection by thin-layer chromatography, silica gel 60 F 254, ethyl acetate, methanol, water, ammonia (100/60/25/1). Spray reagent: 1% aqueous $KMnO_4$ solution.

Received: February 5, 1981 [Z 837b IE]
German version: Angew. Chem. *93*, 800 (1981)

[1] a) *Th. S. Stevens, J. M. Cowan, J. Mackinnon,* J. Chem. Soc. *1931*, 2568; b) *Th. Thomson, Th. S. Stevens, ibid. 1937*, 2607; c) *L. H. Goodson, H. Christopher,* J. Am. Chem. Soc. *72*, 358 (1950); d) *D. Lednicer, J. C. Babcock,* J. Org. Chem. 1962, *27*, 2541; e) *J. Canceill, J. Jaques,* Bull. Soc. Chim. Fr. *1965*, 903.

[2] *J. Yoshimura, Y. Ohgo, T. Sato,* J. Am. Chem. Soc. *86*, 3858 (1964); Bull. Chem. Soc. Jpn. *38*, 1809 (1965).

[3] a) *N. Ishida, K. Kumagai, T. Niida, T. Tsuruoka, H. Yumoto,* J. Antibiot. Ser. *A 20*, 66 (1967); b) *H. Saeki, E. Ohki,* Chem. Pharm. Bull. *16*, 2477 (1968); c) *H. Paulsen, J. Sangster, K. Heyns,* Chem. Ber. *100*, 802 (1967).

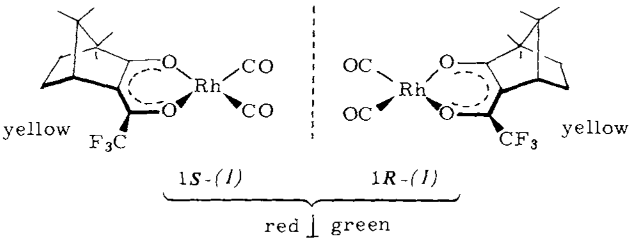
[4] a) *W. Frommer, L. Müller, D. Schmidt, H. P. Krause,* DOS 2726899 (1979), Bayer AG; Chem. Abstr. *91*, P 18359n (1979). b) *E. Truscheit, W. Frommer, B. Junge, L. Müller, D. D. Schmidt, W. Wingender,* Angew. Chem. *93*, 738 (1981); Angew. Chem. Int. Ed. Engl. *20*, 744 (1981); *D. D. Schmidt, W. Frommer, L. Müller, E. Truscheit,* Naturwissenschaften *66*, 584 (1979).

[5] *S. Inouye, T. Tsuruoka, T. Ito, N. Niida,* Tetrahedron *24*, 2125 (1968).

## Chirodichroism of Different Enantiomeric Compositions of a Planar d$^8$-Metal Complex

By *Volker Schurig* [*]

Enantiomeric mixtures of variable composition can exhibit different physical properties in the solid state[1]. A dependence of optical and electrical properties on the enantiomeric composition is to be expected if cooperative phenomena can only occur in a preferred crystal packing. Remarkable differences have been observed between the optical properties of pure enantiomers and racemate in the solid state for the chiral planar d$^8$-metal complex dicarbonylrhodium(I) 3-trifluoroacetylcamphorate *(1)*[2a]—a phenomenon that has been referred to as "chirodichroism"[2b].



The pure enantiomers 1*R*-*(1)* or 1*S*-*(1)* are isolated from *n*-hexane as lemon-yellow crystals (m.p. 134.0 °C (uncorr.)), while the 1 : 1 enantiomeric mixture crystallizes as the deep-red—green dichroic racemate (m.p. 130.5 °C (uncorr.)). When equimolar solutions of the yellow antipodes 1*R*-*(1)* and 1*S*-*(1)* in *n*-hexane are mixed and evaporated to dryness, the red color of the racemate appears spontaneously. This color-effect is especially evident when solutions of the antipodes are added as spots near to each other on filter paper or silica gel plate and chromatographed together: after development of the chromatogram a sharp zone of the red racemate appears at the site of contact, while the regions of the unmixed antipodes remain yellow. The formation of the red racemate can also be followed visually as a solid-state reaction[3] on mixing sublimed samples of the antipodes (10 min). The formation of a red solid phase instantaneously occurs on wetting the yellow mixture with a small amount of solvent ($CHCl_3$).

---

[*] Prof. Dr. V. Schurig
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

The diffuse reflection spectrum[4] of the racemate (550, *ca.* 450 sh, 370, 318 nm) differs markedly from that of the pure enantiomer (385, 318 nm); characteristic is the appearance of additional bands at 550 and 450 nm for the racemate[5].

The racemic form of *(1)* proves to be a real stoichiometric binary compound whose melting point is lowered on addition of pure enantiomers (*e.g.* m.p. 127.5 °C for 1R-*(1)*, *ee* = 28%). No differences are discernible in the scalar physical properties of the pure enantiomers and racemic mixture in dilute solution (UV, VIS, NMR, IR)[6]. The melts of the pure enantiomers and of the racemate are all brown-red.

Planar $d^8$-metal complexes (*e.g.* the dicarbonylmetal acetylacetonates of Rh and Ir) form columnar structures in the crystal lattice with intermolecular metal-metal interaction. These compounds therefore show one-dimensional electric effects as well as anisotropic optical properties in the solid state[7]. The chirodichroism described here for *(1)* is attributed to the different crystal packing of the enantiomers and of the racemate. This assumption is confirmed by the X-ray structure analysis[8]: the oppositely configurated molecules of the racemic compound are ideally stacked alternately in a columnar structure, whereby the formation of linear chains of rhodium atoms (Rh—Rh 3.38 Å) parallel to the *z*-axis promotes occurrence of cooperative phenomena. In contrast, identical configuration of the molecules in the pure enantiomer prevents a packing with intermolecular d-d interaction; thus, the rhodium atoms of the molecules, sited in reversed order in the lattice, can only form a zig-zag chain (Rh—Rh 4.32 Å).

The introduction of chirality into the inner coordination sphere of a metal ion proves, therefore, to be an interesting parameter for the investigation of steric influences of ligands of like constitution, but different configuration, on cooperative properties in the solid state. From the findings on *(1)* it follows that the crystal packing has a dominating influence over that of M—M interaction on the formation of columnar structures[9]. The tailor-made reaction of quasi-racemates starting from quasi-enantiomers with ligands of similar constitution or different central atom appears attractive; thus, *e.g.*, highly ordered structures with chains of alternating metal atoms (Rh(*R*)/Ir(*S*)) could be accessible.

Received: December 8, 1980 [Z 843 IE]
supplemented: March 31, 1981
German version: Angew. Chem. *93*, 806 (1981)

---

[1] Cf. *K. Mislow:* Introduction to Stereochemistry, Benjamin, New York 1965; *M. Leclerq, A. Collet, J. Jacques,* Tetrahedron *32*, 821 (1975).

[2] a) *V. Schurig,* Inorg. Chem. *11*, 736 (1972); b) Angew. Chem. *89*, 113 (1977) and Angew. Chem. Int. Ed. Engl. *16*, 110 (1977), Ref. [8].

[3] Cf. *H. Brockmann, H. Musso,* Chem. Ber. *89*, 241 (1956). It was shown on the basis of the different IR spectra of enantiomers and racemate that mixtures of L- and D-serine convert into the racemate on pressing in KBr disks.

[4] I thank Prof. *D. Oelkrug,* Universität Tübingen, for the measurement (MgO as white standard).

[5] Differences in color (white/yellow) and in the fluorescence spectra of enantiomerically pure and racemic 1-(2-chlorophenyl)ethyl anthroates are described by *M. Lahav, F. Laub, E. Gati, L. Leiserowitz, Z. Ludmer,* J. Am. Chem. Soc. *98*, 1620 (1976).

[6] Differences in the physical properties of enantiomeric mixtures in solution are discussed by *A. Horeau, J. P. Guetté,* Tetrahedron *30*, 1923 (1974).

[7] *F. Bonati, G. Wilkinson,* J. Chem. Soc. *A 1964*, 3156; *K. Krogmann,* Angew. Chem. *81*, 10 (1969); Angew. Chem. Int. Ed. Engl. *8*, 35 (1969); *T. W. Thomas, A. E. Underhill,* Chem. Comm. *1969*, 725; *R. Aberjan, H. J. Keller, H. H. Rupp,* Z. Naturforsch. *A 29*, 1367 (1974).

[8] *F. Frolow, D. Rabinovich, V. Schurig,* unpublished.

[9] Cf. *G. Ciullo, O. Piovesana,* Inorg. Chem. *19*, 2871 (1980).

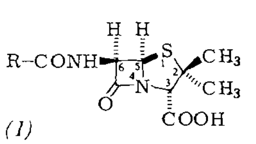
---

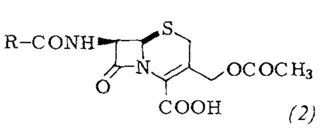
# Stereospecific, One-Step Introduction of a Methoxy Group at C6 in Penicillins and C7 in Cephalosporins

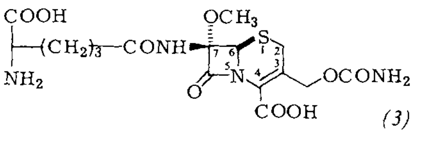
By *Peter Feyen* and *Wilfried Schröck*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

β-Lactam antibiotics such as the penicillins *(1)* and cephalosporins *(2)* are degraded by bacterial β-lactamases. Bacteria which can produce β-lactamase are therefore resistent to derivatives of *(1)* and *(2)*. In cephamycins [*e.g.* cephamycin C *(3)*]—metabolic products of streptomycetes—the cephalosporin ring systems have an α-methoxy substituent at the 7-position which produces improved lactamase stability[1]. In the numerous published syntheses of 7-methoxycephalosporins and 6-methoxypenicillins[2], the carboxy group must always be protected by esterification. The removal of the protecting group—esters have low activity as antibacterial agents—precludes most types of esters in view of the sensitivity of this class of substances[3].


*(1)*


*(2)*


*(3)*

We report here a single-step methoxylation which avoids the use of protecting groups, and which uses penicillinic or cephalosporinic acids with already finished frameworks as starting materials.

The penicillinic or cephalosporinic acids *(1)* and *(2)* are converted into their lithium salts by treatment with lithium methoxide in methanol-tetrahydrofuran (THF) at −50 to −70 °C followed by treatment for *ca.* 30 min at −50 °C with *t*-butyl hypochlorite. Based on earlier investigations on cephalosporin esters[4], the reaction probably proceeds *via* the penicillinic acid *(4)*.

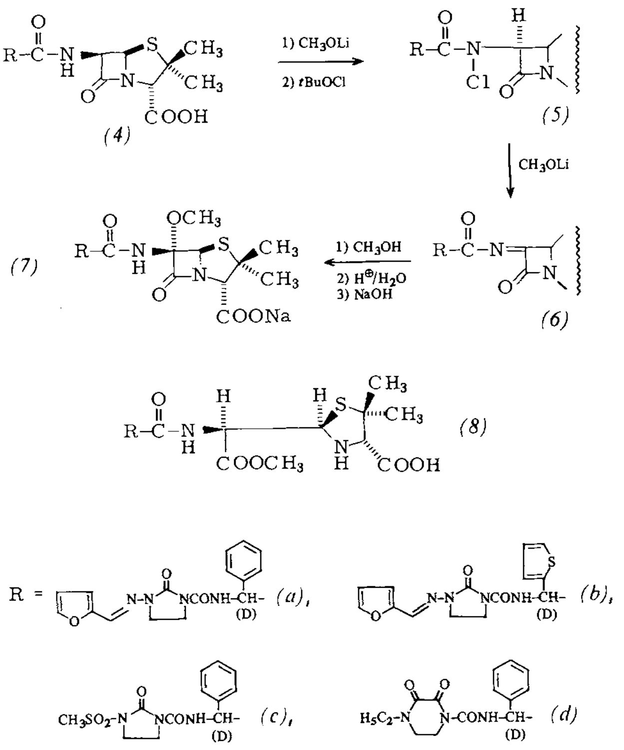
After formation of the acylimine *(6)* from the *N*-chloroamide *(5)*, methanol adds to the sterically less hindered α-side of the molecule with high selectivity (only one methoxy signal in the NMR spectrum). Some methyl penicilloate *(8)* is formed as a by-product *via* direct attack of the methoxide on the β-lactam ring—together with 10—15% other conversion and degradation-products (recognizable by a broad NMR absorption in the region of the signals of the geminal dimethyl groups).

A series of penicillin derivatives, which should have powerful antibacterial activity, were investigated (Table 1). The crude products were purified by crystallization or preparative column chromatography on silica gel.

The 7-methoxycephalosporins were synthesized in an analogous manner. In this way *(9)*[5] was obtained in 60% yield from *(2)*: the crude product contained 75% *(9)* and in addition, 12% of the educt.

---

[*] Dr. P. Feyen
Verf. Entw. PF der Bayer AG
Friedrich-Ebert-Strasse, D-5600 Wuppertal 1 (Germany)
Dr. W. Schröck
Chemisch-wissenschaftliches Labor Pharma der Bayer AG
Aprather Weg, D-5600 Wuppertal 1 (Germany)



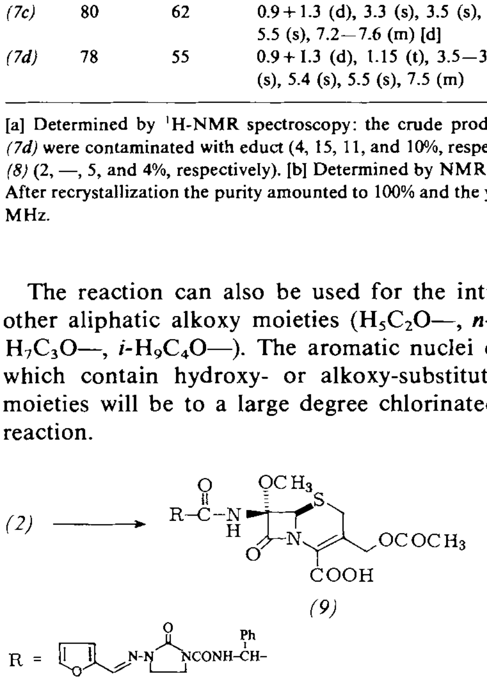
Scheme 1. (D) in substituents *(a)*—*(d)* signifies the asymmetric center to be configuration of the D-amino acid series.

Table 1. Purity, yields and $^1$H-NMR spectroscopic data for *(7a)*—*(7d)*.

| Compound | Product purity [%] [a] | Yield [%] [b] | $^1$H-NMR ($\delta$-value, $CH_3OD$, 100 MHz) |
|---|---|---|---|
| *(7a)* | 84 [c] | 54 [c] | 0.9 + 1.3 (d, $C(CH_3)_2$), 3.5 (s, $OCH_3$), 3.85 (m, —$CH_2$—$CH_2$—), 4.1 (s, 3-H), 5.5 (s, 5-H), 5.55 (s, N—CH—CO), 6.5 (q, $J$ = 3.2 Hz and 1.5 Hz, Furyl-4), 6.85 (d, $J$ = 3.2 Hz, Furyl-5), 7.2—7.6 (m, Furyl-3 + Ph), 7.7 (s, —CH=N—) |
| *(7b)* | 70 | 50 | 1.2 + 1.4 (d), 3.5 (s), 3.9 (m), 4.15 (s), 5.55 (s), 5.85 (s), 6.55 (q), 6.85 (d), 7.0 (d), 7.2—7.4 (m), 7.6 (d), 7.7 (s) |
| *(7c)* | 80 | 62 | 0.9 + 1.3 (d), 3.3 (s), 3.5 (s), 3.85 (m), 4.1 (s), 5.5 (s), 7.2—7.6 (m) [d] |
| *(7d)* | 78 | 55 | 0.9 + 1.3 (d), 1.15 (t), 3.5—3.8 (m, 9H), 4.05 (s), 5.4 (s), 5.5 (s), 7.5 (m) |

[a] Determined by $^1$H-NMR spectroscopy: the crude products from *(7a)*—*(7d)* were contaminated with educt (4, 15, 11, and 10%, respectively) and with *(8)* (2, —, 5, and 4%, respectively). [b] Determined by NMR spectroscopy. [c] After recrystallization the purity amounted to 100% and the yield 38%. [d] 250 MHz.

The reaction can also be used for the introduction of other aliphatic alkoxy moieties ($H_5C_2O$—, *n*-$H_7C_3O$—, *i*-$H_7C_3O$—, *i*-$H_9C_4O$—). The aromatic nuclei of molecules which contain hydroxy- or alkoxy-substituted aromatic moieties will be to a large degree chlorinated during the reaction.



*Procedure*

*(7a)*: A solution of 150 mmol $LiOCH_3$ in methanol at −20 °C is added to a stirred suspension of *(4a)* (50 mmol, 27.7 g) in 550 mL tetrahydrofuran (THF) at −70 °C in such a manner that the internal temperature does not rise above −55 °C. As soon as a clear solution forms, a solution of *t*-butyl hypochlorite (7 g, 65 mmol) in 20 mL $CH_2Cl_2$ is poured in. The temperature rises to −45 °C and is immediately cooled again to −55 °C. The mixture is stirred for 30 min at −55 °C and poured into an ice-cold solution of 75 g $NH_4Cl$ and 10 g $Na_2SO_3 \cdot 10H_2O$ in 750 mL water. Finally, an additional 1000 mL water is added, the pH adjusted to 7—7.5, the mixture washed with ethyl acetate (2 × 500 mL), 500 mL of ethyl acetate added, and the mixture acidified to pH = 2 with HCl. The organic phase is treated with 350 mL water and NaOH is added with constant stirring until the pH = 7. After separation of the ethyl acetate, the mixture is freeze-dried, giving the crude product. Alternatively, the mixture is separated from ethyl acetate, treated with 175 mL acetone, cooled to 5 °C and acidified to pH = 2 with 2 N HCl. During crystallization an additional 150 mL water is added. After 45 min the crystals are filtered-off, suspended afresh in 150 mL water, 2 N NaOH added until the pH = 7 and freeze-dried as the sodium salt. For yield and purity see Table 1.

Received: May 7, 1981 [Z 845 IE]
German version: Angew. Chem. *93*, 814 (1981)

---

[1] *R. Nagarajan, L. D. Boeck, M. Gorman, R. L. Hamill, C. E. Higgens, M. M. Hoehn, W. M. Stark, J. G. Whitney,* J. Am. Chem. Soc. *93*, 2308 (1971); *R. W. Ratcliffe, B. G. Christensen,* Tetrahedron Lett. *1972*, 2907; *G. Albers-Schönberg, B. H. Arison, J. L. Smith, ibid. 1972*, 2911; *T. W. Miller, R. T. Goegelman, R. J. Weston, J. Putter, F. J. Wolf,* Antimicrob. Agents Chemother. *1972*, 132; *E. O. Stapley, M. Jackson, S. Hernandez, S. B. Zimmermann, S. A. Currie, S. Mochales, J. M. Mata, H. B. Woodruff, D. Hendlin, ibid. 1972*, 122.

[2] *D. N. McGregor,* Fortschr. Chem. Org. Naturst. *31*, 1 (1974); *A. K. Mukerjee,* Synthesis *1975*, 547; *E. M. Gordon, H. W. Chang, C. M. Cimarusti,* J. Am. Chem. Soc. *99*, 5504 (1977); *T. Kobayhashi, T. Hiraoka,* Chem. Pharm. Bull. *27*, 2718 (1979).

[3] *L. D. Cama, W. J. Leanza, T. R. Beattie, B. G. Christensen,* J. Am. Chem. Soc. *94*, 1408 (1972); *S. Nakatsuka, H. Tanino, Y. Kishi, ibid. 97*, 5008 (1975); *Y. Sugimura, K. Iino, Y. Iwano, T. Saito, T. Hiraoka,* Tetrahedron Lett. *1976*, 1307; *A. W. Taylor, G. Burton, ibid. 1977*, 3831; *P. H. Bentley, J. P. Clayton, M. O. Boles, R. J. Girven,* J. Chem. Soc. Perkin Trans. I *1979*, 2455; *E. M. Gordon, H. W. Chang, C. M. Cimarusti, B. Töplitz, J. Z. Gougoutas,* J. Am. Chem. Soc. *102*, 1690 (1980).

[4] *J. S. Chalstry, S. S. Israelstam,* Chem. Ind. *1954*, 1452; *J. E. Baldwin, F. J. Urban, R. D. G. Cooper, F. L. Jose,* J. Am. Chem. Soc. *95*, 2401 (1973); *G. A. Koppel, R. E. Köhler, ibid. 95*, 2403 (1973); *R. A. Firestone, B. G. Christensen,* J. Org. Chem. *38*, 1436 (1973).

[5] $^1$H-NMR (200 MHz): $\delta$ = 2.1 (s), 3.25 + 3.6 (AB, $J$ = 18 Hz), 3.6 (s), 4.0 (s), 4.85 + 5.1 (AB, $J$ = 12 Hz), 5.2 (s), 5.9 (d, $J$ = 7 Hz), 6.75 (q, $J$ = 4 Hz and 1.5 Hz), 6.98 (d, $J$ = 4 Hz), 7.3—7.8 (m), 7.9 (d, $J$ = 1.5 Hz), 7.95 (s), 9.2 (d, $J$ = 7 Hz), 9.8 (s).

## 15,16-Dioxo-*syn*-1,6:8,13-bismethano[14]annulene

By *Metin Balci, Rolf Schalenbach,* and *Emmanuel Vogel*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

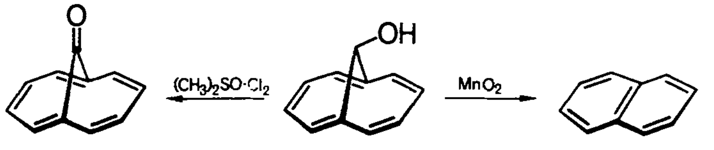
It had originally been assumed that 11-oxo-1,6-methano[10]annulene *(1)* very readily fragments into naphtha-

---

[*] Dr. M. Balci, Dr. R. Schalenbach, Prof. Dr. E. Vogel
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

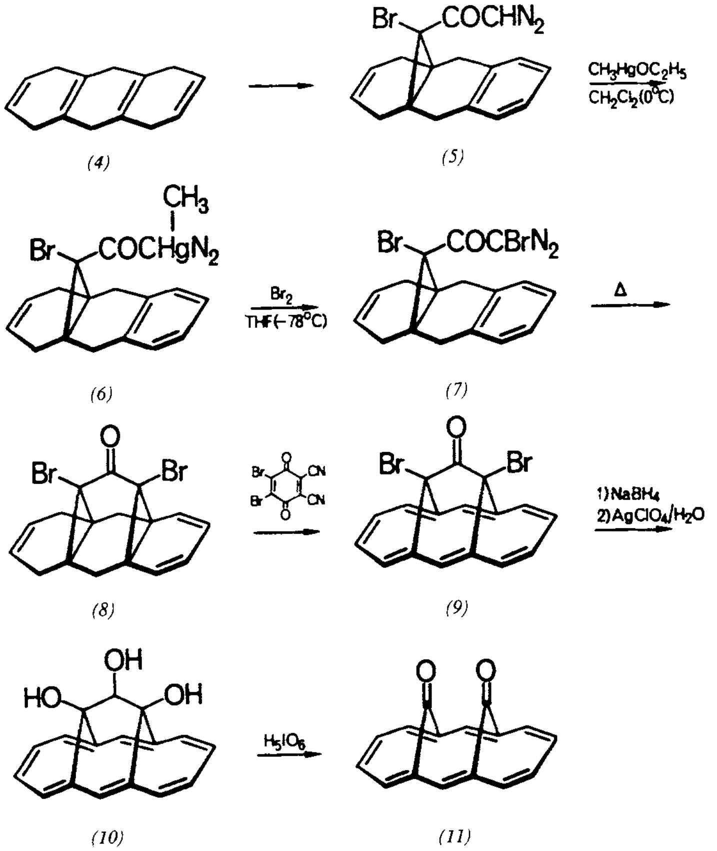
*0570-0833/81/0909-0809 $ 02.50/0*

lene *(3)* and carbon monoxide[1] on heating, since *(3)* was always obtained as reaction product on oxidation of 11-hydroxy-1,6-methano[10]annulene *(2)* with manganese dioxide (in acetone), chromium trioxide-pyridine complex (in dichloromethane) or lead tetraacetate (in pyridine).



In actual fact, *(1)*—first synthesized in 1972 by *Itô et al.*[2] from the [6 + 4]-adduct of tropone and butadiene—is a stable aromatic compound, whose decarbonylation necessitates heating to more than 200 °C! The naphthalene obtained on oxidation of *(2)* with the above mentioned reagents therefore cannot be formed *via (1)* but in all probability arises from tricyclo[4.4.1.$0^{1,6}$]undeca-2,4,7,9-tetraen-11-ol, the valence tautomer of *(2)* containing a cyclopropanol structural unit[3]. It has now been possible to oxidize *(2)* smoothly to *(1)* with the Pfitzner-Moffat reagent as well as with the dimethyl sulfoxide-chlorine complex described by *Corey* (yields 77 and 87%, respectively; no naphthalene formation).

From the properties of *(1)* it could be predicted that its next higher homologue with *syn*-carbonyl groups[4], 15,16-dioxo-*syn*-1,6 : 8,13-bismethano[14]annulene *(11)*, is capable of existence under normal conditions and is distinguished by having aromatic character. True, the annulene ring in *(11)* might be bent as a result of steric and electrostatic repulsion of the carbonyl groups but from experience with the *syn*-1,6 : 8,13-bismethano[14]annulene[5a] no serious loss of resonance is to be expected through this. Possible conjugative interactions between the carbonyl groups and the annulene ring ought to be small, since the $2p_z$ orbitals of the carbonyl groups and the corresponding bridge-base C-atoms are, according to molecular models, arranged almost orthogonally to each other. We have found that these concepts about *(11)* are not at variance and we report here on its synthesis.



The α-diazoketone *(5)*, which has already served as intermediate in the synthesis of 1,6 : 8,13-propanediylidene[14]annulene[5b], is accessible in a five-stage reaction sequence from 1,4,5,8,9,10-hexahydroanthracene *(4)*. The α-bromo-α-diazoketone *(7)* is expediently prepared *via* the mercury compound *(6)*, which is obtained on slow addition of a solution of *(5)* in dichloromethane at 0 °C to a solution of methylmercury ethoxide in ethanol[6]; the compound *(6)* crystallizing out on concentration of the reaction solution is NMR-spectroscopically pure (yield 85—90%). Reaction of *(6)* with an equivalent amount of bromine in tetrahydrofuran (THF) at −78 °C leads to formation of *(7)*, which is not isolated, but, after extensive removal of the original solvent in a vacuum is immediately taken up in hexane (the changeover to this solvent effects precipitation of the Hg-salt) and thermolyzed (reflux, 1 h). Chromatography on silica gel (dichloromethane) furnishes colorless *(8)* [m.p. 189–190 °C (dec.), (from acetonitrile); yield 17%, based on *(5)*]. When a mixture of *(8)* and 2,3-dibromo-5,6-dicyano-*p*-benzoquinone (25% excess) in chlorobenzene is heated for 4 h at 120 °C dehydrogenation of *(8)* takes place to give *(9)*, which is isolated by chromatography on silica gel (dichloromethane) [orange needles (gradual decomposition above 275 °C, from nitromethane); yield 41%]. *(9)* can be smoothly reduced with $NaBH_4$ in THF/methanol (1 : 1) at 0 °C to the alcohol [yellow needles, m.p. 248–250 °C (dec.), from ethyl acetate; yield 90%]. Although, for steric reasons, the bromine atoms of this alcohol should not be very reactive solvolytically, its reaction with an excess of silver perchlorate in acetone/water (3 : 1) leads to almost complete hydrolysis even after 3 hours stirring at room temperature. The main product *(10)* is isolated by transferring the product mixture onto silica gel and successively eluting with dichloromethane (removal of by-products) and ether/methanol (5 : 1) [yellow needles, m.p. 219–221 °C (from ether); yield 56%].

As expected, the triol *(10)* is cleaved by periodic acid in water/acetone, giving *(11)* and not (which had to be reckoned with) a hydrate[7] of *(11)*; it forms air-stable, orange-red rhombic crystals (from acetonitrile), which slowly decompose above 250 °C (yield 51%).

Table 1. Spectral data of *(8)*, *(9)*, *(10)* and *(11)* (cf. also [9]).

*(8)*, $^1$H-NMR ($CDCl_3$): $\delta = 6.23$ and 5.70 (AA′BB′-system, 4 H), 5.58 (m, 2 H), 2.55 (AB-system, 2 × 2 H), 2.33 (m, 4 H); IR (KBr): 1670 $cm^{-1}$ (C=O); MS: $m/z = 396/394/392$ ($M^+$, 5, 10, 5%), 315/313 ($M^+ - Br$, 9), 287/285 ($M^+ - Br, - CO$, 17), 206 ($M^+ - 2Br, - CO$, 100)

*(9)*, $^1$H-NMR ([$D_6$] DMSO): $\delta = 8.10$ (s, 2 H), 7.97—7.54 (AA′BB′-system, 2 × 4 H); UV (dioxane): $\lambda_{max} = 242$ ($\varepsilon = 14250$), 310 (98250), 330 (20600) sh, 362 (9300), 445 (220) sh, 506 nm (1200); IR (CsI): 1750 $cm^{-1}$ (C=O); MS: $m/z = 392/390/388$ ($M^+$, 2, 5, 2%), 311/309 ($M^+ - Br$, 1), 283/281 ($M^+ - Br, - CO$, 1), 202 ($M^+ - 2Br, - CO$, 100)

*(10)*, $^1$H-NMR ($CDCl_3$): $\delta = 7.93$—7.46 (m, 2 × 4 H), 7.78 (s, 1 H), 7.60 (s, 1 H), 1.96 and 1.50 (AB-system, $J = 3$ Hz, 2 H), 0.43 (s, 2 H); UV (dioxane): $\lambda_{max} = 228$ ($\varepsilon = 7700$), 301 (145600), 313 (35550), 252 (7400), 364 (7200) sh, 463 nm (260); IR (KBr): 3500 $cm^{-1}$ (O—H); MS: $m/z = 266$ ($M^+$, 61%), 202 ($M^+ - CO, - 2H_2O$, 36), 178 ($M^+ - C_3H_4O_3$, 100)

*(11)*, $^1$H-NMR ([$D_6$] DMSO): $\delta = 8.53$ (s, 2 H), 8.11 and 7.81 (AA′BB′-system, $J_{2,3} = 9.63$, $J_{3,4} = 9.81$, $J_{2,4} = 0.18$, $J_{2,5} = 0.89$ Hz, 2 × 4 H); $^{13}$C-NMR ([$D_6$]DMSO): $\delta = 194.71$ (C—15, 16), 129.22 (C—7, 14), 129.53, 127.15 (C—2, 3, 4, 5, 9, 10, 11, 12), 125.32 (C—1, 6, 8, 13); UV (dioxane): $\lambda_{max} = 292$ ($\varepsilon = 139100$), 312 (24200), 365 (7550), 442 (80), 509 nm (300); IR (CsI): 1713 (C=O), 1540 $cm^{-1}$ (C=C); MS (120 °C): $m/z = 234$ ($M^+$, 58%), 218 ($M^+ - O$, 2), 206 ($M^+ - CO$, 11), 202 ($M^+ - 2O$, 45), 178 ($M^+ - 2CO$, 100)

The spectra (cf. Table 1) and X-ray structure analysis clearly show that *(11)* is an arene. The $^{1}$H-NMR spectrum, which as expected, consists of a singlet and an AA'BB' system, shows in its parameters—apart from the chemical shifts of H-7, H-14—a qualitative agreement with the partial spectrum of the annulene protons of 1,6:8,13-propanediylidene[14]annulene[5b]. The singlet of H-7, H-14 appears at unusually low field strength, which in the main could be attributed to the fact that these protons are exposed to the inductive effect of both carbonyl groups. The relationship between *(11)* and 1,6:8,13-propanediylidene[14]annulene also extends to the electronic spectrum. Hence, in agreement with model considerations the π-systems of the carbonyl groups and annulene ring in *(11)* are essentially independent of each other. The carbonyl band at 1713 cm$^{-1}$ can be explained in the same terms. As assumed, successive loss of carbonyl groups occurs in the mass spectroscopic fragmentation of *(11)*; interestingly, however, a stepwise cleavage of the two oxygen atoms follows parallel to the decarbonylation and at sample temperatures above 100 °C it even predominates (base peak: $M^{+}-2O$)[8] (this fragmentation pattern is not observed in the case of the *anti*-isomer of *(11)*[9]).

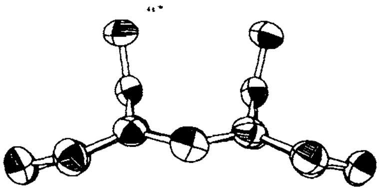


Fig. 1. Longitudinal profile of 15,16-dioxo-*syn*-1,6:8,13-bismethano[14]annulene *(11)*.

The X-ray structure analysis[10] of *(11)* confirms the spectral findings by virtue of demonstrating aromatic CC bonds (lengths 1.376–1.413 Å) in the annulene ring. According to Figure 1 the annulene ring is only slightly bent, even though there must be strong repulsion between the carbonyl groups owing to electrostatic interactions, since the oxygen atoms are forced out of the plane of the corresponding bridge- and bridge-base C-atoms. The bridge bond angle in *(11)* (112.4°) is greater than that in 1,6:8,13-propanediylidene[14]annulene (104.2°), and consequently the transannular distance C1–C6 as well as C8–C13 in *(11)* is greater (2.470 Å) than in the reference compound (2.359 Å).

The outstanding chemical feature of *(11)* is its thermal stability. *(11)* can be subjected to flash pyrolysis at 500 °C in a vacuum without it undergoing fragmentation to anthracene and carbon monoxide or other changes.

Received: May 31, 1981 [Z 847a IE]
German Version: Angew. Chem. *93*, 816 (1981)

---

[1] *E. Vogel, F. Weyres, H. Lepper, V. Rautenstrauch,* Angew. Chem. *78*, 754 (1966); Angew. Chem. Int. Ed. Engl. *5*, 732 (1966).

[2] *S. Itô, H. Ohtani, S. Narita, H. Honma,* Tetrahedron Lett. *1972*, 2223.

[3] Reaction of cyclopropanols with metal ions such as Fe$^{3+}$, Cu$^{2+}$ readily affords *inter alia*, radicals by hydrogen-abstraction from the OH group), which react further with ring-opening: *S. E. Schaafsma, H. Steinberg, Th. J. DeBoer,* Recl. Trav. Chim. Pays-Bas *85*, 70 (1966).

[4] For the dependence of the π-electron delocalization on the steric arrangement of the bridges in bridged [14]annulenes with anthracene perimeters see: *E. Vogel,* Pure Appl. Chem. *28*, 355 (1970).

[5] a) *E. Vogel, J. Sombroek, W. Wagemann,* Angew. Chem. *87*, 591 (1975); Angew. Chem. Int. Ed. Engl. *14*, 564 (1975); b) *E. Vogel, A. Vogel, K.-H. Kübbeler, W. Sturm, ibid. 82*, 512 (1970) and *9*, 514 (1970).

[6] We wish to thank Professor *S. Masamune*, MIT, Cambridge (USA) for this procedure for the transformation of an α-diazoketone into an α-bromo-α-diazoketone.

[7] The monohydration of *(11)* to a hemiacetal with an oxygen bridge between C-15 and C-16 requires relatively drastic conditions [heating in glacial acetic acid/conc. HCl (5:1)]. Analogous hydrations are known in the case of 7H, 14H-cycloocta[1,2,3-de:5,6,7-de'']dinaphthalene-7,14-dione [*W. C. Agosta*, J. Am. Chem. Soc. *89*, 3505 (1967)] and some cage-diketones with spatially adjacent, parallel oriented carbonyl groups [*R. C. Cookson, E. Grundwell, R. R. Hill, J. Hudec,* J. Chem. Soc. *1964*, 3062].

[8] We wish to thank Dr. *M. Linscheid* (Universität Köln) for the mass spectroscopic investigations.

[9] *E. Vogel, R. Nitzsche, H.-U. Krieg,* Angew. Chem. *93*, 816 (1981); Angew. Chem. Int. Ed. Engl. *20*, 811 (1981).

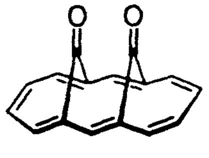
[10] *R. Destro, M. Simonetta,* Acta Crystallogr. *B 33*, 3219 (1977); *M. Simonetta,* Pure Appl. Chem. *52*, 1597 (1980).

## 15,16-Dioxo-*anti*-1,6:8,13-bismethano[14]annulene

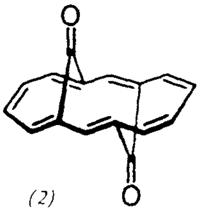
By *Emanuel Vogel, Rudolf Nitsche,* and *Hans-Ulrich Krieg*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

The properties of the *syn-anti* isomeric 1,6:8,13-bismethano[14]annulenes[1] serve as a typical example for illustrating that the bonding in a cyclically conjugated (4n+2)π-electron system can be decisively influenced by the molecular geometry. The *syn*-isomer[1a] is aromatic, even though it has a bent annulene ring[2], whereas the *anti*-isomer, which has a strongly puckered ring, is an olefinic compound with fluxional π-bonds[3].



*(1)*



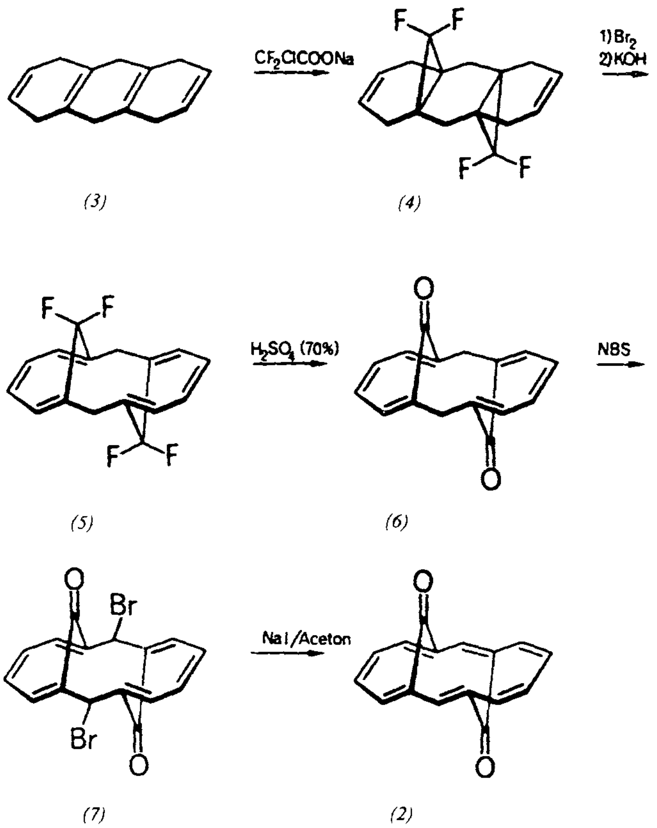
*(2)*

We have found that the transition from the aromatic 15,16-dioxo-*syn*-1,6:8,13-bismethano[14]annulene *(1)*[4] to the *anti*-isomer *(2)* is likewise accompanied by a loss in aromaticity.

The synthesis of *(2)* was achieved—following that of the *anti*-1,6:8,13-bismethano[14]annulene[1b]—using 1,4,5,8,9,10-hexahydroanthracene *(3)* as starting material. Reaction of *(3)* with sodium chlorodifluoroacetate in diglyme at 165 °C[5] (molar ratio 1:2.5) afforded a mixture of mono- and bis-(difluorocarbene) adducts, from which *(4)* could be separated by chromatography on silica gel with pentane [colorless rhombs, m.p. 154–155 °C (from ethanol): yield 22%]. *(4)* readily reacts with bromine in dichloromethane at −78 °C to give the tetrabromide (presumably both stereoisomers) [colorless crystals, m.p. 234–236 °C (dec.) (from ethyl acetate), yield 91%]. If the tetrabromide is transferred slowly into a 15% methanolic KOH solution (five-fold excess) and the mixture heated under reflux for 4 h, dehydrohalogenation takes place to give *(5)*, which is obtained in the form of colorless rhombs [decomp. above 270 °C (from ethyl acetate), yield 35%]. On treatment with 70% (vol-%) sulfuric acid and stirring at room temperature (10 d), *(5)* is hydrolyzed to *(6)*[6] *[yield 95% NMR-spectro-*

---

[*] Prof. Dr. E. Vogel, Dr. R. Nitsche, Dipl.-Chem. H.-U. Krieg
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)



scopically pure *(6)*; colorless rhombs (decomp. above 290 °C, from dichloromethane)]. For the bromination, *(6)* is allowed to react with *N*-bromosuccinimide in boiling benzene in the presence of dibenzoyl peroxide. Subsequent chromatography on silica gel with ether/pentane affords crystalline *(7)* (presumably a mixture of both stereoisomers) in 35% yield, which is immediately dehalogenated by heating (7 h) with an excess of sodium iodide in acetone; after usual work-up and recrystallization from acetone, *(2)* is obtained as carmine-red needles [gradual decomposition above 138 °C, yield 35—45%]. *(2)* very rapidly polymerizes in air and is sensitive to light. It can be stored for some time under argon at *ca.* $-40\,°C$.

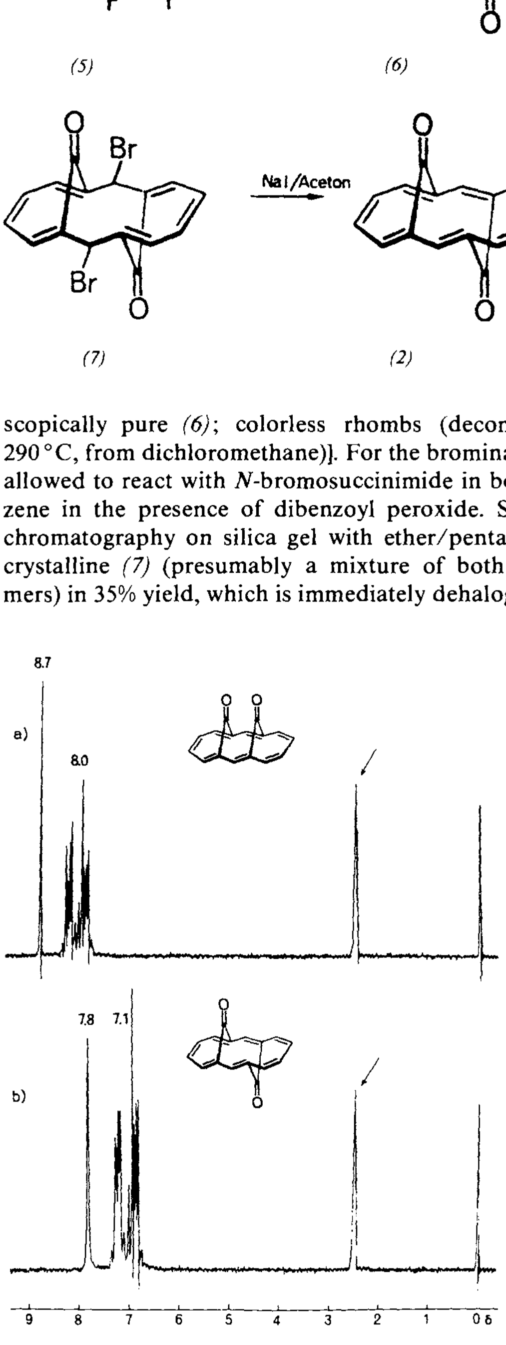


Fig. 1. $^1$H-NMR spectra (90 MHz) of a) 15,16-dioxo-*syn*-1,6:8,13-bismethano[14]annulene *(1)*[4] and b) 15,16-dioxo-anti-1,6:8,13-bismethano[14]annulene *(2)* (both in [D$_6$]DMSO (arrow), TMS as internal standard).

The olefinic nature of *(2)*, suggested by the ready polymerization of the compound, is impressively confirmed by the $^1$H-NMR spectrum. Although this shows the same absorption pattern as that of *(1)* (singlet and AA'BB' system), all the signals are shifted upfield by $\Delta\delta \approx 1$, as is consistent with the transition from an arene to an olefin (Fig. 1). The rapid π-bond shift in *(2)*, inferred from the presence of only one AA'BB' system, has hitherto defied experimental detection. The spectrum remains unchanged at $-130\,°C$[7], the lowest temperature reached, whereas that of the *anti*-1,6:8,13-bismethano[14]annulene already shows strong exchange broadening in the range from $-70$ to $-120\,°C$. The activation energy for the π-bond shift in *(2)* is consequently lower than in the case of the hydrocarbon, which seems plausible, since the opening of the bridge-bond angle effected by the CO group[8] should reduce the torsional angles of the C6—C7 and C7—C8 as well as C1—C14 and C13—C14 bonds. The electronic spectrum of *(2)* has experienced a red-shift compared to that of the hydrocarbon, the main cause of which is to be regarded as a conjugative interaction of the carbonyl groups with the annulene ring, which according to molecular models is sterically possible. However, the CO band at 1695 cm$^{-1}$ is not revealing in this respect. The fragmentation behavior in the mass spectrum is characterized by successive loss of the two carbonyl groups (base peak: $M^+ - 2\,CO$).

Table 1. Spectral data of *(2)*, *(4)*, *(5)* and *(6)*.

*(2)*, $^1$H-NMR ([D$_6$] DMSO): $\delta = 7.78$ (s, 2 H), 7.18 and 6.85 (AA'BB'-system, $J_{2,3} = 9.33$, $J_{3,4} = 10.21$, $J_{2,4} = 0.38$, $J_{2,5} = 0.62$ Hz, 2×4 H); $^{13}$C-NMR [(CD$_3$)$_2$CO]: $\delta = 205.23$ (C-15, 16), 144.89 (C-1, 6, 8, 13), 128.43, 128.29, 125.96; UV (dioxane): $\lambda_{max} = 240$ ($\varepsilon = 27400$), sh, 318 (21800), 384 nm (4400); IR (CHCl$_3$): 1695 (C=O), 1595 cm$^{-1}$ (C=C); MS (120 °C): $m/z = 234$ ($M^+$, 18%), 206 ($M^+ - CO$, 24), 178 ($M^+ - 2\,CO$, 100)

*(4)*, $^1$H-NMR (CDCl$_3$): $\delta = 5.57$ (m, 4 H), 2.70—1.80 (m, 8 H), 1.90 (m, 4 H); IR (KBr): 1675 cm$^{-1}$ (C=C); MS: $m/z = 284$ ($M^+$, 18%), 264 ($M^+ - HF$, 6), 91 ($M^+ - 193$, 100)

*(5)*, $^1$H-NMR (CDCl$_3$): $\delta = 6.80$—6.40 (AA'BB'-system, 2×4 H), 3.85 (br. s, 4 H); UV (MeOH): $\lambda_{max} = 227$ ($\varepsilon = 43400$), 243 (20000), 275 nm (2000); IR (KBr): 1602 cm$^{-1}$ (C=C); MS: $m/z = 280$ ($M^+$, 100%), 178 ($M^+ - 2\,CF_2$, $-H_2$, 47)

*(6)*, $^1$H-NMR (CDCl$_3$): $\delta = 6.74$ (s, 8 H), 4.00 (s, 4 H); UV (dioxane): $\lambda_{max} = 237$ ($\varepsilon = 28000$), 328 nm (3500); IR (KBr): 1670 cm$^{-1}$ (C=O); MS: $m/z = 236$ ($M^+$, 38%), 208 ($M^+ - CO$, 12), 179 ($M^+ - 2\,CO$, $-H$, 100)

The X-ray structure analysis[2,9] of *(2)* surprisingly shows CC bond lengths for the annulene ring like those in arenes. Since the $^1$H-NMR and electronic spectra are clearly consistent with those of an olefin the equalization of the bond lengths is either simulated by crystal defects (most likely case) or confined to the crystalline state of the compound.

Received: May 31, 1981 [Z 847b IE]
German version: Angew. Chem. 93, 818 (1981)

---

[1] a) *E. Vogel, J. Sombroek, W. Wagemann*, Angew. Chem. *87*, 591 (1975); Angew. Chem. Int. Ed. Engl. *14*, 564 (1975); b) *E. Vogel*, Proc. Robert A. Welch Found. Conf. Chem. Res. *12*, 215 (1968); *E. Vogel, U. Haberland, H. Günther*, Angew. Chem. *82*, 510 (1970); Angew. Chem. Int. Ed. Engl. *9*, 513 (1970).

[2] Resumé on X-ray structure analyses of aromatic and olefinic bridged [14]annulenes containing an anthracene perimeter: *M. Simonetta*, Pure Appl. Chem. *52*, 1597 (1980).

[3] *syn*-1,6-Ethano-8,13-methano[14]annulene, which displays increased torsions in the annulene ring compared to in *syn*-1,6:8,13-bismethano[14]annulene was recognized, similarly to the *anti*-1,6:8,13-bismethano[14]annulene, as being an olefinic molecule with fluxional π-bonds, *E. Vogel, H. M. Deger, P. Hebel, J. Lex,* Angew. Chem. *92,* 943 (1980); Angew. Chem. Int. Ed. Engl. *19,* 919 (1980); *H. Günther, H. von Puttkamer, H. M. Deger, P. Hebel, E. Vogel, ibid. 92,* 944 (1980) and *19,* 921 (1980).

[4] *M. Balci, R. Schalenbach, E. Vogel,* Angew. Chem. *93,* 816 (1981); Angew. Chem. Int. Ed. Engl. *20,* 809 (1981).

[5] *J. Hine, D. C. Duffey,* J. Am. Chem. Soc. *81,* 1131 (1959); *J. M. Birchall, G. W. Cross, R. N. Haszeldine,* Proc. Chem. Soc. (London) *1960,* 81.

[6] For the hydrolysis of geminal allylic fluorides see: *J. J. Drysdale, W. W. Gilbert, H. K. Sinclair, W. H. Sharkey,* J. Am. Chem. Soc. *80,* 3672 (1958); *J. D. Park, S. Cohen, J. R. Lacher, ibid. 84,* 2919 (1962).

[7] We thank Professor *H. Günther* (Gesamthochschule Siegen) for the measurements.

[8] The bridge-bond angles measured in *anti*-1,6:8,13-bismethano[14]annulene and *(2)* are 108.8 and 119.8° [9], respectively, and thus show remarkable conformity with those to be expected for $sp^3$- and $sp^2$-hybridized carbon atoms, respectively.

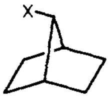
[9] *R. Destro, T. Pilati, M. Simonetta,* Tetrahedron *36,* 3301 (1980).

---

# Intramolecular Interaction between a Tropylium Ion and a Non-Neighboring Cyclopropane Ring[**]

By *Tomoo Nakazawa, Keiji Kubo, Atsuko Okimoto, Jun Segawa,* and *Ichiro Murata*[*]

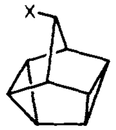
Many examples of remote interaction between a cyclopropane ring and a non-neighboring carbonium ion center are known[1a], the best known example being the solvolysis of the five norbornyl derivatives *(1)*—*(5)*, whose relative rates are 1, 1.7, $10^9$, $10^{10}$, and $10^{12}$, respectively[1]. However, attempts to observe the cation derived from *(5)* directly by spectroscopic methods have been unsuccessful, because the potential precursors are unstable in the acidic media employed[2].



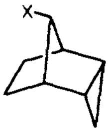
(1)

(2)

(3)

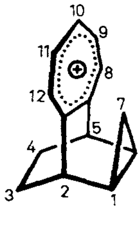


(4)

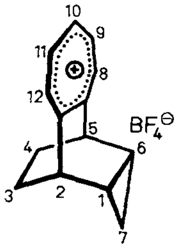


(5)

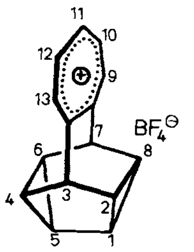
Herein we report the synthesis and some properties of a series of compounds *(6a)*—*(6c)*, in which the tropylium ion and cyclopropane ring are incorporated in a bicyclo[2.2.2]octane. The tropylium ions *(6)* can be synthesized from the benzene derivatives, *(7)* through homologation with diazomethane and a hydride ion abstraction sequence. Thus, for example, cyclopropanation of *endo*-benzotricyclo[3.2.2.$0^{2,4}$]non-6-ene *(7a)*[3a] with $CH_2N_2$ in the presence of CuCl in $CH_2Cl_2$ gave rise to a mixture of two cycloheptatriene isomers *(9a)* and *(10a)* in 28.4% yield. In contrast, the same cyclopropanation of the *exo*-derivative *(7b)*[3a] and 9,10-benzopentacyclo[4.4.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]dec-9-ene (benzosnoutene) *(7c)*[3b] led to a mixture of all three possible isomers, *(8b)*, *(9b)*, and *(10b)* (23%), and *(8c)*, *(9c)*, and *(10c)* (25%), respectively. All of these isomers could be separated by column chromatography on silica gel impregnated with 7% $AgNO_3$ (hexane + benzene) and characterized by $^1$H-NMR spectroscopy.



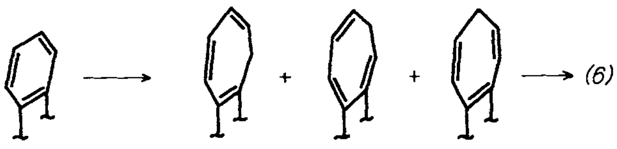
(6a)



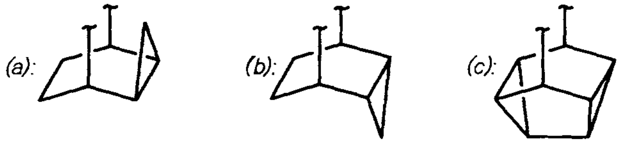
(6b)



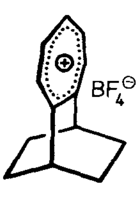
(6c)



(7) (8) (9) (10)

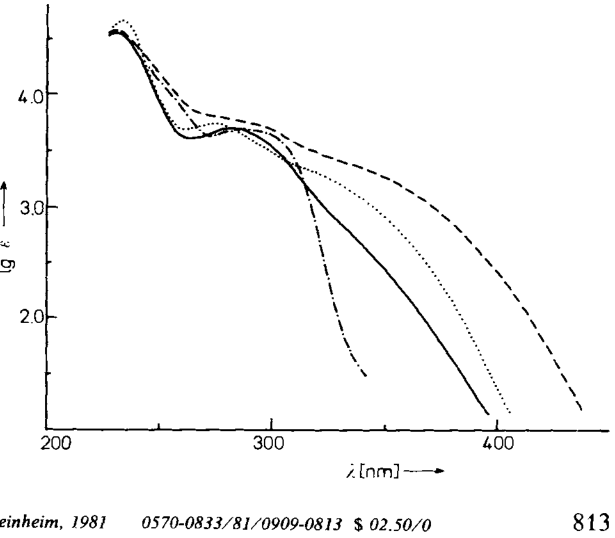


Conversion of these cycloheptatrienes into the desired tropylium ions was readily accomplished using trityl tetrafluoroborate in $CH_2Cl_2$: *(6a)*[4] (yellow leaflets, mp 126—7 °C); *(6b)*[4] (pale yellow prisms, mp 201—3 °C (decomp)); and *(6c)*[4] (lemon-yellow plates, mp 160.5 °C (decomp)).



(11)

In the tropylium ions *(6b)* and *(6c)*, the cyclopropane and tropylium moieties are situated such that interaction can occur *via* an edge of the three-membered ring; this is not the case in *(6a)*. The interactions are evident in the UV/VIS spectra of *(6a)*—*(6c)* (Fig. 1). *(6b)* ($\varepsilon_{350}$ = 900) and *(6c)*



---

[*] Prof. Dr. I. Murata[+], K. Kubo, A. Okimoto, J. Segawa
Department of Chemistry, Faculty of Science, Osaka University
Toyonaka, Osaka 560 (Japan)
Prof. Dr. T. Nakazawa
Department of Chemistry, Medical University of Yamanashi,
Nakakoma-gun, Tamoho-mura, Yamanashi 409-38 (Japan)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by a Grant-in-Aid for Scientific Research (No. 343007) from the Ministry of Education, Japan.

($\varepsilon_{350}=2000$) exhibit strong broad end-absorptions in the long wavelength region, tailing out to 400 and 450 nm, respectively; this is not observed in the spectrum of the reference compound *(11)*. These absorptions undergo blue-shifts upon changing the solvent to the more polar acetonitrile[8]. These results, as well as the concentration independence of their intensities, suggest that the absorptions can be assigned to intramolecular charge-transfer (CT) bands[9]. In contrast, *(6a)* only shows a weak absorption ($\varepsilon_{350}=370$) in this region, a result of the weaker interaction of the cyclopropane "side" with the "remote" tropylium ion.

The intramolecular CT-interaction in *(6a)—(6c)* is also reflected in their ground state properties *e.g.* $pK_{R^+}$-values and their reduction potentials (Table 1).

Table 1. $pK_{R^+}$-values and reduction potential data for the tropylium ions, *(6a)—(6c)*, and *(11)*.

| | *(6a)* | *(6b)* | *(6c)* | *(11)* |
|---|---|---|---|---|
| $pK_{R^+}$ [a] | 8.60 | 8.68 | 8.85 | 8.82 |
| $E_{1/2}$ [b] | −0.450 | −0.473 | −0.492 | −0.455 |

[a] Measured spectrophotometrically in 20% aqueous $CH_3CN$. [b] vs. SCE. Measured by polarography at 25 °C in $CH_3CN$ (25 °C, $CH_3CN$, $Et_4NClO_4$ as supporting electrolyte).

Although the dominant factor affecting the thermodynamic stability of the tropylium ion is the inductive effect of the bicyclo[2.2.2]octane skeleton[7, 10], both the $pK_{R^+}$-values and the reduction potentials increase, although only to a small degree, with increasing charge-transfer interaction in the order *(6a)*, *(6b)*, to *(6c)*.

Studies of the possible interactions in the excited states by MCD spectroscopy and MO (CNDO/S) calculations are presently been undertaken[9].

Received: October 8, 1980 [Z 848 IE]
German version: Angew. Chem. *93*, 820 (1981)

CAS Registry numbers:
*(6a)*, 73745-17-2; *(6b)*, 73701-15-2; *(6c)*, 73701-17-4; *(7a)*, 59331-32-7; *(7b)*, 59273-83-5; *(7c)*, 29443-83-2; *(8b)*, 78805-35-3; *(8c)*, 78805-36-4; *(9a)*, 78805-37-5; *(9b)*, 78854-31-6; *(9c)*, 78805-38-6; *(10a)*, 78805-39-7; *(10b)*, 78854-32-7; *(10c)*, 78805-40-0; *(11)*, 73701-21-0.

---

[1] a) Review: *J. Haywood-Farmer*, Chem. Rev. *74*, 315 (1974); b) *H. Tanida, T. Tsuji, T. Irie*, J. Am. Chem. Soc. *89*, 1953 (1967); *M. A. Battiste, C. L. Deyrup, R. E. Pincock, J. Haywood-Farmer, ibid. 89*, 1954 (1967); *J. Haywood-Farmer, R. E. Pincock, ibid. 91*, 3020 (1969); *H. Tanida*, Acc. Chem. Res. *1*, 239 (1968); *P. K. Freeman, R. S. Raghavan, G. L. Fenwick*, J. Am. Chem. Soc. *94*, 5101 (1972); *R. M. Coates, J. L. Kirkpatrick, ibid. 90, 4162 (1968); 92*, 4883 (1970).

[2] See footnote 120 in [1a].

[3] a) *K. Kitahonoki, K. Sakurawi, K. Tori, M. Ueyama*, Tetrahedron Lett. *1976*, 263; b) *L. A. Paquette, M. J. Kukla, J. C. Stowell*, J. Am. Chem. Soc. *94*, 4920 (1972).

[4] *(6a)*: $^1$H-NMR ($CD_2Cl_2$) $\delta=-1.08$ (1H, dt, $J=7.6$, 3.6 Hz, H-$7_{syn}$), 0.23 (1H, dt, $J=7.6$, 7.6 Hz, H-$7_{anti}$), 1.36—1.71 (4H, m, H-$3_{exo}$, $4_{exo}$, 1,6), 2.62 (2H, m, H-$3_{endo}$, $4_{endo}$), 4.07 (2H, m, H-2,5), 8.90—9.11 (5H, m, H-8—12); $^{13}$C-NMR ($CD_3CN$) $\delta=2.0$ (C-7), 10.3 (C-1,6), 24.0 (C-3,4), 43.2 (C-2,5), 151.5 (C-10), 152.1 (C-8,12), 153.0 (C-9,11), 172.2 (C-5a, 12a). *(6b)*: $^1$H-NMR ($CD_2Cl_2$) $\delta=1.10$—1.50 (4H, m, H-1, 6, $3_{exo}$, $4_{exo}$), 1.57—1.77 (2H, m, H-$7_{syn,anti}$), 1.94—2.19 (2H, m, H-$3_{endo}$, $4_{endo}$), 3.87—4.03 (2H, m, H-2, 5), 9.05 (5H, br, s, H-8—12); $^{13}$C-NMR ($CD_3CN$) $\delta=16.3$ (C-7), 21.2 (C-1, 6), 21.8 (C-3, 4), 42.9 (C-2, 5), 151.5 (C-10), 152.9 (C-8, 12), 153.2 (C-9, 11), 178.7 (C-5a, 12a). *(6c)*: $^1$H-NMR ($CD_2Cl_2$) $\delta=1.96$—2.18 (4H, m, H-2, 4, 6, 8), 2.93 (2H, br. t, $J=5.0$ Hz, H-1, 5), 4.33 (2H, quint, $J=2.9$ Hz, H-3, 7), 8.88—9.11 (5H, m, H-9—13); $^{13}$C-NMR ($CD_3CN$) $\delta=40.5$ (C-2, 4, 6, 8), 41.3 (C-1, 5), 48.9 (C-3, 7), 150.3 (C-11), 151.2 (C-9, 13), 152.2 (C-10, 12), 177.5 (C-7a, 13a); the assignment of signals C-8, 12 and C-9, 11 in *(6a)* and *(6b)*, as well as these of C 9, 13 and C-10, 12 in *(6c)* could also be reversed. Although the $^1$H-NMR spectra of *(6a)*, *(6b)*, and *(6c)* provide no useful information about charge delocalization, the $^{13}$C-NMR data are more informative. Thus, comparison of the $^{13}$C-NMR data for tropylium ions, *(6a)*, *(6b)*, *and (6c)*, with those reported for the corresponding benzo-analogs, *(7a)* [3a], *(7b)* [3b], and *(7c)* [5], indicates that (i) the ethano bridge carbons (C-3 and C-4) of both *(6a)* and *(6b)*, compared with those of *(7a)* and *(7b)*, respectively, are shifted upfield by *ca.* 2 ppm [6], (ii) the signals of C-1 and C-6 in *(6a)* also exhibit slight upfield shifts of 0.9 ppm and (iii) the signals of C-1 and C-6 in *(6b)* and C-2, C-4, C-6, and C-8 in *(6c)* exhibit downfield shifts of 0.7 and 2.8 ppm, respectively. These downfield shifts are indicative of decreased electron densities at these carbon atoms a consequence of the intramolecular CT-interaction in *(6b)* and *(6c)*.

[5] *(7c)*: $^{13}$C-NMR ($CD_3CN$) $\delta=34.5$ (C-1, 5), 37.7 (C-2, 4, 6, 8), 40.9 (C-3, 7), 125.1 (C-10, 11), 124.8 (C-9, 12), 144.1 (C-7a, 12a). The numbering follows that in *(6c)*.

[6] Almost the same high-field shift (1.8 ppm) is observed if the signals of the C atoms in the ethano bridges in *(11)* [7] and in the 6,9-dihydro-6,9-ethanobenzotropylium ion are compared with the signals of the corresponding benzo-annelated derivatives.

[7] *T. Nakazawa, Y. Niimoto, K. Kubo, I. Murata*, Angew. Chem. *92*, 566 (1980); Angew. Chem. Int. Ed. Engl. *19*, 545 (1980).

[8] Cf. *T. Nakazawa, I. Murata*, J. Am. Chem. Soc. *99*, 1996 (1977); *T. Nakazawa, N. Abe, K. Kubo, I. Murata*, Tetrahedron Lett. 1979, 4995; *K. Yamamura, K. Nakatsu, K. Nakao, T. Nakazawa, I. Murata, ibid.* 1979, 4999.

[9] The newly appeared end-absorptions in *(6a)*, *(6b)*, and *(6c)* also appear in their MCD spectra and are interpreted, on the basis of the MO(CNDO/S) method, to be due to the electronic transitions from the cyclopropane to the tropylium-moiety. *A. Tajiri, M. Hatano, K. Nakasuji, T. Nakazawa, I. Murata*, Ber. Bunsenges. Phys. Chem., in press.

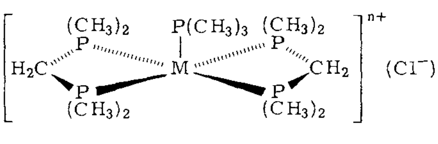
[10] *K. Takeuchi, Y. Yokomichi, T. Kurosaki, Y. Kimura, K. Komatsu, K. Okamoto*, Abstracts M33, 29th Symp. Org. React. Mechanisms, Osaka 1978.

---

## A Triply Bridged Dicobalt Complex with Odd Number of Electrons ($Co_2^{1+}$)[**]

By *Hans Heinz Karsch* and *Beatrix Milewski-Mahrla*[*]

Dinuclear complexes with bridging ligands and direct metal-metal interaction, which contain an odd number of electrons, are accessible in only a few exceptional cases and/or by directed redox reactions[1]. We report here on the spontaneous formation of a novel, triply bridged dicobalt complex with the "mixed" oxidation state $Co_2^{1+}$.



*(1)*, M = Fe
n = 0
*(2)*, M = Co
n = 1
*(3)*, M = Ni
n = 2

In the series of isoelectronic complexes *(1)—(3)*[2] the orange cobalt(I) compound *(2)* is distinguished by the fact that it disproportionates in tetrahydrofuran (THF) solution—slowly at room temperature, rapidly above 40 °C—to give the cobalt(II) compound *(4)* (green crystals, dec. > 115 °C) and a product *(5)* decrystallizing as red-brown, hexagonal platelets.

$$[(Me_2PCH_2PMe_2)_2(Me_3P)Co]Cl \quad (2)$$

$$\text{THF}\ \Big\downarrow\ +40\,^{\circ}\text{C}$$

$$[(Me_2PCH_2PMe_2)(Me_3P)_2CoCl_2] \quad (4)$$

$$+$$

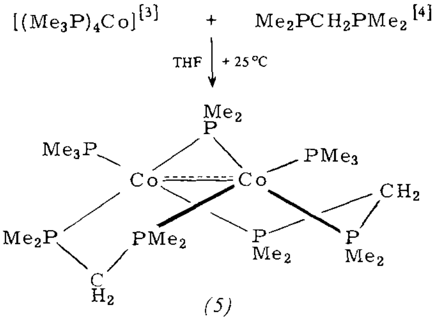
$$[\{(Me_2PCH_2PMe_2)(Me_3P)Co\}_2PMe_2] \quad (5)$$

---

[*] Dr. H. H. Karsch, Dipl.-Chem. B. Milewski-Mahrla
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

The paramagnetic complex *(5)*, which is readily soluble in pentane and is moderately sensitive to air in the solid state, should therefore be formulated as a cobalt(0) compound. According to this, *(5)* is also formed spontaneously in the following reaction.



(5)

However, from the mass spectrum (*m/z* 603), the elemental analysis, and the IR spectrum of *(5)*, a dimeric structure could be deduced in which two cobalt atoms with the formal oxidation number $+1/2$ are linked *via* three bridge ligands (two methylenebis(dimethylphosphane)- and one dimethylphosphido-bridge). This surprising observation is confirmed by the X-ray structure analysis[5].

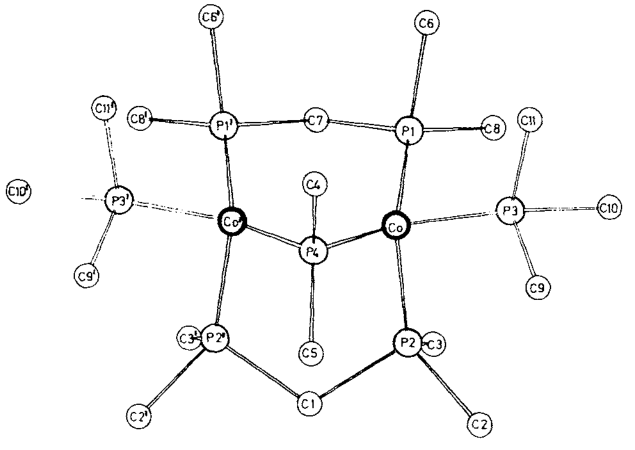


Fig. 1. Structure of the dicobalt complex *(5)* in the crystal. The molecule has a plane of symmetry through C7—P4—C1. Hydrogen atoms not shown. Most important bond lengths and angles: Co—Co 260.3, Co—P1 214.0, Co—P2 217.1, Co—P4 214.4, P1—C7 185.5, P2—C1 184.2 pm; Co—P4—Co' 74.77, P1—C7—P1' 105.43, P2—C1—P2' 113.45, P1—Co—P2 106.65, P1—Co—P3 101.25, P1—Co—P4 137.08, P2—Co—P3 105.39, P2—Co—P4 104.19, P3—Co—P4 98.49, P3—Co—Co' 147.91°.

The distance between the two almost tetrahedrally configurated Co atoms is 260.3(3) pm, a value close to the lower limit in comparable complexes[6]. As model considerations show, a still closer approach of the metal atoms increases repulsion between the bridge- and trimethylphosphane ligands; for minimum repulsion between the bridge ligands only one of the two $CP_2Co_2P$ six-membered rings should adopt a chair conformation, the other a boat conformation; this is in fact observed (Fig. 1). A bond order of 1.5 can be formally assigned to the Co—Co bond (17.5 electrons per Co atom), as is also assumed for the, to our knowledge, hitherto sole comparable complex $[\{(C_5H_5)Co\}_2(\mu\text{-}CO)(\mu\text{-}NO)]$[7]. Regardless of this relationship *(5)* rather corresponds to the "A-frame" complexes[8], whose planar metal coordination (without metal-metal bonding) has now for the first time its tetrahedral pendant (with metal-metal bonding). Whereas the P—C bond cleavage necessary for the formation of *(5)* is not unusual in low-valency phosphanecobalt complexes[6b,9], a "voluntary" reorganization to a bridged molecule with an odd number of electrons is still without example.

Received: December 5, 1980 [Z 853 IE]
German version: Angew. Chem. *93*, 825 (1981)

---

[1] *H. Vahrenkamp*, Angew. Chem. *90*, 403 (1978); Angew. Chem. Int. Ed. Engl. *17*, 379 (1978); and references cited therein.

[2] *H. H. Karsch*, unpublished.

[3] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *108*, 944 (1975).

[4] *H. H. Karsch, H. Schmidbaur*, Z. Naturforsch. *B 32*, 762 (1977).

[5] Hexagonal crystals, space group P63/m, $Z=12$, 273 K: $a=1629.2(7)$, $b=1627.8(7)$, $c=1929.6(6)$ pm; Syntex $P2_1$/XTL, $Mo_{K\alpha}$-radiation, 817 structure factors ($F_0 \geq 4.0\sigma(F_0)$), $R_1=0.068$, $R_2=0.061$.

[6] a) *E. Keller, H. Vahrenkamp*, Z. Naturforsch. *B 33*, 537 (1978); references cited therein; b) *H.-F. Klein, J. Wenninger, U. Schubert, ibid. B 34*, 1391 (1979).

[7] *J. Müller, S. Schmitt*, J. Organomet. Chem. *97*, C 54 (1975); *W. A. Herrmann, I. Bernal*, Angew. Chem. *89*, 186 (1977); Angew. Chem. Int. Ed. Engl. *16*, 172 (1977).

[8] *C. P. Kubiak, R. Eisenberg*, J. Am. Chem. Soc. *102*, 3637 (1980); *M. Cowie, S. K. Dwight, ibid. 102*, 2500 (1980); *L. S. Benner, A. C. Balch, ibid. 100*, 6099 (1978); *M. P. Brown, J. R. Fisher, R. J. Puddephatt, K. R. Seddon*, Inorg. Chem. *18*, 2808 (1979).

[9] *H. H. Karsch*, Dissertation, Universität Würzburg 1974.

---

## Observations on the Structural Chemistry of the Cyclopentadienyl Bridge[**]

By *Wolfgang A. Herrmann, Gangolf Kriechbaum, Christine Bauer, Ernst Guggolz,* and *Manfred L. Ziegler*

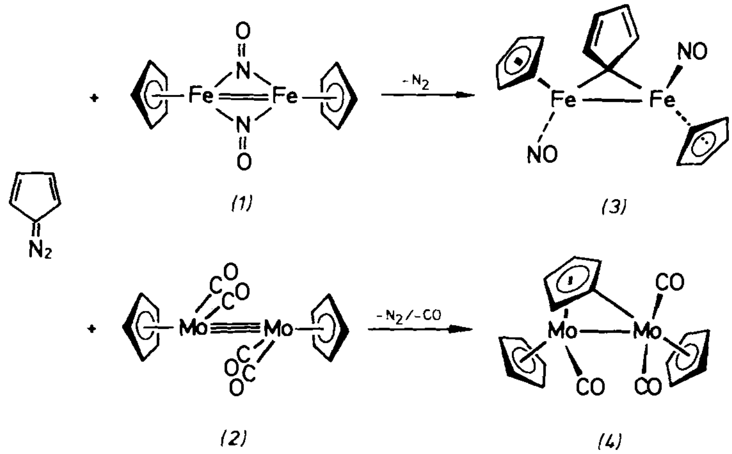
The uniform bonding[1,2] and the consistent structural parameters of all previously investigated $C_5H_4$-bridges have led to their formulation as $\mu(\eta^1:\eta^5)$ ligands, while there are no indications whatever for the alternative $\eta^1$-carbene/$\eta^4$-diolefin coordination. We attempted the realization of this type of structure by employing a precursor compound already containing the $C_5H_4$ ligand, and report here on the carbene addition to metal-metal multiple bonds starting from diazocyclopentadiene.

Reaction of a suspension of the dinuclear nitrosyl complex *(1)*[3], which formally exhibits an FeFe double bond, in tetrahydrofuran (THF), with an excess of diazocyclopentadiene leads with rapid elimination of $N_2$, even at temperatures as low as $-80\,^\circ C$, to the carbene addition product *(3)* which was isolated in pure form in 90—95% yield as air-stable crystals. *(3)* can be stored without decomposition at room temperature and was unequivocally characterized by total elemental analysis and by IR, $^1H$-NMR, $^{13}C$-NMR, and mass spectra (EI and FD) as a $\mu,\eta^1$-cyclopentadienylidene complex[4a]. The smooth formation of *(3)* supports the concept[5] that carbene-transfer with diazoalkanes to sterically accessible metal-metal double bonds com-

---

[*] Prof. Dr. W. A. Herrmann, Dipl.-Chem. G. Kriechbaum, Dipl.-Chem. Ch. Bauer
Institut für Anorganische Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg 1 (Germany)
Prof. Dr. M. L. Ziegler, Dipl.-Chem. E. Guggolz
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[**] Complex Chemistry of Reactive Organic Compounds, Part 36. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and BASF AG.—Part 35: *W. A. Herrmann, G. Kriechbaum, P. Wülknitz, M. L. Ziegler*, Chem. Ber. *114*, 276 (1981).



prises a straightforward general method for the construction of dimetallacyclopropanes.

By way of contrast, the analogous reaction with the molybdenum compound *(2)*[6], which contains an MoMo triple bond, does not lead to the hitherto unknown dimetallocyclopropenes: the sole isolable product at room temperature in only 35—45% yield formed with with concomitant elimination of $N_2$ and CO is the thermally very stable complex *(4)* (total elemental analysis, FD mass spectrum, IR, $^1$H-NMR spectra[4b]). This unexpected compound formally arises from carbonyl/carbene exchange of the precursor *(2)*. The structural determination (Fig. 1) gave a surprising result:

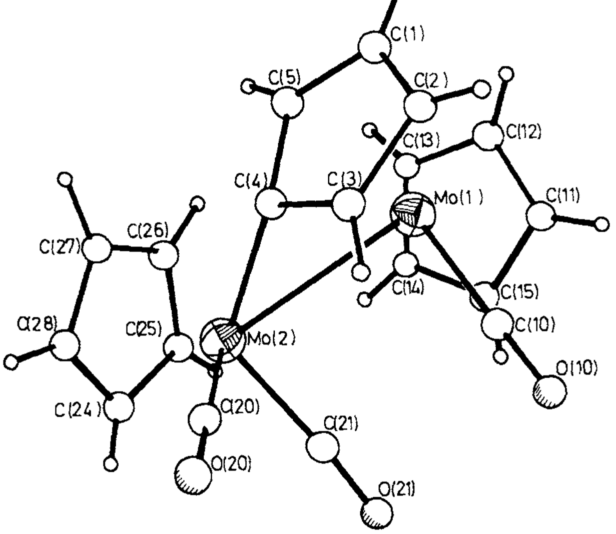


Fig. 1. ORTEP diagram of *(4)* (thermal vibrational ellipsoids drawn with 50% probability).—Monoclinic (from acetone/$CH_2Cl_2$; −35°C), space group $P2_1/n$ ($C_{2h}^5$); $a = 866.66(15)$, $b = 1539.06(35)$, $c = 1222.34(16)$ pm, $\beta = 92.58(1)°$; Syntex P3; $3° \leq 2\theta \leq 70°$; 3966 independent reflections with $I \geq 4\sigma(I)$; $R_{iso} = 0.070$, $R_{aniso} = 0.029$. Selected bond lengths [pm] and angles [°]:

| | | | |
|---|---|---|---|
| Mo(1)—Mo(2) | 309.8(0) | C(2)—C(3) | 142.4(6) |
| Mo(2)—C(4) | 211.1(4) | C(3)—C(4) | 144.2(6) |
| Mo(1)—C(4) | 222.4(4) | C(4)—C(5) | 145.1(6) |
| Mo(1)—C(1) | 230.4(4) | C(5)—C(1) | 141.7(6) |
| Mo(1)—C(2) | 231.5(4) | C(10)—O(10) | 114.0(6) |
| Mo(1)—C(3) | 225.0(4) | C(20)—O(20) | 117.0(6) |
| Mo(1)—C(5) | 226.4(4) | C(21)—O(21) | 115.1(6) |
| Mo(1)—C(11 ·· 15) | 228.3—232.5 | Mo(1)—C(10) | 199.2(4) |
| Mo(2)—C(24 ·· 28) | 233.2—239.1 | Mo(2)—C(20) | 191.3(4) |
| C(1)—C(2) | 139.7(6) | Mo(2)—C(21) | 196.4(4) |
| Mo(1), C(4), Mo(2) | 91.2(1) | C(3), C(4), C(5) | 101.8(3) |
| Mo(1), Mo(2), C(4) | 45.9(1) | C(4), C(5), C(1) | 111.0(3) |
| C(1), C(2), C(3) | 106.4(3) | C(5), C(1), C(2) | 108.3(3) |
| C(2), C(3), C(4) | 112.2(3) | | |

In remarkable contrast to the $\mu,\eta^1$-coordination in *(3)* the $C_5H_4$-group acts as metal-bridging 6-electron ligand with complexation of the entire ring system and concomitant surrender of the MoMo triple bond. The metal-metal distance is about 65 pm longer than in the educt *(2)*[6] and is thus close to the values observed for MoMo "single bonds"[7]. All carbonyl ligands are found to occupy terminal positions; hence for electron balancing reasons (EAN rule), a carbene-diolefin coordination of the bridging ligand is to be expected. However, such a coordination mode is not present on the grounds of the following structural characteristics:

1. The Mo(2)—C(4) bond (211.1(4) pm) is considerably longer than in comparable carbene complexes[8], although a closing up of the two atoms by tilting of the $(C_5H_5)(C_5H_4)$Mo(CO)-fragment in the direction of the second metal atom would encounter no problems, at least geometrically.
2. The Mo(1)—C(4) bond is shorter than the corresponding bond lengths of the remaining ring members of the $C_5H_4$ ligand.
3. The alternance of the C(3)—C(2)-, C(2)—C(1)- and C(1)—C(5)-bond lengths (short, long, short) to be expected for a diolefin-type coordination is not observed. Rather, the C(2)—C(1) bond is significantly shorter than the other CC bonds in the unique cyclic ligand. The observed bond length pattern as a consequence of folding of the $C_5H_4$ ligand about C(3) · · C(5) (3.7°) is also consistent with theoretical calculations[9].

The $\eta^1:\eta^5$-coordination of the cyclopentadienyl bridge thus demonstrated would indicate the formation of a semipolar metal-metal bond of the type Mo(1)→Mo(2), whereby the unequal charge distribution about the metal centers is not mitigated, or alleviated, in the usual way[10] by semibridging, but exclusively by the terminal CO ligands. This is revealed spectroscopically, *inter alia*, by an unusually low-frequency CO vibration[4b] and moreover, is consistent with the significant differences in the Mo—CO and C—O bond lengths, respectively. Some structural details, *e.g.* the markedly acute angle of 59.5° between the plane defined by C(3), C(4), C(5) and the Mo(2)—C(4) vector are in part enforced sterically; nevertheless, the pronounced propensity of the cyclic ring to aromatize appears to be responsible for the general preference of $\eta^1:\eta^5$ complexation over carbene/diolefin fixation, regardless of the method of synthesis, the metal framework, and the electronic nature of the peripheral ligands. As demonstrated by the stability of the compound *(3)* and $(\mu\text{-}C_5X_4)[(\eta^5\text{-}C_5Me_5)Rh(CO)]_2$ (X = H[4a], Cl, Br[11]), the diolefin nature of the $C_5H_4$ bridge is preserved upon carbene-addition to metal-metal multiple bonds if metal-metal single bonds are achieved and/or steric factors or the bonding properties of the additional ligands do not permit further complexation of the ring system. Evidently, cancellation of coordinative and electronic unsaturation of metal-metal multiple bonds plays a pivotal role in determining the final structure of carbene addition products.

## *Procedure*

All operations must be carried out under rigorous exclusion of air and moisture (Schlenk technique).

*(3)*: A suspension of *(1)* (302 mg, 1.0 mmol) in THF (50 mL) is treated at −80°C with *ca.* 5 mmol of diazocyclopentadiene (tosyl azide-free, *ca.* 0.5 M solution in benzene). A color change from olive-green to brown-red occurs, accompanied by immediate evolution of $N_2$; *(1)* goes com-

pletely into solution. The solution is warmed to +25 °C, evaporated down after 20 min *in vacuo*, and the microcrystalline residue extracted with 40 mL of *n*-pentane. The extract is filtered and concentrated to 30 mL. On cooling to −35 °C, *(3)* crystallizes as black needles and/or spear-shaped rods. Decomposition above 184 °C (sealed capillary); very soluble in all common organic solvents, yield 339 mg (93%).

*(4):* A stirred solution of *(2)* (217 mg, 0.5 mmol) in benzene (20 mL) is treated dropwise with 0.5 mmol of diazocyclopentadiene at +25 °C (cf. preceeding preparation). After a few minutes the dark-red solution turns black-brown. Stirring is continued for 12 h and the solution is then evaporated down in a vacuum and the residue chromatographed on silica gel (Merck 7734; Act. II–III; 40 × 1.5 cm column; −20 °C). Unreacted *(2)* (red zone) is first eluted with ether; thereafter the product *(4)* is eluted with $CH_2Cl_2$ as a black-red zone. After recrystallization from acetone/$CH_2Cl_2$ (−35/−80 °C) *(4)* is analytically pure; it forms deep-red prisms which sinter at 155—175 °C and decompose at 222—225 °C (sealed capillary); yield 83—106 mg (35—45%).

Received: January 29, 1981 [Z 856 IE]
German version: Angew. Chem. *93*, 838 (1981)

---

[1] Cf. *L. J. Guggenberger, P. Meakin, F. N. Tebbe*, J. Am. Chem. Soc. *96*, 5420 (1974); *G. P. Pez, ibid. 98*, 8072 (1976); *D. A. Lemenovskii, V. P. Fedin, A. V. Aleksandrov, Yu. L. Slovohotov, Yu. T. Struchkov*, J. Organomet. Chem. *201*, 257 (1980); *A. A. Pasynskii, Yu. T. Struchkov, V. T. Kalinnikov, M. A. Porai-Koshits, A. S. Antsyshkina, G. G. Sadikov, V. N. Ostrikova, ibid. 201*, 269 (1980), and references cited therein; recent example: *P. S. Pregosin, A. Togni, L. M. Venanzi*, Angew. Chem. *93*, 684 (1981); Angew. Chem. Int. Ed. Engl. *20*, 668 (1981).

[2] *R. J. Hoxmeier, J. R. Blickensderfer, H. D. Kaesz*, Inorg. Chem. *18*, 3453 (1979); *R. J. Hoxmeier, C. B. Knobler, H. D. Kaesz, ibid. 18*, 3462 (1979), and references cited therein.

[3] *H. Brunner*, J. Organomet. Chem. *14*, 173 (1968); *J. L. Calderon, S. Fontana, E. Frauendorfer, V. W. Day, D. A. Iske, ibid. 64*, C16 (1974).

[4] a) *(3)*, IR (νCO): 1738 vs, 1718 sh [KBr]; 1744 [*n*-pentane]; $^1$H-NMR ($CDCl_3$, int. TMS, 32 °C): $\delta = 5.05$ (10H, $C_5H_5$, s), 6.38 (4H, $C_5H_4$, symm. m); $^{13}$C-NMR ($CDCl_3$, int. TMS, 29 °C): $\delta = 91.49$ ($C_5H_5$), 116.76, 146.57, 148.59 ($C_5H_4$).—$(\mu\text{-}C_5H_4)[(\eta^5\text{-}C_5Me_5)Rh(CO)]_2$ is formed analogously from $C_5H_4N_2$ and $[(\eta^5\text{-}C_5Me_5)Rh(\mu\text{-}CO)]_2$; air-sensitive red crystals, m.p. 162 °C (sealed capillary); IR (νCO): 1953 vs [KBr]; $^1$H-NMR ($C_6D_6$, int. TMS, 23 °C): $\delta = 1.72$ (30H, $CH_3$, s); 6.63 and 6.39 (4H, $C_5H_4$, symm m); mol. wt. 596 (MS-FD, from acetone); b) *(4)*: IR (νCO): 1945 vs, 1867 vs, 1759 vs [KBr]; 1972 vs, 1883 vs, 1786 vs [$CH_2Cl_2$]; 1962 vs, 1886 vs, 1797 vs, [THF]; $^1$H-NMR ([$D_8$]THF, 25 °C): $\delta = 5.09$ (5H, $C_5H_5$, s), 5.23 (5H, $C_5H_5$, s), 4.16 (1H, $C_5H_4$, m), 5.17 (1H, $C_5H_4$, "s"), 5.34 (1H, $C_5H_4$, "s"), 5.38 (1H, $C_5H_4$, m).—Mol. wt. 474 ($^{98}$Mo; FD-MS, from acetone).

[5] *W. A. Herrmann, Ch. Bauer*, J. Organomet. Chem. *204*, C13 (1981); cf. *W. A. Herrmann*, Adv. Organomet. Chem., in press; Pure Appl. Chem., in press.

[6] *R. J. Klinger, W. M. Butler, M. D. Curtis*, J. Am. Chem. Soc. *100*, 5034 (1978).

[7] *F. A. Cotton, D. M. Collins, R. D. Adams*, Inorg. Chem. *13*, 1086 (1974).

[8] *D. J. Cardin, B. Cetinkaya, M. F. Lappert*, Chem. Rev. *72*, 545 (1972).— The Mo(2)—C(4) bond length is of the same order of magnitude as the bond lengths in alkyl-Mo complexes, cf. *M. H. Chisholm, F. A. Cotton, M. W. Extine*, Inorg. Chem. *17*, 2338 (1978), and references cited therein.

[9] *P. Hofmann*, Universität Erlangen-Nürnberg, personal communication.

[10] *F. A. Cotton*, Prog. Inorg. Chem. *21*, 1 (1976).

[11] *W. A. Herrmann, Ch. Bauer, J. Plank, W. Kalcher, D. Speth, M. L. Ziegler*, Angew. Chem. *93*, 212 (1981); Angew. Chem. Int. Ed. Engl. *20*, 193 (1981), *W. A. Herrmann, Ch. Bauer, G. Kriechbaum, H. Kunkely, M. L. Ziegler, H. Kunkely, E. Guggolz*, Chem. Ber., in press.

---

# BOOK REVIEWS

**Comprehensive Treatise of Electrochemistry. Vol. 1. The Double Layer.** Edited by *J. O'M. Bockris, B. E. Conway* and *E. Yeager*. Plenum Publishing, New York 1980. xix, 453 pp., bound, $ 49.50.

The first of four volumes deals with the electrochemical double layer. In nine review articles written by well-known authors, the fundamental aspects of this extremely important field are clarified by concentrating on particular points. The contributions run as follows: 1) *R. Parsons:* Thermodynamic Methods for the Study of Interfacial Regions in Electrochemical Systems (thermodynamic description of adsorption), 2) *S. Trasatti:* The Electrode Potential (physical description of the electrode potential, role of the work function, absolute electrode potential), 3) *R. Reeves:* The Double Layer in the Absence of Specific Adsorption (double-layer capacity, classical double-layer model), 4) *M. A. Habib* and *J. O'M. Bockris:* Specific Adsorption of Ions (*inter alia* methods of measurement, adsorption isotherms, partial charge transfer), 5) *A. N. Frumkin, O. A. Petrii* and *B. B. Damaskin:* Potentials of Zero Charge (determination, origin, modification), 6) *Yu. V. Pleskov:* Electric Double Layer on Semiconductor Electrodes (space-charge layer, surface states, capacities. The article deals more with semiconductor surfaces than with the special features of the semiconductor-electrolyte interface), 7) *L. I. Boguslavsky:* Insulator/Electrolyte Interface (short review of problems relating to insulator-electrolyte boundary surfaces), 8) *B. B. Damaskin* and *V. E. Kazarinov:* The Adsorption of Organic Molecules (thermodynamic description, results), 9) *R. J. Hunter:* The Double Layer in Colloidal Systems (charge and potential distribution, electrokinetic effects, colloid stability).

The book gives a very good general picture, is well arranged, and is clearly and attractively written. It will be a welcome reference book not only for the electrochemist but also (and indeed especially) for those working in neighboring areas of research who wish to familiarize themselves with electrochemistry. It will also prove useful for undergraduate and postgraduate students. Electrochemists will realize that some of the chapters have already appeared in other series or monographs, but the advantage of having all together in a single volume must not be underestimated. The shortcomings of the collection are marginal. As always, the combination of various contributions places a strain on consistency. Many important fields are hardly touched upon (electrode kinetics), while other aspects are repeated in at least two chapters. A better account of single-crystal metal electrodes could have been given: recent results in this field (*e.g.* from the French group) would have fitted well into this book. An equally justified treatment of metal electrodes and of semiconductor and insulator electrodes would perhaps have gone beyond the bounds of a single volume, but precisely because of this a much more comprehensive literature collection for these two chapters would have been desirable.

While it is impossible to go here more deeply into the individual contributions, it may be said that the title reflects the contents very well. The first three contributions must be singled out because of their clear and didactic construction; the fourth perhaps suffers somewhat from an excessive linkage of the results with particular workers. Contributions 6, 7, and 9 are a most welcome, even if (too) short, supplement on the electrochemistry of metal electrodes.

The external appearance of the book is attractive, the text and the illustrations are clearly arranged, and, happily, there seem to be few printing errors. The price is moderate and the book can be recommended without reservations for the relevant libraries.

*Dieter M. Kolb* [NB 543 IE]

### Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Transport Across Biological Membranes.** By *M. Höfer.* Pitman Books, London 1981, xiii, 184 pp., bound, £ 15.00.— ISBN 0-273-08480-1

**Structure and Bonding. Vol. 43. Bonding Problems.** Edited by *J. B. Goodenough, P. Hemmerich, J. A. Ibers, C. K. Jørgensen, J. B. Neilands, D. Reinen,* and *R. J. P. Williams.* Springer-Verlag, Berlin 1981. v, 220 pp., bound, DM 98.00.—ISBN 3-540-10407-0

**Personal Computers in Chemistry.** Edited by *P. Lykos.* John Wiley & Sons, Chichester 1981. xi, 262 pp., bound, £ 14.57.—ISBN 0-471-08508-1

**Drug Design. Vol. 10. Medicinal Chemistry.** Edited by *E. J. Ariëns.* Academic Press, New York 1980. xi, 432 pp., bound, $ 49.50.—ISBN 0-12-060310-1

**Analytical Chemistry. Vol. 2. Basic Analytical Chemistry.** By *L. Pataki* and *E. Zapp.* Pergamon Press, New York 1980. xiii, 463 pp., bound, $ 55.00.—ISBN 0-08-023850-5

**Landolt-Börnstein. Neue Serie. Band 11 (Ergänzung zu Band 2). Magnetische Eigenschaften der Koordinations- und metallorganischen Verbindungen der Übergangselemente.** Edited by *K.-H. Hellwege* and *A. M. Hellwege.* Springer-Verlag, Berlin 1981. 1002 pp., bound, DM 1190.00.—ISBN 3-540-09908-5

**Advances in Quantum Chemistry. Vol. 12.** Edited by *P.-O. Löwdin.* Academic Press, New York 1980. x, 325 pp., bound, $ 48.00.—ISBN 0-12-034812-8

**The Alkaloids. Vol. 10.** Senior Reporter: *M. F. Grundon.* The Royal Society of Chemistry, London 1981. xii, 263 pp., bound, £ 49.00.—ISBN 0-85186-337-X.—A volume in the series "Specialist Periodical Reports"

**Chemische Kinetik. Fachstudium Chemie. Arbeitsbuch 6.** By *R. Ebisch, E. Fanghänel, W.-D. Habicher, R. Hahn,* and *K. Unverfeth.* Verlag Chemie, Weinheim 1980. 212 pp., bound, DM 36.00.—ISBN 3-527-25871-X

**Isolierung, Fraktionierung und Hybridisierung von Nukleinsäuren.** Edited by *U. Wobus.* Verlag Chemie, Weinheim 1981. 229 pp., bound, DM 55.00.—ISBN 3-527-25860-4

**Solid State Reactions.** By *Hermann Schmalzried.* Verlag Chemie, Weinheim 1981. 2., completely new revised edition. x, 254 pp., bound, DM 98.00.—ISBN 3-527-25872-8

**Wie werden aus Pulvern kompakte Werkstoffe?** By *J. E. Geguzin.* VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1981. 224 pp., bound, *ca.* DM 16.00

**Materials for Advanced Batteries.** Edited by *D. W. Murphy, J. Broadhead,* and *B. C. H. Steele.* Plenum Press, New York 1980. ix, 373 pp., bound, $ 39.50.—ISBN 0-306-40564-4

**Gmelin Handbuch der Anorganischen Chemie.** Springer-Verlag, Berlin 1981. 8th edit. Sc, Y, La—Lu Seltenerdelemente. Verbindungen mit Schwefel (Fortsetzung): Sulfidhalogenide. Sulfate, Salze weiterer Schwefelsäuren sowie entsprechende Alkalidoppelverbindungen. xxxii, 416 pp., bound, DM 1147.00.—ISBN 3-540-093434-0

**Inorganic Reaction Mechanisms. Vol. 7.** Senior Reporter: *A. G. Sykes.* The Royal Society of Chemistry, London 1981. xxi, 442 pp., bound, £ 72.00.—ISBN 0-85186-315-9.—A volume in the series "Specialist Periodical Reports"

**Mathematics for Physical Chemistry.** By *R. G. Mortimer.* Macmillan Publishing, New York 1981. x, 405 pp., bound, $ 10.95.—ISBN 0-02-384000-5

**Molecular Electronic Structures. An Introduction.** By *C. J. Ballhausen* and *H. B. Gray.* Benjamin/Cummings Publishing, Reading 1980. viii, 133 pp., bound, $ 14.50.—ISBN 0-8053-0452-5

---

**Editorial office:** Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 602-1, Telex 465516 vchwh d.

**Editor:** *O. Smrekar.* **Translation Editors:** *I. G. Neil* and *A. Stimson.*

**Publishers:** Verlag Chemie GmbH. (Managing Director *Dr. Helmut Grünewald*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany, Telephone Weinheim (06201) 602-1, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE

Volume 20 · Number 10
October 1981
Pages 819–898

International Edition in English

# α,ω-Diisocyanatocarbodiimides, -Polycarbodiimides, and Their Derivatives

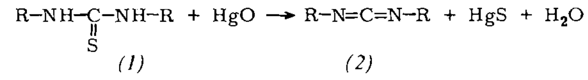
**By Kuno Wagner, Kurt Findeisen, Walter Schäfer, and Werner Dietrich**[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Research in the field of low-molecular weight, oligomeric and polymeric α,ω-diisocyanatocarbodiimides and -polycarbodiimides has been fruitful, not only in connection with these compounds themselves, but also—as so often happens in chemistry—with quite different problems. Novel synthetic methods, discoveries concerning the properties of low-molecular weight carbodiimides and phosphane imide derivatives, as well as results on the fragmentation reactions of four-membered heterocyclic compounds containing oxygen, phosphorus, and nitrogen, and a better understanding of the diisocyanate polyaddition process are among the many by-products of this research. The "high- and low-temperature formation" of polycarbodiimides and the homogeneous and heterogeneous catalysis of this process are described, and the fundamental importance of four-membered ring fragmentation mechanisms resulting in the formation of phosphane imide derivatives is outlined. Interesting building blocks for the diisocyanate polyaddition and polycondensation processes can be synthesized by many derivatization reactions of oligomeric and high-molecular weight polycarbodiimides and polyuretonimines. The *in situ* production of polycarbodiimides *via* matrix reactions in flexible polyurethane foams leads to a cellular arrangement of the material due to the pronounced symmetrical growth processes. Combination-foams with increased carbonation tendencies are formed in this way. Attention is drawn to several industrial applications of α,ω-diisocyanatopolycarbodiimides, of high-molecular weight cross-linked polyuretonimines, and of polycarbodiimide foams.

## 1. Old and New Methods for the Synthesis of Low-Molecular Weight Carbodiimides

The carbodiimide family was first described more than 100 years ago by *Weith*[1]. This was the beginning of an intensive study of these reactive compounds, for the production of which a great variety of methods were subsequently found[2]. The cumulative double bonds make these compounds highly reactive, especially in addition and cycloaddition reactions, with the result that they are versatile building blocks for the synthesis of heterocyclic compounds.



$$\underset{(1)}{R{-}NH{-}\underset{\|}{\overset{}{C}}{-}NH{-}R} + HgO \longrightarrow \underset{(2)}{R{-}N{=}C{=}N{-}R} + HgS + H_2O$$

(1) (2)

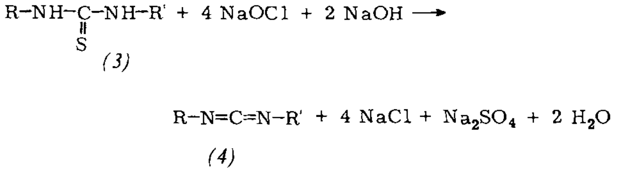
Carbodiimides, especially dicyclohexylcarbodiimide, are important dehydrating reagents—in many cases on polymeric carriers (in Merrifield synthesis[4])—in the synthesis of peptides[3].

---

[*] Dr. K. Wagner, Dr. K. Findeisen, Dr. W. Schäfer
Zentralbereich Forschung und Entwicklung,
Bayer AG, D-5090 Leverkusen, Bayerwerk (Germany)
Dr. W. Dietrich
Anwendungstechnische Abteilung der Sparte Polyurethane,
Bayer AG, D-5090 Leverkusen, Bayerwerk (Germany)

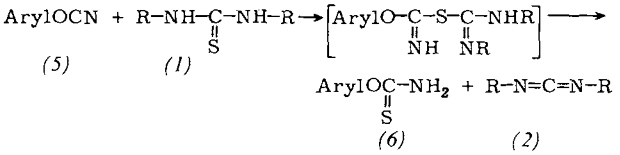
0570-0833/81/1010-0819 $ 02.50/0

Many methods for the synthesis of low-molecular weight carbodiimides were developed by *E. Schmidt et al.*[5-10]. *N,N'*-dialkylthiourea derivatives *(3)* are oxidized to carbodiimides very efficiently by alkaline hypochlorite solution at temperatures below 0 °C, a reaction which is characterized by a wide range of applications. However, the preparation of oligomeric or high-molecular weight polycarbodiimides with more than two carbodiimide units in the molecule is beset with considerable difficulties, however, even when highly effective phase transfer catalysts are used[11].



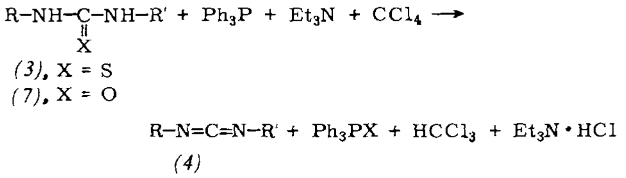
$$\underset{(3)}{\mathrm{R{-}NH{-}\underset{\underset{S}{\|}}{C}{-}NH{-}R'}} + 4\,\mathrm{NaOCl} + 2\,\mathrm{NaOH} \longrightarrow \underset{(4)}{\mathrm{R{-}N{=}C{=}N{-}R'}} + 4\,\mathrm{NaCl} + \mathrm{Na_2SO_4} + 2\,\mathrm{H_2O}$$

*Grigat* and *Pütter*[12] succeeded in obtaining high yields of carbodiimides by reacting aromatic cyanates *(5)* with *N,N'*-substituted thiourea derivatives *(1)*.



$$\underset{(5)}{\mathrm{ArylOCN}} + \underset{(1)}{\mathrm{R{-}NH{-}\underset{\underset{S}{\|}}{C}{-}NH{-}R}} \longrightarrow \left[\mathrm{ArylO{-}\underset{\underset{NH}{\|}}{C}{-}S{-}\underset{\underset{NR}{\|}}{C}{-}NHR}\right] \longrightarrow \underset{(6)}{\mathrm{ArylO\underset{\underset{S}{\|}}{C}{-}NH_2}} + \underset{(2)}{\mathrm{R{-}N{=}C{=}N{-}R}}$$

As discovered by *Appel et al.*[13], the urea derivatives *(3)* and *(7)* can react with $Ph_3P/Et_3N/CCl_4$ to give carbodiimides in yields exceeding 90%.

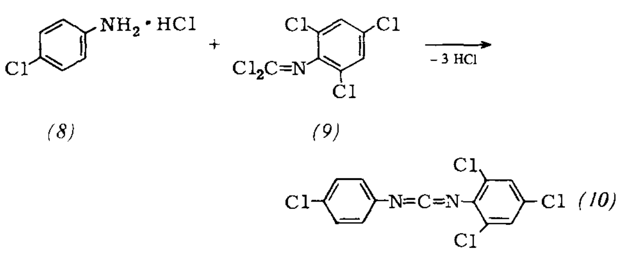


$$\mathrm{R{-}NH{-}\underset{\underset{X}{\|}}{C}{-}NH{-}R'} + \mathrm{Ph_3P} + \mathrm{Et_3N} + \mathrm{CCl_4} \longrightarrow \underset{(4)}{\mathrm{R{-}N{=}C{=}N{-}R'}} + \mathrm{Ph_3PX} + \mathrm{HCCl_3} + \mathrm{Et_3N\cdot HCl}$$

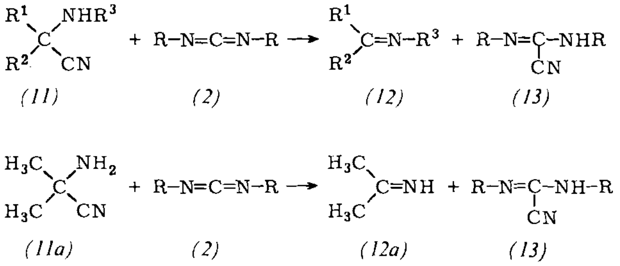
$(3)$, X = S

$(7)$, X = O

One method for the preparation of unsymmetrically substituted carbodiimides, which was subsequently developed by us, is the reaction of isocyanide dichlorides *(9)* with amine hydrochlorides *(8)* in an inert organic solvent[14].



We found that hydrocyanic acid is readily cleaved by aliphatic carbodiimides *(2)* from α-aminonitriles *(11)*[15]. In this way it is possible to obtain the hitherto unknown 2-propanimine *(12a)*, which can be removed by distillation from the simultaneously formed cyanoformamidine derivative *(13)*.



For a variety of reasons, all these methods for the preparation of low-molecular weight carbodiimides were unsuccessful when applied to the synthesis of oligomeric or polymeric polycarbodiimides.

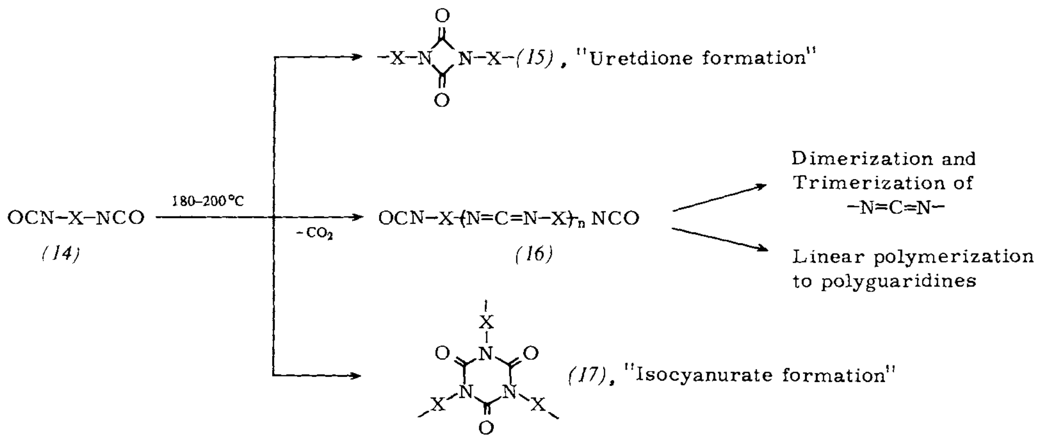
A special study of problems relating to the diisocyanate polyaddition process and an intensive investigation of the side-reactions involved in the preparation of polycarbodiimides from diisocyanates resulted in the development of thermal condensation processes by means of which only low-molecular weight polycarbodiimides with unidentified terminal groups, together with insoluble by-products, were initially obtained.

## 2. Improvements in the Synthesis of Oligomeric α,ω-Diisocyanatocarbodiimides and -Polycarbodiimides

In connection with the diisocyanate polyaddition process, which was devised by *Otto Bayer* in 1937 and subsequently developed by his colleagues[16,17], questions were soon raised about the storage stability of diisocyanatocarbodiimides—questions were even raised concerning their ability to exist at all—as well as about the nature of the side reactions involved in the production of polyisocyanates.

Polyurethane chemistry, the foundations of which were laid by *O. Bayer et al.* more than forty years ago, has since acquired great technical importance throughout the world, polyurethanes now being among the most versatile of plastics. The low-molecular weight and oligomeric building blocks which participate in the diisocyanate polyaddition process form a large group of interesting functional or heterofunctional compounds. *O. Bayer* himself[18] was already interested to ascertain whether isocyanatocarbodiimides could be synthesized and in what manner diisocyanatocarbodiimides, *i.e.* compounds having three cumulative double bond systems in the molecule, can be stabilized by means of cycloaddition processes to form interesting new monomers with heterofunctional groups having different degrees of reactivity. Initially it appeared quite impossible to predict whether a diisocyanate polycondensation process could produce high-molecular weight α,ω-diisocyanatopolycarbodiimides.

It was discovered that monomeric α,ω-diisocyanatocarbodiimides and polymer homologous series of α,ω-diisocyanatopolycarbodiimides could not be formed by thermal condensation of diisocyanates in the presence of highly basic catalysts. The $OH^{\ominus}$-catalyzed reaction leads, *via* the uretedione derivatives *(15)*, to the isocyanurate derivatives *(17)* and to derivatives of *(16)* (Scheme 1).

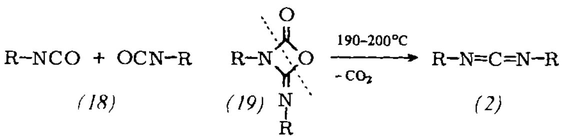


Scheme 1. Side reactions in the production of polyisocyanates; X = aryl, alkyl, or cycloalkyl.

Polyisocyanates are metastable systems having high energy contents; they are only stable and capable of being handled on an industrial scale because the formation of systems *(15)*–*(17)* requires a relatively large amount of activation energy (15–25 kcal/mol[19]).

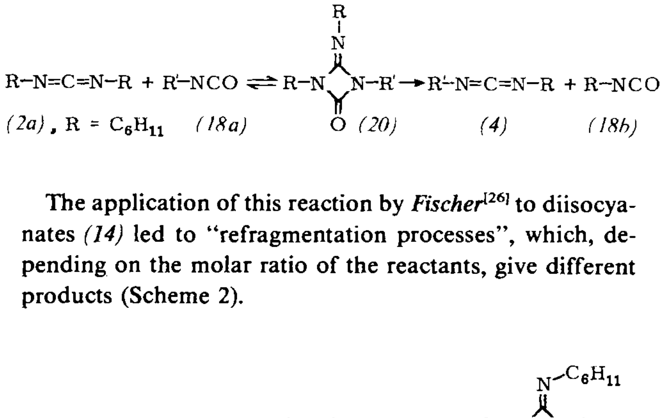
In the absence of diluting agents and in the presence of highly basic catalysts, cross-linked polyisocyanurates (cf. *(17)*) are formed at temperatures between 40 and 210 °C as a result of exothermic reactions which are often violent and in which the NCO groups are trimerized.

One of the best models for the mechanism of purely thermal "high temperature carbodiimidization" was proposed by *Staudinger*[20] in the course of his fundamental work on ketenes[21]. A similar mechanism was postulated independently in 1955 by *Gaylord* and *Snyder*[22]. The symmetrical constitution *(15)* proposed by *Staudinger*[21] for crystalline 1,3-diazetidine-2,4-dione derivatives ("uretediones") was confirmed by X-ray crystallographic analyses performed by *Brown*[23] in 1955. According to *Staudinger*, molten uretediones and liquid monoisocyanates are present, to a small extent, as asymmetrical four-membered ring systems *(19)* at high temperatures; their fragmentation results in the formation of the carbodiimides *(2)*.

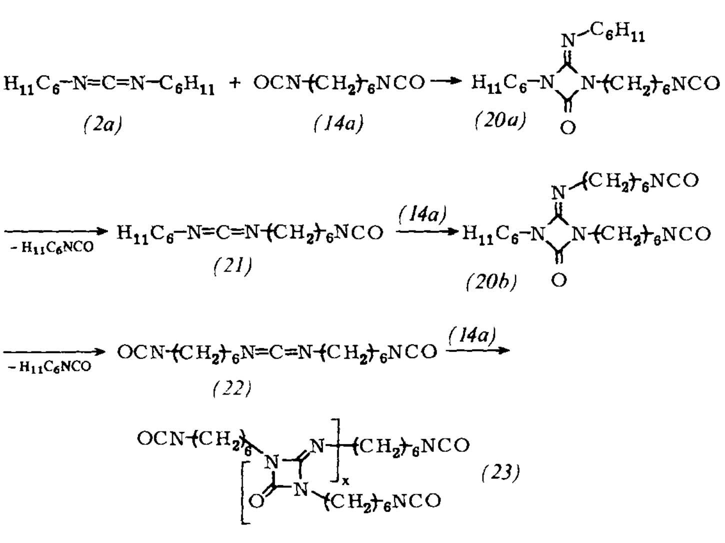


In the course of kinetic investigations we found that the exclusively thermal high-temperature carbodiimidization (at 180–195 °C) of industrially available aliphatic diisocyanates is an extremely slow and entirely unpromising method for the production of low-molecular weight isocyanatocarbodiimides. In the case of hexamethylene diisocyanate, for example, even temperatures of 180–195 °C for 20 h only result in the formation of *ca.* 4–6% of oligomeric isocyanatocarbodiimides. Isocyanatopolyisocyanurates are formed in such reactions, the yield being 18–20%[24].

4-Cyclohexylimino-1,3-diazetidin-2-one-derivatives ("uretonimines") *(20)*, which represent an interesting family of four-membered ring heterocyclic compounds, were first synthesized in the years 1955–1957 by *Hoffmann, Reichle*, and *Moosmüller* in Dormagen, and by *E. Schmidt*[25] in München, from carbodiimides such as *(2a)* and isocyanates such as *(18a)*. *(20)* is formed in an equilibrium reaction which is highly dependent on temperature. This makes it possible[12,13]—when use is made of a mono-isocyanate R′NCO whose boiling point is higher than that of RNCO—for the uretonimine *(20)* to be fragmented in a reversed manner to its formation, provided that RNCO is removed from the reaction mixture by distillation.



The application of this reaction by *Fischer*[26] to diisocyanates *(14)* led to "refragmentation processes", which, depending on the molar ratio of the reactants, give different products (Scheme 2).

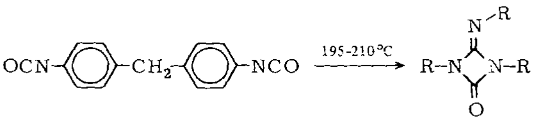


Scheme 2.

The products obtained in this way included polymer-homologous series of uretonimine polyisocyanates *(23)* of hexamethylene diisocyanate *(26)*; they were produced in several addition-elimination steps from *(2a)* and *(14a) via* the uretonimines *(20a)* and *(20b)*, cyclohexyl isocyanate being removed continuously by distillation.

Recent investigations by modern analytical methods, such as gel chromatography, show that, as expected from the laws of *Flory* and *Schultz*, polymolecular mixtures are always obtained. If a large excess of *(14a)* is used the monomeric uretonimine *(23a)*, x = 1, is obtained in the polymer homologous series of the polyuretonimine polyisocyanates at concentrations of up to 60 mol %.

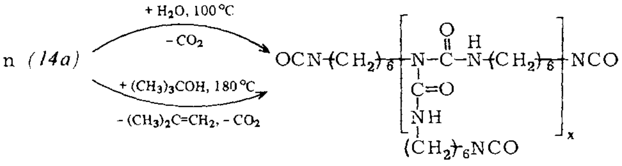
High temperature carbodiimide formation from 4,4′-diisocyanatodiphenylmethane *(14b)* was performed successfully for the first time in 1959, special catalysts being used and solutions of the uretonimine triisocyanate *(24)* being obtained[27,28].



*(14b)* *(24)*, R = $C_6H_4CH_2C_6H_4NCO$

*(24)* is formed in a thermally reversible equilibrium reaction during the cooling phase, through addition of the isocyanate group to the already formed α,ω-diisocyanatocarbodiimide.

Polymer-homologous series of polyisocyanates with the biuret structure *(25)* (Desmodur N, Bayer AG), whose synthesis mechanisms are given in Scheme 3[29–31], are particularly useful non-basic catalysts in the high temperature formation of carbodiimides[28] for the liquefaction of 4,4′-diisocyanatodiphenylmethane.



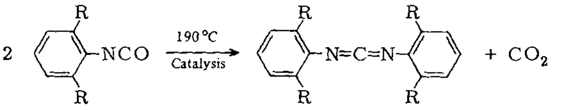
*(25)*, x = 1–6

Scheme 3.

The *in situ* production of the catalysts from aliphatic, cycloaliphatic, or aromatic polyisocyanates can be achieved by adding small amounts of water, *tert*-butyl alcohol, or mono- or diamines.

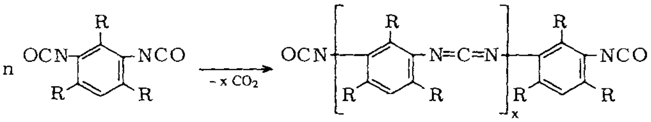
The isocyanatocarbodiimides and polyisocyanatouretonimine synthesized by high temperature carbodiimide formation are, however, contaminated by by-products (isocyanatopolyisocyanourates, isocyanatouretediones), the amounts of which depend largely on the reaction temperature.

Later *Neumann* and *Fischer*[32], using the technique of $OH^{\ominus}$-catalyzed thermal condensation, were also able to synthesize monomeric and oligomeric α,ω-diisocyanatocarbodiimides from mono- and diisocyanates with high degrees of steric hindrance, in a way which excluded side reactions.



*(26)* *(27)*

R = $CH_3$, $C_2H_5$, $CH(CH_3)_2$



*(28)* *(29)*

The bulky isopropyl moieties prevent quantitative formation of uretedione, uretonimine, and polyisocyanurate, as well as the uretonimine cross-linking of the oligomeric diisocyanatopolycarbodiimides formed during the process.

The degrees of polymerization obtainable by this method are, however, low. The oligomeric α,ω-diisocyanatopolycarbodiimides obtained are typical aligomers with mean molecular weights of less than 2000.

A "low temperature polycarbodiimidization" at *ca.* 0—60 °C, in which linear polymers with ten to one hundred —N=C=N-units are obtained, remained impossible until the 1960's.

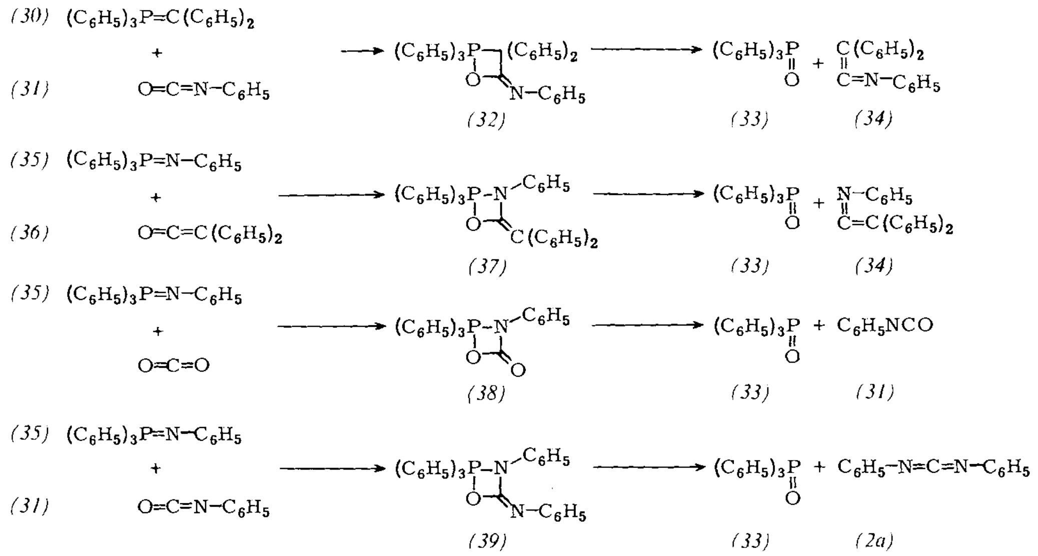
## 3. Catalytic "Low Temperature Carbodiimidization" of Mono- and Polyisocyanates

More than 60 years ago *Staudinger et al.*[33–37] working in Zürich found two important classes of compounds; the substituted phosphorus ylides and the phosphane imides, *e.g.* *(30)* and *(35)* respectively, both of which are characterized by high reactivity towards, *e.g.*, phenyl isocyanate *(31)*.

*(30)* and *(35)* react with reagents containing cumulative double bonds to form four-membered ring heterocyclic compounds (Scheme 4). When heated, these compounds decompose in a manner opposite to that of their formation (a process referred to as "refragmentation"), the decomposition products being the diphenylketenimine derivative *(34)*, the phenyl isocyanate *(31)*, and the diphenylcarbodiimide *(2a)*. Phosphane imides and phosphane oxides play a fundamental part as catalysts in carbodiimidization reactions.

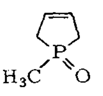
Addition of carbon dioxide to *(35)* to form the heterocyclic compound *(38)* and the fragmentation of the latter to triphenylphosphane oxide and phenyl isocyanate reflect the high energy content of phosphane imide derivatives and the affinity of phosphorus for the oxygen. This is also the key to understanding the four-membered ring mechanism of carbodiimide formation.

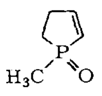
"Low temperature polycarbodiimidization" and the formation of polyuretonimines, starting from diisocyanates, were developed in the years following 1959 after *Campbell et al.*[38,39] of DuPont, and *Schliebs* and *Block* of Bayer had synthesized phospholene oxides, which proved highly active as catalysts for the formation of polycarbodiimides.

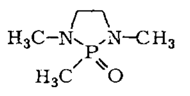


Scheme 4.

*Schliebs* and *Block* optimized the process by which the isomer mixture was obtained from the 1-methyl substituted phospholene oxides *(40)* and *(41)*, a mixture which was

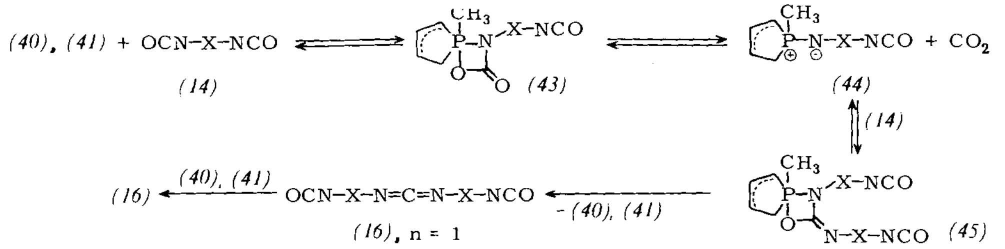

*(40)*


*(41)*


*(42)*

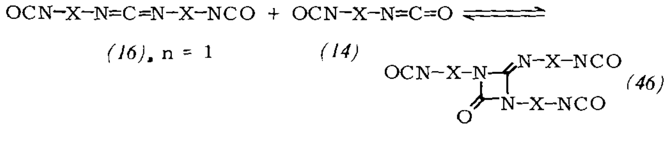
found to be the most effective catalyst of the carbodiimidization in our studies. But the diazophospholidine oxide *(42)*, synthesized by *Däbritz* and *Herlinger*[40], is also an efficient catalyst at temperatures of 60 °C and above.

The mechanism of the polycarbodiimidization, as catalyzed by the mixture of *(40)* and *(41)*, is in accord with the assumptions made by *Staudinger* (Scheme 5).



Scheme 5. Mechanism of formation of polycarbodiimides from diisocyanates. In *(43)*-*(45)* the double bond isomerism is represented by broken lines, X = aryl, alkyl, cycloalkyl.

The isocyanatophosphane imide *(44)*, which is capable of undergoing cycloaddition, is formed just as rapidly as the α,ω-diisocyanatocarbodiimide *(16)*, n = 1, even at temperatures in the vicinity of 0 °C, due to refragmentation.



Repetition of this reaction sequence finally leads to high-molecular weight α,ω-isocyanatopolycarbodiimides.

With aromatic polyisocyanates the polycarbodiimidization with the isomer mixture of the phospholene oxides *(40)*/*(41)* is extremely fast and occurs with continuous elimination of $CO_2$. In the absence of solvents and at a catalyst concentration of about 3% by weight it takes only a few minutes at 20—40 °C. Sterically unhindered aromatic polyisocyanates and oligomeric isocyanate prepolymers react exceptionally rapidly with active phospholene oxides to form polyisocyanatopolycarbodiimides or polyisocyanato(polyurethane)polycarbodiimides. Even when only a few ppm of these catalysts[41] were used we were able to effect the smooth partial carbodiimidization of polyisocyanates. As expected, these carbodiimide isocyanate mixtures undergo changes upon storage. The carbodiimide bands disappear from the IR spectrum, an indication that isocyanatouretonimines such as *(46)* have been formed from the carbodiimides and isocyanates in a thermally reversible equilibrium reaction. The stability of the isocyanatouretonimines in solution is high, and it is possible to deactivate the catalysts adequately with a few ppm of, *e.g.*, anhydrous HCl:

$$(40)/(41) + 2\,HCl \rightleftharpoons [(40)/(41) \cdot 2\,HCl].$$

## 4. Recent Developments

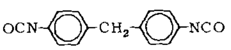
With the advent of highly active phospholene oxide catalysts it become possible for the first time to produce linear, high-molecular weight α,ω-diisocyanatopolycarbodiimides under mild conditions. In this connection we were interested both in the molecular weights obtainable and in the uniformity of the end-groups. Numerous polymer-analogous reactions of high-molecular weight polycarbodiimides appeared to us to be promising, in view of the changes which could be effected in the material properties of the high polymer products. It was also necessary to investigate problems connected with the homogeneous and heterogeneous catalyization. In view of the exceptionally rapid polycarbodiimidization of solventless aromatic polyisocyanates or of highly concentrated solutions of these compounds, we decided to initiate the polycarbodiimide formation in flexible polyurethane foams impregnated with, and swelled by, aromatic polyisocyanates, *i. e.* to perform it as a series of matrix reactions on interconnecting cell walls solvated with polyisocyanates.

## 5. Rates of Formation of α,ω-Diisocyanatopolycarbodiimides

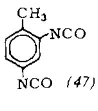
The α,ω-diisocyanatocarbodiimidization and -polycarbodiimidization from 4,4′-diisocyanatodiphenylmethane *(14b)* and 2,4-diisocyanato-1-methylbenzene *(47)* in toluene occur rapidly at temperatures of 5—40 °C (Fig. 1).

$OCN\text{-}(CH_2)_6\text{-}NCO$

*(14a)*



*(14b)*



*(47)*

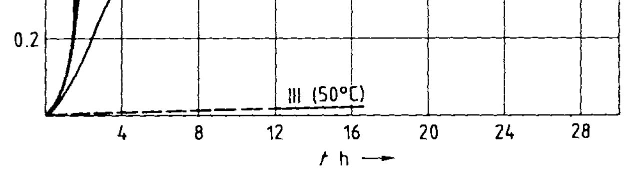


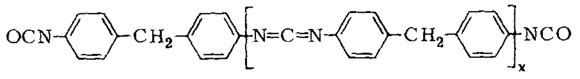
Fig. 1. Carbodiimide formation from *(14b)* (I), *(47)* (II), and *(14a)* (III); *(14b)* and *(47)* were used as 18% solutions in toluene, and *(14a)* as pure substance. The carbodiimide equivalents (calculated from the amount of $CO_2$ released) are plotted as a function of time.

Although we are concerned here with a sterically hindered diisocyanate, the high rate of condensation of *(47)*, both at 40 °C and at 5 °C, and the small differences between the half-lives are remarkable.

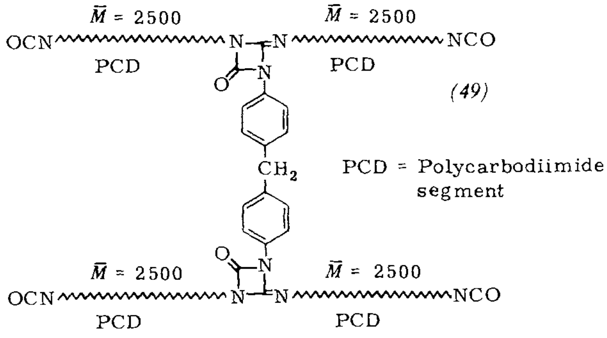
The curve plotted for hexamethylene diisocyanate *(14a)* (III) does not correspond to the actual progress of carbodiimide formation; liberated $CO_2$ reacts immediately, without evaporating, with polar resonance forms of dimeric isocyanatocarbodiimides and of the dimeric hexamethylene diisocyanate even at room temperature (cf. Section 9).

## 6. Linearity of High-Molecular Weight and Oligomeric α,ω-Diisocyanatopolycarbodiimides

In the early part of our investigations we were concerned with discovering whether the powdery polycarbodiimides from 4,4′-diisocyanatodiphenylmethane *(14b)*, which apparently have very high-molecular weights, contained isocyanate end-groups or small amounts of branching and cross-linking sites (uretonimine segments as in *(49)*, and cross-linking isocyanourate or triazine structures, which could have been formed from trimerized carbodiimide units). Since these species are insoluble in all solvents it was at first impossible to determine the average molecular weight. Free NCO groups (1.1—1.4% NCO) were identified using special titration methods. IR spectroscopic data was inconclusive. The oxygen content of 0.4—0.6% found in the elemental analysis was consistent with polymers of the structure shown in *(48)* and *(49)*.



*(48)*, x = 25-27



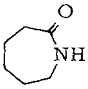
*(49)*

PCD = Polycarbodiimide segment

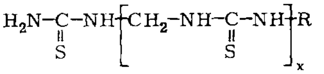
From the NCO content found in the end-group analysis, and from the relations between this content and the amount of $CO_2$ liberated in the polycarbodiimidization, and the oxygen content (high-molecular weight polycarbodiimides with $\bar{M}=25000$ contain only *ca.* 0.13% of oxygen), it was concluded that thermally stable isocyanurate structures could hardly be present in the powdery polycarbodiimides. But the presence of small amounts of cross-linking uretonimine segments could not be excluded.

Thus the highest attainable molecular weights of the white, insoluble polycarbodiimide powders from *(14b)* could only be determined by the classical methods which *Staudinger* had used to investigate the constitution of the polyoxymethylenes. In this connection we were helped by discoveries concerning insoluble polymethylenethioureas which had been made in the 1950's[42,43].

At 80 °C, ε-caprolactam *(50)* is a liquid of low viscosity which readily dissolves polymethylenethioureas of the type *(51)* and *(52)*, which had long been considered to be cross-linked and insoluble.

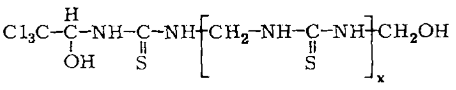


(50), m. p. = 70 °C



$$\mathrm{H_2N{-}\underset{\underset{S}{\|}}{C}{-}NH\left[CH_2{-}NH{-}\underset{\underset{S}{\|}}{C}{-}NH\right]_x R}$$

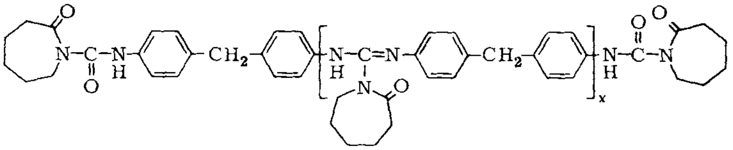
(51), R = H, CH₂OH, x = 4-12



$$\mathrm{Cl_3C{-}\underset{\underset{OH}{|}}{\overset{H}{C}}{-}NH{-}\underset{\underset{S}{\|}}{C}{-}NH\left[CH_2{-}NH{-}\underset{\underset{S}{\|}}{C}{-}NH\right]_x CH_2OH}$$

(52)

Surprisingly, we found that not only is ε-caprolactam an excellent solvent for the otherwise insoluble high-molecular weight polycarbodiimides of *(14b)*, but also that when it is heated to 120 °C (without polymerization of ε-caprolactam), the lactam in the molten material rapidly adds quantitatively to all the carbodiimide groups and to the isocyanato end-groups of the polymer molecule[44]. In the resulting polymers *(53)* the covalently bound lactam content leads to a dramatic increase (from about 0.6 to 5.7%) in the oxygen content of the powdery final product. The polyaddition product *(53)* melts at 210—214 °C, *i. e.* at a temperature *ca.* 70 °C lower than the melting point of the polycarbodiimide. The lactam ring (acylated guanidine segment), which functions as a spacer in the polymer, now renders the polyaddition product soluble in dimethylformamide or *N*-methylpyrrolidone. In this polymer-analogous conversion, chain cross-linking uretonimine segments are quantitatively eliminated by linearization reactions with ε-caprolactam. The linearized polymers can be isolated by precipitation in acetone. Very little uretonimine cross-linking takes place in carbodiimidization at room temperature, *i. e.* about 6000 segment units, at the most, are formed *per* uretonimine segment. According to *Hoffmann* and *Krömer*[45], the polymers treated with ε-caprolactam have a fairly broad molecular weight distribution and a mean molecular weight of *ca.* 11 000. The highest obtainable molecular weights of powdery α,ω-diisocyanatopolycarbodiimides of *(14b)*, with the idealized constitution respresented in *(48)*, $\bar{x}=30$, are never exceed 6000—7000. The increase in the average molecular weight to 10 000—11 000 in the reaction with ε-caprolactam is in good accord with the oxygen content.



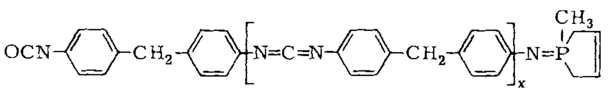
(53), x = 30

Our results on powdery polycarbodiimides can be summarized as follows. The end-groups of these polycarbodiimides are mainly α,ω-NCO groups; but the highest obtainable average molecular weights of the polycarbodiimides, which plastisize at 270 °C, are less than 6000 to 7000. The limiting factors to chain growth ("molecular weight barrier") in many of these compounds are the solvents in which they are synthesized because the solubility limits of the polymers are reached. Even after long reaction times (*e.g.* 40 h at 100—140 °C) the polymers undergo no more chain growth due to topochemical reactions of their end-groups.

## 7. Molecular Weight Jumps in the Melting of High-Molecular Weight α,ω-Diisocyanatopolycarbodiimides

At a temperature of about 180-270 °C the polycarbodiimides described in Section 6 undergo changes which are attributable to the presence of phosphane imide end-groups as impurities in the polymers[44]; structures like *(54)* (where only one phospholene isomer is represented) being present. In the processing of α,ω-diisocyanatopolycarbodiimides as thermoplastics at 270 °C, these polymeric impurities act as catalysts for the molecular weight multiplication. The polycarbodiimide/phopshane imide derivatives with relatively high molecular weights generally have an NCO-content of 1.3%, a P-content of *ca.* 0.05%, and an O-content of *ca.* 0.6%.

The phosphane imide end-groups cause pronounced molecular weight jumps when the powdery polycarbodiimides melt at 240—270 °C, in accord with the mechanism of carbodiimide formation shown in Scheme 5. The processing of these materials to transparent thermally stable linear polymers, *e.g.* as plastics and fibers is difficult because the flowability of these systems decreases continuously, while the softening points rise dramatically; not only do the chain lengths increase, but the materials also undergo cross-linking.



(54), x = 30

At high temperatures, the pronounced polymerization tendencies of the accumulated carbodiimide segments in these powdery polycarbodiimides lead to branching and cross-linking. Transparent molded sheets produced at 270 °C and 250 bar have considerably greater high-temperature bending strength than polycarbonates, but because they have high cross-link densities they have less notched impact strength.

The assumption that cross-linking reactions take place is supported by the fact that polycarbodiimide powders which are molded at 300 °C are no longer soluble in, but are merely swelled by ε-caprolactam. Addition of caprolactam to unpolymerized carbodiimide units is then very difficult.

Thus, the processing of linear α,ω-diisocyanatopolycarbodiimides with average molecular weights of 4000—8000 to produce thermoplastics with the typical characteristics of linear macromolecular materials, *e.g.* with average molecular weights of 20 000—40 000, high degrees of hardness, the ability to cobweb in the molten state, and low brittleness, is prevented by cross-linking polymerization of the numerous carbodiimide groups of the polymer at high temperatures.

The experience gained in connection with polymer-analogous reactions involving ε-caprolactam led us to prepare other polycarbodiimides and mixed condensates with particularly high degrees of thermal stability, *e.g.* mixed condensates from *p*-phenylene diisocyanate and 1,5-naphthylene diisocyanate with softening points of approximately 300 °C. The average molecular weights of these α,ω-diisocyanato mixed polycarbodiimides are very greatly reduced because polymers with three to six carbodiimide units reach their solubility limits in inert solvents, with the result that they do not undergo further condensation. In contrast, ternary mixed carbodiimides from 2,4-diisocyanato-1-methylbenzene *(47)* and the aforementioned aromatic diisocyanates in the ratio 1 : 1 : 1 can acquire average molecular weights of up to *ca.* 3500.

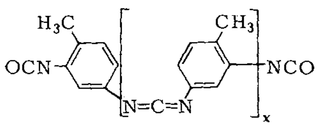
α,ω-Diisocyanato mixed polycarbodiimides can be made elastic with α,ω-diisocyanato polyether—or polyester—urethanes (NCO-prepolymers) and their softening points can be greatly reduced. In aromatic solvent mixtures and isopropanol the chains of polymers containing α,ω-diisocyanatopolyurethane or polyurea groups and having three to four carbodiimide units can be extended with sterically hindered diamines without premature addition of the diamines to the carbodiimide groups, with the result that useful film-forming agents of high-molecular weight are obtained[46].

## 8. Condensation and Polycondensation of 2,4-Diisocyanato-1-methylbenzene in Toluene or Hexane/Petroleum Ether

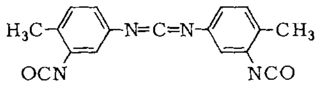
Polymer-homologous compounds of oligomeric α,ω-diisocyanatopolycarbodiimides from 2,4-diisocyanato-1-methylbenzene *(47)*, which are formed at room temperature using phospholene oxides as catalysts, are readily soluble in many chlorinated and aromatic hydrocarbons because of the considerable reduction in mutual association of the chain molecules within certain molecular weight limits. We were also able to show that in such cases the molecular weight is controlled by the solvent. The highest obtainable molecular weight compatible with linearity, which is less than 8000, was determined as described in Section 6; the polymers may be considered to have the constitution given in *(55)*. Using such precipitating agents as cyclohexane and petroleum ether/hexane, we were able to prepare a homologous series of carbodiimides from *(47)*, beginning with the bis(3-isocyanato-4-methylphenyl)carbodiimide *(56)*, using the techniques of fractionating condensation and polycondensation.

These compounds and their addition products to polyethers or polyesters with terminal hydroxy groups, *i.e.* their NCO-containing prepolymers, are useful building blocks in the diisocyanate polyaddition process.

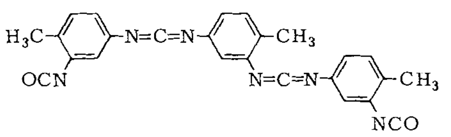
Despite their molecular non-uniformity these polymers are strictly bifunctional; they can be added to all the components used in the diisocyanate polyaddition process by means of selective NCO reactions. Since these powdery products contain 200—400 ppm of phosphane imide end-groups, *i.e.* highly active catalysts, it is necessary to stabilize them with a few ppm of HCl, $BF_3$, or benzoyl chloride.



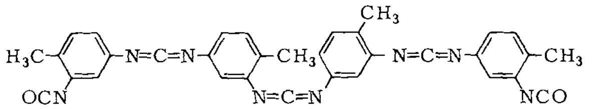
*(55)*



*(56)*, $M$ = 304, % NCO = 27.7



*(57)*, $M$ = 434, % NCO = 19.3



*(58)*, $M$ = 564, % NCO = 14.9

Because the α,ω-diisocyanatocarbodiimides *(56)—(58)* are adequately to freely soluble in many solvents, they have been used for a large number of polymer-analogous reactions[47—52].

These reactions give many interesting polyaddition products with polyurea-, polyisourea-, polyisothiourea-, polyformamidine-, polyacylurea-, polyguanidine-, polyphosphonoformamidine-, and polycyanoformamidine-segments (Table 1).

In this way—through the use of ppm amounts of bases—even such carboxylic acids as acrylic acid and methacrylic acid can readily be added (e in Table 1), without substantial anhydride formation; the polyaddition products obtained being easily polymerizable. Route i in Table 1 leads to *N*-alkoxysilylmethyl-*N*-alkylamino-substituted polyguanidines, which are among the most reactive of those polyaddition products which cross-link *via* siloxane bridges in the presence of atmospheric moisture.

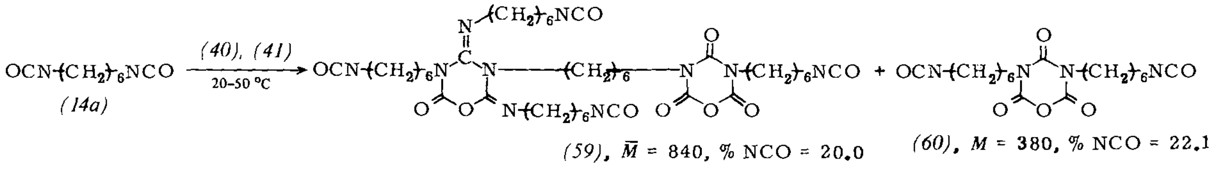
## 9. Possible Errors in the Interpretation of the Reaction Curve for Low-Temperature Polycarbodiimidization of Hexamethylene Diisocyanate

Whereas, we originally thought that only aromatic diisocyanates react at room temperature to form carbodiimides, we later discovered using hexamethylene diisocyanate *(14a)* that this assumption was based on the incorrect interpretation of the respectively determined $CO_2$ balances[53]. Since $CO_2$ was not formed in the phospholene oxide catalyzed reaction of *(14a)* at room temperature, and the characteristic carbodiimide and uretonimine bands were not present in the IR spectra, condensation had not occurred. From the results of NCO-titrations performed at definite time intervals, gel chromatography, and IR spectroscopic investigations of the reaction products, it is clear that ure-

Table 1. Polymer-analogues reactions on oligomeric and high-molecular polycarbodiimides.

| | Educts | | Polyaddition products | |
|---|---|---|---|---|
| a) | $-X\!\left(N{=}C{=}N{-}X\right)_x + H_2O$ | → | $-X\!\left[\overset{H}{N}-\underset{\underset{O}{\Vert}}{C}-\overset{H}{N}-X\right]_x$ | polyurea segments |
| b) | $-X\!\left(N{=}C{=}N{-}X\right)_x + R{-}OH$ | → | $-X\!\left[NH-\underset{\underset{OR}{\vert}}{C}{=}N-X\right]_x$ | polyisourea segments |
| c) | $-X\!\left(N{=}C{=}N{-}X\right)_x + R{-}SH$ | → | $-X\!\left[NH-\underset{\underset{SR}{\vert}}{C}{=}N-X\right]_x$ | polyformamidine segments |
| d) | $-X\!\left(N{=}C{=}N{-}X\right)_x + CH_2\begin{matrix}\diagup Z\\ \diagdown Y\end{matrix}$<br>$Z{=}COOC_2H_5,\ COCH_3;$<br>$Y{=}COOC_2H_5$ | → | $-X\!\left[NH-\underset{\underset{\underset{X\diagup\quad\diagdown Y}{CH}}{\vert}}{C}{=}N-X\right]_x$ | polyisothiourea segments |
| e) | $-X\!\left(N{=}C{=}N{-}X\right)_x + R'{-}COOH$ | → | $-X\!\left[NH-\underset{\underset{O\underset{\underset{O}{\Vert}}{C}-R'}{\vert}}{C}{=}N-X\right]_x$ | → |
| | | | $-X\!\left[NH-\underset{\underset{O}{\Vert}}{C}-\underset{\underset{\underset{\underset{O}{\Vert}}{C}-R'}{\vert}}{N}-X\right]_x$ | polyacylurea segments |
| f) | $-X\!\left(N{=}C{=}N{-}X\right)_x + R{-}NH_2$<br>R = prim. and sec. alkyl | → | $-X\!\left[NH-\underset{\underset{\underset{\underset{R}{\vert}}{NH}}{\vert}}{C}{=}N-X\right]_x$ | polyguanidine segmentes |
| g) | $-X\!\left(N{=}C{=}N{-}X\right)_x + H{-}\overset{\overset{O\ \ OR}{\Vert\diagup}}{P}\diagdown OR$ | → | $-X\!\left[NH-\underset{\underset{O{=}P\left(OR\right)_2}{\vert}}{C}{=}N-X\right]_x$ | polyphosphonoformamidine segments |
| h) | $-X\!\left(N{=}C{=}N{-}X\right)_x + HCN$ | → | $-X\!\left[NH-\underset{\underset{CN}{\vert}}{C}{=}N-X\right]_x$ | polycyanoformamidine segments |
| i) | $-X\!\left(N{=}C{=}N{-}X\right)_x + H_{11}C_6{-}\underset{H}{N}{-}CH_2{-}Si(OEt)_3$<br>or<br>$H_{11}C_6{-}\underset{H}{N}{-}CH_2{-}Si(OEt)_2$ | → | $-X\!\left[NH-\underset{\underset{\underset{H_{11}C_6\diagup\quad\diagdown C_2-Si(OEt)_3}{N}}{\vert}}{C}{=}N-X\right]_x$ | poly-*N*-alkoxysilylmethyl-*N*-alkyl-amino-substituted guanidine segments |
| | | | $-X\!\left[NH-\underset{\underset{\underset{H_{11}C_6\diagup\quad\diagdown CH_2-\overset{\overset{CH_3}{\vert}}{Si}(OEt)_2}{N}}{\vert}}{C}{=}N-X\right]_x$ | |

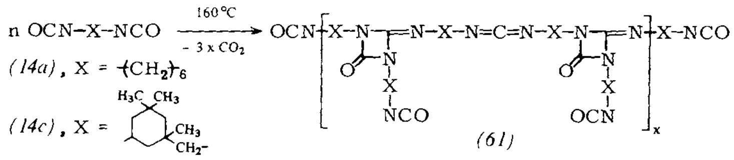
tonimine or carbodiimide units are not found even at room temperature, because the $CO_2$ produced cycloadds immediately after its formation to dimeric, polar intermediates of biscarbodiimides and diisocyanates, leading to compounds with the idealized constitutions given in *(59)* and *(60)*.



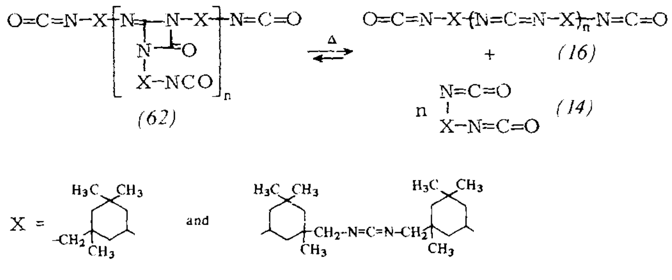
*(59)*, $\bar{M}$ = 840, % NCO = 20.0 *(60)*, *M* = 380, % NCO = 22.1

At temperatures up to 80 °C phospholene oxide derivatives are therefore not selective catalysts of the carbodiimidization; instead they catalyze the oxadiazinetrione ring formation and also the trimerization, thus behaving like phosphane derivatives. The curve reproduced in Figure 1 is therefore misleading with respect to the rate of carbodiimide formation of hexamethylene diisocyanate.

At 150—160 °C, however, even aliphatic polyisocyanates, such as *(14a)* and 3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate *(14c)* (isophorone diisocyanate) react in the presence of phospholene oxide derivatives to form mainly polycarbodiimides *(61)* with the polycarbodiimide-polyuretonimine structure. Provided that a large excess of monomeric diisocyanate is avoided, these polymers participate in the formation of three-dimensional cross-links, accompanied by uretoneimine formation as



the temperature falls, but, however, readily form polyisocyanates again if the temperature is raised. These systems represent masked polyisocyanates which can be used together with polymerization, polyaddition, and polycondensation products containing Zerewitinoff-active hydrogen for many cross-linking reactions at elevated temperatures[54]. The advantage of these compounds, especially of polycarbodiimide-polyuretonimines from *(14c)* is that volatile decomposition products, which do not participate in the cross-linking, are not formed.



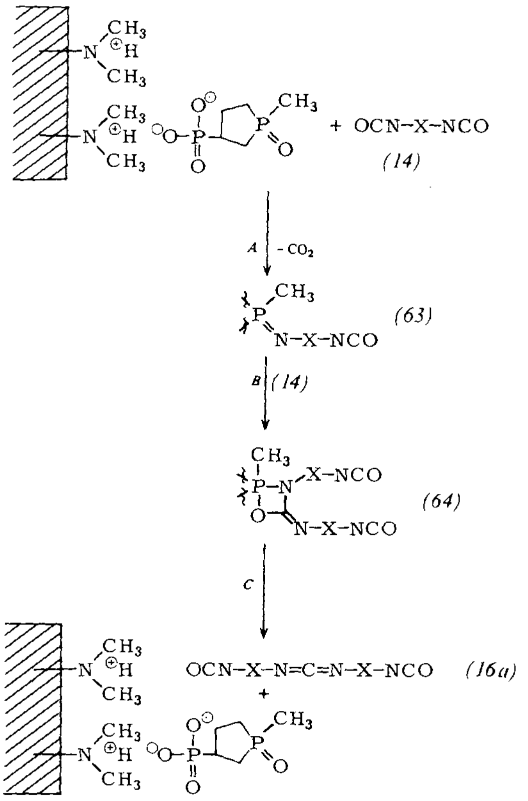
## 10. Heterogeneously Catalyzed NCO Condensations Leading to Oligomeric Isocyanatopolycarbodiimides in Swellable Matrices

With the aid of special phospholene oxide derivatives ionogenically or covalently bound to insoluble but swellable matrices, we investigated whether swellable catalysts are effective in the heteregeneous catalysis of polycarbodiimide formation and how the reaction depends on temperature[55–59]. The high-molecular weight matrix shown in Scheme 6 can be produced by salification of commerical basic ion-exchange resins with phosphonic acid derivatives of the phospholene oxides. Using this matrix those polyisocyanates, which among oligomeric technical polyisocyanates have the lowest molecular weights, can be converted without participation of trifunctional and tetrafunctional polyisocyanates of high molecular weight into isocyanatocarbodiimides provided that they reach the catalytically active anchor group in the matrix. Temperatures of 130 to 165 °C are needed for this purpose.

In the reaction step *C*, the diisocyanatocarbodiimide formed is released from the matrix and hence the high-molecular catalyst is again fully effective.

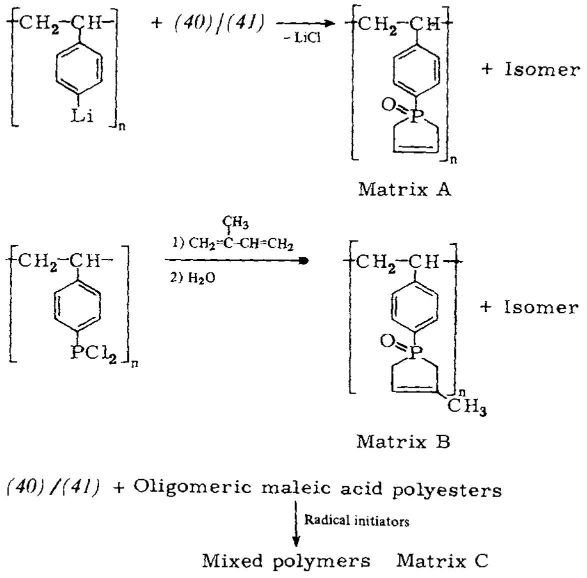
If the process is properly controlled, the oligomeric polyisocyanatocarbodiimides and polyisocyanatouretonimines obtained are completely free of phosphane imide end-groups and can, therefore, be stored.

The use of pore diameters of *ca.* 100—200 Å for the matrices and adjustable porosity, permit the selective formation of the lowest molecular weight polyisocyanatocarbodiimides. Thus, heterogeneous catalysis enables derivatives of polyisocyanate mixtures which are free of phosphane imide end-groups to be produced without loss of catalyst. Another considerable advantage to the process is that the solid catalysts can be removed from the reaction mixture at any time, and can be used again if proper care is taken.



Scheme 6.

Phospholene oxide moieties bound covalently to matrices with pores of 100—200 Å are also catalytically active. They can be produced in the ways indicated in Scheme 7, and also permit the selective formation of polyisocyanatocarbodiimides of low-molecular weight.



Scheme 7.

## 11. High-Molecular Weight Polycarbodiimides and Polyuretonimines in Swellable, Impregnated Flexible Polyurethane Foams

A review article published almost ten years ago[60] reported on growth processes caused by reactions in swellable, cellular matrices and described a universally valid cell arrangement principle which can be applied to any desired organic, cellular substrate and can be effected by any type of organic or inorganic chemical reaction, provided that the reactants exert a sufficient swelling action on the matrices employed. The physical swelling pressure and its irreversible fixation by cellular solid formation were recognized as the driving forces responsible for the observed growth phenomena[61-66].

Results gained so far, indicate that matrix reactions are potentially useful when reactive swelling agents with high energy contents are employed. The essential condition for rapid and irreversible fixation of the state of swelling is that the swelling agents must be able to react very rapidly to form solids in the absence of solvents. For example, since they have high energy contents, flexible polyurethane foam matrices swollen with liquid polyisocyanates, but when previously charged with catalytical amounts of phospholene oxides, need no further energy input to be converted from the cellular, swollen state into a cellular, three-dimensional, and entirely symmetrical solid because of rapid polycarbodiimide formation.

This process gives interesting open-celled, carbonized combination-rigid foams, which show enhanced flame resistance. The interconnecting cell walls of the matrix are considerably stretched by the cellular solid arrangement of the high-molecular weight polycarbodiimides and these forms are fixed irreversibly. It is not until the elongations have acquired the maximum, irreversible degree of fixation that the surfaces of the interconnecting cell walls become—to an increasing extent—the site of the reaction.

A cellular solid arrangement of polyisocyanatopolycarbodiimides arises when the polyurethane matrix is charged with phospholene oxides and then impregnated with any, although preferably aromatic, polyisocyanates and oligomeric and elastifying isocyanate prepolymers of hydroxy-terminated polyethers or polyesters; in this way it is possible to produce rigid or semi-rigid combination-foams whose cells are entirely open and which have carbonization properties and enhanced flame resistance.

## 12. Industrial Applications of Polycarbodiimides, α,ω-Diisocyanatomono-, -Polycarbodiimides, and their Derivatives, and of Polyuretonimines

Through the use of special associates prepared from phospholene oxides and monoalcohols or polyalcohols[67] it has been possible to overcome all the technical difficulties involved in the production of highly cross-linked polycarbodiimide foams with extremely low densities, good high-temperature bending strength, and high degrees of flame resistance. For this purpose it was necessary to specifically increase the stirring, waiting, and rising times of the systems, together with sufficiently short setting times, by systematic variation of the catalyst associates.

The industrial applications of isocyanatocarbodiimides, polycarbodiimides, and uretonimines cover a wide range. This includes anti-hydrolysis agents for polyester-polyurethane plastics and chain extending and cross-linking agents for the diisocyanate polyaddition process. Many of the isocyanato polymers and derivatives described above are interesting diisocyanate liquefiers, reactive fillers, light-fast raw materials for electrostatic powder spraying processes[54], pigment binders, thixotropic agents, starting materials for the manufacture of film[46], coatings[47], or micro-encapsulation devices[68,69], as well as for catalysts used in isocyanate chemistry.

## 13. Conclusion

The chemistry of isocyanates is characterized by the enormous variety of the building blocks that can be used for polyaddition; it can be combined with ring cleavage polymerization and copolymerization processes, and with grafting reactions involving a very wide range of vinyl monomers. In addition, the formation of polycarbodiimides and mixed polycarbodiimides provides a variable polycondensation structural principle; a characteristic of this type of polycondensation is its high rate relative to that of familiar polycondensation processes.

The possibilities of simple *in situ* production of α,ω-isocyanatopolycarbodiimides in monomeric vinyl compounds, together with the ease with which the polymerizable acrylic or methacrylic acid can be added to carbodiimide groups[70,71] to form acylated urea segments, makes interesting polymerizable and graftable polymer combinations feasible.

Owing to the great variability of the diisocyanate polyaddition and diisocyanate polycondensation processes used to produce polycarbodiimides, together with the opportunities for combining these processes with methods involving polymer-analogous reactions on polycarbodiimides, ring cleavage polymerization, copolymerization processes, and with grafting reactions involving many vinyl monomers, solutions to problems encountered in numerous industrially interesting fields of macromolecular chemistry, especially those of polymer blends and multiphase plastics, may be expected.

*We wish to thank Professor K. Büchel, Professor W. Swodenk, and Dr. H. Rudolph for the help and encouragement they have given us. We also wish to thank Drs. G. Baatz, H.-D. Block, W. von Bonin, E. de Cleur, E. Däbritz, M. Dahm, R. Dhein, U. von Gizycki, E. Grigat, P. Fischer, H. Heitzer, H.-J. Hennig, R. Holm, H.-J. Kreuder, La Spina, D. Liebsch, F. Meisert, H.-J. Müller, P. Müller, U. Nehen, W. Oberkirch, G. Oertel, L. Preis, and R. Schliebs, the members of the Anwendungstechnische and Produktionsabteilungen der Polyurethan- and AC-Sparte, the Analytische and Polymerphysikalische Abteilungen des Zentralbereichs Forschung and Entwicklung and the Zentralbereich*

*Patente, Marken and Lizenzen of Bayer AG for close interdisciplinary cooperation.*

Received: February 2, 1981
German version: Angew. Chem. *93*, 585 (1981)

---

[1] *W. Weith*, Chem. Ber. *6*, 1395 (1873).
[2] *H. G. Khorana*, Chem. Rev. *53*, 145 (1953); cf. also *M. Mikolajczyk, P. Kielbasinski*, Tetrahedron *37*, 233 (1981) and *F. Kurzer, K. Douraghi-Zadeh*, Chem. Rev. *67*, 107 (1967).
[3] *J. C. Sheehan, G. P. Hess*, J. Am. Chem. Soc. *77*, 1067 (1955).
[4] *R. B. Merrifield*, J. Am. Chem. Soc. *85*, 2149 (1963).
[5] *E. Schmidt, F. Hitzler, E. Lahde*, Chem. Ber. *71*, 1933 (1938).
[6] *E. Schmidt, M. Seefelder et al.*, Justus Liebigs Ann. Chem. *571*, 83 (1951).
[7] *E. Schmidt, W. Striewsky*, Chem. Ber. *73*, 286 (1940).
[8] *E. Schmidt, W. Striewsky*, Chem. Ber. *74*, 1285 (1941).
[9] *E. Schmidt, W. Striewsky, F. Hitzler et al.*, Justus Liebigs Ann. Chem. *560*, 222 (1948).
[10] *E. Schmidt, W. Striewsky, M. Seefelder, F. Hitzler et al.*, Justus Liebigs Ann. Chem. *568*, 192 (1950).
[11] *K. Wagner*, Bayer AG, unpublished results.
[12] *E. Grigat, R. Pütter*, Chem. Ber. *98*, 1168 (1965).
[13] *R. Appel, R. Kleinstück, K. D. Ziehn*, Chem. Ber. *104*, 1335 (1971).
[14] *E. Kühle*, DBP 1149712 (1963), Bayer AG.
[15] *K. Findeisen*, DOS 2714770 (1977), Bayer AG.
[16] *O. Bayer*, DRP 728981 (1937).
[17] *O. Bayer*, Angew. Chem. *59*, 267 (1947).
[18] *O. Bayer*, Bayer AG, unpublished results.
[19] *G. Pfisterer*, Bayer AG, unpublished results; cf. also *A. Davis*, Makromol. Chem. *66*, 196 (1963) and *R. E. Buckles, L. A. McGrew*, J. Am. Chem. Soc. *88*, 3582 (1966).
[20] *H. Staudinger*, unpublished results, 1921.
[21] *H. Staudinger:* Die Ketene, Enke-Verlag, Stuttgart 1912.
[22] *G. Gaylord, J. A. Snyder*, Chem. Ind. London *1955*, 145.
[23] *C. J. Brown*, J. Chem. Soc. *1955*, 2931.
[24] *K. Wagner*, Bayer AG, unpublished results.
[25] *R. Hofmann, E. Schmidt, A. Reichle, F. Moosmüller*, DBP 1012601 (1955/1957).
[26] *P. Fischer*, DBP 1122057 (1960/1962), Bayer AG.
[27] *P. Fischer, E. Meisert*, DBP 1092007 (1959/1960), Bayer AG.
[28] *H.-J. Hennig, P. Fischer*, EP 1200432 (1969), Bayer AG.
[29] *K. Wagner*, Angew. Chem. *74*, 799 (1962).
[30] *K. Wagner*, DBP 1101394 (1958), Bayer AG.
[31] *J. W. Britain*, DBP 1543178 (1965), Mobay.
[32] *W. Neumann, P. Fischer*, Angew. Chem. *74*, 801 (1962); Angew. Chem. Int. Ed. Engl. *1*, 621 (1962).
[33] *H. Staudinger, J. Meyer*, Helv. Chim. Acta *2*, 612 (1919).
[34] *H. Staudinger, J. Meyer*, Helv. Chim. Acta *2*, 619 (1919).
[35] *H. Staudinger, J. Meyer*, Helv. Chim. Acta *2*, 635 (1919).
[36] *H. Staudinger, E. Hauser*, Helv. Chim. Acta *4*, 861 (1921).
[37] *H. Staudinger, E. Hauser*, Helv. Chim. Acta *4*, 887 (1921).
[38] *T. W. Campbell, J. J. Verbanc*, US-Pat. 2853473 (1956/1958), DuPont.
[39] *T. W. Campbell*, US-Pat. 2941966 (1956/1960), DuPont; *K. C. Smeltz*, US-Pat. 2941983 (1957/1960), DuPont; siehe auch *T. W. Campbell*, Angew. Chem. *74*, 127 (1962).
[40] *E. Däbritz, H. Herlinger*, F 45356 (1965), Bayer AG.
[41] *K. Findeisen, K. Wagner, W. Schäfer, H.-J. Hennig*, DOS 2537685 (1977), Bayer AG.
[42] *H. Staudinger, K. Wagner*, Makromol. Chem. *12*, 168 (1954).
[43] *H. Staudinger, K. Wagner*, Makromol. Chem. *12*, 181 (1954).
[44] *K. Wagner, K. Findeisen, W. Schäfer, W. Dietrich*, Bayer AG, Tagungsheft des Makromol. Kolloquiums, Freiburg, March 1980.
[45] *M. Hoffmann, H. Krömer*, Bayer AG, unpublished results.
[46] *W. Schäfer, K. Wagner, H.-J. Müller*, DOS 2436740 (1974), Bayer AG.
[47] *W. Schäfer, K. Wagner*, DOS 2436741 (1974), Bayer AG.
[48] *W. Schäfer, K. Wagner, K. Findeisen*, DOS 2504334 (1975), Bayer AG.
[49] *W. Schäfer, K. Wagner, K. Findeisen*, DOS 2714289 (1977), Bayer AG.
[50] *W. Schäfer, K. Wagner, K. Findeisen*, DOS 2714292 (1977), Bayer AG.
[51] *W. Schäfer, K. Wagner, K. Findeisen*, DOS 2714293 (1977), Bayer AG.
[52] *W. Schäfer, K. Wagner, K. Findeisen*, DOS 2941253 (1979), Bayer AG.
[53] *K. Wagner, W. Schäfer, G. Baatz*, Bayer AG, unpublished results.
[54] *E. de Cleur, R. Dhein, H. Rudolph, H.-J. Kreuder, P. Müller, W. Schäfer, K. Wagner, K. Findeisen*, DOS 2819827 (1978), Bayer AG.
[55] *K. Wagner, H.-D. Block, W. Schäfer*, DOS 2504331 (1975), Bayer AG.
[56] *K. Wagner, H.-D. Block, W. Schäfer*, DOS 2504334 (1975), Bayer AG.
[57] *K. Wagner, H.-D. Block, W. Schäfer*, DOS 2504400 (1975), Bayer AG.
[58] *W. Schäfer, K. Wagner, H.-D. Block*, DOS 2552340 (1975), Bayer AG.
[59] *W. Schäfer, K. Wagner, H.-D. Block*, DOS 2552350 (1975), Bayer AG.
[60] *K. Wagner, M. Dahm*, Angew. Chem. *84*, 1001 (1972); Angew. Chem. Int. Ed. Engl. *11*, 990 (1972).
[61] *K. Wagner*, Angew. Makromol. Chem. *37*, 59 (1974).
[62] *K. Wagner*, DBP 1911644 (1970), Bayer AG.
[63] *K. Wagner*, DBP 1911643 (1970), Bayer AG.
[64] *K. Wagner, M. Dahm*, DBP 1911645 (1970), Bayer AG.
[65] *K. Wagner*, DBP 1953347 (1971), Bayer AG.
[66] *K. Wagner, M. Dahm, D. Liebsch, J. Zirner*, DOS 2037613 (1972), Bayer AG.
[67] *La Spina, W. Dietrich, R. Schliebs*, DOS 2245634 (1972), Bayer AG.
[68] *G. Baatz, M. Dahm, W. Schäfer*, DOS 2520892 (1975), Bayer AG.
[69] *G. Baatz, M. Dahm, W. Schäfer, K. Wagner*, DOS 2523586 (1975), Bayer AG.
[70] *W. von Bonin, L. Preis, U. von Gizycki, M. Dahm*, DOS 2536493 (1975), Bayer AG.
[71] *W. von Bonin, L. Preis, U. von Gizycki*, DOS 2624198 (1976), Bayer AG.

# Analysis of Low Molecular Weight Homologues of Fiber-Forming Polycondensates[**]

By V. Rossbach[*]

*Dedicated to Professor Helmut Zahn on the occasion of his 65th birthday*

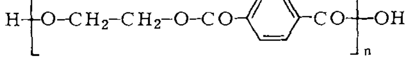
Oligomers belong to the gray area between low molecular weight chemistry and macromolecular chemistry. Although they represent an undesirable "natural impurity" in fiber-forming polycondensates, they serve as useful model compounds for the corresponding polymers in fundamental research. Whereas for many years new classes of oligomers were being made preparatively accessible and the isolation of higher oligomers in pure form was being pursued, at the present time the emphasis is on analysis. By a combination of classical chemical and instrumental methods of analysis from polymer and organic chemistry, the identification of oligomers of unknown structure, the analytical control of their synthesis and the determination of their content in technical polymers has meanwhile become a routine task.

## 1. Introduction

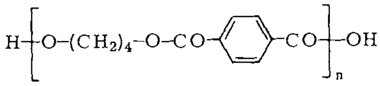
Apart from in a few special processes, the technical synthesis of polymers does not only yield macromolecules. On the contrary, plastics, fibers, varnishes and adhesives often contain low molecular weight precursors of the polymer as "natural impurities". They have the same structure as the corresponding polymer molecules, only the number of repeat units from which they are constructed is smaller. *Van der Want* and *Stavermann*[1] introduced the term "oligomers" for these short-chain homologues of the polymer. *Kern*[2] later narrowed the concept of oligomers to be those low molecular weight polymer homologues which differ sufficiently in their properties so that they can be separated into individual chemical species. This definition is now accepted. Nowadays an oligomer is understood as being a "chemically pure" substance, whereas with a polymer it is tacitly assumed that it can consist of polymer chains of various lengths and frequently also contains oligomer molecules.

In accordance with this definition of oligomers, their classification depends on the efficiency of the methods of separation used. Thus a polystyrene with 38 repeat units, which can be separated chromatographically from its neighboring polymer homologues[3a], would be classified as an oligomer. In the case of the fiber-forming polycondensates (cf. Fig. 1) one would have to speak of polymers at much lower n-values (degree of oligomerization or polymerization), for here the lower polymer homologues with molecular masses of 1000 to 2000 g/mol can no longer be separated. In view of this, the definition by *Zahn* and *Gleitsmann*[3b] appears less ambiguous. They define oligomers as those molecularly uniform initial members of polymer-homologue series which do not yet have the typical physical structure (secondary and tertiary structure) of the particular polymer. The higher members, for which this definition no longer suffices, although they may be prepared in a pure form, can be termed pleionomers. In spite of these various definitions, in this publication oligomers are to be understood quite generally as the lower polymer homologues.

As a result of studies by *Zahn* and his group, considerable experimental material about the oligomers of the fiber-



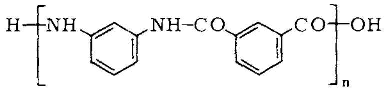
Polyethylene terephthalate



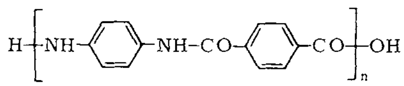
Polybutylene terephthalate
(Polytetramethylene terephthalate)

$H-[NH-(CH_2)_5-CO-]_nOH$
Polyamide 6 (Polyhexanamide)

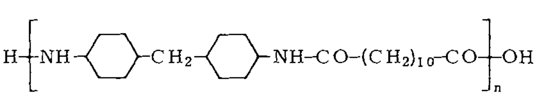
$H-[NH-(CH_2)_6-NH-CO-(CH_2)_4-CO-]_nOH$
Polyamide 6,6 (Polyhexamethylene adipamide, poly-ε-caprolactam)



Poly(*m*-phenylene isophthalamide) (Nomex type)



Poly(*p*-phenylene terephthalamide) (Kevlar type)



Poly(4,4'-methylenedicyclohexyldodecanamide) (Qiana type)

Fig. 1. Structural formulas of the most important fiber polymers of the polycondensate type.

---

[*] Prof. Dr. V. Rossbach
Deutsches Wollforschungsinstitut an der Technischen Hochschule
Veltmanplatz 8, D-5100 Aachen (Germany)
Present address:
Textilchemisches Laboratorium der Fachhochschule Niederrhein
Adlerstr. 32, D-4150 Krefeld (Germany)

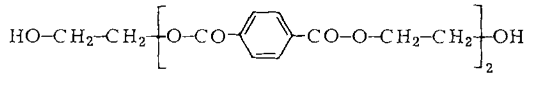
[**] Based on a lecture delivered at the GDCh Extension Course, "Schutzgruppenchemie - Methoden zur Umsetzung polyfunktioneller Moleküle", October 11, 1979 in Aachen (Germany).

forming polycondensates is available. In the course of three decades, it has been possible to achieve the preparative isolation of the various oligomer classes and to spur on the preparation of pure samples of the higher oligomers[4-8]. In recent times however, the emphasis has shifted towards analysis of these oligomers.

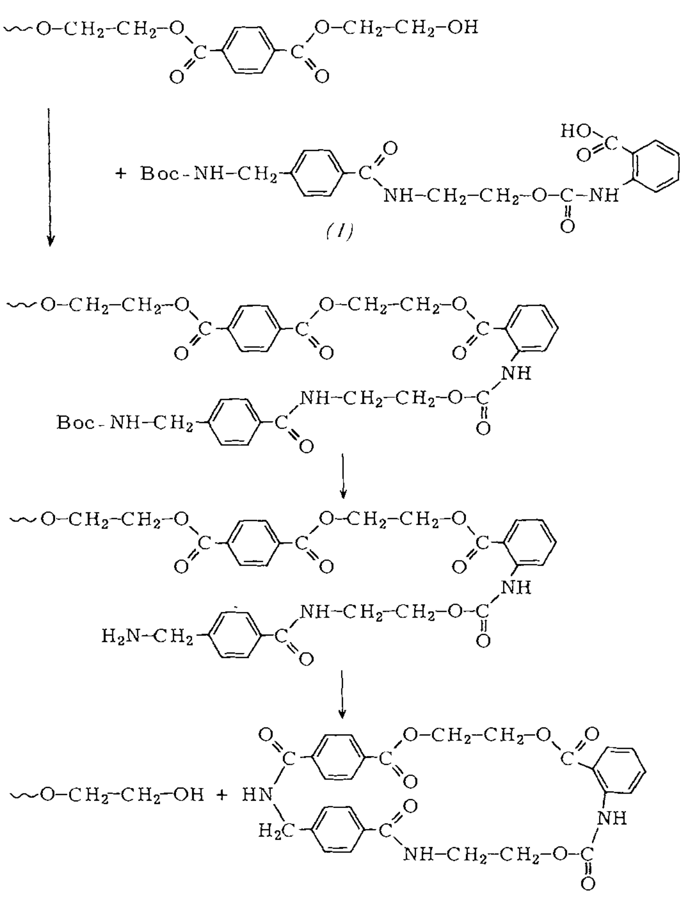
## 2. Importance of Analysis

Analysis of oligomers from fiber-forming polycondensates is, for various reasons, of great scientific and technical significance. Lower polymer homologues serve as model compounds for the elucidation of important textile and polymer properties, such as dyeability, viscosity and melting characteristics[3b,9] as well as secondary and tertiary structure[10] and thermal stability[11]. Furthermore, oligomers are used to calibrate methods of investigation used in polymer chemistry, *e.g.*, as internal standards for gel permeation chromatography[12a] or in the calibration of end-group determinations with polyesters[12b] and polyamides[12c].

Oligomers have also proved to be useful tools for macromolecular chemistry in the development of new analytical procedures. Thus it was possible to show, using the dimeric diol of ethylene terephthalate



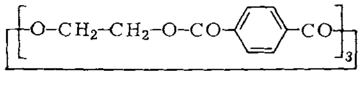
that the reagent *(1)*, m.p. = 181 °C, is suitable for the sequential degradation (and therefore for sequential analysis) of copolyesters containing ethylene terephthalate units[13].



The method for the sequential degradation of ethylene terephthalate oligomers and polymers—binding of the reagent to the hydroxy end groups, cleavage of the Boc protective groups (Boc = *tert*-butyloxycarbonyl), thermal ester aminolysis with ring closure—corresponds to the Edman degradation[14] used in protein chemistry, in that a ring compound (m.p. = 146 °C) is formed which contains the terminal monomer unit. The latter can thus be identified and determined quantitatively. Furthermore, a new hydroxy end group is formed, to which the reagent can again bind. The degradation can thus be repeated. Before this method (the first to allow chemical sequencing of copolyesters) can be used to give satisfactory and complete analyses of products with unknown composition a number of tasks still have to be completed, such as the preparation of molecularly uniform fractions and degradation studies on the corresponding cooligoesters.

It is obvious that, in order to act as model or calibration compounds, oligomers have to be absolutely pure, *i.e.* molecularly homogeneous, which can only be ascertained by efficient analytical methods. Often the task in hand is namely to study changes in certain parameters as a function of chain length.

However, the importance of analysis of oligomers from fiber-forming polycondensates is not confined to producing well-characterized model and calibration compounds for textile and polymer chemistry. On the contrary, the determination of the low molecular weight polymer homologues is important in itself. Thus, for example, by analytical separation of the cyclic oligomers in polyethylene terephthalate[15a], polybutylene terephthalate[15b], polypropylene terephthalate[15b], polyamide 6[16], polyamide 11[17a], and polyamide 12[17] it was possible to come closer to an elucidation of the relationship between the chain conformation of the polymer and its tendency to form cyclic oligomers. There is an increasing tendency to use oligomer analysis in applied problems *e.g.* the clarification of faults in materials. A disproportionately large content of linear oligomers in polyethylene terephthalate is an indication that the material has been subjected to hydrolytic damage[18] and the content of cyclic trimer *(2)* is actually a criterion of quality for polyethylene terephthalate. On account of its low solubility in water the cyclic trimer *(2)* causes difficulties during the processing and finishing of polyethylene terephthalate fibers. During cooling of dye-baths used in high-temperature dyeing, the oligomer *(2)* crystallizes out in the water and on the fiber[19]. The crystalline, sharp-edged deposits which are thereby formed on the fiber surface (cf. Fig. 2) can damage guide rollers during further processing of the fibers. In addition, oligomer crystals which collect on rollers can discharge onto the material and lower its quality.



*(2)*

Although it has been accepted, with resignation, that one "has to live with oligomers"[20], it has recently been shown possible to suppress oligomer formation in polyethylene terephthalate[21] or to remove oligomers once formed[22].

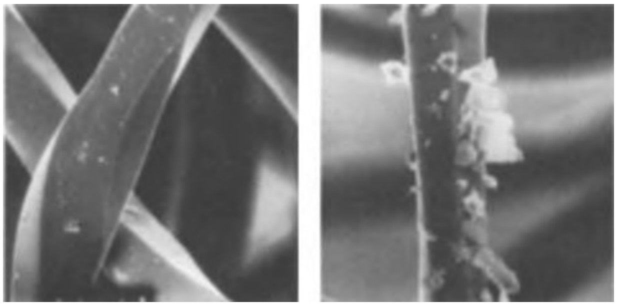
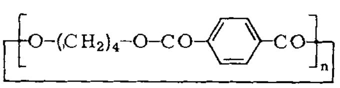


Fig. 2. Surface of a polyethylene terephthalate fiber before dyeing (left) and after dyeing, with considerable oligomer deposition (right) (SEM micrograph from Dr. *P. Kusch*, magnification 450 × ).

In the case of the other currently important fibrous polymers of the polycondensate type (cf. Fig. 1), oligomers present no very great problems during processing and finishing, since they all exhibit good solubility in water. This is also true for the cyclic oligomers of polybutylene terephthalate, which, surprisingly, are about 3 to 5 times more soluble in water than the sparingly soluble polyethylene terephthalate oligomers[23].



n = 2-5

The (readily soluble) oligomers from fiber-forming aliphatic polyamides can, however, give rise to dust formation if they are present in large quantities in the fiber polymer[24]. In the case of aromatic polyamides such as poly(*p*-phenylene terephthalamide) (Kevlar), oligomer analysis has no direct practical importance since, on account of the manufacturing process used, the commercially available fiber polymers contain no oligomers[25].

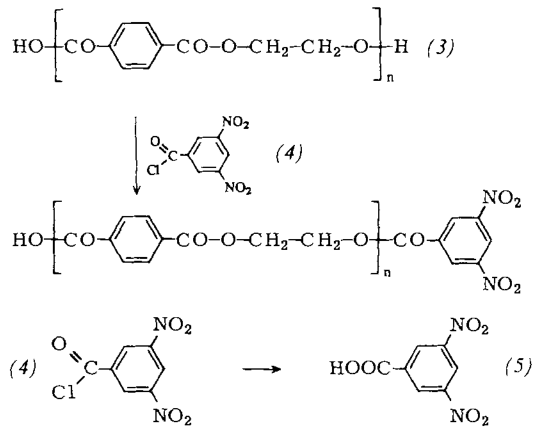
In spite of the great importance which oligomers have as model compounds, calibration compounds, and (undesirable) low molecular weight by-products in fiber-forming polyesters and polyamides, it cannot be overlooked that since about 1970 the number of publications on oligomer preparation has declined steadily. This tendency arises from the fact that in the last decade hardly any new polymers have achieved commercial importance, and the activities of the producers have therefore been concentrated on modifying the polymers already available and optimizing the processing procedures or developing new ones. Parallel to this development in the polymer field, interest in new classes of oligomers is also declining. This development is regrettable in as much as analytical methods are now available which allow even very complicated molecules to be identified and complex oligomer mixtures to be separated. In contrast to this declining activity in the preparative field, there have been numerous publications either touching on, or dealing with, the analytical aspects of oligomer chemistry. However, these are almost entirely restricted to the already well-known oligomer classes[11,15-22,24,26-37].

## 3. Special Aspects of Oligomer Analysis

As polymer homologues with a low degree of polymerization, oligomers occupy a place between monomers and polymers. They are thus, according to a definition of *Lehn et al.*[38], to be classified as "mesomolecules" *i.e.*, they belong neither to the "micromolecules" of organic chemistry (molecular mass $<500$ g/mol), nor to the macromolecules of polymer chemistry and biochemistry (molecular mass $>5000$ g/mol). This special position occupied by the oligomers also holds for their analysis: in many cases they cannot be characterized either by the methods of organic or of macromolecular chemistry.

This may be illustrated by two examples. In organic chemistry, a standard method for the separation of complicated mixtures is gas chromatography. Since, like polymers, oligomers (especially the higher ones) cannot be vaporized without decomposition, this important analytical principle generally cannot be applied to oligomer analysis. Gas chromatography can only be used—as with the corresponding polymer—to analyze monomer units. For example, after trifluoroacetylation of the *N,N'*-diaryldiamines from oligo- and polyamides[39] and trimethylsilylation of ω-amino acids[40] they can be separated and identified, using gas chromatography. The methods of organic chemistry can only be used after the poly- and oligoamides have been converted by hydrolysis into micromolecules.

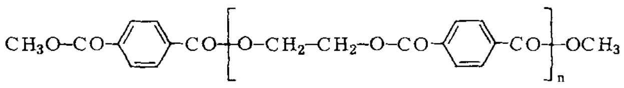
Similarly, the methods of polymer analysis are also generally not applicable to oligomers. This can be illustrated by an example from polyester analysis. A simple and reliable method for determining the hydroxy end groups in polyethylene terephthalate *(3)* is to react them with an excess of 3,5-dinitrobenzoyl chloride *(4)*, followed by hydrolysis of the excess reagent with pyridine/water to 3,5-dinitrobenzoic acid *(5)*, which is then determined potentiometrically[41].



Before the titration the polymer has to be precipitated from the analysis solution with acetone/water. Otherwise the carboxy end-groups of the polymer would also be titrated, thus leading to erroneous values for the hydroxy end group content. This procedure can only be used with considerable reservations for the oligoesters, since they have different solubility characteristics. In addition, the solubility of the individual members differs considerably, as shown in Table 1 for the dicarboxylic acid dimethyl esters of the polyethylene terephthalate series (cf. also Fig. 3).

Whereas the lower members of this dimethyl ester series are adequately soluble in the solvent dioxane, which is

Table 1. Solubility, melting point and elemental analysis of the dicarboxylic acid dimethyl esters of the polyethylene terephthalate series [42—44]. $n$ = Number of repeat units. DMF = $N,N$-dimethylformamide, TCE = 1,1,2,2-tetrachloroethane.



| $n$ | Solvent | M.p. [°C] | Analysis calc. [%] C | H | found [%] C | H |
|---|---|---|---|---|---|---|
| 1 | Dioxane | 168—170 | 62.17 | 4.70 | 62.12 | 4.62 |
| 2 | Dioxane | 196—198 | 62.28 | 4.53 | 62.24 | 4.50 |
| 3 | Dioxane | 215—217 | 62.33 | 4.45 | 62.11 | 4.32 |
| 4 | Dioxane | 231—232 | 62.37 | 4.41 | 62.22 | 4.38 |
| 5 | DMF | 242—243 | 62.39 | 4.35 | 62.27 | 4.21 |
| 6 | DMF | 248—249 | 62.41 | 4.33 | 62.54 | 4.16 |
| 7 | DMF | 250—252 | 62.42 | 4.32 | 62.57 | 4.40 |
| 8 | Dioxane/TCE | 251—253 | 62.43 | 4.30 | 62.22 | 4.21 |
| 9 | TCE | | 62.44 | 4.29 | 62.26 | 4.21 |
| 10 | TCE | 254—256 | 62.44 | 4.28 | 62.36 | 4.39 |

well suited to analytical purposes, the higher members are only soluble in such solvents as $N,N$-dimethylformamide and 1,1,2,2-tetrachloroethane, which for various reasons are less suitable for analytical studies. The higher solubility of the lower oligomers has often been made use of in spectroscopic investigations.

Thus, for example, the UV spectrum of the polyethylene terephthalate oligomers (in solution) was recorded long before the spectrum of polyethylene terephthalate itself[45]. It should be noted, however, that with the discovery of the various fluorinated solvents such as 1,1,1,3,3,3-hexafluoroisopropyl alcohol for polyethylene terephthalate, polyamide 6 and polyamide 6,6 as well as 2,2,2-trifluoroethanol for aliphatic polyamides, suitable solvents are now also available for the most important fiber polymers of the polycondensate type.

The chemistry of low molecular weight polymer homologues, especially their analysis, had its beginnings in peptide chemistry and analysis. *Zahn et al.*[46] described their first synthetic oligoamides as "nylon-peptides". This should not, however, obscure the fact that there are great differences between peptide analysis and oligomer analysis (including oligoamide analysis). These result from the different chemical structure of these classes of compounds. Firstly, peptides consist of *heterogeneous* amino acids, whereas the most important oligoamides and oligoesters are the lower members of the corresponding *homo*polymers (polyamide 6 and 6,6 or polyethylene terephthalate). It is true that cooligoamides are known, *e.g.*, from ε-aminohexanoic acid[*] and ω-aminoundecanoic acid[47], but they are of minor importance. Secondly, among the technically important oligomers of the polycondensate type are some in which — in contrast to peptides — the functional groups leading to chain extension are distributed between two different monomer units. Combinations of practical importance are diamine/dicarboxylic acid and diol/dicarboxylic acid. Such oligomers of the AABB type show a greater variety of structure than the oligomers (and peptides) in which the chain-extending functional groups are contained in the same monomer unit (AB type). Figure 3 illustrates this in the case of the oligomers of ethylene terephthalate.

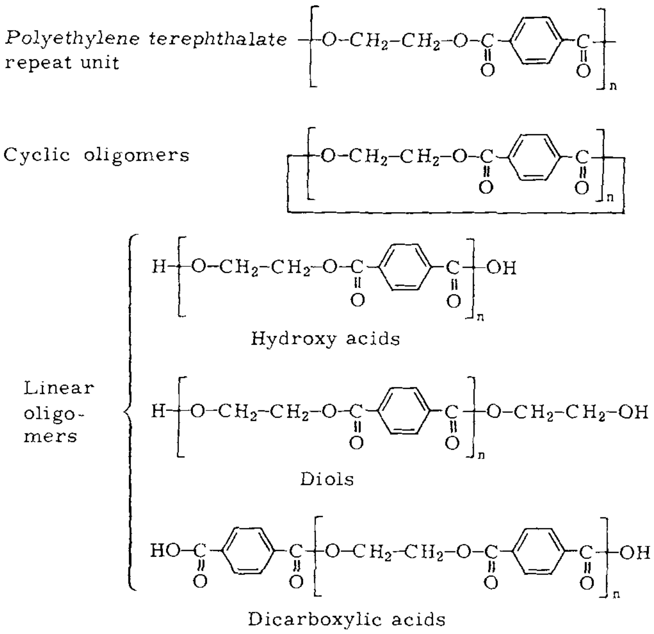
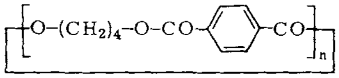


Fig. 3. Structure of the possible oligomers of ethylene terephthalate.

These characteristic differences in the structure of peptides as opposed to the technically important oligoesters and oligoamides have various consequences for their analysis.

On account of the different chemical structure of the individual amino acids, the short-chain peptides differ quite considerably from each other after every coupling step. As a consequence, their purification and the proof of purity do not present any great difficulties. In contrast to this, because of their homogeneous construction, the technically important oligoesters and oligoamides resemble each other chemically to such an extent, after a few coupling steps, that it is hardly possible to purify and separate them using simple methods (*e.g.* recrystallization). The classical criteria of purity (*e.g.* elemental analysis, melting point) also cannot be used (cf. Table 1). For cyclic oligomers this statement is true only with limitations. It is true that elemental analysis is of little value, since all homologues must give the same results, but the melting point determination gives more information, because, in contrast to the linear oligomers, the melting point does not gradually approach that of the polymer (cf. Table 1). As Table 2 shows, in the

Table 2. Melting points, elemental analyses and molecular masses (*via* mass spectroscopy) of cyclic oligomers of butylene terephthalate [23]. $n$ = Number of repeat units.



| $n$ | M.p. [°C] | Analysis found [%] [a] C | H | Molecular mass [g mol⁻¹] calc. | found |
|---|---|---|---|---|---|
| 2 | 199 | 65.50 | 5.50 | 440.40 | 440 |
| 3 | 171.5 | 65.40 | 5.90 | 660.60 | 660 |
| 4 | 250—251 | 65.13 | 5.49 | 880.80 | 880 |
| 5 | 207 | 65.40 | 5.48 | 1101.00 | [b] |

[a] Calculated values C 65.45, H 5.49%. [b] No molecular ion.

---

[*] IUPAC name for ε-aminocaproic acid.

case of the cyclic oligomers of polybutylene terephthalate, the melting points develop discontinuously.

Analysis of the monomer units is much more critical for peptides than for oligomers, since for complete characterization of peptides the sequence and configuration of the amino acids have to be determined in addition to the quantitative composition. In cases where the analysis of the monomer units in oligomers is based on chemical cleavage into these units, it has to be borne in mind that, in the case of the lower cyclic polymer homologues, Flory's principle of equal reactivity of functional groups[48] does not always hold. After ring formation, not only can the lower polymer homologues have a slower rate of hydrolysis compared to the polymer, as has long been known for oligoamides[49,50], but also the reverse can occur: the ester groups in the cyclic trimer of ethylene terephthalate hydrolyze in alkali 50 to 60 times faster than the ester groups in the corresponding polymer[51].

End-group analysis of oligomers with chemical reagents is simplified because, in contrast to peptides, the end-groups in any one series have chemically identical surroundings, independent of the chain length. This means that the reactivity only varies within narrow limits[4,12c].

Peptides are usually synthesized with the aim of obtaining biologically active substances. In these cases, biological activity is the most unequivocal criterion of purity. In the case of the oligomers of technically important polycondensates this aspect does not apply, since they exhibit no biological activity.

Table 3. Eluents for thin-layer chromatographic separation of oligomer mixtures.

| Oligomer Type | Eluent |
|---|---|
| Linear oligomers with free or blocked end groups and cyclic oligomers of polyamide 6- and 6,6-type | *sec*-Butyl alcohol/formic acid/water 75:15:10 ("SBA") or *sec*-butyl alcohol/10% $NH_3$ 85:15 ("SBN") |
| Higher molecular weight linear oligomers of polyamide 6,6-type | Amyl alcohol/formic acid/water 60:30:10 |
| *N*-(2,4-Dinitrophenyl)oligomers of polyamide 6- and 6,6-type | Chloroform/methanol/acetic acid 95:5:1 ("CMA") |
| Oligomers of Qiana- and Kevlar-type | *sec*-Butyl alcohol/formic acid/water/acetic acid 75:21.5:15:8.5 ("WESBA") |
| Cyclic oligomers of ethylene terephthalate (linear oligomers remain at origin) | Chloroform/ether 9:1 |
| Cyclic oligomers and linear oligomers of diol type of ethylene terephthalate | Benzene/dioxane 10:1 |
| Linear oligomers of ethylene terephthalate (cyclic oligomers remain at origin) | Chloroform/ethanol 9:1 |
| Linear oligomers of diacid type of ethylene terephthalate | Ethanol/triethylamine/glycol 65:25:10 |
| Linear oligomers of hydroxy acid type of ethylene terephthalate | 1-Propanol/28% $NH_3$/ammonia/water 70:25:3 |
| Cyclic oligomers of butylene terephthalate | Dioxane/toluene 1:9 |

[a] Qiana and Kevlar, see Fig. 1.

## 4. Monitoring the Course of Reaction during Oligomer Synthesis

### 4.1. Synthesis of Oligomers in Solution

Synthesis of oligomers in solution[3b,4] is the most important method for their production besides isolation from the technical polycondensate. The course of the synthesis can be followed easily and rapidly with thin-layer chromatography. A large number of eluents are available for the various oligomer series, some of them having remarkable specificity[18,25,52,53].

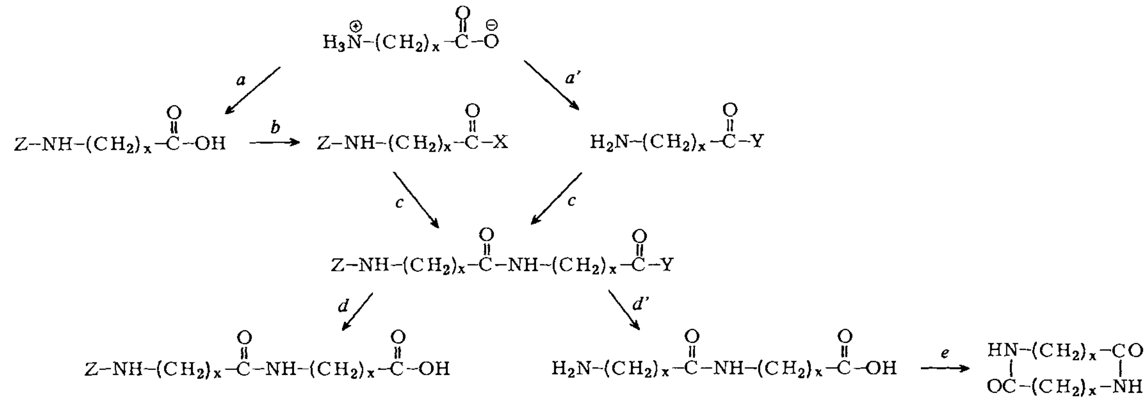


Fig. 4. General scheme for oligomer synthesis in solution, using an oligoamide of the AB type as example. *a,a'*: introduction of the protective group; *b*: activation; *c*: coupling; *d,d'*: removal of protective group; *e*: cyclization.

As Table 3 shows, sufficient eluent mixtures are available for quantitatively following all important steps of an oligomer synthesis, such as introduction of protective groups, coupling, cleavage of protective groups and, if necessary, cyclization (cf. Fig. 4).

In addition to ascending thin layer chromatography, the technique usually used, the descending method is also used for some higher molecular weight oligomers.

There are various possibilities for the detection of the compounds on thin layer chromatograms. If the oligomers contain aryl groups (*e.g.* in the oligomers of ethylene terephthalate, butylene terephthalate, *m*- and *p*-phenylene-terephthalamide), the spots can be detected by quenching of fluorescence under UV light, so long as thin layer plates with a fluorescent indicator are used. In general, the "chlorine" method of *Zahn* and *Rexroth*[54] can be used for oligoamides. If they also contain free amino groups, oligoamides can be detected by spraying with ninhydrin. It has to be remembered however, that with increasing chain length (corresponding to a decreasing amino group content) the detection becomes less sensitive. With both methods the hue and intensity of the colors obtained on the thin layer plates varies quite markedly between the individual oligoamide series.

### 4.2. Oligomer Synthesis on Polymer Carriers

Oligomer synthesis on polymer carriers[6,55] only yields pure oligomers if the reaction steps are kept under strict analytical control. If an *insoluble* carrier resin with chloromethyl groups is used, as in the classical Merrifield peptide synthesis, it is not easy to follow the course of the reaction analytically. For example, in the synthesis of ε-aminohexanoic acid oligomers the following steps (1—4) have to be checked[53].

1. Binding of the first amino acid on the resin:

$$\sim\!\!\sim CH_2{-}Cl + HOOC{-}(CH_2)_5{-}NH{-}Boc \rightarrow \sim\!\!\sim CH_2{-}O{-}CO{-}(CH_2)_5{-}NH{-}Boc$$

(Boc = *tert*-butyloxycarbonyl)

N elemental analysis and Moore-Stein analysis of the total amino-acid carrying resin can be used to follow the reaction analytically.

2. Total blocking with benzyl thioalcohol[56] of excess chloromethyl groups which have not reacted with Boc-ε-aminohexanoic acid:

$$\sim\!\!\sim CH_2{-}Cl + HS{-}CH_2{-}C_6H_5 \rightarrow \sim\!\!\sim CH_2{-}S{-}CH_2{-}C_6H_5$$

This step can be checked by an S elemental analysis.

3. Cleavage of the Boc protective group from the resin-bound ε-aminohexanoic acid with trifluoroacetic acid in $CH_2Cl_2$:

$$\sim\!\!\sim CH_2{-}O{-}CO{-}(CH_2)_5{-}NH{-}Boc \rightarrow \sim\!\!\sim CH_2{-}O{-}CO{-}(CH_2)_5{-}NH_2$$

Various methods are available for determining the resulting free amino groups. *Lee* and *Loudon*[57] recently reviewed their efficacy. In the case of controlled pore glass, the picric acid method is especially suitable. In this method, picric acid initially binds to the amino groups in stoichiometric amounts. The picrate is then cleaved with *N,N*-diisopropylethylamine and the amount of amine-picrate complex formed is determined spectrophotometrically at 358 nm.

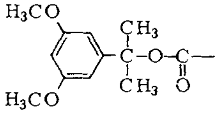
The pyridinium chloride method[58] is also useful. The amino groups bind to the chloride ions of pyridinium chloride. Washing with triethylamine removes the chloride ions, which are then determined potentiometrically.

4. Coupling of the second ε-aminohexanoic acid molecule onto the resin with *N,N'*-dicyclohexylcarbodiimide:

$$\sim\!\!\sim CH_2{-}O{-}CO{-}(CH_2)_5{-}NH_2 + HOOC{-}(CH_2)_5{-}NH{-}Boc \rightarrow \sim\!\!\sim CH_2{-}O{-}CO{-}(CH_2)_5{-}NH{-}CO{-}(CH_2)_5{-}NH{-}Boc$$

Determination of the unreacted amino groups using the methods described above gives a direct estimate of the amount of coupling.

The course of the reaction in the Merrifield synthesis is especially easy to follow if easily identifiable protective groups such as the 3,5-dimethoxy-α,α-dimethylbenzyloxycarbonyl group are used.



To determine the degree of binding to the polymer, the protective group is cleaved and the carrier material washed until the filtrate shows no UV adsorption. Cleavage and washing are repeated to test completeness of reaction. The combined filtrates are then condensed and the concentration of cleaved protective groups determined by UV spectroscopy[59,60]. To the author's knowledge, this elegant technique has not yet been applied to oligomer synthesis.

Attempts to synthesize ethylene terephthalate oligomers on polymeric carriers have so far been without success[42].

## 5. Determination of Oligomer Content in Polymers

Technical fiber polymers of the polycondensate type almost all contain low molecular weight fractions, present in the individual polymers to quite different extents (Table 4).

Table 4. Content of low molecular weight fractions in some fiber polymers [3b, 23, 25, 61a] (see Fig. 1).

| Polymer | Low molecular weight fraction (wt.-%) | Extraction solvent |
|---|---|---|
| Polyamide 6 | 11—12 | Methanol |
| Polyamide 6,6 | 2.0—2.2 | Glacial acetic acid |
| Polyamide 11 | *ca.* 7 | Glacial acetic acid |
| Qiana polyamide | 2.4 | Butanol |
| Kevlar polyamide | 0 | Various solvents |
| Polyethylene terephthalate | 1.3—1.7 | Dioxane |
| Polybutylene terephthalate | 0.8—1.9 | Dichloromethane, dioxane |

These differences are not only due to the fact that during polymer synthesis the lower polymer homologues are formed in varying amounts, but rather that different technologies are used in their manufacture and processing. Thus the reason no extraction residue is obtained from technical Kevlar polyamide is to be found in the production process for the polymer, using condensation polymerization in solution and wet spinning[25,62].

The oligomers are often separated from the polymer in order to estimate them. This can take place in two ways: by extraction with a solvent for the oligomer or by reprecipitation of the polymer.

Extraction techniques are very common in oligoester and oligoamide analysis and are applied in many different ways. The solvents most often used are listed in Table 4. A special problem, common to all extraction techniques is the *complete* removal of the low molecular weight fraction. As was recently shown in the case of polyamide 6, when determining the content of extractable matter on coarse material (*e.g.* cord and granules) the extraction times are often not sufficient to completely remove the low molecular weight fraction[30]. On the other hand, in some situations it is not required to extract exhaustively. With polyethylene terephthalate it often suffices to extract and determine the surface oligomers, since only these are responsible for problems arising during textile processing and finishing (cf. Section 2). Differentiation between surface oligomer and total oligomer content can be carried out by grading the extraction conditions with respect to solvent, and time and temperature of extraction[31].

The second possibility for separating the low molecular weight fraction consists in dissolving the whole polymer sample (including the oligomers) in a suitable solvent and then precipitating the high molecular weight fraction with a precipitating agent which leaves the oligomer fraction in solution (*i.e.* fractionation). Suitable solvent/precipitant systems are *e.g.* 1,1,1,3,3,3-hexafluoroisopropyl alcohol/dioxane for polyethylene terephthalate[32], and 2,2,2-trifluoroethanol/ethanol for polyamide 6 and 6,6[63]. A problem with all such reprecipitation techniques is that, on addition of the precipitant, the coagulating polymer can occlude oligomers, making them unavailable for analysis.

There are various possibilities for quantitative determination of oligomers in extracts and reprecipitated solutions. The simplest is weighing of the solid residue after evaporation of the solvents (gravimetry). It has to be borne in mind here that foreign matter, such as stabilizers, spinning oils *etc.* is also included in the weighing and can thereby falsify the results. Optical methods are more specific, *e.g.* UV spectroscopy for the oligomers of ethylene terephthalate[64] and refractometry and interferometry for the oligomers of polyamide 6 and 6,6[33]. However, these detection techniques are also liable to interference by foreign substances. In recent times, therefore, preference has been given to analytical methods in which the oligomers are separated from foreign matter before detection, *e.g.* by thin layer chromatography, gel chromatography and adsorption chromatography, in the last case especially as high pressure liquid chromatography (HPLC). These methods have the further advantage that they allow separation of the various oligomers in the mixtures. Information is thus obtained about the content of the individual oligomers in the polymer, which can further be used for the analysis of faults (cf. Section 2). A selection of various chromatographic methods which have been used for analytical problems is given in Table 5.

High pressure liquid chromatography in particular has made it possible to analyze technical extracts of chemically very similar oligomers with great speed and precision. Figure 5 shows this for the monomeric cycloamides of the Qiana-type, which differ only in their configuration.

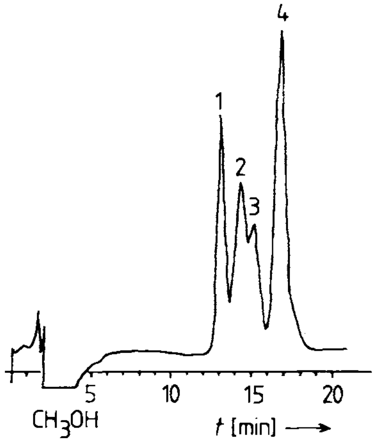


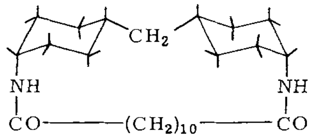
Fig. 5. HPLC chromatogram of an extracted isomeric mixture of the monomeric cycloamides of the Qiana-type [61a]. 1—4, see text.

By comparison with synthetically prepared cycloamides, it can be shown that the peaks 1—4 in Figure 5 can be attributed to the isomers *(6a)—(6d)*[61a].

The search for suitable eluting agents is a problem with HPLC. In the case of the ethylene terephthalate oligomers, nano-thin layer chromatography can be used to advantage for this purpose[65].

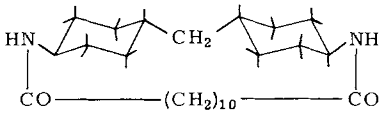
Table 5. Selection of chromatographic methods for quantitative oligomer analysis. GPC = gel permeation chromatography, HPLC = high pressure liquid chromatography, Ads = adsorption chromatography, TLC = thin layer chromatography.

| Area of Application | Principle of Separation | Mobile Phase | Detection | Ref. |
|---|---|---|---|---|
| Linear monomers and oligomers of polyamide 6-, 6,6- and 12-type | GPC after reaction with 1-fluoro-2,4-dinitrobenzene | 0.05 N HCl/Methanol | UV-VIS spectroscopy | [34] |
| Cyclic monomers and oligomers of polyamide 6- and 6,6-type | GPC | 0.1 N HCl | UV spectroscopy | [35] |
| Cyclic monomers and oligomers of polyamide 11- and 12-type | GPC | *o-tert*-Butylphenol | No information | [17a] |
| Isomeric mixtures of the cycloamides of the Qiana-type | HPLC | Methanol/water | Refractometry | [61a] |
| Cyclic trimer of ethylene terephthalate | TLC | Benzene/dioxane | Quenching of fluorescence | [19] |
| Cyclic oligomers of ethylene terephthalate | GPC | Chloroform | Refractometry | [15a] |
| Cyclic oligomers of ethylene terephthalate | Ads. | Chloroform/ether, chloroform/ethanol, $CH_2Cl_2$/hexane | UV spectroscopy | [27, 28] |
| Cyclic oligomers of butylene terephthalate | HPLC | Methanol/water | UV spectroscopy | [23] |
| Cyclic oligomers of ethylene terephthalate | Ads. | Hexane/dioxane | UV spectroscopy | [32] |

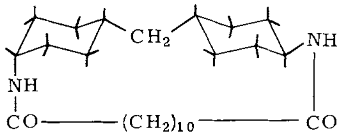


(6a), *cis, cis*, m.p. = 254-257 °C

(6b), probable conformer of (6a)



(6c), *trans, trans*, m.p. = 310-314 °C



(6d), *cis, trans*, m.p.= 269-272 °C

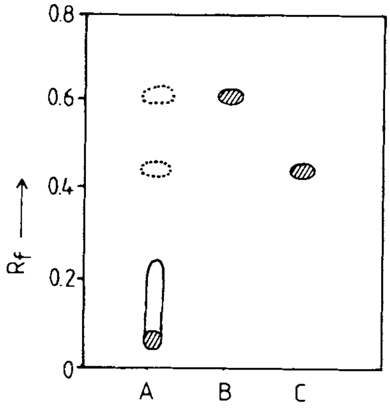
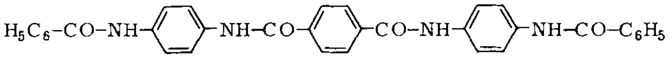


Fig. 6. Thin layer chromatogram of an *N,N*-dimethylformamide extract of poly-(*p*-phenyleneterephthalamide) (A) and the reference compounds *N,N'*-dibenzoylphenylenediamine (B) and *(7)* (C) (Eluent: WESBA, cf. Table 3).

The errors associated with separation of oligomers can be avoided by using techniques which enable the low molecular weight homologues to be determined directly along with the polymer. Examples of this are gas chromatographic[36a] and IR spectrophotometric[29] determination of ε-caprolactam in polyamide 6, or the determination by adsorption chromatography of the cyclic oligomers of ethylene terephthalate[27]. For routine absolute determinations, this method of determining the low molecular weight polymer homologues in the presence of polymer appears particularly promising.

The chromatographic techniques described above can be used in conjunction with authentic reference compounds for the identification of oligomers in polymers. Thus in the *N,N*-dimethylformamide extracts of poly(*p*-phenyleneterephthalamide), manufactured according to the relevant company patent for Kevlar[62], *N,N'*-dibenzoylphenylenediamine and the dibenzoyl derivative *(7)* of the monomeric diamine (m.p. >385 °C) could be identified, along with higher condensed products, by means of thin layer chromatography[25] (cf. Fig. 6).



*(7)*

The formation of these benzoylated low molecular weight homologues can be attributed to the use of benzoic acid, as prescribed in the patent[62], as a molecular weight regulator in the polycondensation.

## 6. Characterization of Oligomers

The methods described above for following the course of reactions in solution (Section 4.1) and for determining the oligomer content of the polymer (Section 5) can also be applied to characterization of the oligomers. They have to be supplemented, however, by further techniques. The methods normally used in organic chemistry, *i.e.* elemental analysis plus UV, IR and NMR spectroscopy, generally are sufficient to assign an oligomer to a certain series. Further information is given by the processes used to determine the monomeric units of the relevant polymers. Table 6 lists a selection of methods for quantitative analysis of monomeric units.

In Table 6 the *N*-propionylpropylamides of ε-aminohexanoic acid and the methyl esters of terephthalic acid have been included as especially useful model compounds ("oligomers free of end groups") for polyamide 6 and polyethylene terephthalate, respectively[3b].

If the chain length and exact oligomer type are to be determined (cf. Fig. 3 in the case of the ethylene terephthalate oligomers) the methods of organic chemistry and polymer chemistry as described above are not sufficient. Fur-

Table 6. Selection of methods for quantitative analysis of monomeric units.

| Area of Application | Preparatory Steps | Principle of Separation | Determination | Ref. |
|---|---|---|---|---|
| Propylamine and propionic acid in *N*-propionyl-propylamides of aminocarboxylic acids, especially ε-aminohexanoic acid | Hydrolysis with $H_2SO_4$ | Distillation | Titration | [66] |
| Various diamines, amino carboxylic acids and dicarboxylic acids from aliphatic polyamides; aromatic diamines from aliphatic-aromatic polyamides | Trifluoroacetylation, methylation or trimethylsilylation after hydrolysis with HCl | Gas chromatography | Retention time (reference compounds) | [39, 40, 67] |
| Methyl ester groups in polyethylene terephthalate | Hydrazinolysis with formation of methanol | Gas chromatography | Retention time | [68] |
| Terephthalic acid units in polyesters | Hydrazinolysis with formation of terephthalic acid dihydrazide and monohydrazide | No separation | Polarography | [69, 70] |
| ε-Aminohexanoic acid units | Hydrolysis with HCl | Ion exchange | Moore-Stein analysis | [71] |

ther chemical and instrumental methods have to be applied.

Although mass spectroscopy was used by *Repin*[72] in 1968 to characterize the cyclic diesters of terephthalic acid and ethylene glycol, it is only in recent years that it has become a standard method in oligomer research. This is due firstly to further refinement of the apparatus[73,74], and also to the fact that since that time reliable data on the fragmentation of the various classes of compounds in the mass spectrometer have become available. This enables the structure of the higher oligomers to be clarified even though they are completely fragmented in the mass spectrometer and hence give no molecular ion.

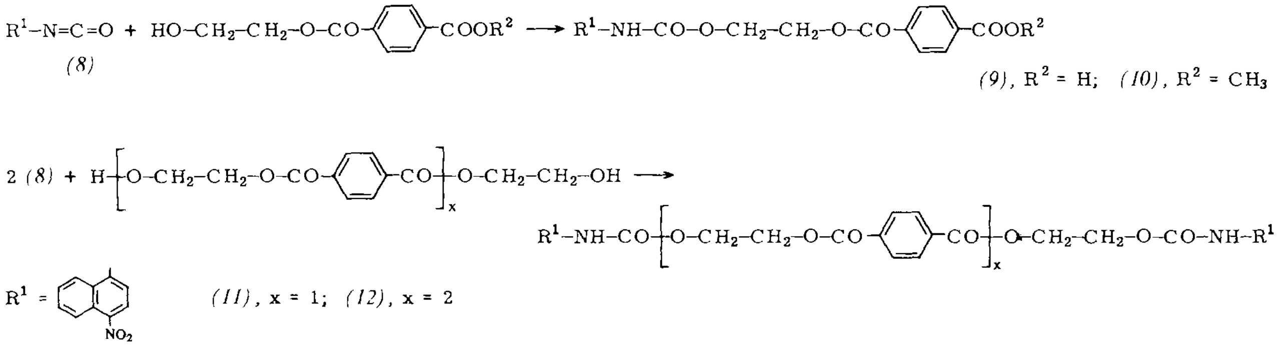
Determination of the molecular mass by identifying the relevant molecular ion is especially applicable to the *cyclic* oligomers, which can be sublimed without decomposition. This technique has been used successfully for the cyclic dimer[36b] and trimer[37a] of ethylene terephthalate, the cyclic oligomers of butylene terephthalate up to the tetramer[23,37b] (cf. Table 2) and the cyclic monomeric and oligomeric amides of various polyamides (Qiana-type[61a], polyamide 6-type[61b], polyamide 4-, 7-, 12- and 4,10-, 6,6-6,10-, 11,6-, 12,12-type[61c]. Mass spectrometry is therefore a useful supplement to the methods of molecular weight determination frequently used in oligomer analysis, *viz.* vapor pressure osmometry and end group analysis[52], since the latter methods are not universally applicable. Vapor pressure osmometry yields values with good reproducibility if the oligomers have a cyclic structure or the end-groups are blocked with non-ionic residues, but it cannot be used for linear oligomers with ionic end groups, *e.g.* for the linear oligomer of ε-aminohexanoic acid and hexamethylene adipamide with unprotected end-groups. However, for these oligomer series a number of chemical and instrumental methods of end-group determination are available, which respond specifically to amino, carboxy and hydroxy end-groups[75].

All these methods have been developed, however, for the corresponding polymers and therefore in some cases they have to be modified before being used with oligomers. Considerable information is obtained from methods of end-group determination which are based on an "oligomer-analogous reaction", *i.e.* a reaction in which, according to *Staudinger*'s criterion, chemical modification takes place without changing the number of repeat units. With this technique it is not only possible to determine the molecular mass according to the following equation:

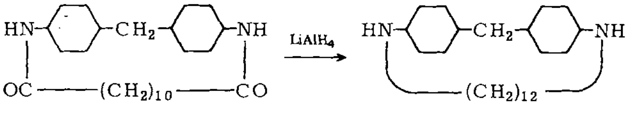
$$M = \frac{2}{E} \times 10^6$$

($E$: end-group content in meq/kg; $M$: molecular mass in g/mol)

In addition, the modified oligomers can be tested for homogeneity using the methods described previously. An example of such a procedure is the reaction of ethylene terephthalate oligomers *(9)–(12)* containing hydroxy groups with 4-nitronaphthyl 1-isocyanate *(8)*, as described by *Nissen*[12b].



The molecular mass of the oligomers can be calculated from the absorption of the introduced chromophore. In addition, information about the homogeneity of the oligomers can be obtained from the melting point, elemental analysis, and chromatographic behavior. Another oligomer-analogous reaction which has proved valuable for analysis is the reduction of cyclic oligoamides to cyclic oligoamines. This was first used by *Spoor* and *Zahn*[76] to determine the oligomers of polyamide 6. In the case of the *cis,trans*-isomeric cycloamides *(6)* of the Qiana-type, this technique proved to be especially useful for characterization since the resulting isomeric diazacycloalkanes *(13)* can, in contrast to the cycloamides, be distinguished by thin layer chromatography[61a].



*(6)* *(13)*

For the identification of known oligomers, *e.g.* in extracts from technical polymers, mention should be made of the clearly arranged table by *Rothe*[77]. This lists physical data and literature references for all oligomers which were characterized up to *ca.* 1970.

*Thanks are expressed to Prof. Dr. H. Zahn for introducing the author to oligomer chemistry. The financial support of the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen, Deutsche Forschungsgemeinschaft (Grant No. Ro 432/2) and the Verband der chemischen Industrie is acknowledged with thanks.*

Received: December 12, 1979 [A 385 IE]
Supplemented: August 11, 1981
German version: Angew. Chem. *93,* 866 (1981)
Translated by Dr. *E. Finnimore,* Aachen (Germany)

[1] *G. M. van der Want, A. J. Stavermann,* Recl. Trav. Chim. Pays-Bas *71,* 379 (1952).
[2] *W. Kern,* Chem.-Ztg. *76,* 667 (1962).
[3] a) *E. Klesper,* Angew. Chem. *90,* 785 (1978); Angew. Chem. Int. Ed. Engl. *17,* 738 (1978); b) cf. *H. Zahn, G. B. Gleitsmann, ibid. 75,* 722 (1963) and *2,* 410 (1963); and references cited therein.
[4] Cf. *G. Heidemann* in *H. F. Mark, G. Gaylord, N. M. Bikales:* Encyclopedia of Polymer Science and Technology, Interscience, New York 1968, Vol. 9, p. 485.
[5] Cf. *M. Rothe, W. Dunkel,* J. Polym. Sci. *B 5,* 589 (1967).
[6] Cf. *P. Kusch,* Kolloid-Z. *208,* 138 (1966).
[7] Cf. *H. Zahn, J. F. Repin,* Chem. Ber. *103,* 3041 (1970).
[8] Cf. *R. Pénisson, H. Zahn,* Makromol. Chem. *133,* 25 (1970).
[9] *H.-W. Hässlin, M. Dröscher, G. Wegener,* Makromol. Chem. *181,* 301 (1980).
[10] *G. I. Asbach, K. G. Drexhage, G. Heidemann, W. Glenz, H. G. Kilian,* Makromol. Chem. *139,* 115 (1970); *H.-W. Hässlin, M. Dröscher,* Polym. Bull. *2,* 769 (1980).
[11] *V. Rossbach,* Forschungsber. Landes Nordrhein-Westfalen Nr. 2344 (1979).
[12] a) *G. N. Patel,* J. Appl. Polym. Sci. *18,* 3537 (1974); b) cf. *D. Nissen,* Forschungsber. Landes Nordrhein-Westfalen Nr. 2455 (1975); c) *V. Rossbach, D. Nissen, H. Zahn,* Angew. Makromol. Chem. *43,* 1 (1975).
[13] *F. P. Schmitz,* Dissertation, Technische Hochschule Aachen 1978; *J. Windeln,* Diplomarbeit, Technische Hochschule Aachen 1980; *J. Windeln, F. P. Schmitz, V. Rossbach,* Makromol. Chem., in press.
[14] *P. Edman,* Acta Chem. Scand. *4,* 283 (1950).
[15] a) *D. R. Cooper, J. A. Semlyen,* Polymer *14,* 185 (1973); b) *K. Burzin, W. Holtrup, R. Feinauer,* Angew. Makromol. Chem. *74,* 93 (1978).
[16] *J. A. Semlyen, G. R. Walker,* Polymer *10,* 597 (1969).
[17] a) *R. Feldmann, R. Feinauer,* Angew. Makromol. Chem. *34,* 9 (1973); b) *M. Bohdanecký, B. Lánská, J. Sebenda, Z. Tuzar,* Eur. Polym. J. *15,* 45 (1979).
[18] Cf. *J. Derminot,* Ind. Tex. (Paris) No. 1083, p. 677 (Nov. 1978).
[19] *P. Kusch, G. Böhm,* Text.-Prax. *27,* 485 (1972).
[20] *P. Senner,* Chemiefasern/Text.-Ind. *4,* 344 (1973).
[21] *R. Humbrecht,* Melliand Textilber. *61,* 450 (1980).
[22] *G. Stein, S. Dugal, G. Heidemann, G. Valk,* Chemiefasern/Text.-Ind. *9,* 829 (1976).
[23] *F.-J. Müller,* Dissertation, Technische Hochschule Aachen 1978.
[24] *V. Rossbach:* Analysis of Faults in Industrial Felts - Methods of Investigation and their Applicability, Monograph in the Technical Proceedings, Organisation of the Felt Industry in Europe, Den Haag 1978.
[25] Cf. *F.-J. Müller,* Diplomarbeit, Technische Hochschule Aachen 1976.
[26] *P. Kusch,* Text.-Prax. *28,* 96 (1973).
[27] *S. Dugal, H. Krüssmann, G. Stein,* Text.-Prax. *28,* 345 (1973).
[28] *B. Lang, H. Makart,* Melliand Textilber. *56,* 647 (1975).
[29] *S. Mori, K. Okazaki,* J. Polym. Sci. *A-1, 5,* 231 (1967).
[30] *E. O. Schmalz,* Faserforsch. Textiltech. *29,* 269 (1978).
[31] Cf. *B. Bogatzki, B. Nittka,* Faserforsch. Textiltech. *25,* 120 (1974).
[32] *J. P. Luttringer, J. Majer, G. Reinert,* Melliand Textilber. *60,* 160 (1979).
[33] Cf. *E.-O. Schmalz,* Faserforsch. Textiltech. *29,* 599 (1978).
[34] *S. Mori, T. Takeuchi,* J. Chromatogr. *50,* 419 (1970).
[35] *S. Mori, T. Takeuchi,* J. Chromatogr. *49,* 230 (1970).
[36] a) *H. F. Dinse,* Faserforsch. Textiltech. *23,* 304 (1972); b) *S. Shiono,* J. Polym. Sci., Polym. Chem. Ed. *17,* 4123 (1979).
[37] a) *I. Lüderwald, H. Urrutia, H. Herlinger, P. Hirt,* Angew. Makromol. Chem. *50,* 163 (1976); b) *K. Burzin, P.-J. Frenzel, ibid. 71,* 61 (1978).
[38] *J.-M. Lehn, J. Simon, J. Wagner,* Angew. Chem. *85,* 621 (1973); Angew. Chem. Int. Ed. Engl. *12,* 578 (1973).
[39] *S. Mori, M. Furusawa,* J. Chromatogr. Sci. *8,* 477 (1970).
[40] *S. Mori, M. Furusawa, T. Takeuchi,* Anal. Chem. *42,* 959 (1970).
[41] *H. Zimmermann, A. Tryonadt,* Faserforsch. Textiltech. *18,* 487 (1967).
[42] *R. Pénisson, H. Zahn,* Makromol. Chem. *133,* 13 (1970).
[43] *H. Zahn, R. Krzikalla,* Angew. Chem. *67,* 108 (1955).
[44] *H. Zahn, R. Krzikalla,* Makromol. Chem. *23,* 31 (1957).
[45] *B. Seidel,* Z. Elektrochem. Ber. Bunsenges. Phys. Chem. *62,* 214 (1958).
[46] Cf. *H. Zahn, P. Rathgeber, E. Rexroth, R. Krzikalla, W. Lauer, P. Miro, H. Spoor, F. Schmidt, B. Seidel, D. Hildebrand,* Angew. Chem. *68,* 229 (1956).
[47] *H. Zahn, W. Pieper,* Makromol. Chem. *53,* 103 (1962).
[48] *P. J. Flory:* Principles of Polymer Chemistry, Cornell University Press, Ithaka 1953; cf. *M. Rätzsch, V. Phien,* Faserforsch. Textiltech. *26,* 99 (1975).
[49] *P. H. Hermans,* Nature *177,* 127 (1956).
[50] *D. Heikens,* J. Polym. Sci. *22,* 65 (1956).
[51] *G. Heidemann,* remark made during the lecture by *J. P. Luttringer* at the 6th Joint Conference of the Aachener Textilforschungsinstitute and the 'Wollfadens', Aachen, September 27, 1979.
[52] Cf. *G. Heidemann, P. Kusch, H.-J. Nettelbeck,* Z. Anal. Chem. *212,* 401 (1965).
[53] Cf. *P. Friese,* Dissertation, Technische Hochschule Aachen 1971.
[54] *H. Zahn, E. Rexroth,* Z. Anal. Chem. *148,* 181 (1955).
[55] Cf. *H. Zahn, P. Kusch,* Z. Gesamte Textilind. *69,* 880 (1967).
[56] *H. Klostermeyer,* Chem. Ber. *101,* 2823 (1968).
[57] *C. C. Y. Lee, G. M. Loudon,* Anal. Biochem. *94,* 60 (1979).
[58] *L. C. Dorman,* Tetrahedron Lett. *28,* 2319 (1969).
[59] *C. Birr,* Justus Liebigs Ann. Chem. *1973,* 1652.
[60] Cf. *C. Birr:* Aspects of the Merrifield Peptide Synthesis, Springer, Berlin 1978, p. 39.
[61] a) Cf. *G. E. Hahn,* Dissertation, Technische Hochschule Aachen 1978; b) *I. Lüderwald, F. Merz, M. Rothe,* Angew. Makromol. Chem. *67,* 193 (1978); c) *I. Lüderwald, F. Merz, ibid. 74,* 165 (1978).
[62] *T. I. Bair, P. W. Morgan,* DOS 1816106 (1968), Du Pont.
[63] *H. Zahn,* Melliand Textilber. *53,* 1317 (1972).
[64] *G. Valk, E. Loers, P. Küppers,* Melliand Textilber. *51,* 504 (1970).
[65] *W. R. Hudgins, K. Theurer,* Abstr. Papers, ACS/CSJ Chemical Congress, Honolulu, April 1.–6., 1979, Part I, Anal. 8.
[66] *B. Dallmann,* Dissertation, Technische Hochschule Aachen 1961.
[67] *S. Mori, M. Furusawa,* Anal. Chem. *42,* 138 (1970).
[68] *H. Zimmermann, D. Becker,* Faserforsch. Textiltech. *22,* 458 (1971).
[69] *W. Berger, K.-H. Ewert,* Faserforsch. Textiltech. *24,* 377 (1973).
[70] *G. Stein, M. Saglam,* Melliand Textilber. *57,* 920 (1976).
[71] *V. Rossbach, F. P. Schmitz, J. Föhles,* Angew. Makromol. Chem. *90,* 1 (1980).
[72] *J. F. Repin,* Dissertation, Technische Hochschule Aachen 1968.
[73] *W. D. Lehmann, H.-R. Schulten,* Chem. Unserer Zeit *10,* 147 (1976).
[74] *W. D. Lehmann, H.-R. Schulten,* Chem. Unserer Zeit *10,* 163 (1976).
[75] Cf. *D. Nissen, V. Rossbach, H. Zahn,* Angew. Chem. *85,* 691 (1973); Angew. Chem. Int. Ed. Engl. *12,* 602 (1973); cf. *R. G. Garmon* in *Ph. E. Slade:* Polymer Molecular Weights, Part I, Dekker, New York 1975, p. 31.
[76] *H. Spoor, H. Zahn,* Z. Anal. Chem. *168,* 190 (1959).
[77] *M. Rothe* in *J. Brandrup, E. H. Immergut:* Polymer Handbook, 2nd Edit., Wiley, New York 1974, Vol. VI, p. 1ff.

# The Critical Screening and Assessment of Scientific Results without Loss of Information—Possible or Not?

**By Reiner Luckenbach, Reinhard Ecker, and Josef Sunkel**[*]

*Dedicated to Professor Leopold Horner on the occasion of his 70th birthday*

The critical assessment of information as a means of screening and selecting scientific results, leading to a procedure for condensing the flood of data from the primary literature into the secondary literature, is reviewed (here, exemplified for organic chemistry). The criteria for critical assessment without loss of content, developed and tested by the Beilstein Institute on the basis of a hundred years' experience, are presented. The possible extent to which data can thus be reduced is demonstrated for a number of examples.

## 1. Introduction

One of the corner stones of international chemical documentation, Beilstein's Handbook of Organic Chemistry, looks back this year on a hundred years of activity in the field[1-3][**]. The principal objective of this work was, and still is, to provide its user with a comprehensive "concentrate" of the primary literature[**] as a tool for day-to-day research work. This objective can only be attained if the results published in the primary chemical literature are subjected to a scientifically critical appraisal, *i.e.* are checked for their general soundness and consistency with other findings. In addition, it must be ensured that the data reduced by this selective processing reach the user without loss of informational content.

Before discussing the general and specific requirements for attaining this objective, the present-day situation of the "information consumer" will be reviewed.

## 2. The Situation of Scientists Seeking Information Today

The process of communication between scientists—one of the fundamental requirements for all intellectual work—is influenced to an increasing extent these days by the ever greater flood of information. This can become an intolerable burden for the individual scientist who finds it less and less possible to select relevant data from the flood of information reaching him. The number of reports appearing annually in Chemical Abstracts amply demonstrates the extent to which this situation is worsening (Table 1).

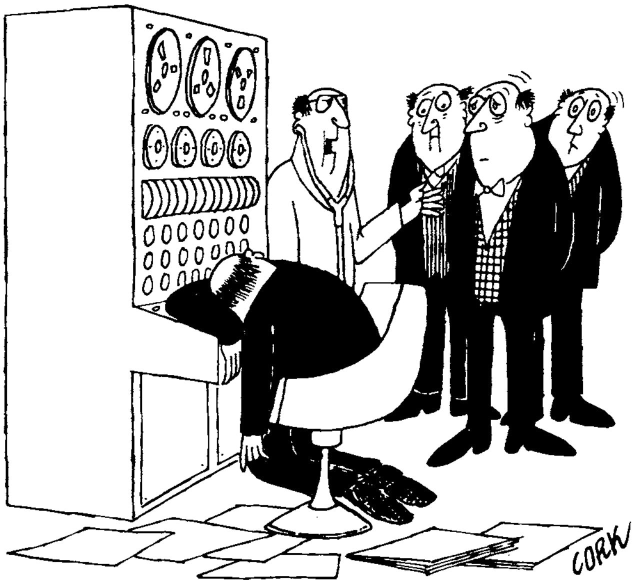


Fig. 1. From *Der Leitende Angestellte 1978* (7), 14: "He died of an overdose of data ...".

Appeals to publish less and to refrain from founding new journals have apparently gone unheeded. As a result, many scientists have adopted the practice of restricting their literature studies to cover only the latest information available at the time. This means that as a result of ignorance of valuable older information numerous duplicate and multiple publications, not infrequently containing already well-known material, have appeared. Scientists specialized in the field of documentation, who made an intensive study of the problems generated by this development, initially believed they had found a solution by the increased use of electronic data processing. Experience has already shown, however, that the non-selective storage of all incoming information once again leads into a blind alley: the percentage of ballast produced in research is con-

Table 1. Number of reports in Chemical Abstracts [5].

| Year | 1909 | 1919 | 1929 | 1939 | 1949 | 1959 | 1969 | 1979 |
|---|---|---|---|---|---|---|---|---|
| Number of Abstracts | 15459 | 15240 | 48293 | 67108 | 53441 | 127196 | 252320 | 436887 |
| Total number of Abstracts to date | 42475 | 236796 | 530883 | 1152697 | 1603461 | 2478814 | 4435451 | 8068661 |

---

[*] Prof. Dr. R. Luckenbach, Dr. R. Ecker, Dr. J. Sunkel,
Beilstein-Institut für Literatur der Organischen Chemie
Varrentrappstrasse 40–42, D-6000 Frankfurt/M. 90 (Germany)

[**] Ref. [4] considers the English usage of the terms "handbook" and "primary and secondary literature".

*0570-0833/81/1010-0841 $ 02.50/0*

stantly on the increase and the end-user is forced to make a time-consuming selection of the relevant information from a large number of ballast-loaded sources (multiple publications, ignorance of long-discovered errors *etc.*). Since this critical screening on any particular subject has to be carried out afresh by every individual seeking information, the entire process must be viewed as making nonsense of any kind of informational economy.

It would thus appear meaningful and rational not to leave it to each individual end-user to rid the material of ballast himself but instead to make the information available after critical screening and assessment by a competent "information analysis center"— a demand which has repeatedly been made over the past years[6] and which has in fact been put into practice by the great chemical handbooks for over a century. More recent attempts to implement this demand have so far mainly failed because of the necessarily high investment costs and the problem of simultaneously avoiding loss of information.

The terminology "critical screening and assessment" is intended to denote the competent scientific appraisal of a piece of information with regard to its soundness (compatibility with generally known facts and analogous material), its novelty, and its general scientific significance. Returning to the experience accumulated during production of the Beilstein Handbook, it will be shown that under certain conditions it is possible, with the aid of this critical scientific screening and appraisal, to make decisive progress in the field of informational economy and accessibility.

## 3. Critical Screening in Science

Critical screening and sifting of information according to quality and usefulness are general reactions of the human intellect towards the flood of information confronting it from day to day. All scientific work also involves critical screening. Before a result is made public, the person or group responsible will normally have filtered out insignificant, uncertain or questionable results since the expenditure required for their publication does not appear to be justified, or further studies are necessary.

Following this rather "subjective" appraisal, the next step is an objective assessment of form and content of the publication or patent application by the editor and referee appointed by the journal, or by the patent attorney. This critical publisher-evaluation of manuscripts submitted to journals has a long tradition in the field of chemistry and is well-illustrated by *Justus von Liebig*'s activities in the course of publication of his "Annalen der Chemie"[7]. In 1871, it was *Friedrich Konrad Beilstein* himself who asked *Emil Erlenmeyer* to referee the increasingly numerous studies submitted to the journals for publication: "... You have now attained the peace of mind necessary to skin the average villain, without the fury of earlier days but in a leisurely and collected fashion over a good cigar ..."[8]. Today too, this critical editorial assessment is frequently exercised in full measure. For example, the editors of the "Chemische Berichte" in 1979 turned down about 17% of the manuscripts submitted and returned just under 50% to the authors for revision (and shortening)[9]. Although it is certain that many of the rejected manuscripts, or parts of them, were subsequently published in other journals, these figures show clearly to what extent potential research ballast is filtered out prior to publication[*]. Once scientific information has become available in the form of a primary publication, it can be taken over by the secondary literature. The function of the secondary literature is to select, analyze, order, and selectively store[10] the information contained in the primary literature.

The greater part of the secondary literature can be subdivided into the *"selective* secondary literature" and that providing *"comprehensive coverage* of the primary literature".

The "selective secondary literature" is intended to provide the user with information of an exemplary nature by grouping scientific results and illustrating common properties of the group in terms of an individual example. The user himself has to bear the risk involved in making analogies with his individual special case. Examples of the "selective secondary literature" are review articles, monographs and textbooks.

The function of the "comprehensive secondary literature" is to provide the user with *all* the information available in the fields covered. The user is thus presented with the individual case itself and all known facts about it.

In addition to the well-established abstracting journals (which provide a comprehensive, mainly uncritical, continuous listing and registration of the contents of the primary literature: a catalogue of all known information) the "comprehensive secondary literature" also includes the scientific handbooks.

If certain rules are observed, these handbooks can be so designed that not only is the primary literature fully covered but also:

- multiple publications with the same content and well-known results are filtered out,
- corrections to earlier findings can be taken directly into account,
- conflicting data on a subject can be recognized and, where possible, clarified,
- individual results on a subject can be correlated with analogous cases and errors brought to light.

Observation of these criteria would satisfy the definition of a critically assessing handbook as a well-ordered, corrected, up-to-date and low-ballast compilation of all known facts. In contrast to the abstracting journal, the handbook does not merely pass on information but is also equipped to recognize and correct mistakes and is thus in a position to exclude ballast.

The absolute necessity of this critical processing was also recognized by *F. K. Beilstein* during preparations for the first edition of his handbook. Here are two further quo-

---

[*] It would of course be unjustified to view publication or non-publication as the sole yardstick of the significance of a scientific result, since frequently there are strong personal, political, military or commercial reasons why the publication of important results is blocked.

tations from his letters to *Erlenmeyer*[8] "... It is truly appalling to see just what has been thrown together so far—the question marks and the inconclusive and contradictory material I have already had to read ...". Elsewhere he deplores that "... a conceited boastfulness is becoming widespread in chemistry, quite insignificant results are blown up into a great discovery, and the publication of watered-down material is becoming the order of the day ...".

## 4. Critical Screening and Assessment as Practised in the Beilstein Handbook of Organic Chemistry

The general criteria outlined above for the compilation of works in the category of "scientific handbooks" are of course also fulfilled by the great handbooks in the field of chemistry (Beilstein, Gmelin, Landolt-Börnstein).

The Beilstein Handbook covers the field of Organic Chemistry *i.e.* it includes a description of all carbon compounds dealt with in the scientific literature (with the exception of CO, $CO_2$ and inorganic carbonates).

In the following discussion it will be shown to what extent it is possible, using a proper scientific approach and methodology to carry out a critical screening and assessment without loss of information.

### 4.1. The Requirements for Critical Screening without Loss of Information

Before the individual criteria for critical screening are discussed, a few general requirements will be mentioned and illustrated in terms of the preparation of Beilstein's Handbook of Organic Chemistry.

#### 4.1.1. Working Procedure

The most important requirement is a suitable working procedure which permits the original literature to be evaluated without informational loss in its first stage and subsequently, after checking, to be stored according to a suitable systematic arrangement. The working procedure includes a number of firm rules for the evaluation of material, established on the basis of many years' experience. Optimal application of these rules is ensured by independent checking of all scientific decisions on at least two levels. This procedure has been supplemented in recent times by a variety of error-determining routines using the most modern data-processing technology (*e.g.* the checking of empirical formulas, checking and standardization of nomenclature *etc.*).

#### 4.1.2. Systematic Classification (Beilstein's System)

In view of the enormous volume of the material to be processed, its classification along strictly logical lines is vital, not only in terms of its later accessibility to the user, but also for those compiling it. The classification of scientific material must ensure that chemically-related compounds be located in close proximity to one another and that all the information available on a compound be immediately retrievable. This in turn ensures that any number of cross-comparisons during compiling of a handbook entry are possible, which again facilitates the uncovering and clarification of any contradictory information which may have been recorded.

These requirements made of the classification system cannot be met by alaphabetical arrangement of the compounds according to their names, nor by arrangement according to their empirical formulas, nor by any other derived or artificial criteria. The Beilstein System is the only system of classification which meets all these requirements for all organic compounds known to date. The basic outlines of the system were developed by Beilstein for the first edition of his handbook, published in 1881, and then refined to their final form, which has stood the test up to the present day, by *B. Prager* and *P. Jabobson*.

The Beilstein System is based on the constitutional formula of the compound as the sole classifying feature and only takes account of the given structural properties ("morphology") of the compound; the essential feature of the system is that it represents a *natural* classification.

The principal classifiable criteria of the system can be summarized as:

A. Main subdivision (acyclic, isocyclic and heterocyclic compounds, the latter of which are further subdivided according to the type and number of the ring heteroatoms),
B. Functional groups (—OH, =O, —COOH, —$NH_2$ *etc.*),
C. Degree of saturation ($C_nH_{2n-x}$),
D. C-number (total number of carbon atoms),
E. Skeletal structure (unbranched, branched, monocyclic, bicyclic, ...).

For further details on the Beilstein System see ref.[11].

#### 4.1.3. Qualifications of the Scientific Editors

Every decision as to whether to include or reject information requires specialized knowledge of the field concerned by the scientific editor. For this reason, more than a hundred scientists (chemists), all of whom participate in continuous further schooling to keep fully up-to-date, are involved in the compilation of the Beilstein Handbook. These scientists are supported by a number of specialists fully familiar with the fields bordering on organic chemistry (*e.g.* biochemistry, organometallic chemistry, physics) or other special areas (*e.g.* nomenclature).

Table 2 shows which of the most important processing stages are absolutely dependent on specialized knowledge, *i.e.* in which processing is carried out by a qualified scientist.

#### 4.1.4. Scientific Aids

Alongside the pre-sorted material, a number of scientific aids are also available to the scientific editors of the handbook. These include, first of all, an extensive library con-

Table 2. Processing stages and compiling editors of the Beilstein Handbook.

| Processing Stage | Compiling Editor |
|---|---|
| Critically selective coverage of the original literature and checking the literature extracts | Specialized scientist (chemist) |
| Arrangement of the abstracts according to the Beilstein System | Chemical documentationalist and/or data processing |
| Preparation of the handbook entries | Specialized scientist (chemist) |
| Checking the entries (in two stages) | Specialized scientist (chemist) |
| Nomenclature and preparation of the indexes | Specialized scientist (chemist) and data processing |

taining all journals and patents as well as a large number of monographs and special publications covering the entire field of organic chemistry. For all important foreign languages translating chemists are available to provide an accurate translation of texts with thorough coverage of the contents.

### 4.2. General Criteria for Critical Screening without Loss of Information

Even today, the fundamental concept developed for the first edition of Beilstein's Handbook provides the basis for the critical processing carried out by the Beilstein editors. *F. K. Beilstein* formulated this concept in the preface to his work as follows[12]: "I have attempted in this work to provide as clear a review as possible of all analyzed organic compounds ... to exclude trivial and superficial information as well as properties and reactions *et cetera* which have not been studied exactly ... to include in its entirety all information which contributes to our precise understanding of substances, such as melting point, boiling point, specific gravity, solubility and so forth as well as precisely studied reactions and rearrangements of the substances ... to extract all data from the *original publications* of the authors ..."

In view of the enormous increases in the number of publications and the progress of chemistry over the last hundred years, the criteria laid down by Beilstein have of course had to be refined, further developed and adapted to keep pace with the advancement of knowledge. The demand for new, reliable and scientifically well-founded information has always been kept in the foreground, and then as now, first priority given to the documentation of all information of interest to the chemist for every organic compound. To combine this objective with simultaneous efforts to achieve maximal data reduction (elimination of redundant information) the criteria for critical screening without loss of content, discussed in the following, must be adhered to.

#### 4.2.1. The Material Correctness of the Information

The first stage of critical screening is to check whether the given information is consistent with current general chemical principles, whether it is compatible with all so far known facts about the compound, and whether contradictions are apparent with regard to data on homologous or analogous compounds. Where discrepancies arise, more detailed research becomes necessary, as a result of which corrections or reservations are noted in the report on the compound involved.

#### 4.2.2. Depth of Information

As experience shows, a depressing feature of the everyday search for information is that the abstracting journals often refer to the primary literature, which, when consulted, proves not to have been worth the effort after all. During compilation of the handbook it is therefore verified that the information possesses a certain "minimal depth" (minimal "content").

If information on a subject is available from *several* publications, it is determined whether some of the data cannot be disregarded in the interests of optimal reduction. A number of factors influencing selection in such cases are considered in the following section.

#### 4.2.3. Completeness of the Information

A publication can be considered as being maximally informative when all relevant details are described exactly, and all important parameters given. This is clearly required if the results given are to be reproducible, which is certainly to be aimed for.

#### 4.2.4. Objectives of the Publication

A further significant criterion for critical selection is consideration of the purpose and objectives of the publication. It is of considerable help in the assessment of a document to know whether the information presented is at the center of the author's interest, and thus of the publication, *i.e.* an essential objective of the work—or is merely an incidental finding. Obviously the "information consumer" is going to give more attention to a result presented in a publication which considers the theoretical background, and larger context, than to one from an otherwise equivalent publication in which the measured result is recorded without comment.

#### 4.2.5. Accessibility of the Information

Although a handbook is primarily concerned with the "documentation of facts" and only serves as a "source of references" for more complex issues, the availability, intelligibility (language) and age of the original publication are also of interest to user and compiler alike. Where more than one publication of comparable informational depth and coverage is available on the same subject, that published in the more easily procurable journal, in the more easily understandable language or of more recent date will generally be preferred.

### 4.2.6. Origin of the Information

A criterion which certainly merits a great deal of caution in its application concerns the competence of the author and the reputation of the journal. However, the knowledge that the author is a known specialist or that the research group involved has considerable experience in the field, and that the publication appeared in a journal with particularly strict rules for acceptance, is—in conjunction with the previously mentioned criteria—sometimes of assistance in making a decision.

## 4.3. Subject-Related Criteria for Critical Screening without Loss of Information

Whereas the criteria reviewed so far include considerations valid for all handbook information, those to be discussed now are more specifically relevant to the factual material dealt with in Beilstein in terms of the most important groups of features used for the description of organic compounds ("compounds meriting inclusion", "preparation", "physical properties", "analysis" and "chemical behavior").

### 4.3.1. Criteria for the Choice of Compounds to be Included

Fundamentally, in a critically assessed collection of chemical data, it would only appear meaningful to describe *isolated* or *definitely identified* compounds of *unambiguous* constitution.

#### *Identity of a Compound*

The most important requirement for the description of a compound—and thus for its nomenclature, documentation and retrievability—is knowledge of its identity, *i.e.* its chemical structure, which is determined by its constitution, configuration and by its conformation.

Compounds of unknown constitution, even when their empirical composition (elemental analysis) has been established with certainty, cannot be described with sufficient unambiguity to permit meaningful classification in the data collection and retrievability with an acceptable degree of effort (*e.g.* "compound $C_8H_{14}O_2$ with m.p. 184—186 °C"). Only where a slight degree of uncertainty exists for an otherwise established constitution (*e.g.* the position of a methyl group in a side chain, or of a C=C double bond) is the retrievability guaranteed to any extent and this condition for the inclusion of a compound fulfilled. (By contrast, the configuration of a species does not necessarily need to be known with certainty; even substances of uncertain or mixed configuration should be retrievable if their constitution is known.)

The constitution or configuration of a compound can be considered as certain when the described mode of formation is unambiguous in terms of general experience and when it has been verified by elemental analysis and physical measurements (*e.g.* spectra) or chemical methods (*e.g.* specific degradation).

Should doubts exist as to the correctness of the assignment of constitution or configuration to a compound, the critical assessment requires a literature search for further data on possible structures. If this research is unfruitful, the search for related compounds whose structure has been verified becomes necessary. This may enable the actual constitution or configuration of the compound in question to be clarified by analogy.

#### *Characterizing Data*

The reporting of the existence alone of a compound is not sufficient to justify its inclusion in the handbook since this information on its own is of little use.

In addition to the verified identity, at least one piece of data, such as details of the method of synthesis used, a characteristic parameter (physical property or information on its chemical behavior) or appropriate information on a salt or derivative should also be available.

The characterizing data must also be meaningful; most important is that the parameter measured is not influenced by existing uncertainties in the molecule itself. For example, data on the optical rotatory power of a compound of non-uniform configuration are just as unsuitable for characterization as the melting point of a mixture of diastereoisomers. The following loosely defined and general criteria can be regarded as a guideline for the inclusion of compounds:

- —Compounds of verified constitution which have been isolated in a configurationally uniform state and for which at least one piece of characterizing data is available are basically suitable for inclusion.
- —Should doubts exist as to a relatively unessential part of the otherwise known constitution of a compound, the configurational uniformity and assignment of the "main part" must be conclusive and adequate characterizing data available, so that where possible comparison with suitable material published at a later date may permit subsequent confirmation.
- —If the constitution of a configurationally non-uniform or questionable substance has been verified, data whose magnitude is not dependent on the configuration should be available.

### 4.3.2. Criteria for the Assessment of Data on Preparation

#### *General*

The information supplied in the primary literature on the preparation of compounds often provides wide scope for rigorous pruning of obsolete material during critical screening.

Thus, the inclusion of modes of formation of no apparent preparative value is invariably suppressed when other useful procedures for the preparation of the compound are already known; strict criteria are to be applied here, particularly for compounds which are frequently described.

Details on already well-known methods of preparation should only be included if an improvement, or at least an equally useful variation of the earlier procedure, is described. Chemical reactions occurring under conditions clearly chosen with a view to isolating another compound are only taken into consideration if no other preparatively useful methods have been described. The question must thus always be asked in assessing a preparational method as to whether the objective of the reaction described was to synthesize a compound, or merely to provide proof of the identity of its precursor by degradation or derivatization.

*Procedure for Critical Screening of Preparational Methods*

Where various methods for the preparation of a compound have been described, it is to be recommended that each individual piece of information be checked in accordance with the scheme shown in Table 3 during critical screening of these data.

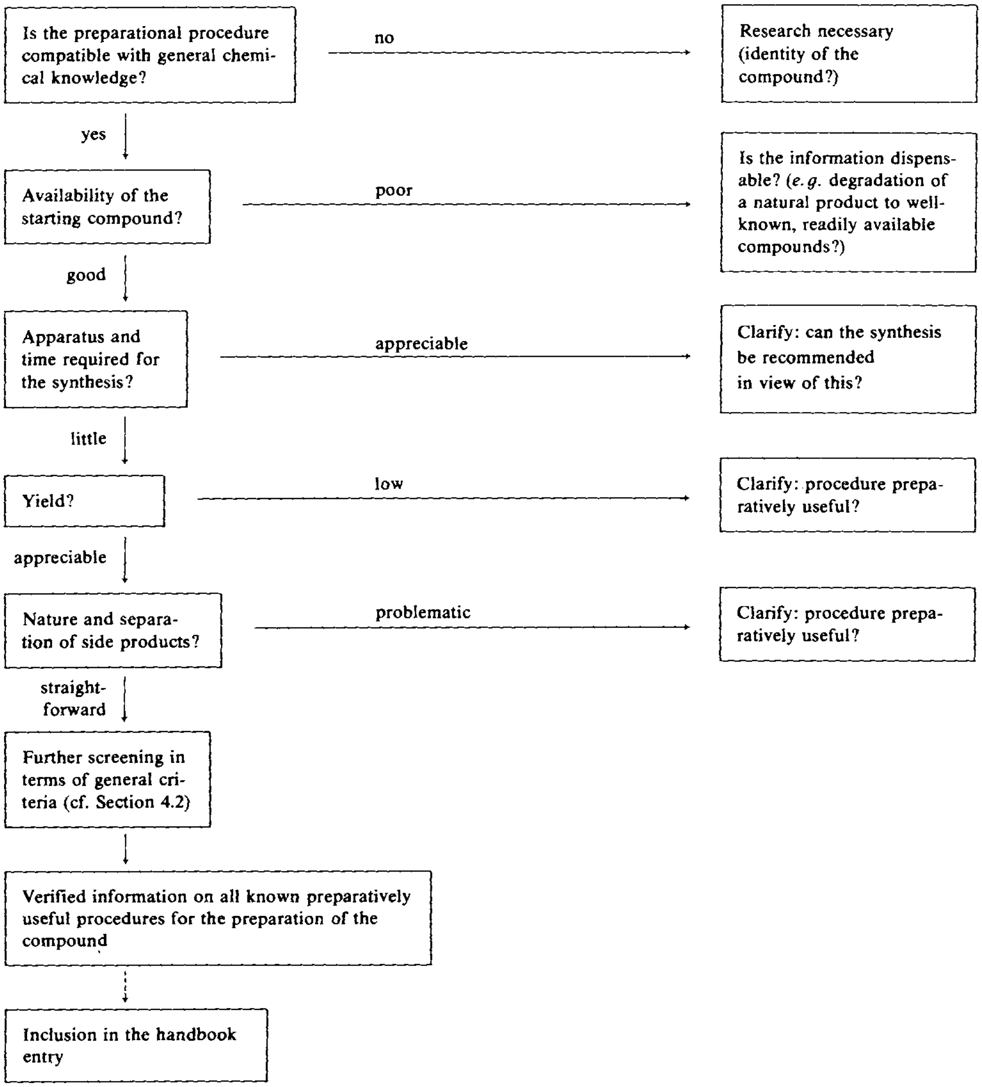
The first question is directed at determining whether the chemical reactions taking place during the synthesis are compatible with general chemical knowledge at all, and thus touches on the problem of the identity of the compound, already discussed in Section 4.3.1. If serious doubts should arise, clarifying research becomes absolutely necessary. If an affirmative response to the first question still leaves a choice of several methods of preparation it must now be examined how readily (relatively) the starting material is available, what experimental effort (apparatus and time) is required for the synthesis, how high the yield is, the nature of the side products and how these can be separated. If this scheme is properly applied, particularly where a large number of preparative methods have been described the best and most important procedures can be determined. A final screening according to the general criteria mentioned in Section 4.2 permits a further selection to be made among multiple publications of the same content.

### 4.3.3. Criteria for the Assessment of Data on Physical Properties

*Purity of the Substance*

The first and most essential criterion for assessment is the purity of the substance (uniformity of constitution and configuration). First indications of this are provided by the elemental analysis. After this, it must be determined

Table 3. Scheme for the critical screening and assessment of information on the preparation of a compound.



whether the author had been at particular pains to isolate the substance in the pure state by recrystallization, distillation, chromatography *etc.*, or whether the substance had been obtained only as an intermediate or crude product for further processing.

*The Method of Measurement and Completeness of the Description of the Experimental Conditions*

First of all, the method of measurement used to determine the physical property under discussion is examined. If a classical, well-known parameter (*e.g.* melting point, boiling point, refractive index *etc.*) is involved, the method of measurement plays a less important role than where the parameter is determined with the aid of a modern technique such as NMR, NQR, ESR spectroscopy *etc.* In the latter case, the stage of development of the instruments used is decisive in assessing the quality of the measurement. A further criterion is provided by the description of the experiment, which, depending on the ease with which it can be performed, permits a more or less exact reproduction.

*Completeness and Accuracy of the Data*

Publication of a physical result is only of value if all the necessary parameters are given. A further indication of the quality of the result is provided by the limits of error, where supplied, as well as a complete and exact description of the units.

*Specific Criteria*

Alongside these general principles—valid for the assessment of all factual information of a physical nature—there also exist a number of specific criteria relating to the nature of the information, which in view of their great number cannot all be mentioned. Three representative examples will show how these detailed deliberations take shape.

a) IR Spectrum: To be taken into account here are the method of preparation of the sample (film, KBr, Nujol or $CCl_4+CS_2$ *etc.*), the resolution of the IR spectrometer used, as well as details of the range of measurement and the way in which the spectrum is reported in the publication (a table of wave numbers or the complete spectrum? Size and precision of reproduction of the spectrum?).

b) Dipole Moment: An important aid to assessment is the method of measurement (microwave spectrum or measurement in solution). It must further be asked which solvents were used (nonpolar or polar) and which method was used for determining the value from the measurements (Debye, Onsager, Kirkwood *etc.*); is the molecule capable of free rotation, and was the resulting temperature dependence of the dipole moment taken into account?

c) Dissociation Constant[13]: Again, the method of measurement is to be considered first of all (*e.g.* determination of the values by potentiometric, conductometric, spectrophotometric or kinetic procedures) since these methods are associated with very different sources of error. It must further be noted whether the ionic strength was taken into account and, in the case of precision measurements, the interface and transport potentials. For measurements carried out in non-aqueous solutions, attention must also be paid to exact definition of the pH value.

Altogether, these three examples show how essential it is that the application of assessment criteria be carried out by capable scientists who are familar with the particular field in question.

### 4.3.4. Criteria for the Assessment of Analytical Data

In view of the increasing use of physical methods in analysis, the criteria mentioned in Section 4.3.3 with regard to physical properties also apply here. It must be added that only properties which relate to the individual substance can be considered; analytical properties which are typical of a certain class of compounds (*e.g.* color reactions of phenols) are not considered. Particular emphasis is laid on the unambiguity and reproducibility of the analytical proof.

### 4.3.5. Criteria for the Assessment of Data on Chemical Behavior

The first thing to be considered here is whether the course of reaction given is consistent with general chemical knowledge, and whether constitution and configuration of the reaction products have been determined with certainty, or whether they have only been conjectured.

Where *qualitative studies* are involved, particular attention must be paid to whether the clarification of the course of the reaction was the object and an essential part of the publication. In studies concerned with the preparation of a compound or determination of the structure (*e.g.* by degradation experiments on natural products), the novelty of the reactions described are used as a criterion. All known reactions can be disregarded if these have already been studied for many other analogous compounds and have thus become general knowledge. By contrast, for *quantitative studies* (kinetics and equilibria) involving substance-specific properties, corresponding data for every compound described should be included. Here again, however, it must also be checked how exact the description is and what relevant parameters are given. In kinetic studies the quality of the measurements and the interpretation of the equation describing the reaction warrant particular attention. The question of configurational uniformity again becomes important here since it almost invariably decisively influences the course of reaction.

## 5. The Significance of Critical Screening and Assessment in Documentation Today and Tomorrow

Following the naming and discussion of the most essential criteria for the critical selection and appraisal of findings in terms of the Handbook of Organic Chemistry, the value of the resulting compacted information is to be considered in conclusion, and an idea of the possibilities for recognition and correction of erroneous information provided, together with a word on the significance of these effects for those seeking information.

### 5.1. Examples of the Extent to Which Data Reduction without Loss of Information is Possible

The efficiency of the system for critical screening and assessment, discussed above, will now be illustrated in terms of its practical application to three compounds, in order to demonstrate just how far data may be reduced by judicious use of the criteria outlined. The results of this test, based on a comparison of the publications cited in an abstracting journal which covers the entire primary literature (Chemical Abstracts), and in the Beilstein Handbook, are summarized in Table 4. (Detailed records of this test can be made available to those interested by the Beilstein editorial staff.)

The test was restricted to material published between 1950 and 1959 for examples 1 and 2, and between 1930 and 1959 for example 3[*]. The information was compared with data already available in earlier volumes of the Beilstein Handbook and checked for its documentational merit. The data in Table 4 show that for the examples chosen a reduction in the number of sources by about one half was possible. It may be added that Beilstein editorial experience shows this reduction by about 50% to be usual for compounds treated with moderate frequency in the literature—between once and 5 times annually. For very frequently discussed compounds, the extent of reduction is considerably higher; in extreme cases, less than 10% of the original citations on a particular category of results are included in the handbook. On the other hand, the situation is necessarily very different for compounds only described in a single original document. In such cases, a critical comparison of data from various sources is not possible and the question of data reduction is limited to a check on whether the conditions for inclusion of the compound are fulfilled at all.

### 5.2. Examples of the Recognition and Correction of Erroneous Primary Literature

As implied in Section 4, the elimination of redundant material is only one aspect of the critical processing of primary information. A further essential feature, of self-evident significance for the user, is the recognition and correction of erroneous data in the original literature. An analysis of Volume 19 of the Beilstein Handbook[*] showed that for more than 2500 compounds, either corrections to the original constitution, given in later publications, had to be taken into account, or, for the first time, unambiguous constitutional assignments had to be made by the Beilstein staff with the aid of analogies or on the basis of genetic relationships to reaction precursors or products. The net result was that critical processing led to a correction or verification of the constitution of almost every tenth compound. A similar situation applies for all other groups of features—particulary for all numerical values.

### 5.3. Significance for the User

The test examples presented in Table 4 demonstrate the efficiency of the procedure described for "critical screening without loss of information". The analysis of the contents of Volume 19 of Beilstein's handbook, mentioned above, shows the significant extent to which errors can be brought to light by critical processing. Application of these procedures represents the greater part of the day-to-day work of the Beilstein scientific staff.

What are the advantages and benefits of a collection of facts and data compiled in this way for those in search of information?

—Improved confidence in the accuracy of the tested data,

—Diminished risk of false conclusions and non-optimal experimental planning as a result of inexact literature results,

—Better possibilities for ballast-free research by concentrating on dependable data,

—Intensive intellectual "reexamination" of selected data unnecessary—greater time saving,

—Guarantee that no relevant information is lost.

In 1880, possibly in premonition of the success of his handbook, *Friedrich Konrad Beilstein*'s "ready tongue", which, in his own words, "God had seen fit to place in his head", formulated the benefits of critical processing in the

Table 4. Extent of information reduction in the Beilstein Handbook by critical screening.

| Name of the compound, Beilstein citation | Number of citations | | Eliminated during Beilstein processing since | | | Reduction in the number of citations in Beilstein [i] | Number of citations only to be found in Beilstein for this compound "*c*" |
|---|---|---|---|---|---|---|---|
| | in Beilstein "*a*" | in Chemical Abstracts "*b*" | contents already known and described in earlier Beilstein series | duplicate publication (prior publication) | does not merit documentation according to other criteria | | |
| 9-Bromoanthracene<br>E IV *5* 2295 [a] | 14 [b] | 24 [b] | 1 [e] | 3 | 7 [h] | 2:1 | 1 |
| 3-Aminocrotonic acid ethyl ester<br>E IV *4* 2841/2 | 5 [b]<br>(+2) [c] | 10 [b] | 4 [f] | 1 | 2 [h] | 3:I | 2 |
| 3,6-Dimethoxypyridazine<br>E III/IV *23* 3089/90 | 12 [d] | 15 [d] | 0 [g] | 3 | 1 [h] | 4:3 | 1 |

[a] E IV *5* 2295: Beilstein, Supplementary Series 4, Volume 5, p. 2295. [b] Literature period: 1950—1959. [c] One result on the constitution (tautomerism) and one correction of earlier information on the chemical behavior of the compound from the literature period from 1960—1981. [d] Literature period: 1930—1959. [e] Literature results from the period before 1950, are to be found in the following Beilstein Series: Basic Series, *5*, p. 665; Supplementary Series I, *5*, p. 326; Supplementary Series II, *5*, p. 576; Suplementary Series III, *5*, p. 2134. [f] Literature results from the period before 1950 are to be found in the following Beilstein Series: Basic Series, *3*, p. 654, Supplementary Series I, *3*, p. 228; Supplementary Series II, *3*, p. 423; Supplementary Series III, *3*, p. 1199. [g] No literature results available from the period before 1930. [h] Mainly data given in more detail in other publications. [i] *b*: (*a*—*c*).

---

[*] For the classification of essential features (*e.g.* constitution and configuration) the latest results, appearing in the literature right up to the time of publication of the sub-volume, are taken into account during processing of the Beilstein reports.

[*] Beilstein Supplementary Series III and IV of volume 19 describe about 26000 compounds on over 5000 pages of text. Our thanks are due to Dr. *Th. Schmitt*, Beilstein Institute, for performing the analysis.

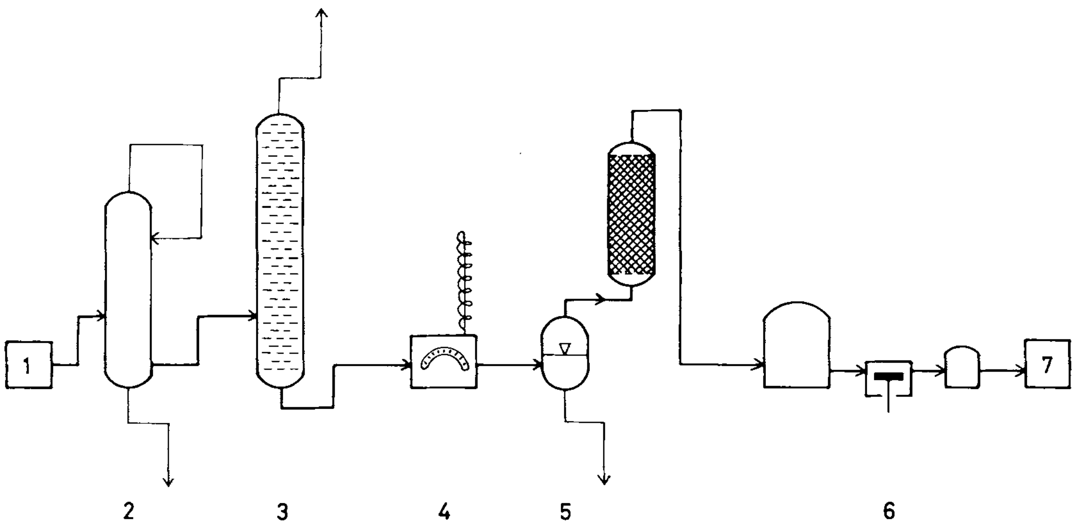


Fig. 2. The procedure of critical screening: In view of its enormous volume, processing of the scientific primary literature has almost reached the dimensions of "industrial" processing. The individual stages of critical assessment are thus readily adapted to the symbolism of industrial technology: 1) primary literature; 2) extraction of the primary literature; 3) "volatile" information distilled off; 4) analysis and evaluation; identification of erroneous data; 5) separation of duplicate information; adsorption of erroneous data; 6) concentration of the information; 7) scientifically assessed information.

following way: "... How delighted such people as *Richter, Wislecenus, Kolbe* and other producers of little books will be, now that everything has been cut to size and they can scoop wisdom by the *bushel* from my well-filled sacks and redistribute it by the *teaspoonful* ..."[8].

### 5.4. Summary and Prospects

In the previous sections, a selection of important considerations, criteria and guiding principles has been reviewed which make it possible for a competent scientist to screen and selectively evaluate data and facts published within his special discipline (here chemistry) and subsequently record and pass them on to the consumer without loss of information. This procedure has not only proved entirely satisfactory for specialized authors of monographs, writing within a narrower field, but also for editors of scientific handbooks, whose task involves critical screening of the literature for an entire discipline (here organic chemistry).

The hundred-year tradition of Beilstein's Handbook of Organic Chemistry testifies to its lasting value and authority, and shows what importance is attached by users to the continuity of the basic concept and the tested dependability of the work. The future task of those entrusted with its compilation will be to retain the well-established conceptual principles of the Beilstein Handbook as a work of critical assessment, but at the same time to remain flexible in the practical business of compilation and able to adapt to current and future developments both in terms of technical innovation and user requirements. It will only be possible to accommodate the steadily increasing volume of data in future if even stricter standards are imposed on the originality and accuracy of results included.

The creation of a computerized "information retrieval" facility for Beilstein is currently under development. It is also being considered to what extent a link-up, useful to the Beilstein user, with other established computer-oriented chemical information systems can and should be implemented.

However, even by stepping up the use of electronic data processing in chemical documentation and information, there is likely to be little change in the significance of the critical screening discussed above. Quite the contrary, sooner or later, in view of the increasing volume of information, critical prior assessment is likely to be of more significance even where data are to be stored in computer information retrieval systems, since this is the only way in which the plethora of data can be reduced. Worthy of note in this connection is that this critical assessment invariably requires the specialized scientist with appropriate training who is able to take into account the criteria and necessary premises on which an acceptance of data depends. Since many of the assessment criteria, with due modification to detail, are certainly of a significance which extends above and beyond the field of chemistry discusssed here, it can be generally said that the procedure of critical screening also provides *one* possibility for other scientific disciplines to direct the current (and future) flood of information into orderly channels.

Received: March 16, 1981 [A 386 IE]
German version: Angew. Chem. *93*, 876 (1981)
Translated by Dr. *M. H. Donbavand*, Berlin

[1] *R. Luckenbach, J. Sunkel,* Naturwissenschaften *68,* 53 (1981).

[2] *R. Luckenbach,* Chem. Unserer Zeit *15,* 46 (1981).

[3] *D. A. O'Sullivan,* Chem. Eng. News *59* (20), 21 (1981).

[4] *K.-C. Buschbeck, W. Lippert, E. Ühlein,* Naturwissenschaften *55,* 379 (1968).

[5] CAS Today, American Chemical Society, Columbus, Ohio 1980.

[6] a) *S. A. Goudsmit,* Phys. Today *19,* 52 (1966); b) *R. Abbel,* Nachr. Dok. *21,* 95 (1970).

[7] *J. P. Phillips,* Chymia *11,* 89 (1966).

[8] *O. Krätz:* Beilstein-Erlenmeyer, Briefe, Neue Münchner Beiträge zur Geschichte der Medizin und Naturwissenschaften, Naturwissenschaftshistorische Reihe Bd. 2, Werner Fritsch, München 1972.

[9] Nachr. Chem. Tech. Lab. *28,* 501 (1980).

[10] *E. Ühlein,* Nachr. Dok. Beih. *14* (1966).

[11] a) How to Use Beilstein, an Informative Guide to Beilstein's Handbook of Organic Chemistry, Springer-Verlag, Berlin 1979; b) *R. Luckenbach, R. Ecker, E. Hoffmann, J. Sunkel,* to be published.

[12] *F. Beilstein:* Handbuch der Organischen Chemie, 1st. Edit., L. Voss-Verlag, Hamburg und Leipzig 1881.

[13] *G. Kortüm, W. Vogel, K. Andrussow:* Dissociation Constants of Organic Acids in Aqueous Solution. Butterworths, London 1961, p. 191ff.

# Replication and Evolution in Inorganic Systems[**]

By Armin Weiss[*]

Using layer silicates as models, the principle of replication, *i.e.* the spontaneous self-multiplication of a carrier of information, can be shown to be a general property of certain macromolecular systems. Errors in replication and feedback together with environmental influences may lead to mutants with higher or lower replication rates, thus enabling evolution. In the light of these findings, the question of whether or not chemical evolution resulted directly in the nucleic acid/protein system, *i.e.* the genetic principle common to all living systems known up to now, has to be answered. It seems conceivable that as a first step a much simpler replicating system was formed: such a system might then have undergone an evolution of replicating systems, resulting in the final nucleic acid/protein system.

## 1. Introduction

During the course of galactic evolution, the first solid rocks on our earth formed about $4.5 \times 10^9$ years ago. The earth's independent chemical evolution, therefore, stems from this date. Almost all specialists agree that the oldest microfossils are found in rocks which are 3.3 to $3.5 \times 10^9$ years old. These microfossils indicate that biological evolution had already started at this time, and strongly influenced the chemical evolution on earth *via* feedback mechanisms.

In the course of chemical evolution on the prebiological planet, a large number of molecules (amino acids, purines, pyrimidines, fatty acids, and sugars) were synthesized from $H_2$, $H_2O$, $NH_3$, $(CN)_2$, CO, $CO_2$, HCHO, and $H_2S$—the constituents of the primordial atmosphere. Most of these syntheses could have been induced by the action of electrical discharges and UV-radiation from the sun. This radiation was much more intense than that of today, due to the absence of the protecting ozone layer in the stratosphere. Probably, the first free oxygen on earth was generated by photosynthesis of living systems.

Yields obtained in simulation experiments lead to the conclusion that the primordial oceans corresponded to a "chicken broth" with respect to their amino acid content. Normal and selective adsorption may have accumulated many of these compounds in huge amounts. Furthermore, many molecules may have been brought to earth from extraterrestial sources *via* meteors. With increasing concentrations, condensation and polymerization reactions could have become more frequent and macromolecules could have developed. According to *Fox*[1], peptides and protoproteins may also have been formed at this stage. Hydrophobic interactions caused amphiphilic molecules to arrange in structured aggregates or membrane-like systems.

There is a gap in our knowledge concerning the next step. In the course of the chemical evolution of macromolecules and organized molecule aggregates, proteins and nucleic acids, *i.e.* the genetic material, must have been formed. The appearance of the genetic principle is a milestone in the process of chemical evolution: it is chemically the same in all forms of life known to date, and is involved in the replication of information which is fixed in the nucleic acids in the well-known helix or double-helix model; with it, biological evolution could start.

The starting point for our experiments was the question: are nucleic acids the only systems capable of replica-

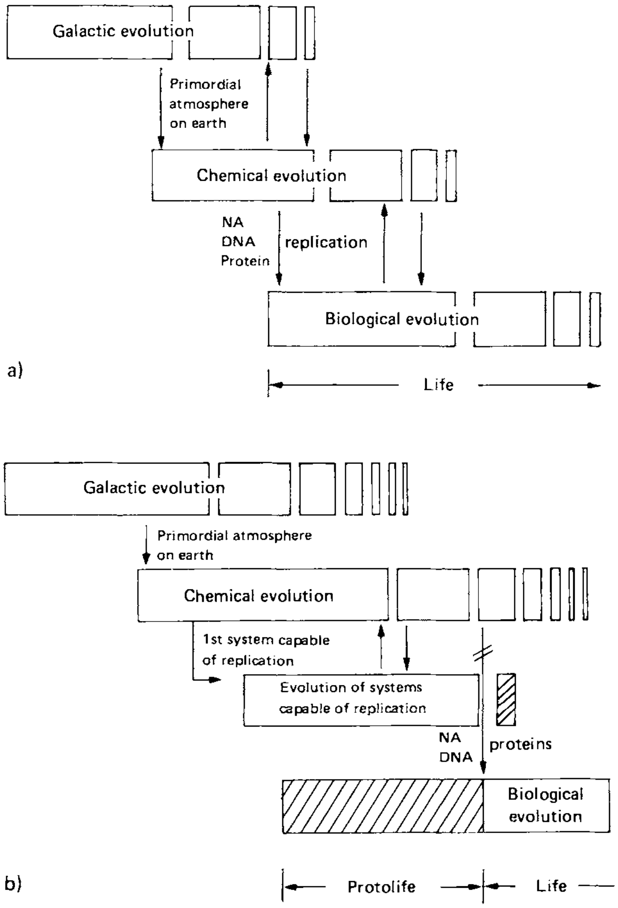


Fig. 1. Scheme of Evolution. a) Direct formation of the genetic nucleic acid (NA)-protein system within the context of chemical evolution; b) between chemical and biological evolution, an evolution of replicative systems (protolife) has been inserted.

---

[*] Prof. Dr. A. Weiss
Institut für Anorganische Chemie der Universität München
Meiserstr. 1, D-8000 München 2 (Germany)

[**] Delivered at the 11th Congress of the Gesellschaft Deutscher Naturforscher und Ärzte, September 23, 1980, Hamburg.

0570-0833/81/1010-0850 $ 02.50/0

tion, *i.e.* was the principle of replication uniquely bound with living systems, or do other replicating systems based on different, perhaps simpler chemistry exist? If replication of a carrier of information is a more general property of chemical systems, the DNA/protein system might only be a highly perfect realization of this principle, far superior to all others with respect to maximum replication rate, entropy production, and adaptability to an environment, changing permanently due to chemical evolution and therefore exclusively used by all life as we know it today.

A consequence of this reasoning leads to the conclusion that further considerations (Fig. 1b) must be added to the previously discussed scheme of evolution (Fig. 1a).

In the course of chemical evolution a primitive replicating system could have developed at a very early stage in the history of the earth[2]. This principle might have undergone an evolution of its own and the evolution of the replicating systems might have culminated in the DNA/protein system. In this case, we would have to concede the existence of alien life not based on DNA/protein. We could refer to this as protolife.

## 2. Conditions for a Simple, Replicating System

A system may be looked upon as replicating, only if it can undergo a spontaneous self-multiplication process in which information is transferred from the mother to the daughter units. The information may be written in full-length or coded in shorthand, as in the DNA/protein system. In practice, the information has to contain either the instructions for the synthesis of a large number of catalysts for the most important chemical reactions like hydrolysis, condensation, oxidation, reduction, and polymerization or has to contain all these catalytic sites in its own replicating structure. These conditions are restricted to macromolecular systems or aggregates. Long-term storage of several pieces of information in isolated small molecules is impossible.

The chemistry of the system should be simple. Synthesis should be possible either with or without ubiquitous catalysts like $H^+$ or $OH^-$: compounds with a macromolecular carbon skeleton are, therefore, eliminated. Bonds and conformations have to be sufficiently stable under the environmental conditions necessary for the self-multiplying process. This also precludes compounds which preferentially adopt pure ionic bonds.

The process of replication, *i.e.* the transfer of information from a matrix onto the replicas, must be precise. Errors may occasionally occur, changing the instructions for the synthesis of at least one catalyst or changing a catalytic property itself. In addition, errors in replication should either accelerate or retard further replication. Retardation can eliminate erroneous replica, acceleration may lead to dominance of the changed information. The chemistry of the system should allow separation of the matrix and replica by an appropriate mechanism, thus enabling the replica to act as matrix on its own.

This latter postulate excludes all simple phenomena of crystal growth. It is well known that many crystals are able to incorporate different information *via* structural defects. For example a screw dislocation which reaches the external surface may decrease the activation energy for many reactions, and act as an active site in catalysis[2]. The distance between these defects, the dislocation density, may alter the catalytic capabilities, quantitatively or even qualitatively. Such a crystal will grow in an appropriate solution and, in general, the screw dislocations will grow along with it, *i.e.* the catalytic capability will be reproduced. However, old and new parts of the crystal cannot be separated by any simple process. Only under the influence of external force, will the crystal be randomly broken into smaller pieces, each of which can act as a growth nucleus for a new crystal. Independent crystals with dislocations will grow from all pieces with dislocations. Their distribution in the different crystals will, however, be random.

Spontaneous separation of matrix and replica, *i.e.* multiplication, requires special mechanisms. In order to store a large number of pieces of information simultaneously, macromolecules or complex systems of small units are required. If these undergo replication, there is strong mutual adherence due to the many sites of contact. This is well known from adsorption and desorption experiments on macromolecules. Usually good separation only becomes possible when the environment is changed; this either alters the surface charge or produces a reversible conformational change.

## 3. Layer Silicates as Models

A simple mechanism of reversible separation, the intracrystalline swelling of montmorillonites and its homologues are silicates with layer structures, and within the indicovered by *U. Hofmann* in 1933, allows the reversible separation of montmorillonite crystals into individual layers of only 9—10 Å thickness[3]. Montmorillonite and its homologues are silicates with layer structures and within the individual crystals the layers are arranged parallel to each other (Fig. 2a). If water is added to such a crystal, water molecules penetrate into the interlayer region, thus increasing the distance between the parallel layers. The equilibrium distance is determined by the electrolyte concentration of the water (Fig. 2b). The lower the ionic strength, the greater the spacings. In the case of 1 : 1 electrolytes the attraction potential approaches the order of the thermal energy at electrolyte concentrations of less than $10^{-3}$ M. The crystals then disintegrate into the individual layers, each of these becoming an independent kinetic unit (Fig. 2c).

Individual layers of a disintegrated crystal, when introduced into an appropriate culture medium containing the necessary ingredients, may act as nuclei for new crystals. Formation of a new layer is highly influenced by the nucleation step. The activation energy for nucleation of montmorillonite layers is decreased by a factor of 0.25—0.35, relative to that for homogeneous nucleation, in the presence of "matrix layers"[*].

---

[*] Experimental determination of the activation energy for nucleation is extremely time-consuming. The degree of error is high when absolute values are to be determined.

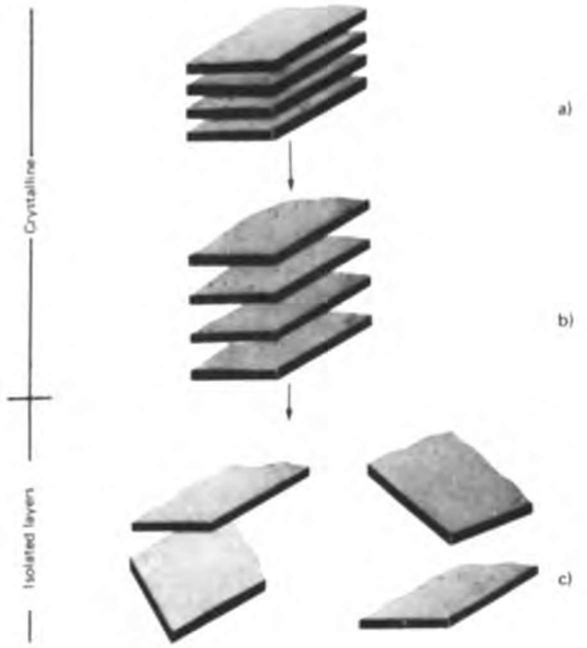


Fig. 2. Scheme for the reversible dissociation of a montmorillonite crystal. a) Layers of a crystal, stacked parallel to each other; b) increase in basal spacing (layer distance), following uptake of water (reduction of electrolyte concentration); c) disintegration of a crystal into individual, kinetically independent layers at low electrolyte concentration ($c \leq 1 \times 10^{-3}$ M of a 1,1-electrolyte).

On decreasing the electrolyte concentration, crystals having newly synthesized layers may also undergo disintegration, thus representing a powerful self-multiplying system. In nature, the external conditions may be provided by each cycle of thawing or by the change from rain to drought. The electrolyte concentration in melting ice is so low that disintegration into individual layers becomes possible. Simultaneously, the suspension of layers becomes highly dilute. As a consequence of the solubility of rocks and soils, and subsequent evaporation of water during drought periods, conditions are created for the synthesis of new layers on the previously existing matrix layers. In addition to cycles of thawing or rain and drought periods, the synthesis requires a distinct ratio of $Mg^{2+}$ and $Ca^{2+}$ to $K^+$ and $Na^+$ ions during the growth phase; the absolute concentrations must not exceed a certain limit. $Mg^{2+}$ and $Ca^{2+}$ limit the uptake of water and expansion of the interlayer distance up to a maximum of *ca.* 12 Å.

As shown in Section 5, individual montmorillonite layers carry quite a number of pieces of different information. If the growth of new layers, nucleated on matrix layers, is connected with the transfer of this information onto the new layers, the self-multiplying montmorillonite could be viewed as a true replicating system. Experiments aimed at investigating the transfer of information in repeated cycles,

disintegration of the matrix into individual layers and subsequent high dilution→

synthesis of new layers on isolated matrix layers→

redisintegration into individual layers and subsequent high dilution→

resynthesis of new layers on isolated matrix layers,

had little success. The transfer of information could not be clearly recognized, even in the first generation. This can, however, be rationalized on the basis of the structure of the individual siicate layers; they have a thickness of *ca.* 9.2 Å and consist of six atomic layers (Fig. 3).

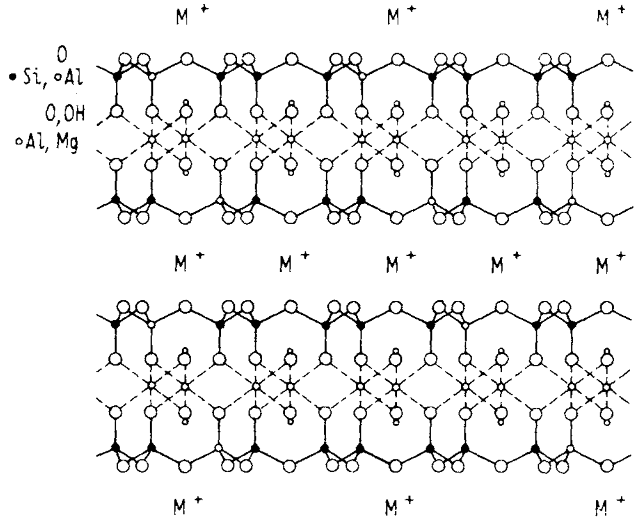


Fig. 3. Structural scheme of a single layer of montmorillonite. $M^+$ = univalent cation.

The Si atoms are tetrahedrally coordinated by four O atoms; neighboring tetrahedrons share common corners, thus forming a two-dimensional $Si_2O_5$-layer. In the idealized structure three of the oxygens, which simultaneously belong to two tetrahedra, lie in one plane. The fourth O atom of each $SiO_4$-tetrahedron protrudes perpendicularly from the layer but is uniformly orientated towards one side of the latter. Two of these tetrahedral layers are interconnected by an octahedral Al(O,OH)-layer. On an atomic scale the information, which should be transferred onto the replica layers during synthesis consits, in general, of isomorphous substitutions of $Si^{4+}$ by $Al^{3+} + M^+$ or of $Al^{3+}$ by $Mg^{2+} + M^+$. A true image of these defects in the replica layers requires long-range forces (up to *ca.* 23 Å, undisturbed by the several sheets of the matrix).

## 4. The Intercalating Synthesis of Silicate Layers

Formally, a different mechanism for a replicating synthesis in such silicates can be postulated. By careful choice of concentration and composition of electrolytes in the growth solution, the interlayer distance can be stabilized at just that value which allows nucleation and growth of new layers in the interlayer region.

From studies of intercalation mechanisms it is well known that the layers can be elastically deformed. Instead of intercalation of small molecules, a newly synthesized layer could grow into the interlayer region, pushing along the frontier of the elastic deformation of the matrix layers (Fig. 4a).

In this way, information on structural irregularities could be transferred from the bottom sheets of the top matrix layer to the top sheets of the new silicate layer, and from the top sheets of the bottom matrix layer onto the bottom sheets of the new silicate layer. Special long-range forces would not be necessary. In principle, this mechanism could be viewed as a primitive two-dimensional analogue of the replication of the double helix of DNA. This is illustrated in simplified form in the scheme in Figure 4b.

varies with water content; appropriate conditions result in total disintegration into individual layers. In contrast to montmorillonite, the smallest kinetically independent units are not single silicate layers, but pairs of layers. Correspondingly, the intercalating synthesis of new layers can only occur in each second interlayer. This permits a simple experimental proof.

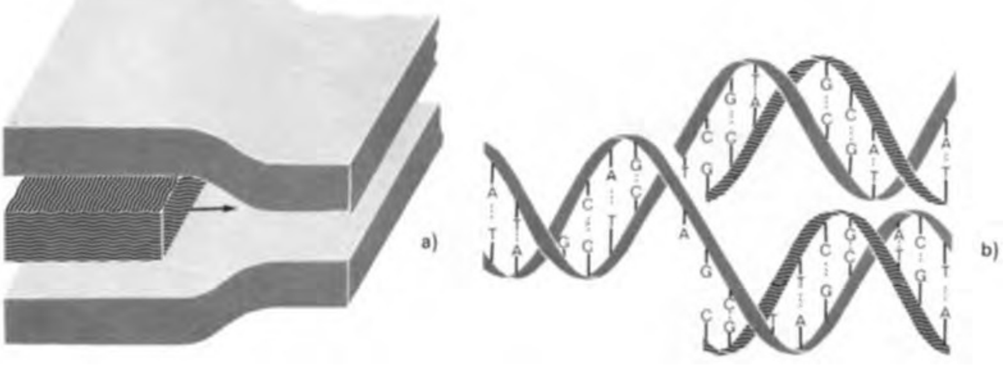


Fig. 4. Comparison of the intercalating synthesis into montmorillonite with the replication of DNA. a) Intercalating synthesis of a silicate layer; b) simplified scheme of the replication of DNA. (Matrix: dark; replica: shaded).

Intercalating synthesis in layer silicates has been known for some time. Under slightly hydrothermal conditions, layers of *e.g.* $Mg(OH)_2$ or $Al(OH)_3$ can be intercalated into the montmorillonite layers, resulting in the formation of chlorites. This synthesis is important in chloritization processes in nature[4].

Unequivocal experimental proof for the intercalating synthesis of montmorillonite silicate layers in montmorillonite, however, meets with considerable difficulties. In those cases where the replica- and matrix-layers are identical, there is no way of differentiating matrix and replica after the synthesis. Moreover, there is no way of distinguishing new layers synthesized either by intercalation or by nucleation on an external basal plane of the matrix. The intercalating synthesis of new montmorillonite layers was eventually unambiguously proven using the rare layer-silicate allevardite[5] as model. The layers of allevardite closely resemble those of montmorillonite; in contrast, however, they are highly asymmetric. The extent of isomorphous substitution of $Si^{4+}$ by $Al^{3+} + M^{+}$ in the two tetrahedral Si—O units of a layer, differs by a factor of three. The stacking of the layers within a crystal is such, that the opposite tetrahedral sheets of adjacent layers have alternately both high or low degrees of substitution. Each replacement of $Si^{4+}$ by $Al^{3+}$ creates an excess negative charge within the layer. For charge balance, cations of equivalent charge have to enter the interlayer space. The typical stacking of the asymmetric allevardite layers thus results in interlayers with regularly alternating very high and very low densities of interlayer cations. The high density corresponds to that of micas. Here the electrostatic attraction between the negatively charged layers and the interlayer cations is of such strength, that under normal experimental conditions hydration of the latter becomes impossible. The interlayer distance is, therefore, fixed at that of closest approach. The low interlayer cation density corresponds to the situation in montmorillonite. The interlayer cations can be hydrated and the interlayer distance

The identity period in allevardite comprises two layers. Therefore, the basal spacing determined by X-ray measurements corresponds to 24.6 Å under normal conditions; 10.2 Å (mica-like part) and 14.4 Å for the montmorillonitic part (silicate layer + 2 layers of $H_2O$) (Fig. 5a). After the intercalating synthesis of one layer in each montmorillonitic interlayer the measured spacing *d* becomes *ca.* 39 Å ($d = 10.2\ \text{Å} + 14.4\ \text{Å} + 14.4\ \text{Å} = 39.0\ \text{Å}$). Shortly after the start of the synthesis, broad first and second order reflections appear. After *ca.* 48 h the original first and second order (001)-reflections disappear, and the new series of reflections become sharper (Fig. 5b). If the synthesis is performed over several weeks another series of (001)-reflections is observed with a spacing of *ca.* 68 Å (Fig. 5c). This results from the intercalation of two additional layers be-

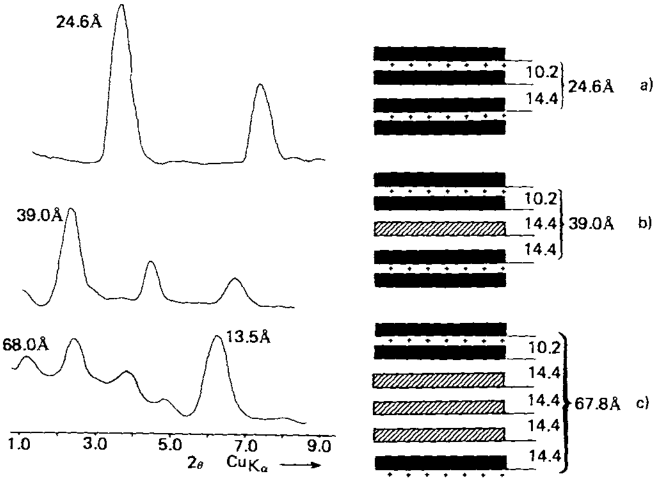


Fig. 5. Evidence for the intercalating synthesis of montmorillonite layers into allevardite. Left: intensities of (001)-reflections in the region $2\theta = 1.0-9.0$ at a water vapor pressure of 6 torr ($Cu_{K_\alpha}$-radiation): right: stacking of layers. The repeat period in the direction normal to the layers is shown in brackets. a) Allevardite, the starting material; b) sample at the end of the intercalating synthesis of the first layer; c) far advanced stage in the synthesis of three new layers (matrix: dark; replica: shaded).

tween the interlayers of the matrix layers and the first intercalated montmorillonite layer ($d = 10.2$ Å + 14.4 Å + 14.4 Å + 14.4 Å + 14.4 Å = 67.8 Å).

To achieve this intercalating synthesis of montmorillonite layers, the experimental conditions must be carefully controlled. We used allevardite from Sarŏspatak (Hungary). The overall electrolyte concentration must not exceed 0.02 N and the ratio of $Na^+ : K^+ : Mg^{2+}$ has to be kept within sharp limits during the synthesis. $Al^{3+}$ was applied as a low charged complex and $SiO_2$ as $Si(OH)_4$.

Systematic experiments have shown that the activation energy for nucleation of a new layer is much smaller in the intercalating synthesis than in synthesis on top of a single matrix layer. The decrease is in the order of one half to one third. Therefore, experimental conditions can be chosen which certainly do not allow homogeneous nucleation from the solution.

## 5. The Information Capacity of a Silicate Layer

The individual silicate layers have only been well characterized structurally but not chemically; they belong to a nonstoichiometric series with a wide range of composition and degree of isomorphous substitution. The substitution of $Si^{4+}$ by $Al^{3+}$, or $Al^{3+}$ by $Mg^{2+}$ creates, in addition to the excess negative charge, a Lewis base site. Such sites are distributed more or less randomly within each layer with areas of higher and lower densities. Correspondingly, there are Lewis acid sites in the interlayer space.

As is well known, Lewis base- and Lewis acid-sites represent sites of high catalytic activity. The different densities of such sites within a layer consitute different catalytic properties. A layer, therefore, might be viewed as a primitive model of a multienzyme complex. The transfer of these catalytic properties from a matrix layer onto the replica would transform the intercalating synthesis into a true replication.

Relations between charge densities and catalytic properties of layers silicates have been studied in detail. In this review article examples have been selected which elucidate the wide variety of catalytic properties stored in the silicate layers.

### 5.1 Dimerization and Oligomerization of Unsaturated Aliphatic Acids

Montmorillonites are widely used as catalysts in industrial processes *e.g.* the dimerization of unsaturated fatty acids to dicarboxylic acids. The annual requirement for this catalyst amounts to several thousand tons. Only a few of the many existing deposits from different localities are highly active, this being governed equally by the charge density and the type of interlayer cations.

In Figure 6 the yield of unaltered oleic acid, $C_{36}$-dimeric, $C_{54}$-trimeric, and $C_{\geq 72}$-oligomeric acids is shown as a function of isomorphous substitution. At high charge densities ($>0.60e/(Si,Al)_4O_{10}$), *cis-trans*-isomerization and redox-disproportioning to diunsaturated $C_{18}$-acids and stearic acid occurs to some extent, but no catalytic dimerization or oligomerization. The oleic acid used as starting material is recovered almost quantitatively as a fraction of $C_{18}$-monocarboxylic acids. At charge densities of 0.28 $e/(Si,Al)_4O_{10}$ the yield of dicarboxylic acids shows a pronounced maximum (*ca.* 66%). The maximum yield of tricarboxylic acids occurs at lower charge density. At still lower densities oligomers, which block the internal surfaces, are formed.

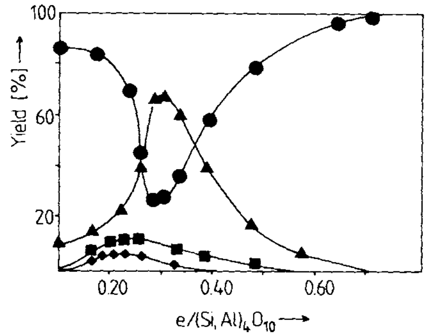


Fig. 6. Oligomerization of oleic acid to di-, tri-, and oligocarboxylic acids with $(CH_3)_4N$-montmorillonite as catalyst as a function of the charge density. Starting material: oleic acid 98%; 0.5 g catalyst per 100 mL oleic acid. ●: Oleic acid + stearic acid ($C_{18}$); ▲: Dicarboxylic acids ($C_{36}$); ■: Tricarboxylic acids ($C_{54}$); ◆: Oligocarboxylic acids ($\geq C_{72}$).

In addition, the effect of charge density on this reaction is interesting because of the influence of the polar end-group of the organic monomer. Only the dimerization of the carboxylic acid is catalyzed, and not that of the corresponding alcohol or nitrile. One would expect the polar end-group not to govern the reactivity of the double bond between C-9 and C-10. All three compounds—acid, alcohol, and nitrile—form intercalation complexes with the montmorillonite catalyst, the only difference being in the structure of these complexes. Alcohols and nitriles have their chains arranged perpendicular or inclined at a large angle to the silicate layers; the $\pi$ bond is, therefore, far removed from the silicate layer and cannot be activated. In the oleic acid complex, the alkyl chain lies flat on the layer; the double bond is in direct contact with the silicate layer and, therefore, can be activated, probably by interaction with an empty 3d orbital on silicon. The charge density provides additional steric effects because the initial intercalation complex is influenced by the interlayer cations $M^+$ which remain in the interlayer region. At high cation density, neighboring acid molecules are separated from each other by the interlayer cations (Fig. 7a). Hence, dimerization cannot occur, although the double bonds are activated. With decreasing interlayer cation density an increasing number of pairs of acid molecules is present. Activation leads to the dimeric acid (Fig. 7b). At still lower cation density, triplets of acid molecules are present, separated from each other by cations. These triplets form trimers. Figure 7c shows a complex with four molecules of acid between the cations, which can react to a tetracarboxylic acid.

### 5.2 Isomerization Reactions

A large number of isomerization reactions are known to occur on and in montmorillonites. A very simple example is the isomerization of cationic complexes, *e.g.*

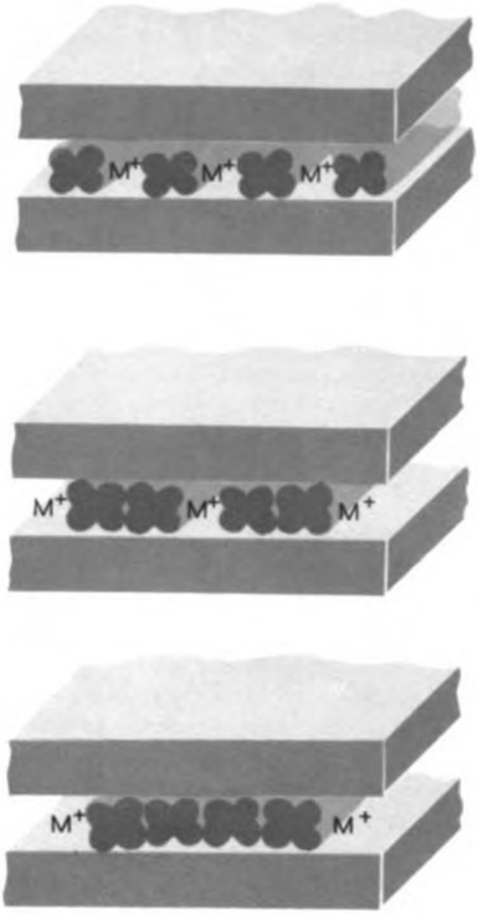


Fig. 7. Effect of the packing density of interlayer cations on the oligomerization of oleic acid (simplified scheme). a) Neighboring molecules in the oleic acid-montmorillonite intercalation complex are separated from each other by interlayer cations: no dicarboxylic acid produced. b) Pairs of acid molecules separated from each other by interlayer cations: maximum yield of dicarboxylic acid. c) Groups of 4 acid molecules separated by interlayer cations: formation of tetracarboxylic acids.

$$[Cr(H_2O)_5Cl]^{2+} + H_2O \rightleftharpoons [Cr(H_2O)_6]^{3+} + Cl^-$$

which can be followed spectrometrically. At high charge densities the complex $[Cr(H_2O)_6]^{3+}$ is stable, at low charge density the stability of $[Cr(H_2O)_5Cl]^{2+}$ is much higher. The behavior is mainly determined by electrostatic interaction. In areas of high charge density, the higher charged interlayer cation is preferred rather than a lower charged one, and the converse. The activation energy for the isomerization reaction varies with charge density by *ca.* 14 kJ/mol.

### 5.3. Redox Reactions

Redox reactions can also be catalyzed by montmorillonites. Industrial applications of this phenomenon are well known, *e.g.* in modern copying papers. The coated front of the paper is filled with an appropriate, mostly acidic montmorillonite, which catalyzes the oxidation of leukobases. The leukobase is fixed on the coated back of the original and is squeezed onto the coated front by the pressure of writing[7]. The oxidizing agent may be any oxidant or oxygen from the air.

The degree of isomorphous substitution is immaterial if the reduced or oxidized compounds are neutral molecules. If cations are involved, however, the charge density becomes a dominant factor, *e.g.* the reaction

$$2CoL_n^{3+} + 2H_2O \rightleftharpoons 2nL + 2Co^{2+} + 2H^+ + H_2O_2$$

In the interlayer space of highly charged montmorillonites the cation with cobalt in the oxidation state +3 is stable, while it is reduced to +2 in low-charged samples. The $H_2O_2$, which develops simultaneously with the cobalt 2+, immediately decomposes to $O_2$ and $H_2O$.

The reduction of the cobalt and the decomposition of the complex are again caused by the electrostatic interaction of the interlayer cations with the fixed negative charges of the layers. At very low charge density, the balance of the excess charges by the complex trivalent cation would imply charge separation.

The effect of charge density on the oxidation of aromatic amines by oxygen of the air is even more pronounced. Aniline, for example, is easily oxidized to a black "polymer" at high charge densities, and at medium densities to a red or blue "oligomer"; at low charge densities it remains unaltered. Correspondingly, the black polymer is hydrolyzed and reduced at low charge densities[8].

### 5.4. Condensation and Hydrolysis

The catalytic action of layer silicates on condensation reactions is not only restricted to montmorillonites. In kaolinite, intercalated ammonium acetate is dehydrated to acetamide even at 60—70 °C. A similar reaction occurs with ammonium salts of amino acids yielding peptides. The same reaction takes place in montmorillonites. The temperature necessary for condensation increases with increasing charge density. In this thermal condensation di-, tri-, and hexapeptides (or other peptides consisting of 3n amino acids) are favored. Similar results were obtained by *Paecht-Horovitz*, *Katchalsky et al.*[9] with activated amino acids and montmorillonite as catalyst. The preference for 3n-peptides is probably related to the pseudohexagonal symmetry of the matrix layers.

Whereas condensation is favored in montmorillonites of low charge density, peptides and proteins can be hydrolyzed at high charge densities if $H_3O^+$ ions are present in the interlayer region. The size of the hydrolysis product of this reaction depends upon the charge density on the silicate layers, and the content of ε-amino- and guanidino-groups of the protein, *i.e.* on the content of lysine and arginine. At a given charge density of the silicate, the more peptide bonds are cleaved the lower the content of lysine and arginine. For a given protein at constant pH, the more bonds are cleaved the higher the charge density of the silicate[8].

There is a simple explanation for this highly selective cleavage of peptide bonds, which is governed by the charge density and its distribution on the silicate. The $H_3O^+$-interlayer cations react with the ε-amino- and guanido groups, forming ammonium ions. In this way the proteins are bound as cations in the interlayer region and spread in layers of 4.5—8 Å thickness. At high charge den-

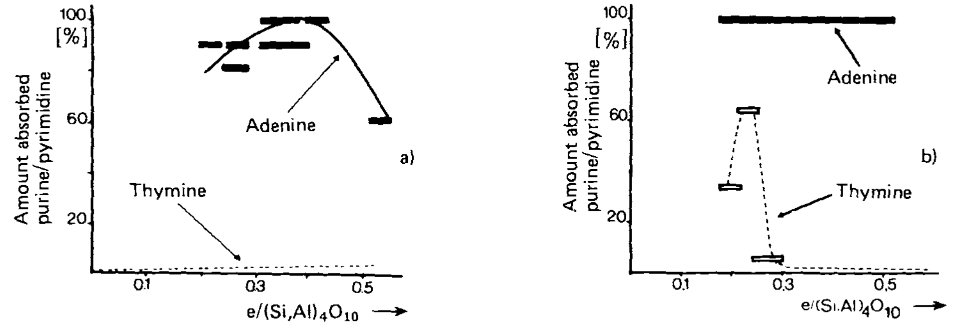


Fig. 9. Adsorption of adenine and thymine on layer silicates of different charge density ($10^{-5}$ M solutions at pH = 4.0). a) Adsorption of pure thymine or adenine; b) Adsorption of mixtures of thymine and of adenine (1 : 1) or adsorption of adenine, followed by adsorption of thymine on the adenine loaded sample.

sity and low lysine and arginine levels, only a fraction of the $H_3O^+$ ions is consumed in ammonium ion formation. The others hydrolyze peptide bonds, which are forced into their neighborhood by the electrostatic interaction of the fixed negative charges and the ammonium groups on the protein. The $H_3O^+$ concentration may correspond to a 10 N acid. Thus, the reaction is a simple acid hydrolysis: the stereospecificity is brought about by the charge density.

### 5.5. Selective Adsorption

In some cases selective catalytic reactions, which depend upon the charge density, are caused by selective adsorption on the silicates. The effect of charge density on such selective adsorptions has been studied with mixtures of amino acids and with mixtures of purines and pyrimidines.

In aqueous solutions of cysteine with another amino acid X, in a molar ratio 1 : 1, one of these is usually adsorbed preferentially. In Figure 8, equilibrium ratios of the adsorbate on the montmorillonite are shown as a function of the charge density.

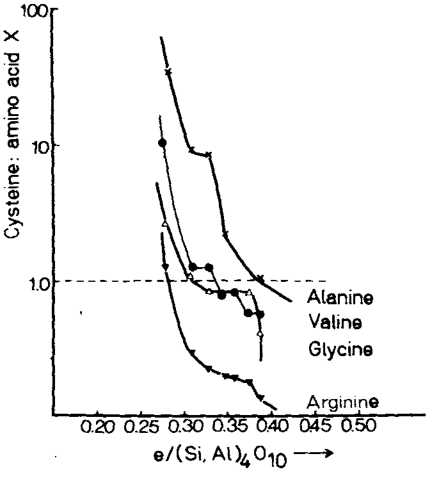


Fig. 8. Effect of charge density on the selective adsorption of amino acids on montmorillonite. Starting mixture; cysteine : amino acid X = 1 : 1 (molar ratio). Ratio in the figure; molar ratio cysteine: amino acid X in the adsorbate at equilibrium. Equilibrium concentration was chosen such that it just reached the plateau of the adsorption isotherm; in every case this is of the Langmuir-type.

At low charge densities the cysteine is enriched, at high charge densities the more basic amino acid accumulates. Similar results have been obtained with many other pairs of amino acids, indicating that the degree of isomorphous substitution has a strong effect on selective adsorption.

The results of adsorption experiments with adenine and thymine, and $10^{-5}$ M solutions of mixtures of these at pH = 4.0[10] also indicate a high sensitivity to charge density. Thymine is bound only to a slight extent, while a broad maximum is observed at medium charge densities in the adsorption of adenine (Fig. 9a).

Adsorption of a mixture of thymine and adenine in the molar ratio 1 : 1, yields quite different results: adenine is adsorbed over the whole range of charge density. In addition, thymine is adsorbed to a high degree at a particular charge density (Fig. 9b). A similar specific adsorption on montmorillonite is found with all corresponding pairs of purines and pyrimidines, but is not observed with non-corresponding pairs.

The particular value of the charge density, at which the specific adsorption is found, is determined by the surface area requirements of the pair. The stronger base is bound as a cation, while the weaker one is chiefly fixed by hydrogen bonds and dispersion forces.

The ring planes of the bases lie parallel to the silicate layers. Hydrogen bonds to the neighboring base are, therefore, only favorable with corresponding pairs. The effect of charge density and charge distribution on the silicate is shown schematically in Figure 10. The cations of the stronger base occupy those sites on the silicate layers which are closest to the fixed negative charges (Fig. 10a). At the particular charge density there is just enough space for pair formation between the cations (Fig. 10b). At higher charge densities, pair formation on the adsorbed monolayer is prevented due to steric effects (Fig. 10c). At lower charge densities the space requirements are sufficient (Fig. 10d). However, in this case the specific adsorption of the pairs is suppressed by kinetic hindrance caused by the strong decrease in the interlayer distance. A state of equilibrium is, therefore, not reached.

From these examples it can be concluded that the areas of different charge densities present in each silicate layer represent, both qualitatively and quantitatively, different catalytic functions and selectivities. Each silicate layer contains a considerable amount of information and corre-

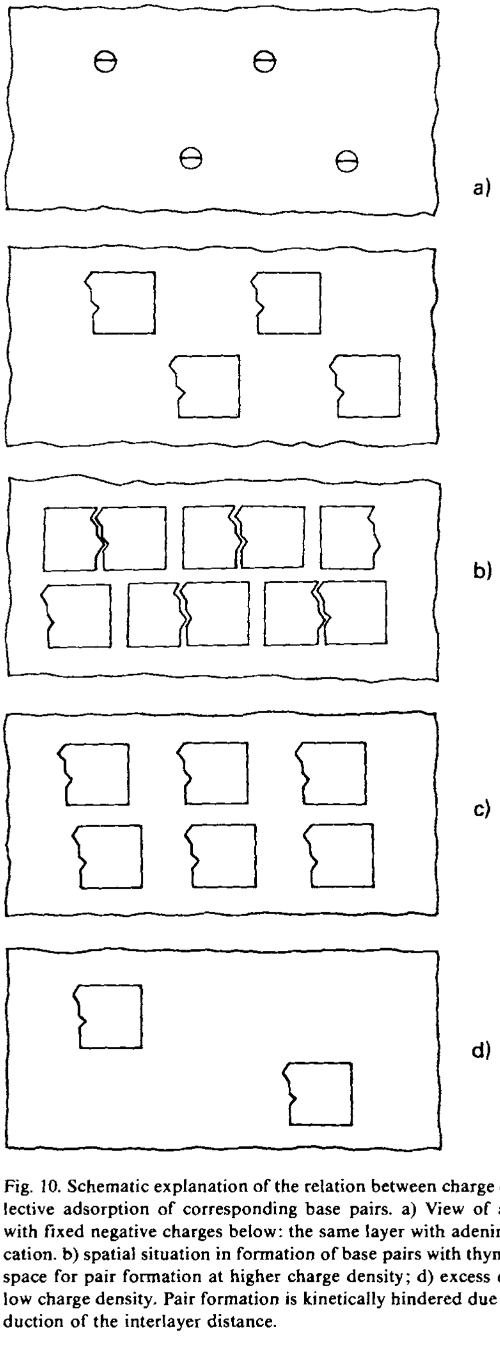


Fig. 10. Schematic explanation of the relation between charge density and selective adsorption of corresponding base pairs. a) View of a silicate layer with fixed negative charges below: the same layer with adenine as interlayer cation. b) spatial situation in formation of base pairs with thymine; c) no free space for pair formation at higher charge density; d) excess empty space at low charge density. Pair formation is kinetically hindered due to a drastic reduction of the interlayer distance.

sponds, at least partially, to multienzyme complexes. Different catalytic capabilities are only partially independent of each other.

## 6. Experimental Proof of Replication

Experiments to establish that every piece of information is transferred from the matrix to the replica layers during the intercalating synthesis were carried out using carefully selected and purified matrix material (montmorillonite from Lower Bavaria and from Cyprus). This matrix material was used as the "parent generation" ($F_0$). Approximately $10^{-8}$ to $10^{-9}$ g of the parent-silicate was added to each run. The breeding solution contained $Na^+$, $K^+$, $Mg^{2+}$, $Al^{3+}$, and $Si(OH)_4$ in concentrations which only resulted in an intercalating synthesis in the model investigations with allevardite, and did not lead to nucleation in the free solution. Concentrations were about half that necessary to cause nucleation in the matrix free solution within three months in the absence of seeds.

The optimum growth rate was determined experimentally by variation of the ionic strength. Part of the $Al^{3+}$ and orthosilicic acid were complexed by pyrocatechol. The intercalating synthesis was interrupted when *ca.* $10^{-5}$–$10^{-6}$ g of new montmorillonite had formed. The product ($F_1$-generation) was examined by X-rays, and characterized chemically by catalytic reactions. The average charge density and its upper and lower limits were determined by the alkylammonium method.

About $10^{-8}-10^{-9}$ g of this $F_1$-generation was used as a matrix for the analogous synthesis of the $F_2$-generation. In order to obtain homogeneous matrix material, the pure $Na^+$ derivative was prepared by a cation exchange reaction and washed with water to an electrolyte concentration less of than $10^{-5}$ N. The $F_n$-generation was bred in the same way, using $10^{-8}-10^{-9}$ g of the $F_{n-1}$-generation as matrix.

The results of such a series of experiments are shown in Figure 11. The composition of the "breeding" solution was such that homogeneous nucleation in the absence of matrix layers, and at twice the concentration, yielded montmorillonites with isomorphous substitution of 0.42 e/$(Si,Al)_4O_{10}$-unit. The matrix layers ($F_0$-generation) had an excess charge of 0.28 e/$(Si,Al)_4O_{10}$.

The distribution of charge densities and its mean value for generations $F_1$ to $F_{22}$ are shown in Figure 11. Up to the 10th generation the spread is low. From the 16th to the 18th generation the number of errors increases rapidly. In

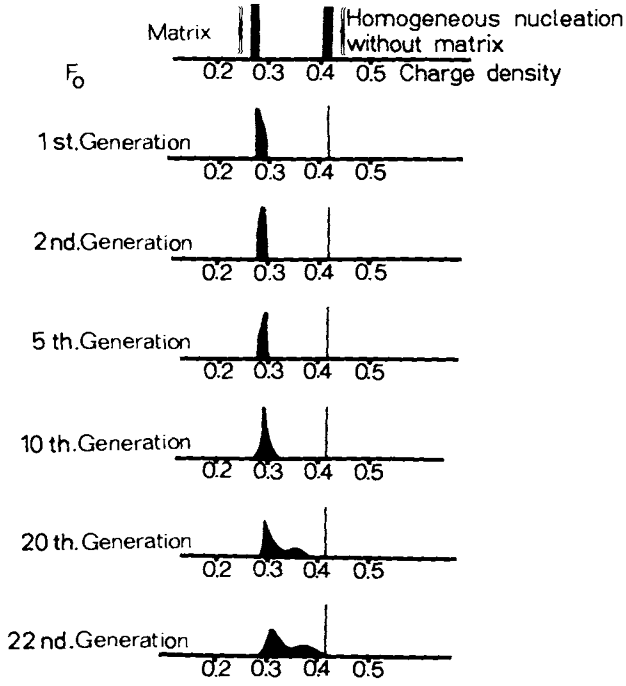


Fig. 11. Charge density distribution in the generations $F_0$ to $F_{22}$. $F_0$-generation: 0.28e/$(Si,Al)_4O_{10}$; the composition of the breeding solution yields 0.43e/$(Si,Al)_4O_{10}$ in the absence of matrix layers at higher concentrations.

the generation $F_{20}$ a significant portion has a charge density higher than 0.33 $e/(Si,Al)_4O_{10}$, and almost no material with the original value of 0.28 $e/(Si,Al)_4O_{10}$ remains; this indicates rapid decay in replication quality.

Results of complementary series of experiments are shown in Figure 12. Here the parent material had a charge density of $0.42e/(Si,Al)_4O_{10}$, while homogeneous nucleation in the solution in the absence of seeds gave densities of $0.26-0.29e/(Si,Al)_4O_{10}$.

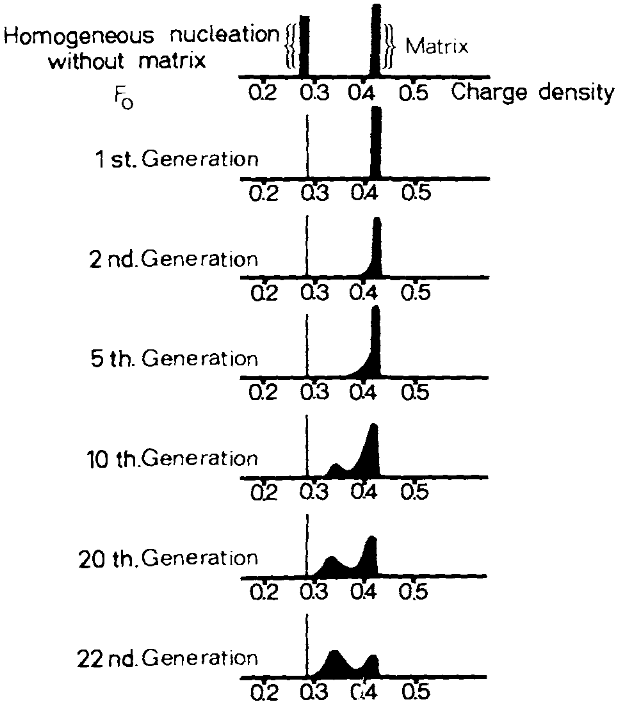


Fig. 12. Charge density distribution in the generations $F_0$ to $F_{22}$. $F_0$-generation: $0.43e/(Si,Al)_4O_{10}$; the composition of the breeding solution yields $0.28e/(Si,Al)_4O_{10}$ in the absence of matrix layers.

In this series, the frequency of replication errors is much higher than in the previous one. By the 10th generation, a second charge density maximum at *ca.* $0.34e/(Si,Al)_4O_{10}$ is observed.

Catalytic activities are affected by errors to a different extent. This is clearly shown in measurements of catalytic activities of individual generations (Fig. 13). These generations were grown under the same experimental conditions as those of Figures 11 and 12. The activities are normalized to samples with maximum activity (=100%). With low charged $F_0$-samples loss of activity for the reduction $Co^{3+} + e \rightarrow Co^{2+}$ is observed, even at the 6th generation. In the 31st generation any influence of the original matrix ($F_0$) has disappeared. With the higher charged $F_0$-matrix ($0.42e/(Si,Al)_4O_{10}$) increased activity for the reduction is clearly displayed after the 20th generation. The activity for oxidation reactions, which was studied using the reaction of aniline with atmospheric oxygen, begins to decrease from the 20th generation in the series with the higher charged $F_0$-generation (Fig. 13b). It increases considerably from the 12th generation in experiments with the low charged $F_0$-matrix.

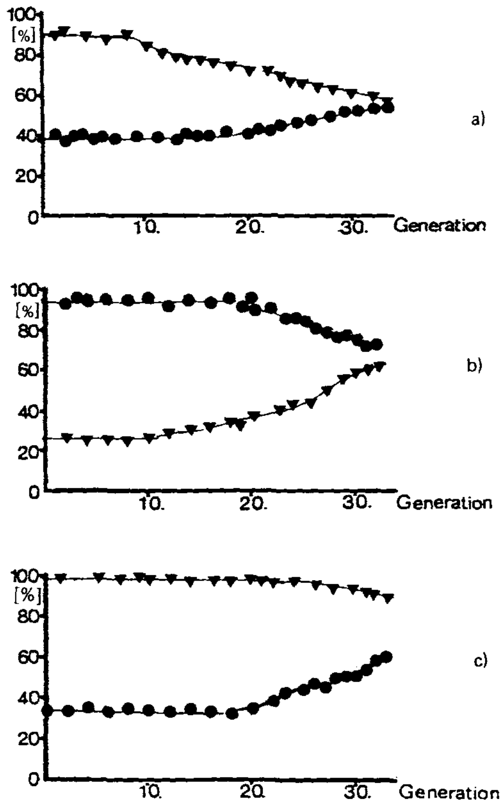


Fig. 13. Change in catalytic activity in the generations $F_0$ to $F_{33}$. a) Activity for reduction of $Co^{3+}$ to $Co^{2+}$; b) activity for the oxidation of aniline; c) activity for the selective adsorption of the pair adenine/thymine. Results from samples, bred according to the conditions described in Fig. 11 (▼) and 12 (●). Charge density ($F_0$): 0.28 or $0.43e/(Si,Al)_4O_{10}$.

The capacity to selectively adsorb the pair adenine/thymine remains unaltered up to the 26th generation in samples which are derived from the lower charged matrix. Improvement becomes significant in the complementary series from the 20th generation onwards (Fig. 13c). Information on distribution and clustering of the errors in replication is obtained from detailed analyses of the data in Figure 13.

The experiments demonstrate that the information contained in the matrix-layer is transferred to the daughter-layers, and prove the intercalating synthesis to be a true replication process. The high margin of error seems to be connected with the two-dimensional nature of the carrier of the information which has many disadvantages compared to a one-dimensional system like DNA. However, it should be borne in mind that our experimental technique[11] may not yet be optimal.

## 7. Replication and Evolution

The results mentioned so far indicate that clay minerals such as montmorillonite, which can swell to a large degree, are capable of replicative self-multiplication. These minerals may, therefore, be looked upon as models for protolife, or possibly for most primitive life; their catalytic capabilities and selectivities can be altered, thus leading to acceleration or retardation of the rate of self-multiplication.

A typical mechanism of retardation becomes active when additional areas of high charge density are produced by the errors. In such areas *e.g.* $K^+$ ions are bound selectively. Beyond a critical concentration of interlayer potassium, the variation of layer distance with variable electrolyte concentration is blocked. Adjacent layers become fixed irreversibly at the distance of closest approach, and water molecules are squeezed out from the interlayer region. In consequence, new layers can no longer be synthesized by intercalation.

Retardation or suppression of the self-multiplication step also occurs if one of the catalytic processes of a mutant leads to a product with much higher molecular weight. This product is bound more or less irreversibly and hence excludes these "mutants" from further replication.

## 8. Differentiation

One of the problems in replication, caused by a two-dimensional carrier of information, is location of the starting point of the replicative synthesis. With a one-dimensional matrix there are only two possibilities. In the two-dimensional system the starting point may occur randomly at the crystal boundary or selectively at distinct charge density sites. Experiments, in which the replicative synthesis was interrupted before the amount of newly synthesized material reached 40% (by weight) of the matrix material, indicate a highly selective start which depends upon the ratio $Na^+ : K^+ : Mg^{2+}$ and the average charge density of the matrix. At relatively high charge density and high $K^+ : Na^+$ ratios, synthesis begins in areas of low charge density, at low $K^+ : Na^+$ ratios in areas of high charge density. Premature interruption of the replication process thus allows the distinct information to be gained. The diameter of the platelets when the synthesis is prematurely interrupted is much smaller than that of the matrix layers. In our experiments the matrix diameter was 600—800 Å; the areas selected by premature interruption were only 80—160 Å in diameter. Unfortunately, these extremely small particles are less stable than the matrix. Therefore, this way of differentiation is very limited in this model system. However, the procedure offers a method of synthesizing highly specific silicate catalysts. Due to their diminished colloid stability, these smaller particles can be flocculated selectively during the self-multiplicating process.

Another disadvantage of our model is the absence of information about the growth of a new layer when the intercalating layer reaches the size of the matrix layers. In nature, this problem seems to be solved in a satisfactory way. The isomorphous substitution obviously induces strain in the lattice. Therefore, when growth reaches the limiting size, nucleation and growth of a new layer becomes energetically more favorable than further growth of the strained layer. In model experiments, however, such information had to be artifically incorporated into the system. This was achieved by reacting the hydroxy groups bound to Si on the edges of the matrix layers with $(CH_3)_3SiCl$, to the produce $(CH_3)_3SiO$ groups. In this way, growth of the matrix layers was prevented and, in addition, growth of the new layers beyond the matrix layer was hindered.

Without the artificial stop-marker in model experiments, the matrix and replica layers would have grown beyond the original size. Thus, the replica layers would obtain all the "genetic" information from the matrix; however, they would acquire additional information in their own genetic index, which is determined by the environment. This newly gained information could be transferred genetically to the next generation. In this way the system would be a simple experimental realization of ***Lamark***'s hypothesis on heritability.

In our experiments, growth of daughter-layers beyond the size of the matrix-layers would have invalidated the results on replication. All experiments were, therefore, interrupted at the earliest possible time; additionally, the trimethylsilyl chloride treatment was administered to the matrix layers of each generation in order to implant the artificial "stop".

## 9. The Possibility of an Evolution of Replicating Systems

With the proof that replication is not restricted to the nucleic acid/protein system, it must be considered whether an evolution of protolife, *i.e.* an evolution of systems capable of replicating, can be inserted between the processes of chemical and biological evolution as shown in Figure 1b.

In a discussion of evolution of the replicating principle, it must first be established whether the principle of a replicating synthesis can be transferred from one system to a chemically different one. In spite of the different chemical composition, the daughter-layer should take over all the information of the matrix.

Information storage implies relatively stable chemical systems, *i.e.* strong bonds and conformational stability: these have to be synthesized in the absence of specific enzymes and hence, the choice of systems is very limited.

For our experiments we chose graphitic acid (graphite oxide), which is obtained from graphite by oxidation with $ClO_2$, $NO_2$, or $Mn_2O_7$[12]. It consists of two-dimensional layers of predominantly $sp^3$-hybridized carbons. Three bonds are used for the carbon layers, the fourth is saturated with a functional group, often OH groups of different acidity. Over a wide range of pH, the layers can be considered as two-dimensional macroanions with interlayer cations for charge balance. With decreasing electrolyte concentration, the interlayer cations form diffuse double layers. The electrostatic repulsion of the latter and simultaneous uptake of water lead to an increase of the interlayer distance, which may lead to the total disintegration into individual, kinetically independent layers as in the case of montmorillonite (Fig. 2). The charge density in graphitic acid can readily be controlled by the pH. In spite of these properties and the very close similarity to montmorillonite, graphitic acid cannot be viewed as a replicating system. There are no catalysts which enable the direct synthesis of two-dimensional layers with carbon-carbon bonds from low molecular weight starting material under conditions in which the crystals are disintegrated into individual layers, or at distances which allow the intercalating synthesis. However, we were able to use graphitic acid as a matrix in the intercalating synthesis of montmorillonite layers.

In the first step, a regular interstratification montmorillonite : graphitic acid = 1 : 1 is formed; at longer reaction times the ratio 3 : 1 is obtained. Finally a montmorillonite with randomly interstratified graphitic acid layers is formed. After the synthesis, the mixed layer crystal was disintegrated into individual layers by lowering the electrolyte concentration to $< 10^{-4}$ M. The effective charge of the graphitic acid layers could be changed by altering the pH, and this enabled the layers to be flocculated into pure montmorillonite and graphitic acid crystals. The separated montmorillonite then was used as a matrix for further intercalating and replicating syntheses of montmorillonite layers.

In this sequence of reactions, the charge density distribution is transferred almost entirely from graphitic acid onto the montmorillonite. Using a breeding solution, which under conditions of homogeneous nucleation and higher concentration would have led to a montmorillonite of mean charge density of $0.25e/(Si,Al)_4O_{10}$, silicate layers with 0.54 or $0.43e/(Si,Al)_4O_{10}$, respectively, were grown in two experiments by intercalating synthesis in different high charged graphitic acid matrices. The charge density on graphitic acid can be varied not only by pH changes, but also by methylation of acidic groups or by acetylation. By use of graphitic acid matrices, whose charge density has been altered in this way, charge density transcription from the graphitic acid onto the montmorillonite layers could also be established.

## 10. Conclusions

The principle of replication and self-multiplication is not restricted to the nucleic acid/protein system; it is a more general property of distinct macromolecular systems. More primitive forms of life or types of protolife, therefore, must also be discussed in the context of the origin of life. Possibly, the question of how nucleic acids and proteins were formed and aptly selected in the course of the chemical evolution has been incorrectly phrased. Both might have developed in the course of the evolution of replicating systems.

The highly-expanding clay minerals are an excellent replicating system model; in the course of an immense number of replications they might have passed on an evolution and a selection, forced on the system by the environment, in just the manner expected for the most primitive forms of protolife.

The question of whether these clay minerals were a real link in the chain of replicating systems, cannot yet be answered. There is no doubt, however, that these clay minerals were abundant on the prebiological earth and were possibly the most abundant macromolecular chemical systems. Certainly, a large number of these would have been excluded from replicating syntheses due to adsorption of basic and neutral C—H—N-compounds, from photochemical reactions, electrical discharges or extraterrestrial sources. This portion was able to accumulate and store labile molecules. The remainder may have propagated replicatively. Each cycle of thawing, or rains and drought could provide the external conditions necessary for one cycle of replication in these systems.

Another indication is obtained, if we assume that *Haeckel*'s postulate "The ontogeny of individuals is an image of the phylogeny" is also valid for protolife systems or the evolution of replicating systems. In this case, three characteristic properties of the clay system may have a deeper meaning:

1) The remarkable $K^+/Na^+$ selectivity,
2) the pronounced selectivity for corresponding pairs of purine/pyrimidine and
3) the possibility of forming ferredoxine-like redox catalysts.

Depending on the charge density, potassium may be accumulated from ratios of 3 : 1 up to 30 : 1 from solutions with $K^+ : Na^+ = 1 : 1$. All living systems known hitherto function within such an accumulation factor.

The corresponding base pairs purine/pyrimidine are fundamental to all types of life based on nucleic acids and proteins, beginning with the most primitive archaebacteria and blue-green algae up to the highly developed mammals.

Ferredoxines represent the biogenetically oldest enzyme system having the same principle: at least two SH groups at a distance which allows formation of metal-sulfur bonds —S—M—S—. Redox properties are mainly determined by the S—M— bond length. These lengths are coerced by the rigid nature of the cysteine groups in the two different peptide helices and the tertiary structure thereof. In models with montmorillonites, the S—M-bond length is determined by the distance of the negative charges, which are fixed in the silicate layers, and the electrostatic interactions between these charges and the $—NH_3^+$ group of cysteine. The selectivity is, therefore, not very pronounced; pair-formation —S—M—S— can occur with all neighboring cysteine units. Their number is higher in the two-dimensional system.

In contrast, the selectivity is higher if the SH groups belong to two different peptide chains, and is still more pronounced if 4 —SH groups are coordinated to a metal ion, as in the phylogenetically younger ferredoxines.

Received: July 15, 1981 [A 384 IE]
German version: Angew. Chem. *93*, 843 (1981)

---

[1] *S. W. Fox*, Nature *205*, 328 (1965); The Sciences *1*, 18 (1980).

[2] *A. G. Cairns-Smith*, J. Theoret. Biol. *10*, 53 (1966); The Life Puzzle, Oliver & Boyd, Edinburgh 1971.

[3] *U. Hofmann, K. Endell, D. Wilm*, Z. Kristallogr., *A*, *86*, 340 (1933).

[4] *S. Caillère, S. Hénin*, Mineral. Mag. *28*, 612 (1949); *S. Caillère, S. Hénin, J. Esquevin*, Bull. Soc. Fr. Minér. *76*, 300 (1953); *S. Hénin, O. Robichet*, Clay Miner. Bull. *2*, 110 (1954).

[5] *A. Weiss, H. O. Becker, G. Lagaly*, Proc. Int. Clay Conf. 1969, Vol. 2, p. 67, Israel University Press, Jerusalem, p. 67; *F. Veniale, H. W. van der Marel, ibid.*, p. 78.

[6] *W. B. Johnston*, U.S.-Pat. 2347562 (1944); *F. O. Barrett, C. G. Goebel, K. M. Peters*, U.S.-Pat. 2793219 (1957); DBP 1134666 (1962); U.S.-Patent 3076003 (1963); U.S.-Patent 3157681 (1964); *M. J. A. M. den Otter*, Fette, Seifen, Anstrichm. *72*, 667, 875, 1056 (1970).

[7] *K. Barrett, R. Green, R. W. Sandberg*, U.S.-Pat. 2550469 (1951).

[8] *A. Weiss*, Clays Clay Miner. *10*, 191 (1963).

[9] *M. Paecht-Horowitz, J. Berger, A. Katchalsky*, Nature *228*, 636 (1970).

[10] *G. E. Lailach, T. D. Thompson, G. W. Brindley*, Clays and Clay Miner. *16*, 285, 295 (1968); *17*, 95 (1969).

[11] Unpublished results; published in part in *G. Mai*, Dissertation, Universität München 1969; *P. Brunner, ibid.*, 1978, *S. Fritz, ibid.*, 1978.

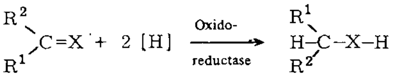
[12] *U. Hofmann, A. Frenzel*, Ber. Dtsch. Chem. Ges. *63*, 1248 (1930); *U. Hofmann, E. König*, Z. Anorg. Allg. Chem. *234*, 311 (1937); *W. Scholz, H. P. Boehm*, Z. Anorg. Allg. Chem. *369*, 327 (1969); *R. Krüger*, Dissertation, Universität München 1980.

# Electro-Enzymatic and Electro-Microbial Stereospecific Reductions[**]

By *Helmut Simon, Helmut Günther, Johann Bader,* and *Wilhelm Tischer*[*]

*Dedicated to Professor Helmut Holzer on the occasion of his 60th birthday*

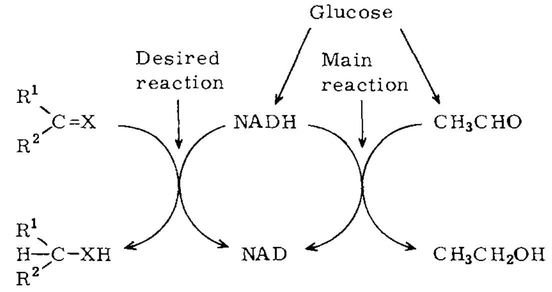
Numerous chiral substances are formed in nature by the reduction of unsaturated compounds with oxidoreductases, which display a relatively large substrate width and complete stereospecificity[1] [eq. (a)]. The two reduction equivalents frequently originate from NADH or NADPH.



$$R^2R^1C{=}X + 2\,[H] \xrightarrow[\text{reductase}]{\text{Oxido-}} H{-}CR^1R^2{-}X{-}H \qquad (a)$$

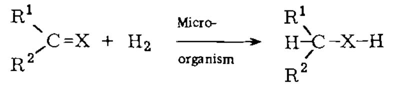
Preparative scale reactions cannot be performed using reduced pyridine nucleotides due to their prohibitively high cost. Therefore, NADH has to be used in catalytic amounts only and regenerated. Reactions of this type have been performed for many years as cofermentations; these have the disadvantage that the desired reaction can principally only occur as a side reaction. Hence, *e.g.*, most of the NADH formed as an intermediate in the fermentation of glucose (electron donor) by yeast is reoxidized in the reduction of acetaldehyde (electron acceptor) [eq. (b)].

We have improved this state of affairs by using $H_2$ as the electron donor[2] in conjunction with anaerobic microorganisms which are provided by a hydrogenase [eq. (c)].



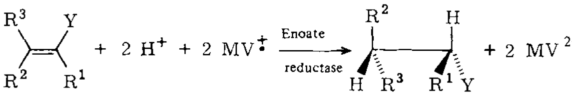
(b)

Reactions of this type are strongly exergonic, and side reactions rarely occur. By this means we have transformed numerous prochiral compounds into chiral species on a preparative scale[2b]. If instead of microorganisms, more or less pure pyridine nucleotide-dependent reductases are used and NAD(P)H is regenerated, systems which are hardly suitable for preparative purposes consisting of two enzymes, two substrates, and two products are formed.



$$R^1R^2C{=}X + H_2 \xrightarrow[\text{organism}]{\text{Micro-}} H{-}CR^1R^2{-}X{-}H \qquad (c)$$

We isolated the enzyme which reduces enoates in Clostridia (anions of α,β-unsaturated carboxylic acids) in an NADH-dependent reaction[3] and have now discovered that this enzyme-type catalyzes two further reactions [eq. (d) and (e)].



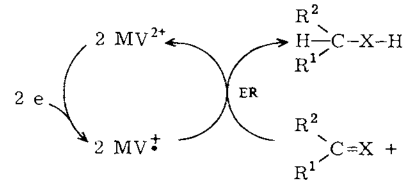
(d)

Y = $COO^-$, CHO;
$R^1$ = H, Me, Et, OMe, NHCHO, F, Cl, Br;
$R^2$ = Alkyl, Aryl, Alkoxycarbonyl (slightly limiting);
$R^3$ = H, Me, Et, etc.

$$2\,MV^{+\cdot} + NAD^+ + H^+ \xrightarrow[\text{reductase}]{\text{Enoate}} NADH + 2\,MV^{2+} \qquad (e)$$

$MV^{+\cdot}$ = Methylviologen radical cation
$MV^{2+}$ = Methylviologen dication
(1,1′-Dimethyl-4,4′-bipyridinium dication)

The dication of the cheap and stable methylviologen can be continuously reduced at an electrode[4]. This produces the system outlined in eq. (f).



(f)

e = Electrons from a cathode; ER = Enoate reductase, $>C{=}X$, the substrate given in eq. (d) or $NAD^+$, eq. (e).

At pH 6.4 even a 0.3 mM solution of $MV^{+\cdot}$ exhibits a half-maximum rate for the reaction described in eq. (d). The

---

[*] Prof. Dr. H. Simon [+], Dr. H. Günther, Dr. J. Bader
Lehrstuhl für Organische Chemie und Biochemie
der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)
Dr. W. Tischer
Boehringer Mannheim GmbH, Biochemica Werk Tutzing 1
Bahnhofstrasse 9, D-8132 Tutzing (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Fonds der Chemischen Industrie. We acknowledge the skilfull technical assistance of Frau *C. Frank.*

enoate reductase can be used as shown in eq. (f) *(electro-enzymatic reduction),* or in the form of bacterial cells *(electro-microbial reduction).* (2*R*)-2-Methyl-3-phenylpropionate can be prepared in 95% yield using the enoate reductase from *Clostridium* La 1. By analogy, hydrogenations can be carried out using whole cells (50 mg dry weight) or *e.g.* with cells immobilized in polyurethane. The initial rates lie, however, *ca.* 40% and 25%, respectively, below the initial rate of the reaction with the pure enzyme; this decrease in rate results essentially from different diffusion processes.

Not only substrates of enoate reductase can be stereospecifically reduced but also those of all the NAD-dependent enzymes [eq. (e)] which occur in addition to enoate reductase in the cells used.

To date, we have detected enoate reductase in three Clostridia[5]. In this way, using whole cells (*Clostridium sporogenes,* ATCC 3584), we have *e.g.* converted phenyl pyruvate into (2*R*)-phenyl lactate, and other α-keto acids into amino acids by reductive amination. The transformation of phenyl pyruvate can also be achieved using *Proteus mirabilis* (DSM 30115). In properly grown cells, 1—2% of the protein is enoate reductase[3] and 400—500 units of the enzyme can be obtained in a working day, since the method of isolation was simplified[6]. One mg of enoate reductase in the presence of 2 mM $MV^{+\cdot}$ reduces *ca.* 10—12 μmol (*E*)-2-methyl cinnamate *per* minute at 25 °C and pH 6.4. The rates of numerous other enoates lie in the region 5—20 μmol/min.

The question of whether enzymes which catalyze the reaction shown in eq. (e) also occur in aerobic enzymes appeared interesting. We found that *Enterobacter agglomerans*[7] (CDC 1461—67) contains an NADH-dependent fumarate reductase, which can be reduced in the presence of $MV^{+\cdot}$.

A prerequisite for the electro-enzymatic and electro-microbial reductions is that the unsaturated compounds neither react spontaneously at the electrode nor with the reduced mediator. This prerequisite can readily be tested in most cases by means of cyclovoltammetry and by spectrophotometry, and seems to be met in most cases.

We believe that this process, which does not show most of the disadvantages of cofermentations and those which use isolated enzymes with NAD(P)H-regeneration, will enable many chiral compounds to be prepared *e.g.* 21 compounds were reduced using whole cells and hydrogen gas[2b]. Compounds can readily be stereospecifically deuterated using $^2H_2O$ buffers. In cofermentation processes, the quotients, gram glucose/equivalent isolated reduction product, and gram catalyst (*e.g.* microorganisms)/equivalent isolated reduction product, respectively, lie between 500 and 10000[8]; the corresponding values in our process are 10—100 times better.

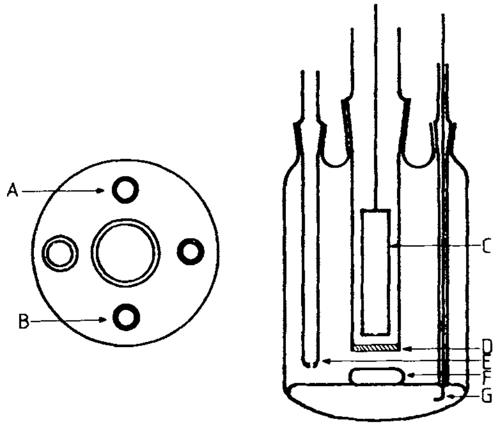


Fig. 1. Side view (right) and plan view (left) of a reaction vessel suitable for electro-enzymatic and electro-microbial reductions; volume 25—160 mL. A = inlet tube, B = outlet tube and sample removal, C = Pt anode, D = diaphragm, E = reference electrode, F = stirrer, G = Hg cathode.

*Procedure*

The cathode compartment of the electrochemical cell (Fig. 1), which contains 85 mL of a solution consisting of 0.1 mol/L phosphate buffer (pH 6.4), 0.1 mmol/L EDTA, 2.5 mmol/L $MV^{2+}$, as well as 40 mg bovine serum albumin (not necessary if the reaction time is less than 20 h), and 1.12 g sodium (*E*)-2-methylcinnamate, is flushed with nitrogen to remove the oxygen. The anode compartment is separated from the cathode compartment by a polyacrylamide plug and is filled with *ca.* 2 mL 0.1 M phosphate buffer (pH 9). The $MV^{2+}$ is prereduced at a −800 mV potential, measured relative to a 0.1 M KCl-calomel electrode, and 0.5 mg eneoate reductase added. By controlling the cathode potential, the reaction proceeds as shown in Figure 2. The pH value of the catholyte is regulated several times by addition of $H_3PO_4/H_2O$ (1 : 1). If Vycor® tips are used as a diaphragm, the anode compartment can be filled with 0.1 M $K_2SO_4$, and adjustment of the pH is unnecessary.

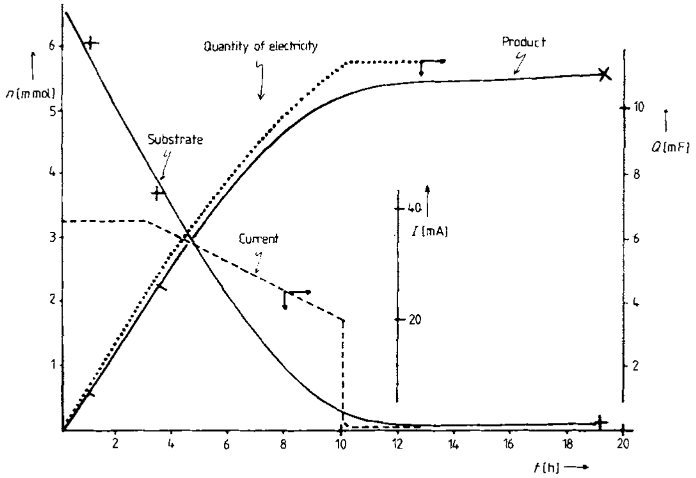


Fig. 2. Course of the electro-enzymatic reduction of (*E*)-2-methyl cinnamate, catalyzed by enoate reductase in the presence of electrochemically continuously regenerated methylviologen radical cation, as a function of time.

The course of the reaction can be followed on the current-curve, or by quantitative high pressure liquid chromatography. After reaction has ceased, the mixture is acidified, extracted with ether, and (*R*)-2-methyl-3-phenylpropionic acid isolated (yield 95%), $[\alpha]^D$ −23.5°; the values for the pure enantiomers have been reported as $[\alpha]^D$ +20.4 and $[\alpha]^D$ −24.6[9].

Received: March 20, 1981 [Z 861 IE]
German version: Angew. Chem. *93,* 897 (1981)

CAS Registry numbers:
Sodium (*E*)-2-methylcinnamate, 79044-44-3; (*R*)-2-methyl-3-phenylpropionic acid, 14367-67-0

---

[1] *J. B. Jones, J. F. Beck* in *J. B. Jones, C. J. Sih, D. Perlman:* Applications of Biochemical Systems in Organic Chemistry, (Techn. Chem. Vol. X) Wiley, New York 1976, Part I, p. 236.

[2] a) *H. Simon, B. Rambeck, H. Hashimoto, H. Günther, G. Nohynek, H. Neumann,* Angew. Chem. *86,* 675 (1974); Angew. Chem. Int. Ed. Engl. *13,* 608 (1974); b) *H. Simon, J. Bader, B. Rambeck, E. Krezdorn, W. Tischer* in *H. W. Dellweg:* 4. Symp. Techn. Mikrobiol., Berlin 1979, p. 325.

[3] *W. Tischer, J. Bader, H. Simon,* Eur. J. Biochem. *97,* 103 (1979).

[4] *E. Steckhan, Th. Kuwana,* Ber. Bunsenges. Phys. Chem. *78,* 253 (1974).

[5] *M. Bühler, H. Giesel, W. Tischer, H. Simon,* FEBS Lett. *109,* 244 (1980).

[6] *J. Bader, H. Simon,* Arch. Microbiol. *127,* 279 (1980).

[7] *R. Holländer*, Zentralbl. Bakteriol. Parasitenkd. Infektionskr. Hyg. Abt. 1: Orig. Reihe C *1*, 243 (1980).
[8] *V. E. Althouse, D. M. Feigl, W. A. Sanderson, H. S. Mosher*, J. Am. Chem. Soc. *88*, 3595 (1966); *H. G. Leuenberger, W. Boguth, R. Barner, M. Schmid, R. Zell*, Helv. Chim. Acta *62*, 455 (1979); *S. F. Lee, G. Barth, C. Djerassi*, J. Am. Chem. Soc. *103*, 295 (1981).
[9] *M. B. Watson, G. W. Youngson*, J. Chem. Soc. C *1968*, 258; *A. W. Schrecker*, J. Org. Chem. *22*, 33 (1957).

---

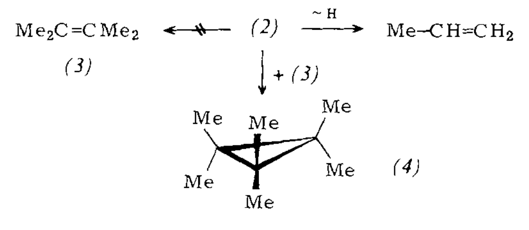
## Cyclopropanation with Dimethylcarbene

By *Peter Fischer* and *Gerhard Schaefer*[*]

Dimethylcarbene, $(CH_3)_2C$: *(2)*, has so far been missing from the broad spectrum of methylene derivatives employed synthetically. Addition of *(2)* to 2,3-dimethyl-2-butene *(3)*, for instance, would be an obvious and elegant route to hexamethylcyclopropane *(4)*[1], which we required in the course of a systematic $^{13}C$-NMR investigation of methylcyclopropanes[2]; the procedures given in the literature afford *(4)* only in low yield[3a] or as a minor by-product[3b].

All attempts at the generation and reaction of *(2)* by thermolysis of 2-diazopropane[4a], dimethylketene[4b] or dimethyldiazirine[4c] yielded only propene. Evidently, intermediary $(CH_3)_2C$: isomerizes much too fast under these conditions for either the dimer *(3)*[4b] or, in the presence of olefins, for cyclopropane derivatives to be formed[4c]. If, on the other hand, 2-diazopropane is decomposed in the presence of NO, the stabilized iminoxyl radical $(CH_3)_2{=}NO^{\ominus}$ can be detected by ESR spectroscopy, and thus the existence of *(2)* established indirectly[5]. So far only the carbenoid, obtainable from 2,2-dibromopropane and chromium(II) salts in DMF/water, has been used with success for $(CH_3)_2C$-addition to olefins which are soluble in this system, *e.g.* allyl alcohol[6].

In principle, α-elimination from 2,2-dihalopropane should also be feasible in a non-polar medium. We have therefore examined the reaction of 2,2-dibromopropane *(1)*[7] in diethyl ether with alkyllithium compounds in the presence of tetramethylethene *(3)* as carbene scavenger (molar ratio 1:1:1). With *n*-butyllithium at −30 °C, the cycloadduct *(4)* could indeed be isolated, apart from unchanged *(3)*; the yield was about 20% with respect to the olefin consumed in the reaction. On the other hand, when methyl- or isopropyllithium were employed as metalating agents, at best traces of *(4)* could be detected by gas chromatography (GC) or GC/MS. These findings are in accord with the gradation of alkyllithium activity reported by *Gilman* for metal-halogen exchange[8].



If, as described by *Schlosser*[9], tetramethylethylenediamine (TMEDA) or potassium *tert*-butoxide is added to the reaction mixture to enhance the metalating potential of the butyllithium, cyclopropanation fails completely since these auxiliary bases themselves react with *(1)*; simultaneous addition of TMEDA and butyllithium does not improve the cyclopropane yield compared to the reaction without auxiliary bases. When, on the other hand, the reaction temperature is lowered from −30° to −70 °C, the yield of *(4)* increases to almost 50% (further reduction giving no further improvement). All further experiments to optimize the cyclopropanation conditions were therefore carried out at −70 °C.

Since in all experiments 35—45% of *(3)* was recovered unchanged[10], the olefin fraction was halved; the yield of *(4)*, relative to the amount of *(3)* consumed, however, remained unchanged. Identical yields of *(4)* (45—50%) were also obtained on doubling the butyllithium fraction or on using a fourfold excess of olefin. In the first case, *n*-octane is formed as by-product, which is much more difficult to separate, while in the second case only half of the excess olefin can be recovered.

Table 1. Addition of dimethylcarbene *(2)* to olefins.

| Olefin | Olefin recovered [%] [a] | Yield relative to olefin consumed [%] [b] |
|---|---|---|
| $(CH_3)_2C{=}C(CH_3)_2$ | 45 | 46 |
| Cyclooctatetraene | 24 | 16 |
| Cyclohexene | 55 | 27 |
| 2-Norbornene | 68 | — |
| $Ph{-}CH{=}CH_2$ | 12 | 44 |
| 1-Dodecene [c, d] | 83 | 9 |
| $Ph{-}CH{=}C(CH_3)_2$ [d] | 86 | 3 |
| $Ph{-}CH{=}CH{-}OCH_3$ [d] | 78 [e] | 6 |

[a] Substrate recovered in pure form by rectification or preparative gas chromatography (in % of total amount employed). [b] All compounds are characterized unequivocally by comparison with authentic material or from their spectral data ($^1H$-, $^{13}C$-NMR, MS). [c] With double solvent volume because of lower solubility at −70 °C. [d] Due to the extremely low carbenation yields, these reactions had to be run with four times the quantities given in the general procedure. [e] The *E/Z*-ratio for the cycloadduct corresponds exactly to that of the styrene precursor (60:40 each).

We have investigated the reaction of dimethylcarbene with a series of other CC-double bond systems, under the conditions optimized for *(3)* (Table 1). The yield decreases drastically on going from *(3)* through cyclohexene to 1-dodecene, indicating that $(CH_3)_2C$-addition puts a rather severe demand on the nucleophilicity of the olefinic substrate. On the other hand, the poor yields obtained in the case of β,β-dimethyl- and β-methoxystyrene (~1% of the olefin employed) are probably due to direct attack of these substrates by butyllithium.

### *Experimental*

A 1.0 M solution of *n*-butyllithium[11] (20 mL) in diethyl ether is added dropwise at −78 °C to a solution of 20 mmol each of elefin and 2,2-dibromopropane[7] in 20 mL of anhydrous diethyl ether; the reaction is carried out under argon atmosphere and with absolute exclusion of moisture, and the rate of addition is so regulated that the internal temperature does not rise above −70 °C to −75 °C (*ca.* 1 h). The reaction mixture is allowed to warm to room temperature (12 h, a colorless precipitate being formed after *ca.* 1 h), 30 mL of water is added, the aqueous phase repeatedly extracted with ether, and the organic phase dried over

---

[*] Prof. Dr. P. Fischer, Dipl.-Chem. G. Schaefer
Institut für Organische Chemie, Biochemie
und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

$MgSO_4$. The solvent is carefully distilled off, and the residue either fractionated or separated by preparative GC (HUPE APG 402, columns 400 × 1 cm, packed with 10% SE 30 on chromosorb P, carrier gas $N_2$). On reaction of 1.68 g of *(3)*, 0.66 g of *(4)* is obtained, besides 0.73 g of unchanged *(3)* (yield 26%, relative to total amount of *(3)* employed).

Received: February 6, 1981 [Z 859 IE]
German version: Angew. Chem. *93*, 895 (1981)

CAS Registry numbers:
*(1)*, 594-16-1; *(2)*, 40852-89-9; *(3)*, 563-79-1; *(4)*, 2570-81-2; PhCH=CMe$_2$, 768-49-0; (*E*)-PhCH=CHOMe, 4110-75-2; (*Z*)-PhCH=CHOMe, 14371-19-8; cyclooctatetraene, 629-20-9; cyclohexene, 110-83-8; 2-norbornene, 498-66-8; styrene, 100-42-5; 1-dodecene, 112-41-4; 1,1,2,2-tetramethyl-3-phenylcyclopropane, 7654-12-8; *cis*-1,1-dimethyl-2-methoxy-3-phenylcyclopropane, 78986-95-5; *trans*-1,1-dimethyl-2-methoxy-3-phenylcyclopropane, 78986-96-6; cyclooctatetraene cyclopropanization product, 79055-75-7; 7,7-dimethylnorcarane, 1460-19-1; 1,1-dimethyl-2-phenylcyclopropane, 7653-94-3; 1,1-dimethyl-2-decylcyclopropane, 78986-97-7

---

[1] Satisfactory yields from 1,3-dipolar cycloaddition of 2-diazopropane and subsequent decomposition of the pyrazolines thus formed are obtained only with electron-deficient olefins.—*M. Franck-Neumann*, Angew. Chem. *80*, 42 (1968); Angew. Chem. Int. Ed. Engl. *7*, 65 (1968); *M. Schneider, A. Rau*, Angew. Chem. *91*, 239 (1979); Angew. Chem. Int. Ed. Engl. *18*, 231 (1979).

[2] *G. Schaefer*, Dissertation, Univ. Stuttgart 1981.

[3] a) *R. G. Kelso, K. W. Greenlee, J. M. Derfer, C. E. Boord*, J. Am. Chem. Soc. *77*, 1751 (1955); b) *H. U. Hostettler*, Tetrahedron Lett. *1965*, 1941.

[4] a) *J. M. Figuera, E. Fernandez*, An. Quim. *67*, 213 (1971); b) *R. A. Holroyd, F. E. Blacet*, J. Am. Chem. Soc. *79*, 4830 (1957); c) *H. M. Frey, I. D. R. Stevens*, J. Chem. Soc. *1963*, 3514.

[5] *A. R. Forrester, J. S. Sadd*, J. Chem. Soc. Chem. Commun. *1976*, 631.

[6] *C. E. Castro, W. C. Kray*, J. Am. Chem. Soc. *88*, 4447 (1966).

[7] *W. Kirmse, B. Graf v. Wedel*, Liebigs Ann. Chem. *666*, 1 (1963).—For the carbenation reaction to be successful, the dibromopropane must be absolutely free from acetone and/or α-bromoacetone.

[8] *H. Gilman, F. W. Moore, O. Baine*, J. Am. Chem. Soc. *63*, 2479 (1941).

[9] *M. Schlosser, J. Hartmann*, Angew. Chem. *85*, 544 (1973); Angew. Chem. Int. Ed. Engl. *12*, 508 (1973).

[10] That *(3)* is reformed by dimerization of *(2)*, can be ruled out, *inter alia*, from the reactions with other olefins where no trace of 2,3-dimethyl-2-butene is detectable either by GC or GC/MS.

[11] *H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn, L. S. Miller*, J. Am. Chem. Soc. *71*, 1499 (1949).

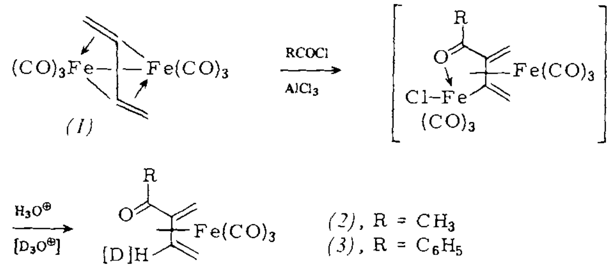
## 2-Acylbutadienes and Their Tricarbonyliron Complexes from Butatriene(hexacarbonyl)diiron Complexes *via* Friedel-Crafts Acylation[**]

By *Michel Franck-Neumann*, *Daniel Martina*, and *Francis Brion*[*]

Butadiene and simple methylated butadienes, as tricarbonyliron complexes, can readily be acylated in the 1-position under Friedel-Crafts conditions[1].

In contrast, open chain 1,3-dienes which carry an acyl group in the 2-position are difficultly accessible[2]; neither 2-acetyl- nor 2-benzoylbutadiene are known.

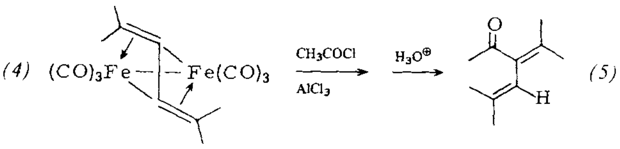
We describe here a route to 2-acylbutadienes, which we required for another purpose[3], using a reaction related to Friedel-Crafts acylation. Reaction of 2-butynes, halogenated in the 1,4-positions, with carbonyliron compounds gives complexes[4a] having the stoichiometry butatriene-$Fe_2(CO)_6$, whose X-ray structural analysis indicates two Fe—C σ-bonds at the 2- and 3-positions[4b]. 2-Substituted butadienes could be formed by electrophilic attack on this species. Indeed, the 2-substituted butadieneiron complexes *(2)* and *(3)*, which were isolated as air stable compounds in 80 and 45% yields, respectively, are formed directly from butatriene(hexacarbonyl)diiron *(1)*[5] and acetyl or benzoyl chloride in the presence of aluminum chloride.



*(2)*, R = $CH_3$
*(3)*, R = $C_6H_5$

The organic ligand of complex *(1)* is not only acylated but also hydrogenated. The latter process most probably occurs during work-up in highly acidic media *via* an insertion complex; a similar reaction pathway has been postulated for the reaction of 2-bromo- or 2,3-dichlorobutadiene with $Fe_2(CO)_9$[6]. This is also corroborated by the fact that both $AlCl_3$ and RCOCl must be used in excess in the reaction and that in the preparation of *(2)*, work-up with $D_2O$ leads to the 3-deuterio analogue of *(2)*.

The tetramethylbutatriene complex *(4)*[7] reacts directly with acetyl chloride and $AlCl_3$ to give the free 3-acetyl-2,5-dimethyl-2,4-hexadiene(2-acetyl-1,1,4,4-tetramethylbutadiene) *(5)* (volatile, therefore only isolated in 40% yield[8]), since the cisoid-configuration necessary for formation of the complex is no longer possible[9].



In contrast, we have been unable to isolate free 2-acetylbutadiene. The dimer *(6)*[10], a colorless liquid, was obtained in 75% yield when the complex *(2)* was cleaved, and in the presence of cyclopentadiene the Diels-Alder adducts *(7)*, *(8)*, and *(9)* were obtained in 95% total yield (see Table 1).

Both of the norbornene derivatives *(7)* and *(8)* undergo rearrangement to the bicyclic ketone *(9)*, whereby *(8)* must only be warmed for a short time (*ca.* 1 h) in benzene at 80 °C; *(7)* reacts more slowly at the same temperature (half-life *ca.* 3 h) and only in the presence of a free radical initiator such as azobisisobutyronitrile (AIBN).

The increased reactivity of 2-acetylbutadiene, which on the one hand may depend on the preferential s-*cis* conformation[11a] and on the other on an extreme radicophilic character[11b], makes it all the more advantageous to have available this diene as a stable tricarbonyliron complex.

### *Procedure*

A solution of *(1)* (8.0 g, 24 mmol) in 50 mL $CH_2Cl_2$ is added dropwise, within 15 min, to a mixture of anhydrous $AlCl_3$ (8.0 g, 60 mmol) and acetyl chloride (8.8 g, 110 mmol) in 120 mL $CH_2Cl_2$ at room temperature. The mixture is stirred for 1 h, cooled to 0 °C, and treated with 100

---

[*] Prof. Dr. M. Franck-Neumann, Dr. D. Martina, Dr. F. Brion
Equipe de Recherche Associée au CNRS n° 687
Institut de Chimie de l'Université Louis Pasteur
1, rue Blaise Pascal, F-67008 Strasbourg (France)

[**] This work was supported by the Délégation Générale à la Recherche Scientifique et Technique (Aide DGRST n°. 77-7-0760). BASF AG is thanked for a gift of pentacarbonyliron.

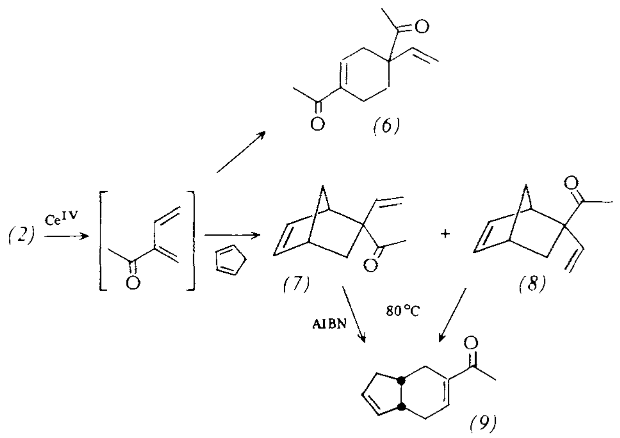


Table 1. IR and $^1$H-NMR spectroscopic data of compounds *(6)*—*(9)* [a].

*(6)*: IR ($CHCl_3$): $\nu=1700$, 1655 cm$^{-1}$ (C=O); $^1$H-NMR ($CDCl_3$/TMS): $\delta=2.12$ (s, 3 H), 2.26 (s, 3 H), other H as multiplets between 1.75 and 2.80 (6 H), 5.13 (dd, $J=1.3$ and 16.6 Hz, 1 H), 5.25 (dd, $J=1.3$ and 10.4 Hz, 1 H), 5.90 (dd, $J=10.4$ and 16.6 Hz, 1 H), 6.93 (m, 1 H)

*(7)* [b]: $^1$H-NMR ($C_6D_6$/TMS): $\delta=1.35$ (broad s, 2 H), 1.51 (dd, $J=3.5$ and 12 Hz, 1 H), 1.80 (s, 3 H), 2.17 (broad d, $J=12$ Hz, 1 H), 2.58 (m, 1 H), 2.80 (m, 1 H), 4.91 (d, $J=11$ Hz, 1 H), 4.97 (d, $J=17$ Hz, 1 H), 5.75 (dd, $J=11$ and 17 Hz, 1 H), 5.76—6.06 (m, 2 H)

*(8)*: IR ($CCl_4$): $\nu=1715$ (C=O), 1645 cm$^{-1}$ (C=C); $^1$H-NMR ($C_6D_6$/TMS): $\delta=1.91$ (s, 3 H), 2.32 (dd, $J=4$ and 12 Hz, 1 H), 2.58 (m, 1 H), 3.10 (m, 1 H), 4.78 (d, $J=17$ Hz, 1 H), 4.86 (d, $J=11$ Hz, 1 H), 5.65 (dd, $J=11$ and 17 Hz, 1 H), other H as multiplets between 0.95 and 1.50 (3 H) as well as 5.80 and 6.10 (2 H)

*(9)*: IR ($CCl_4$): $\nu=1675$ (C=O), 1635 cm$^{-1}$ (C=C); $^1$H-NMR ($CDCl_3$/TMS): $\delta=2.31$ (s, 3 H), 5.64 (broad ABm, 2 H), 7.09 (broad t, $J=5$ Hz, 1 H), other H as multiplets between 1.85 and 3.15 (8 H)

[a] The compounds *(7)*, *(8)* and *(9)* formed in the ratio 2 : 3 : 5; could be separated by HPLC on silica gel Si 60 (5—15 μ) hexane/ether (20 : 1). [b] The IR spectrum of *(7)* shows the same characteristic bands as *(8)*.

mL ice-water. After extraction with $CH_2Cl_2$ (2 x 50 mL) the organic extract is dried over $MgSO_4$. The solvent is removed under reduced pressure and the residue chromatographed on silica gel (Merck Si 60) using hexane/ether (9 : 1); *(2)*, 4.47 g (79%) is isolated as a yellow-orange oil. IR ($CCl_4$): $\nu=2060$, 1995, 1985 (CO); 1690 cm$^{-1}$ (C=O); $^1$H-NMR ($CDCl_3$): $\delta=0.23$ (d, $J=3.0$ Hz, 1 H), 0.57 (dd, $J=2.0$ and 10.0 Hz, 1 H), 2.06 (dd, $J=2.0$ and 7.0 Hz, 1 H), 2.35 (dd, $J=3.0$ and 1.3 Hz, 1 H), 2.47 (s, 3 H), 6.17 (broad dd, $J=7.0$ and 10.0 Hz, 1 H).

Received: January 19, 1981 [Z 862 IE]
German version: Angew. Chem. 93, 900 (1981)

CAS-Registry-Numbers:
*(1)*, 12211-98-2; *(2)*, 12082-23-4; *(3)*, 12087-05-7; *(4)*, 12212-46-3; *(5)*, 58143-80-9; *(6)*, 79044-47-6; *(7)*, 79044-48-7; *(8)*, 79044-49-8; *(9)*, 79044-50-1; $CH_3COCl$, 75-36-5; $C_6H_5COCl$, 98-88-4

---

[1] *E. O. Greaves, G. R. Knox, P. L. Pauson*, Chem. Commun. *1969*, 1124; *R. E. Graf, C. P. Lillya*, J. Organomet. Chem. *166*, 53 (1979).

[2] Cf. *e.g. R. Lantzsch, D. Arlt*, Justus Liebigs Ann. Chem. *1976*, 1757.

[3] *M. Franck-Neumann, D. Martina, F. Brion*, Angew. Chem. *90*, 736 (1978); Angew. Chem. Int. Ed. Engl. *17*, 690 (1978).

[4] a) *K. K. Joshi*, J. Chem. Soc. *A 1966*, 594; b) *D. Bright, O. S. Mills*, J. Chem. Soc. Dalton Trans. *1972*, 2465.

[5] *(1)* was prepared in 45% yield from a solution of 1,4-dibromo-2-butyne and $Fe_2(CO)_9$ (1 : 2.8) at 80°C. (11% from 1,4-dichloro-2-butyne and $Fe_2(CO)_9$ [4a].)

[6] *R. N. Greene, C. H. Depuy, T. E. Schroer*, J. Chem. Soc. *C 1971*, 3115; *S. M. Nelson, C. M. Regan, M. Sloan*, J. Organomet. Chem. *96*, 383 (1975).

[7] *(4)* can be obtained, as described in [4a], in 65% yield from free cumulene and $Fe_3(CO)_{12}$. The preparation is, however, more straightforward if 2,5-dibromo-2,5-dimethyl-3-hexyne is treated with $Fe_2(CO)_9$ (45% yield).

[8] *(5)* has previously been isolated from the mixture of photolysis products of 4-acetyl-5-isopropyl-3,3-dimethyl-3*H*-pyrazole using preparative gas chromatography: *C. Dietrich-Buchecker, M. Franck-Neumann*, Tetrahedron *33*, 751 (1977).

[9] *E.g.* 2,5-dimethyl-2,4-hexadiene (1,1,4,4-tetramethylbutadiene) reacts with $Fe(CO)_5$ to give the tricarbonyliron complex of 1-isopropyl-3-methyl-1,3-butadiene): *G. F. Emerson, J. E. Mahler, R. Kochhar, R. Pettit*, J. Org. Chem. *29*, 3620 (1964).

[10] The diester corresponding to the diketone *(6)* is known, and this simplified its identification: *L. K. Snydes, L. Skattebøl, C. B. Chapleo, D. G. Leppard, K. L. Svanholt, A. S. Dreiding*, Helv. Chim. Acta *58*, 2061 (1975); *J. M. McIntosh, R. A. Sieler*, J. Org. Chem. *43*, 4431 (1978).

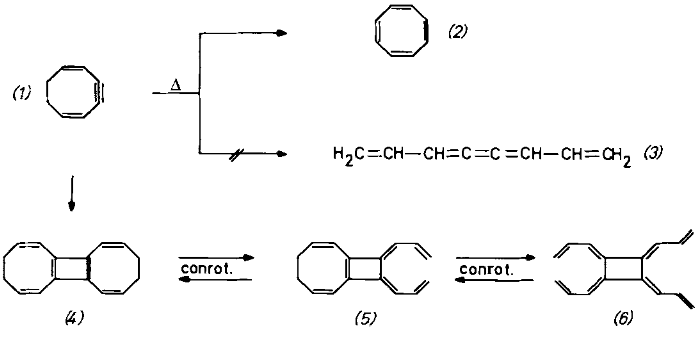
[11] a) See *e.g. A. J. P. Devaquet, R. E. Townshend, W. J. Hehre*, J. Am. Chem. Soc. *98*, 4068 (1976); b) *H. G. Viehe, R. Merényi, L. Stella, Z. Janousek*, Angew. Chem. *91*, 982 (1979); Angew. Chem. Int. Ed. Engl. *18*, 917 (1979).

# Investigation of Valence Isomerism Cyclobutadiene—Bismethylenecyclobutene—[4]Radialene[**]

By *Herbert Meier*, *Toni Echter*, and *Oswald Zimmer*[*]

The short lifetime of highly strained cyclic alkynes often results from di-, tri-, and oligomerization reactions, which *e.g.* occur with cyclohexyne[1a] or 1,2-didehydrocyclooctatetraene[1b].

The 1,5-cyclooctadien-3-yne *(1)*[2], isolated by us, isomerizes to 1,3,5,7-cyclooctatetraene *(2)* at high temperatures. In contrast, at room temperature—by avoiding alkaline media—an almost quantitative dimerization to the cyclobutadiene *(4)* is observed. A 0.3 M solution of *(1)* in chloroform has a half-life of *ca.* 2 h. *(4)* can stabilize itself *via* a conrotatory electrocyclic ring opening process, forming the bicycle *(5)*, a bismethylenecyclobutene, or even the monocycle *(6)*, a [4]radialene. The $^1$H- and $^{13}$C-NMR spectra of the dimeric stage indicate an equilibrium whose position lies almost completely to the side of *(5)*. In contrast to the colorless educt *(1)*, *(5)* is intensely yellow. The 400 MHz $^1$H-NMR spectrum[3] demonstrates that six types of chemically non-equivalent olefinic protons are present. The protons $H_f$ and $H_{f'}$ absorb at the lowest field position ($\delta=6.84$). Their coupling with $H_e$, $H_g$, and $H_h$, and $H_{e'}$, $H_{g'}$, and $H_{h'}$ respectively was ascertained by means of decoupling experiments ($\delta=5.90$, 5.28, 5.17). The protons of the

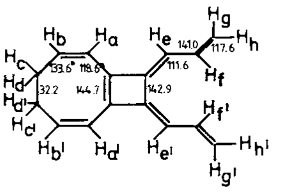


---

[*] Prof. Dr. H. Meier, Dipl.-Chem. T. Echter, Dipl.-Chem. O. Zimmer
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.

intact eight-membered ring approximately form an ABXX' system. $H_a$ and $H_{a'}$ appear as a doublet at $\delta=6.27$, and $H_b$ and $H_{b'}$ as a multiplet at $\delta=6.23$. The chemical equivalence of $H_c$ and $H_{c'}$, as well as that of $H_d$ and $H_{d'}$, is based on an inversion process which occurs at room temperature. The eight $^{13}$C absorptions recorded for *(5)* yield two singlets, four doublets and two triplets under off-resonance conditions. The given assignments shown in the formula are consistent with the $^{13}$C data for bis(methylene)cyclobutene in the literature[4].

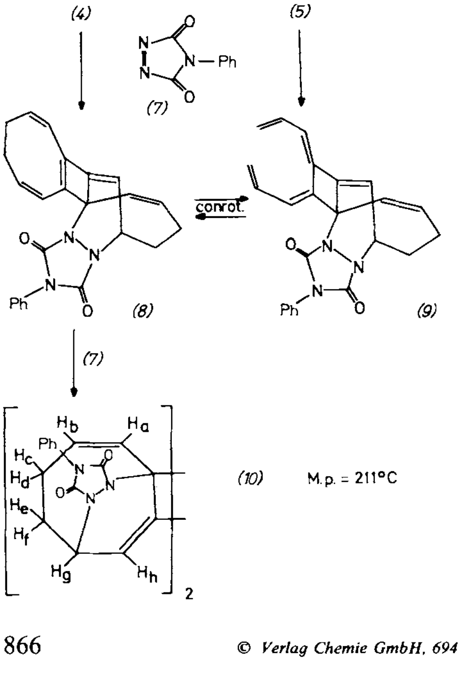


*(5)*

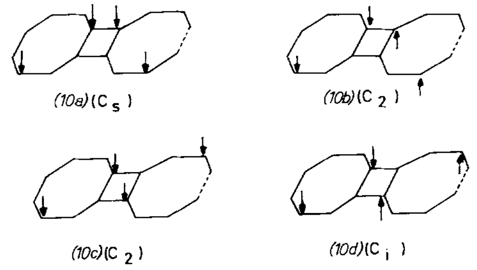
In principal, *(5)* could also be formed *via* an electrocyclic ring opening process of *(1)* to 1,3,4,5,7-octapentaene *(3)*, which reacts with *(1)* in a $[2_\pi+2_\pi]$-cycloaddition step. This route is, however, precluded, since the monomolecular reaction *(1)*→*(3)* would then have to be observed already in the gas phase in the preparation of *(1)*. In the $^1$H-NMR spectrum of a solution of *(5)* in chloroform kept for a few days at room temperature, the signals for protons $H_a$ and $H_b$ become smaller and those of the protons of the open chain become larger. This indicates a further valence isomerization to the radialene system *(6)*. Unfortunately, this process is accompanied by polymerization which makes its investigation difficult.

*cis,cis*-1,3,5,7-Octatetraene undergoes extremely rapid and complete cyclization to 1,3,5-cyclooctatriene[5a]. *Huisgen et al.*[5b] were able to extensively investigate the position of equilibrium and stereochemistry of the dimethyl compounds. The cyclooctatriene was shown to dominate the equilibrium at room temperature. A low energy barrier for this $[_\pi8_s]$-valence isomerization is also indicated by our example. Because of the energetically unfavorable cyclobutadiene structure of *(4)*, the equilibrium lies to the side of *(5)*.

In contrast to *(1)*, the dimeric stage reacts spontaneously with the highly reactive dienophile 4-phenyl-1,2,4-triazolidine-3,5-dione *(7)*. By this means a 20% yield of the bisadduct *(10)*, a derivative of cyclobutadiene *(4)*, is obtained. This can be rationalized in two different ways: either the tricycle *(4)* reacts preferentially *via* the monoadduct *(8)* to *(10)* and thereby displaces the position of the equilibrium *(4)*⇄*(5)*, or the monoadduct *(9)* is formed from *(5)* *via* selective addition to the side of the eight-membered ring, which then is further transformed in an electrocyclic ring closure to *(8)* and hence leads, *via* a second cycloaddition, to *(10)*. The constitution of *(10)* was elucidated using homonuclear double-resonance experiments. Apart from the signals of five aromatic protons ($\delta=7.5$), the $^1$H-NMR spectrum ($CDCl_3$) consists of a doublet for $H_h$ (6.9, $^3J=6.8$ Hz), a multiplet for $H_a$ and $H_b$ (6.0), a multiplet for $H_g$ (5.2), and a broad absorption for $H_c$, $H_d$, $H_e$, and $H_f$ ($1.9\leq\delta\leq2.6$). When all couplings to the saturated protons $H_{c-f}$ are eliminated, residual AB- and AX-systems remain for $H_{a,b}$ and $H_{g,h}$, respectively. The possible structures of *(10)* are obtained by applying one of the following symmetry operations to the half-molecules shown in formula *(10)*: *(10a)*: Reflection in a plane of symmetry σ lying right angles to the plane of the four-membered ring. *(10b)*: Rotation about a $C_2$ axis lying in the plane of the four-membered ring. *(10c)*: Rotation about a $C_2$ axis perpendicular to the plane of the four-membered ring. *(10d)*: Inversion i through the middle of the four-membered ring.

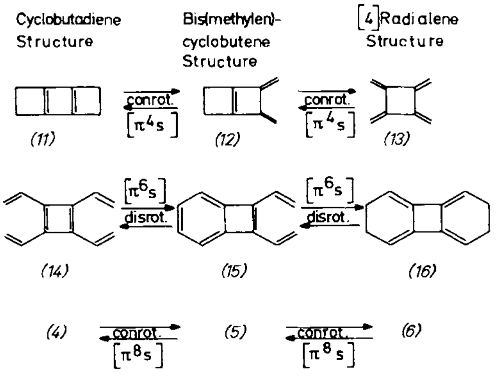


In principle, the double Diels-Alder reaction could lead to four adducts. In this connection it is immaterial whether the direct route *(4)*→*(8)*→*(10)*, or the indirect route *(4)*→*(5)*→*(9)*→*(10)* is followed. The various possible modes of attack of the dienophile *(7)* and the point groups of the resulting adducts are shown in Scheme 1.



Scheme 1.

Apart from the $C_{16}H_{16}$-system with $2\cdot8\pi$- or σ-electrons described here, valence isomerization between cyclobutadiene, bis(methylene)cyclobutene, and [4]radialene systems is also conceivable in the $C_{12}H_{12}$- and $C_8H_8$-systems (Scheme 2). The steric course shown refers to the thermally allowed synchronous reactions. The behavior is reversed under photolytic conditions.



Scheme 2.

The experimental verification of the hypotheses appears to be considerably easier in the $C_{12}H_{12}$ series than with $C_8H_8$[6]. We hope that our investigations will be an impetus to finding further electrocyclic reactions at four-membered rings with four π-centers.

Received: March 13, 1981 [Z 864 IE]
German version: Angew. Chem. *93*, 901 (1981)

CAS Registry numbers:
*(1)*, 68344-46-7; *(4)*, 79084-09-6; *(5)*, 79084-10-9; *(7)*, 4233-39-4; *(10)*, 79084-11-0

---

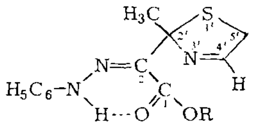
[1] a) *G. Wittig, U. Mayer*, Chem. Ber. *96*, 342 (1963); b) *A. Krebs, D. Byrd*, Justus Liebigs Ann. Chem. *707*, 66 (1967).
[2] *H. Meier, T. Echter, H. Petersen*, Angew. Chem. *90*, 997 (1978); Angew. Chem. Int. Ed. Engl. *17*, 942 (1978).
[3] Dr. *U. Siehl* is thanked for recording the 400 MHz spectra.
[4] *A. J. Jones, P. J. Garratt, K. P. C. Vollhardt*, Angew. Chem. *85*, 260 (1973); Angew. Chem. Int. Ed. Engl. *12*, 241 (1973).
[5] a) *W. Ziegenbein*, Chem. Ber. *98*, 1427 (1965); b) *R. Huisgen, A. Dahmen, H. Huber*, J. Am. Chem. Soc. *89*, 7130 (1967); Tetrahedron Lett. *1969*, 1461; *A. Dahmen, R. Huisgen, ibid. 1969*, 1465.
[6] The tetrakis(methylene)cyclobutane *(13)* (*G. W. Griffin, L. I. Peterson*, J. Am. Chem. Soc. *84*, 3398 (1962)) and the bicyclo[2.2.0]hex-1(4)-ene (*K. B. Wiberg, G. J. Burgmaier, P. Warner, ibid. 93*, 246 (1971)) as basic frameworks of *(12)* are known. For the tricyclic compound *(11)* see *E. Kloster-Jensen, J. Wirz*, Helv. Chim. Acta *58*, 162 (1975).

---

## Reactions of a Heterocyclic System Having Ambidentate Reactivity[**]

By *Johann Gasteiger, Ulrich Strauß*, and *Ulrich Schubert*[*]

α-Phenylhydrazono-2,5-dihydro-2-thiazole acetates *(1)*[1] offer various sites for attack, both by electrophilic[2] and nucleophilic reagents.



*(1a)*, R = $CH_3$
*(1b)*, R = $C_2H_5$
*(1c)*, R = $C(CH_3)_3$

This makes them useful models for the study of ambidentate reactivity. Nucleophilic attack could occur at both C atoms (1 and 2) of the acetic acid system and at C-4′ of the dihydrothiazole ring. A sufficiently basic nucleophile could abstract the NH-proton followed by rearrangement or fragmentation processes. We investigated whether, under these circumstances, the ester group could be hydrolyzed in alkaline solution.

Reaction of *(1a)* with ethanolic potassium hydroxide gave a product in which the methyl group had been lost and an ethyl group had been incorporated. However, the product was not *(1b)*, as its independent synthesis proved, but rather an isomer of *(1b)*. Structure elucidation was aggravated, since $^1$H-NMR spectra showed that the product consisted of a mixture of two compounds which were only moderately soluble in $CDCl_3$.

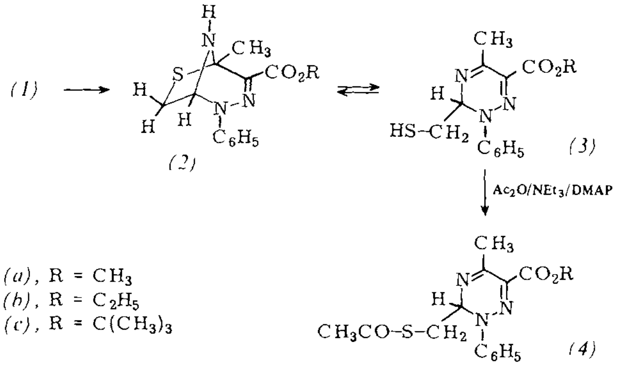
Reaction of *(1c)* with methanolic sodium hydroxide produced a product which was sufficiently soluble in $CDCl_3$ to allow the determination of $^{13}$C-NMR spectra. It was apparent that a *tert*-butyl group was still present, but that a rearrangement had occurred. Hence, in the reaction of *(1a)* with ethanolic potassium hydroxide the incorporation of the ethyl group is not necessarily coupled to the rearrangement reaction, but is rather a secondary process, a transesterification which does not occur with the *tert*-butyl ester.

Additional information on the mechanism was gathered from the reaction of the rearranged methyl ester with acetic anhydride/triethylamine/4-dimethylaminopyridine. By this means, the acetyl derivative *(4)* of the minor component of the product mixture was isolated; sufficient material was collected in this way to allow structural assignments[3]. The constitutional changes express themselves particularly clearly in the $^{13}$C-NMR spectra (Table 1). The course of the reaction is thus as follows: in alkaline media deprotonation of the hydrazono group takes place first, followed by nucleophilic attack at the azomethine group to give the 6-thia-2,3,8-triazabicyclo[3.2.1]oct-3-ene system *(2)*. This compound has a thiohemiaminal structure which can rearrange to the 3-thiomethyl-2,3-dihydro-1,2,4-triazine derivative *(3)*.

Table 1. Selected $^{13}$C-NMR data (in $CDCl_3$; δ-values) of *(1c)*–*(4c)*. C-atoms which are related to each other through the structural changes in the reactions are displayed in the same columns.

| | | | | |
|---|---|---|---|---|
| *(1c)* | 45.9 (C-5′) | 158.3 (C-4′) | 93.1 (C-2′) | 129.0 (C-2) |
| *(2c)* | 43.0 (C-7) | 73.2 (C-1) | 67.7 (C-5) | 140.2 (C-4) |
| *(3c)* | [a] ($CH_2S$) | 71.6 (C-3) | 156.7 (C-5) | [a] (C-6) |
| *(4c)* | 27.9 ($CH_2S$) | 68.2 (C-3) | 157.1 (C-5) | 133.5 (C-6) |

[a] Hidden by lines of *(2c)*.



*(a)*, R = $CH_3$
*(b)*, R = $C_2H_5$
*(c)*, R = $C(CH_3)_3$

The equilibrium *(2)*⇄*(3)* is solvent dependent. At room temperature the amount of *(3c)* in $CDCl_3$ is 25%, in $CD_3COCD_3$ 5%. Acylation of this equilibrium mixture only leads to the acetyl derivative *(4)*.

An X-ray structure determination of the rearranged methyl ester was performed[4], and showed that only *(2a)* was present in the crystal (Fig. 1).

In the thiazolidine ring, the atoms C2, S, C7 and C1 are approximately coplanar (torsion angle C2—S—C7—C1 4.7°). In the six-membered ring, all atoms except N3 are also approximately coplanar. This observation, in conjunction with the bond lengths and the trigonal planar configuration of N2, indicates conjugation of the C=N double bond with N2.

---

[*] Priv. Doz. Dr. J. Gasteiger [+], Dr. U. Strauß
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)
Priv. Doz. Dr. U. Schubert
Anorganisch-chemisches Institut der Technischen Universität München,
Lichtenbergstrasse 4, D-8046 Garching (Germany)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

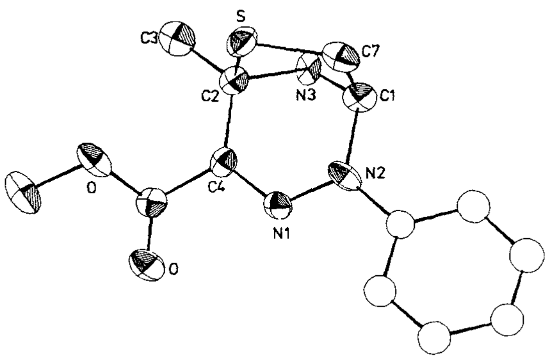


Fig. 1. Structure of *(2a)* in the crystal N1—N2 134.1(6), C4—N1 128.6(6), C1—N2 148.3(6), C1—N3 143.4(6), C2—N3 145.8(8), C2—C4 151.9(7), C2—S 183.8(6), C7—S 181.1(6) pm; C2—S—C7 91.5(3), C2—C4—N1 121.9(5), C4—N1—N2 118.9(4), C2—N3—C1 107.6(4)°.

### *Procedure*

*(2a):* A solution of *(1a)* (6.00 g, 21.6 mmol) in 100 mL dioxane and 40 mL water is treated for 1 h with 21.6 ml 1 N KOH. After dilution with 100 mL ice-water, the mixture is extracted three times with $CH_2Cl_2$. After washing, drying, and evaporation of the solvent, 5.52 g of crude product is obtained from which yellow prisms, 2.36 g (39%) *(2a)*, are isolated by recrystallization from ether and then from acetone.

*(4a): (2a)* (1.80 g, 6.5 mmol) is suspended in benzene and treated with acetic anhydride (8.3 mL, 9.0 g, 88 mmol), triethylamine (3.6 mL, 2.6 g, 26 mmol), and 4-dimethylaminopyridine (0.1 g). Within a few min the solution becomes clear. After 20 h at room temperature, the mixture is washed with sodium bicarbonate solution. After evaporation of the solvent, the product is dissolved in 10 mL methylene chloride, 100 mL cyclohexane added, and the solution concentrated to 50 mL. *(4a)* 1.80 g (87%) crystallizes as fine yellow needles.

Received: July 14, 1980 [Z 866a IE]
supplemented: April 9, 1981
German version: Angew. Chem. *93*, 931 (1981)

CAS Registry numbers:
*(1a)*, 77362-54-0; *(1b)*, 77362-55-1; *(1c)*, 77362-56-2; *(2a)*, 79043-69-9; *(2c)*, 79043-70-2; *(3c)*, 79057-58-9; *(4a)*, 79043-71-3; *(4c)*, 79043-72-4

---

[1] *J. Gasteiger, U. Strauß*, Chem. Ber., *114*, 2336 (1981).

[2] *J. Gasteiger, U. Strauß*, Heterocycles *16*, 199 (1981).

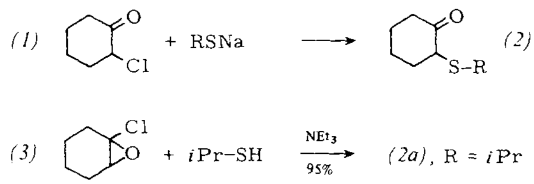
[3] Elemental analyses and spectral data (IR, MS, $^1H$- and $^{13}C$-NMR) agree with the structures given. M.p.: 99—100°C *(1a)*; 107—108°C *(1b)*; 117°C *(1c)*; 150—151°C *(2a)*; 151—152°C *(2c)*; 128°C *(4a)*.

[4] Monoclinic, $P2_1/c$; $a = 972.5(11)$, $b = 1634(2)$, $c = 883.4(8)$ pm, $\beta = 112.10(7)°$. Syntex $P2_1$/XTL, $Mo_{K\alpha}$ (graphite monochromator) $\lambda = 71.069$ pm). 1407 structure factors, $F_0 \geqq 4.2\sigma(F_0)$, $2° \leqslant 2\theta \leqslant 48°$. $R_1 = 0.071$, $R_2 = 0.066$.

## The 2-Chlorooxirane—α-Chloroketone Reactivity Spectrum[**]

By *Johann Gasteiger* and *Christian Herzig*[*]

α-Hydroxy-[1b], α-amino-[1c], and α-mercaptoketones[1d,2] and their derivatives are important synthetic building blocks. An obvious entry to these classes of compounds is presented by the reaction of α-haloketones with nucleophiles. Thus, 2-alkylthiocyclohexanones *(2)* can be obtained from 2-chlorocyclohexanone *(1)* and thiolates, but only in moderate yields[3].

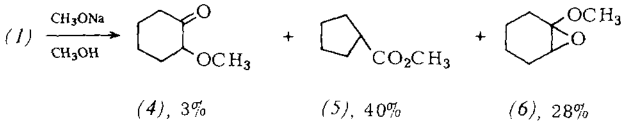


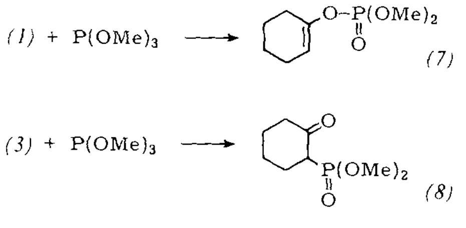
In investigations of nucleophilic substitutions of 2-chlorooxiranes, we found that the α-alkylthioketones *(2)* can be obtained from 1-chloro-7-oxabicyclo[4.1.0]heptane[4] *(3)*, which is isomeric to *(1)*. The reactions proceed under milder conditions, and give higher yields. In comparison with α-chloroketones, 2-chlorooxiranes offer not only the advantage of improved yields, but also might give a different spectrum of products.

Reactions of α-haloketones with nucleophiles often create problems, as a number of side reactions can occur[1]. Thus, 2-chlorocyclohexanone *(1)* only gives minor amounts of 2-methoxycyclohexanone *(4)* with methanolic sodium methoxide. The main reaction is a Favorski rearrangement to *(5)*. In addition, a sizeable amount of 1-methoxy-7-oxabicyclo[4.1.0]heptane *(6)* is formed[5].

Under the same reaction conditions, *(3)* leads to *(4)* in nearly quantitative yield[6].

*(1)* gives 1-cyclohexenyldimethyl phosphate *(7)* with trimethyl phosphite in a Perkov reaction. *(3)*, on the other hand, undergoes a Michaelis-Arbuzov reaction yielding dimethyl 2-oxocyclohexyl phosphonate *(8)*[7].





The reactions of *(1)* and *(3)* with sodium methoxide and with trialkyl phosphites show that in reactions with nucleophiles, 2-chlorooxiranes can follow pathways different from those of α-chloroketones. In other words, reactions of 2-chlorooxiranes do not go through an initial rearrangement to α-chloroketones. This conclusion is supported by the fact that 2-chlorooxiranes have a higher reactivity than α-chloroketones. In the course of the reaction, the strain energy of the three-membered ring is released. Therefore, reactions with nucleophiles occur under mild conditions, and also with less reactive reagents.

To test for the limits of the synthetic utility of 2-chlorooxiranes, *(3)* was reacted with 2-mercaptopropionic acid/triethylamine and with dimethyl sulfide.

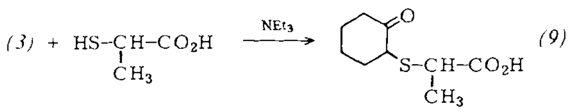
---

[*] Priv. Doz. Dr. Johann Gasteiger [+], Dr. C. Herzig
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[+] Author to whom correspondence should be addressed.

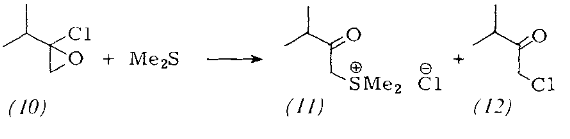
[**] This work was supported by the Deutsche Forschungsgemeinschaft.

0570-0833/81/1010-0868 $ 02.50/0



While (9) could be isolated in 88% yield, no reaction between (3) and dimethyl sulfide was observed. In this case only (1), the product of rearrangement of (3), was obtained.

On the other hand, dimethyl sulfide can still be alkylated by 2-chloro-2-isopropyloxirane[4b] (10). The sulfonium salt (11) was isolated in 30% yield. In addition, rearrangement of (10) to (12) (isolated in 60% yield) occurred.



The fact that (12) could be isolated from this reaction mixture underlines particularly well the lower alkylating power of α-chloroketones relative to that of 2-chlorooxiranes. On attempted reaction of the 2-chlorooxirane (3) with dimethyl sulfide, rearrangement is faster than the nucleophilic substitution. In the case of the 2-chlorooxirane (10), the reaction with dimethyl sulfide can still compete with the rearrangement to the α-chloroketone. (10) can even alkylate triethylamine at room temperature; the ammonium salt (13) was obtained in 40% yield.

2-Chlorooxiranes have a higher reactivity than α-chloroketones toward nucleophilic reagents, give products under milder conditions and in higher yields, and over and above lead to different products.

### *Procedure*

*(2a):* A solution of 2-propanethiol (3.14 g, 40 mmol) and of triethylamine (4.04 g, 40 mmol) in 10 mL $CH_2Cl_2$ is added to (3) (2.66 g, 20 mmol) at −10 °C. After 1 h the mixture is allowed to warm to room temperature, and is stirred for an additional 16 h. After evaporation of the solvent at room temperature (12 torr), the residue is digested with ether and filtered. The filtrate is concentrated, and then distilled to give 3.29 g (95%) of (2a) at 59.5 °C/0.5 torr.

*(11):* Dimethyl sulfide (3.10 g, 50 mmol) in 6 mL $CH_2Cl_2$ is added at 0 °C to (10) (1.21 g, 10 mmol). The sulfonium salt (11) precipitates within 1 h in a slightly exothermic reaction, and is isolated in the form of highly hygroscopic crystals after filtration and washing with ether: 0.54 g (30%); m. p. 101 °C. From the reaction solution the chloroketone (12) can be isolated in 60% yield.

Received: August 1980 [Z 866b IE]
supplemented: April 9, 1981
German version: Angew. Chem. 93, 933 (1981)

CAS Registry numbers:
(1), 822-87-7; (2a), 69763-36-6; (3), 51595-54-1; (4), 7429-44-9; (5), 4630-80-2; (6), 79043-65-5; (7), 3719-53-7; (8), 76002-23-8; (9), 79043-66-6; (10), 76002-26-1; (11), 79043-67-7; (12), 17687-63-7; (13), 79043-68-8; 2-mercaptopropionic acid 79-42-5

---

[1] a) *Houben-Weyl-Müller:* Methoden der Organischen Chemie, Bd. VII/2c, Thieme, Stuttgart 1977; b) *D. Mayer* in [1a], p. 2171; c) *D. Mayer*, p. 2251; d) *H. Horstmann*, p. 2317.

[2] *D. Seebach, M. Teschner*, Chem. Ber. *109*, 1601 (1976).

[3] *L. Bateman, F. W. Shipley*, J. Chem. Soc. *1955*, 1996; *M. Oki, W. Funakoski, A. Nakamura*, Bull. Chem. Soc. Jpn. *44*, 828 (1971); *J. J. Looker*, J. Org. Chem. *31*, 2973 (1966).

[4] a) *M. Mousseron, R. Jacquier*, Bull. Soc. Chim. Fr. *1950*, 698; b) *J. Gasteiger, C. Herzig*, J. Chem. Res. (S) *1981*, 113; (M) *1981*, 1101.

[5] *M. Mousseron, R. Jacquier, A. Fontaine*, Bull. Soc. Chim. Fr. *1952*, 767.

[6] *M. Mousseron, R. Jacquier* (Bull. Soc. Chim. Fr. *1950*, 698) obtained (5) and (6) as products from (3). Our investigations show that (3) only leads to (4). With the other authors (3) had probably already rearranged to (1).

[7] *J. Gasteiger, C. Herzig*, Tetrahedron Lett. *1980*, 2687.

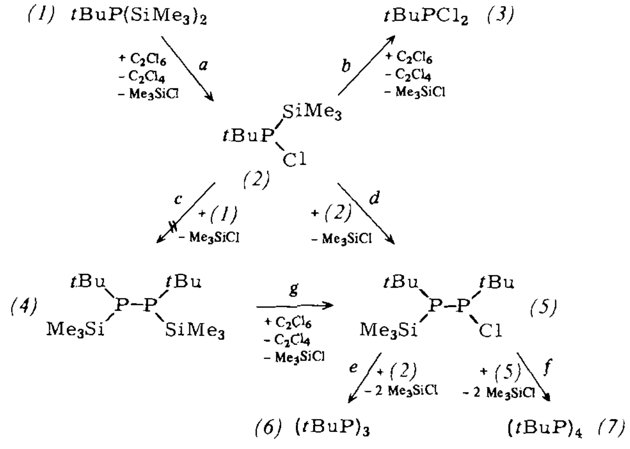
---

# $Me_3C$—P(Cl)—$SiMe_3$, the First *P*-Halogenated Silylphosphane[**]

By *Rolf Appel* and *Wilfried Paulen*[*]

*Dedicated to Professor Hans-Dieter Beckey on the occasion of his 60th birthday*

Attempts to prepare a *P*-halogen-*P*-silylphosphane have been unsuccessful until now[1]; the halosilane was always cleaved off. To obtain a synthetic building block containing this structurally interesting moiety, however, we reacted *tert*-butylbis(trimethylsilyl)phosphane (1) with the stoichiometric amount of hexachloroethane[2]. The desired product (2) is thus almost quantitatively formed in solution as an unstable intermediate.



As expected, the second silyl function could also be exchanged for chlorine when an excess of $C_2Cl_6$ was used (step *b*). In contrast to the phenyl derivative[3], however, intermolecular condensation (step *c*) of (2) and the educt (1) still present could be observed under the reaction conditions. The formation of the P—P bond in (4) is here kinetically suppressed by the steric demands of the components (1) and (2).

(2) was unequivocally characterized as *tert*-butylchloro(trimethylsilyl)phosphane by elemental analysis, molecular weight (MS), as well as by $^{31}P\{^1H\}$-, $^{13}C\{^1H\}$-, and $^1H$-NMR results[4]. The condensation (step *d*) can be cited as additional proof of the structure. Even at room temperature, (2) reacts slowly in toluene under $Me_3SiCl$-cleavage to produce the novel unsymmetrical diphosphane (5), which in the presence of (2) cyclizes to the cyclotriphos-

---

[*] Prof. Dr. R. Appel, Dipl.-Chem. W. Paulen
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[**] Phosphorus-Carbon-Halogen Compounds, Part 29.—Part 28: *R. Appel, A. Westerhaus*, Tetrahedron Lett., in press.

phane *(6)*[5], or alternatively undergoes self-condensation to the cyclotetraphosphane *(7)*[6] (steps *e* or *f*, respectively). The dissociation of *(2)* to its thermodynamically stable end-products *(6)* and *(7)* shows a characteristic solvent dependence; a polar medium accelerates formation of the cyclophosphane, and simultaneously causes a shift of the $^{31}P\{^1H\}$ signal of *(2)* to low-field.

The diphosphane *(5)* could not be isolated as a reactive intermediate until now. Its identification by $^{31}P$-NMR spectroscopy in solution (significant AB spectrum[7]) was corroborated by independent synthesis (step *g*) from *(4)* and hexachloroethane using an analogous procedure to that of step *a*.

Silyl- and halogen-functionalized phosphanes are, in addition, suitable educts for gas phase pyrolysis, a process which may hinder the intermolecular condensation discussed here. In this way, *(2)* could form a phosphanediyl[8] *via* a 1,1-elimination and *(5)* an analogue of an azo compound *via* a 1,2-elimination[10].

### *Procedure*

A solution of $C_2Cl_6$ (22.0 g, 93 mmol) in toluene is slowly added to a stirred solution of *(1)*[9] (21.8 g, 93 mmol) in 30 mL toluene under ice cooling. The mixture is stirred for 30 min at room temperature. The toluene solution contains *(2)* in practically quantitative yield. After purification by distillation, *(2)* 3.7 g (20% yield), b.p. 28 °C/0.05 torr) remains in the distillation receiver (−78 °C) (half-life of *(2)* at 34 °C: 13 min from $^{31}P\{^1H\}$-NMR spectrum).

Received: March 16, 1981 [Z 867 IE]
German version: Angew. Chem. *93*, 902 (1981)

CAS Registry numbers:
*(1)*, 42491-33-8; *(2)*, 79044-45-4; *(3)*, 25979-07-1; *(4)*, 55793-25-4; *(5)*, 79044-46-5; *(6)*, 61695-12-3; *(7)*, 5995-07-3; $C_2Cl_6$, 67-72-1

---

[1] *M. Baudler, A. Zarkadas,* Chem. Ber. *104*, 3519 (1971); *M. Baudler, M. Hallab, A. Zarkadas, E. Tolls, ibid. 106*, 3962 (1973); *E. A. V. Ebsworth, C. Glidewell, G. M. Sheldrick,* J. Chem. Soc. *A 1969*, 352.

[2] *R. Appel, K. Geisler, H.-F. Schöler,* Chem. Ber. *110*, 376 (1977).

[3] *H.-F. Schöler,* Dissertation, Universität Bonn 1977.

[4] *(2):* $^{31}P\{^1H\}$-NMR (toluene/$C_6D_6$, 32.2 MHz, $H_3PO_4$ ext.): $\delta = 94.7$ [s]; $^{13}C\{^1H\}$-NMR ($C_6D_6$, 22.6 MHz, TMS int.): $\delta = -1.24$ [d, $^2J(PSiC) = 11.2$ Hz, $SiCH_3$], 28.17 [d, $^2J(PCC) = 16.6$ Hz, $CCH_3$], 33.8 [d, $J(PC) = 34$ Hz, PC]; $^1H$-NMR ($C_6D_6$, 90 MHz, TMS int.): $\delta = 0.2$ [d, $^3J(PSiCH) = 2.7$ Hz, $SiCH_3$], 1.15 [d, $^3J(PCCH) = 13.5$ Hz, $CCH_3$].

[5] *M. Baudler, J. Hahn, H. Dietsch, G. Fürstenberg,* Z. Naturforsch. *B 31*, 1305 (1976).

[6] *K. Issleib, M. Hoffmann,* Chem. Ber. *99*, 1320 (1966).

[7] *(5):* $^{31}P\{^1H\}$-NMR (toluene/$C_6D_6$, 32.2 MHz, $H_3PO_4$ ext.): $\delta = -47.2$ [d, $J(PP) = 358.5$ Hz, PSi], 145.1 [d, $J(PP) = 358.5$ Hz, PCl].

[8] *U. Schmidt,* Angew. Chem. *87*, 535 (1975); Angew. Chem. Int. Ed. Engl. *14*, 523 (1975).

[9] *G. Becker, O. Mundt, M. Rössler, E. Schneider,* Z. Anorg. Allg. Chem. *443*, 42 (1978).

[10] Compound of this type: *J. Shina, N. Juamoto,* lecture delivered at the International Conference on Phosphorus Chemistry, Durham 1981.

## A Boron-Boron One-Electron π-Bond[**]

By *Hartmut Klusik* and *Armin Berndt*[*]

*Dedicated to Professor Siegfried Hünig on the occasion of his 60th birthday*

The boron-boron one electron π-bond in the radical anion *(2a)* derived from tetraneopentyldiborane(4) *(1a)* represents the simplest B—B π-bond[1–4]. *(1a)*, which is accessible from tetramethoxydiborane(4) and neopentyllithium, can be reduced to a persistent radical. The ESR spectrum of the radical derived from *(1b)*, in which all 36 H atoms of the *tert*-butyl groups have been replaced by D atoms, is shown in Figure 1. The spectrum can be analyzed by hyperfine coupling constants of 0.380 and 0.465 mT for two sets of four equivalent protons and 0.08 mT for two equivalent $^{11}B$ atoms[5]. The assignment of the larger coupling constants to the methylene protons has been experimentally verified by D atom substitution. In the ESR spectrum of the radical derived from *(1a)*, neither the nonequivalence of the methylene protons nor the splitting of the two equivalent boron atoms, which is essential for the proof of the structure, are detectable due to the additional splitting of the *tert*-butyl protons ($a^H = 0.013$ mT).

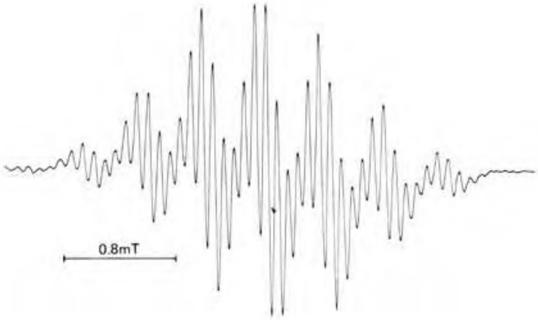
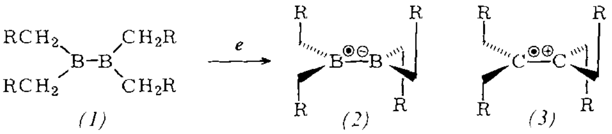


Fig. 1. ESR spectrum of the radical anion *(2b)* in dimethoxyethane at 30 °C.

The nonequivalence of the methylene protons indicates that the neopentyl groups adopt a preferred conformation in which the $CH_2$—$C(CH_3)_3$ bond forms a torsion angle of *ca.* 2° with the axis of the p-orbital of the neighboring boron atom[6]. For steric reasons, *(2)* therefore exists in a conformation in which each pair of *tert*-butyl groups of *trans*-standing neopentyl groups shields both boron atoms from above and below.



*(a)*, R = $C(CH_3)_3$; *(b)*, R = $C(CD_3)_3$

This shielding effect, which is reproduced insufficiently in the formula shown, may be one reason for the remarkable persistence of radical *(2)*, which can easily be investigated by ESR spectroscopy up to +140 °C ($t_{1/2} \approx 15$ min). In contrast, *(1)* decomposes, even at +20 °C ($t_{1/2} \approx 20$ min), to produce trineopentylborane and, as yet, unidentified products. The persistence of the reduced diborane(4) is reminiscent of that of tetramethoxydiborane(4) and of tetra(dimethylamino)diborane(4) in which the electron deficiency of the two boron atoms, which must be responsible for the high reactivity of diboranes(4), is partially removed *via* the electron pairs on oxygen and nitrogen. The electron deficiency in *(2)* is decreased by the unpaired electron.

The structure *(2)* is further corroborated by the properties of the isoelectronic radical cation *(3a)*, which we prepared by oxidation of tetraneopentylethylene with $SbCl_5$ in dichloromethane. The nonequivalence of the methylene protons in *(3a)* ($a^H = 0.987$ and 1.040 mT, for each 4 H) es-

---

[*] Prof. Dr. A. Berndt, Dipl.-Chem. H. Klusik
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and by Hoechst AG.

tablishes a conformation corresponding to that of *(2)*, which accounts for the notable persistence of *(3a)* ($t_{1/2}\approx 1$ h at +40 °C).

The coupling constant of the methylene protons in *(2)* (*ca.* 0.4 mT) is considerably smaller than in *(3a)* (*ca.* 1.0 mT). This is consistent with the structure of a radical anion: coupling constants of β-protons are always much smaller in radical anions than in the corresponding radical cations[7].

The $^{11}B$ coupling constant of 0.08 mT is surprisingly small[8]. Splittings of this magnitude can remain undiscovered in broad lines of incompletely resolved ESR spectra. Attempts to reduce persistent tetraalkyldiboranes(4) to radical anions were previously interpreted as unsuccessful[9], because the ESR spectra showed no splitting from the two boron atoms. The results found with *(2)*, however, indicate that this could be accounted for by the linewidth of 0.36 mT. The persistence of the radical observed on reduction of 1,2-di-*tert*-butyl-1,2-dineopentyldiborane(4) is comparable to that of *(2)*, indicating that another species with a B—B one electron π-bond is involved.

Received: March 13, 1981 [Z 869 IE]
German version: Angew. Chem. *93*, 903 (1981)

CAS Registry numbers:
*(1a)*, 79057-63-9; *(2a)*, 79044-42-1; *(3a)*, 79044-43-2

---

[1] Boron-boron π-bonds also accur in two $C_2B_3H_5^{4-}$-heterocycles which are isoelectronic with $C_5H_5^-$. These, however, are only known as the central ligands of tripledecker sandwich complexes [2].

[2] *W. T. Robinson, R. N. Grimes*, Inorg. Chem. *14*, 3056 (1975), and references cited therein.

[3] The structure $[\mathrm{aryl_2B{-}Baryl_2}]^{\cdot-}$, aryl = $p$-$(CH_3)_2N{-}C_6H_4$, with B—B π-bond contribution has been suggested by *Leffler et al.* [4] for a radical formed reversibly from $Ar_3B$ and Na/K, and which shows a 1:2:3:4:3:2:1 multiplet with 0.31 mT intervals in the ESR spectrum. This structure, however, is not consistent with the absence of a splitting from the 8 *o*-protons which should be *ca.* half the magnitude of that in $(C_6H_5)_3B^{\cdot-}$ ($a^H = 0.199$ mT [4]).

[4] *J. E. Leffler, G. B. Watts, T. Tanigaki, E. Dolan, D. S. Miller*, J. Am. Chem. Soc. *92*, 6825 (1970).

[5] The combination $^{11}B{-}^{11}B$ occurs with 65.9% probability. The lines expected for the combination $^{11}B{-}^{10}B$ (30.6%) ($a^{^{11}B} = 0.08$ and $a^{^{10}B} \approx 0.027$ mT) are not resolved due to an experimental linewidth of 0.025 mT.

[6] Calculated with $a^H = B\cdot\cos^2(60\pm\phi)$, $\phi$ = torsion angle.

[7] Review: *K. Scheffler, H. B. Stegmann*: Elektronenspinresonanz, Springer-Verlag, Berlin 1970, p. 461 pp.

[8] Assuming that the Karplus-Fraenkel relationship $a^X = (Q_1^X - Q_2^X)\cdot\rho$ is valid for X = B, the σ-π parameters $Q_1^X$ and $Q_2^X$, whose values are considerably different (*ca.* 4.0 and 1.4 mT) when X = C, must be approximately equal ($Q_1^B - Q_2^B \approx 0.16$ mT) when X = B.

[9] *K. Schlüter, A. Berndt*, Angew. Chem. *92*, 64 (1980); Angew. Chem. Int. Ed. Engl. *19*, 57 (1980).

---

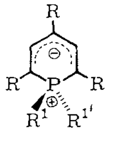
# Novel Reactions of $\lambda^5$-Phosphorins and Their Tricarbonylchromium Complexes

By *Karl Dimroth* and *Hans Kaletsch*[*]

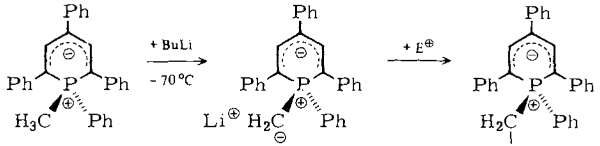
*Dedicated to Professor Sigfried Hünig on the occasion of his 60th birthday*

2,4,6-Trisubstituted $\lambda^5$-phosphorins of type *(1)*[1] are not "non-classical" 6π-heteroarenes, but cyclic phosphorus ylides whose negative charge is delocalized over the pentadienyl moiety and whose positive charge, depending on the substituents $R^1$, $R^{1'}$ is, to a greater or lesser extent, localized on the phosphorus atom[2a]. This can be established from the $^{13}C$-NMR signals of C-2/6 and C-4, and the $^{13}C$-$^{31}P$ coupling constants[2], as well as from the ESR spectra of free radicals formed by the oxidation of *(1)*[3]. We describe the first chemical evidence for the ylide character of *(1)* using a strong base to remove a proton from the α-position of suitable P-substituents (primary or secondary alkyl groups). A "double" ylide *(3)* is obtained which adds electrophiles (E), such as $D^+$, $CH_3^+$, or $PhCH_2^+$, to give *(4)*.

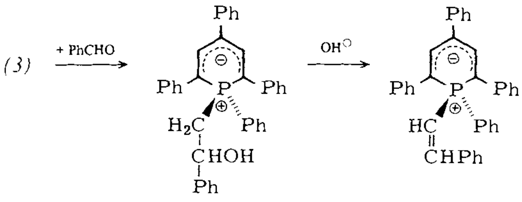
*(4b)*, E = Me, can be deprotonated again, and yields the 1-isopropyl derivative *(4d)* with MeI. Benzaldehyde reacts with *(3)* to give the β-hydroxy compound *(5)*, which forms the olefin *(6)* with alcoholic solutions of sodium hydroxide. No Wittig olefination is observed.



*(1)*, R = Ph, *t*Bu
$R^1$, $R^{1'}$ = Me, Et, Ph,
$NR_2^2$, OMe, SEt, Cl, Br, F, etc.

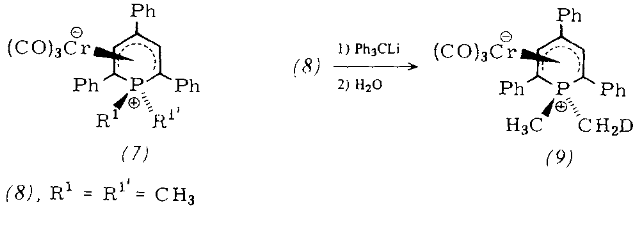


*(2)* *(3)* *(4)*



*(5)* *(6)*

In the nonplanar[4], highly stable[5] *P,P*-substituted tricarbonyl($\eta^5$-2,4,6-triphenyl-$\lambda^5$-phosphorin)chromium derivative *(7)*, the ylide character is strengthened by the electronic buffer-effect of the $Cr(CO)_3$ moiety[6] which leads to increased delocalization of the negative charge. Compounds of type *(7)* are obtained either from reaction of $\lambda^5$-phosphorins with $Cr(CO)_6$, whereby the *larger* residue $R^{1'}$ assumes the *exo*-position[5b], or from tricarbonyl(2,4,6-triphenyl-$\lambda^3$-phosphorin)chromium[7] *via exo*-addition of nucleophiles and subsequent reaction with electrophiles (at the *endo*-position)[8]. If $R^1$ and/or $R^{1'}$ are primary or secondary alkyl groups, the same sequence of deprotonation and addition of electrophiles as in the $\lambda^5$-phosphorins can be performed. However, with the bulky base $Ph_3C^-$ only the *exo*-methyl group of the 1,1-dimethyl complex *(8)* is deprotonated and subsequently deuterated to *(9)* with $D_2O$, while with BuLi both the *exo*- and *endo*-$CH_3$ groups are deprotonated to almost an equal extent. With $D_2O$, therefore, a mixture of *(9)* and its *endo*-$CH_2D$ isomer is obtained. The 1-*endo*-methyl-1-*exo*-phenyl complex, which



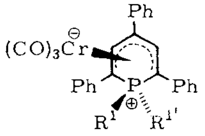
*(7)* *(9)*

*(8)*, $R^1 = R^{1'} = CH_3$

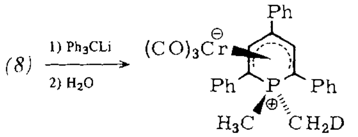
---

[*] Prof. Dr. K. Dimroth, H. Kaletsch
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

produced the "double" ylide complex with BuLi [cf. *(2)*→*(3)*], was thoroughly investigated. $D^+$ and $CH_3^+$ give *(10a—b)*, and benzaldehyde *(11)* from which *(12)* is obtained.



(7)



(9)

(8), $R^1 = R^{1'} = CH_3$

Careful oxidation of the $Cr(CO)_3$ complex resulted in cleavage of the tricarbonylchromium moiety, by analogy to carbocyclic $\eta^6$-tricarbonylchromium benzene complexes[9], whereby $\lambda^5$-phosphorins having the novel substituents $R^1$ and $R^{1'}$ at phosphorus are produced.

*Procedure*

1.2 Stoichiometric amounts of *n*BuLi are added to a solution of *(2)*, or its tricarbonylchromium complex, in anhydrous tetrahydrofuran (THF) under argon, and the mixture stirred for 30 min. $D_2O$, $CH_3I$, $PhCH_2Br$, or PhCHO are then added, and the mixture stirred for a further 30 min, allowed to warm up to room temperature, the solvent removed by evaporation, and the residue chromatographed on $Al_2O_3$ (neutral) using benzene, or in the case of *(10a, b)* on $SiO_2$ using $CH_2Cl_2$/petroleum ether (70—80°C) 1:1; *(12)* is purified by HPLC.

| Comp. | E | M.p. [°C] | Yield [%] | MS ($M^+$, [%]) |
|---|---|---|---|---|
| *(4a)* | D | 169—170 | 70 | 417 (100) |
| *(4b)* | Me | 160—161 | 70 | 430 (81) |
| *(4c)* | $CH_2Ph$ | noncryst. | 60 | 506 (35) |
| *(4d)* | *i*Pr | 173—175 | 70 | 444 (41) |
| *(5)* | | 150—152 | 57 | 522 (55) |
| *(6)* | | 179—181 | 65 | 504 (100) |
| *(10a)* | D | 265—267 | 90 | 553 (44) |
| *(10b)* | Me | 239—241 | 90 | 566 (11) |
| *(11)* | | 205—207 | 50 | 658 (100) |
| *(12)* | | 220 | 50 | 640 (100) |

*(8)* (0.4 g) is treated with the stoichiometric amount of $Ph_3CNa$ in THF and after 30 min, 1 mL of $D_2O$ is added. *(9)*[5b] (0.350 g, 90%, m.p. 276—277°C, MS 491 (13%)) is obtained after chromatography on $SiO_2$.

Received: April 27, 1981 [Z 870 IE]
German version: Angew. Chem. *93*, 898 (1981)

CAS Registry numbers:
*(2)*, 13689-25-3; *(3)*, 79044-36-3; *(4a)*, 79044-37-4; *(4b)*, 20442-47-1; *(4c)*, 79044-38-5; *(4d)*, 79044-39-6; *(5)*, 79044-40-9; *(6)*, 79044-41-0; *(8)*, 79101-61-4; *(9)*, 79101-62-5; *(10a)*, 79101-63-6; *(10b)*, 79101-64-7; *(10c)*, 79101-65-8; *(11)*, 79101-66-9; *(12)*, 79121-00-9

---

[1] *K. Dimroth*, Fortschr. Chem. Forsch. (Top. Curr. Chem.) *38*, 1 (1973).

[2] a) *K. Dimroth, St. Berger, H. Kaletsch*, Phosphorus Sulfur, in press; b) *T. Bundgaard, H. J. Jacobsen, K. Dimroth, H. H. Pohl*, Tetrahedron Lett. *1974*, 3179.

[3] *K. Dimroth, W. Heide*, Chem. Ber. *114*, 3004, 3019 (1981).

[4] *T. Debaerdemaeker*, Acta Crystallogr. *B 35*, 1686 (1979).

[5] a) *M. Lückoff, K. Dimroth*, Angew. Chem. *88*, 543 (1976); Angew. Chem. Int. Ed. Engl. *15*, 503 (1976); b) *K. Dimroth, M. Lückoff, H. Kaletsch*, Phosphorus Sulfur, in press.

[6] *W. M. McFarlane, S. O. Grim*, J. Organomet. Chem. *5*, 147 (1966).

[7] a) *J. Deberitz, H. Nöth*, Chem. Ber. *103*, 2541 (1970); b) Tricarbonyl(2,4,6-tri-*tert*-butyl-$\lambda^3$-phosphorin)chromium (m.p. 135—137°C) can readily be obtained (in 70% yield) as a crystalline compound from the reaction of 2,4,6-tri-*tert*-butyl-$\lambda^3$-phosphorin with $Cr(CH_3CN)_3(CO)_3$, and reacted with nucleophiles and electrophiles.

[8] *K. Dimroth, H. Kaletsch*, Pol. J. Chem. in press.

[9] *H. F. Semmelhack, H. T. Hall, R. Farina, M. Yoshifuji, G. Clark, T. Barger, K. Hirotsu, J. Clardy*, J. Am. Chem. Soc. *101*, 3535 (1979).

## Bis(trimethylgermyl)magnesium, the First Organogermylmagnesium Compound Isolated[**]

By *Lutz Rösch*[*]

*Dedicated to Professor Ferdinand Bohlmann on the occasion of his 60th birthday*

Organogermylmagnesium compounds have frequently been postulated as intermediates[1]. We now wish to report the successful isolation of bis(trimethylgermyl)magnesium·2 DME (=dimethoxyethane) *(1)* and hence establish the ability of organogermylmagnesium to exist.

*(1)* is synthesized in an analogous manner to the homologous silyl compound *(2)*[2] (see procedure). The well-formed colorless crystals of *(1)* decompose immediately on contact with the air, however, without the spontaneous ignition observed with *(2)*[2]. Apart from the signals from the coordinated DME, the $^1H$-NMR spectrum of *(1)* in benzene shows only one sharp signal for the trimethylgermyl protons (in the vicinity of the TMS-signals); the ratio DME:$Me_3Ge$ amounts to 1:1. Decomposition of *(1)* with water or $D_2O$ produces trimethylgermane or deuterio(trimethyl)germane, respectively. The results of the elemental analysis were corroborated by the mass spectrum. This shows a weak signal from the molecular ion with the expected isotopic splitting, as well as signals from the expected cleavage products. *(1)* melts at 90°C, accompanied by slight discoloration. A sample which is heated to 100°C for 10 min with dilute HCl yields, apart from trimethylgermane, a small amount of methane. This indicates that dimethylgermanediyl is produced during the decomposition and that the latter proceeds relatively slowly at this temperature.

$Mg[Ge(CH_3)_3]_2\cdot 2C_4H_{10}O_2$ *(1)*

$Mg[Si(CH_3)_3]_2\cdot C_4H_{10}O_2$ *(2)*

*Procedure*

All reactions were conducted under conditions of rigorous exclusion of air and moisture under argon. $(Me_3Ge)_2Hg$ (9 g) is dissolved in 70 mL of anhydrous DME and stirred with Mg (4 g) until the initially formed red color disappears (*ca.* 3 d). The dark solution is then filtered through a glass frit; the volatile fraction of the filtrate is removed using an oil vacuum pump. The solid residue is taken up in *ca.* 40 mL of anhydrous $Et_2O$. The solution is allowed to settle and separated from the undissolved material. Approximately 5 g of colorless *(1)* crystallizes out at −20°C, m.p. ≈90°C (decomp.).

Received: March 16, 1981 [Z 872 IE]
German version: Angew. Chem. *93*, 894 (1981)

CAS Registry numbers:
*(1)*, 79121-08-7; $(Me_3Ge)_2Hg$, 13915-91-8

---

[*] Priv.-Doz. Dr. L. Rösch
Institut für Anorganische und Analytische Chemie
der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

[1] Review: *M. Lesbre, P. Mazerolles, J. Satgé:* The Organic Compounds of Germanium, Wiley, London 1971, p. 656; more recently: *F. Carre, R. Corriu,* J. Organomet. Chem. *73,* C49 (1974); *E. Colomer, R. Corriu,* J. Chem. Soc. Chem. Commun. *1976,* 176.

[2] *L. Rösch,* Angew. Chem. *89,* 257 (1977); Angew. Chem. Int. Ed. Engl. *16,* 247 (1977).

## ENDOR Investigation of a Novel Organic Tetraradical in the Quintet State[**]

By *Burkhard Kirste, Wolfgang Harrer,* and *Harry Kurreck*[*]

*Dedicated to Professor Georg Manecke on the occasion of his 65th birthday*

Little is known about the dipolar coupling and scalar exchange interaction of the unpaired electrons and hyperfine interaction in organic tetraradicals. Reports have appeared in the literature only on ESR investigations of a tetrakisverdazyl[1a], of tetrakisnitroxides[1b], and on the detection of the quintet state of some *m*-dicarbenes and *m*-dinitrenes in the solid state[1c].

Following successful ESR and ENDOR (electron-nuclear double resonance) experiments on diradicals in the triplet state[2a] and on triradicals in the quartet state[2b], we wished to test whether these techniques could also be applied to tetraradicals in the quintet state. The following difficulties must, however, be considered:

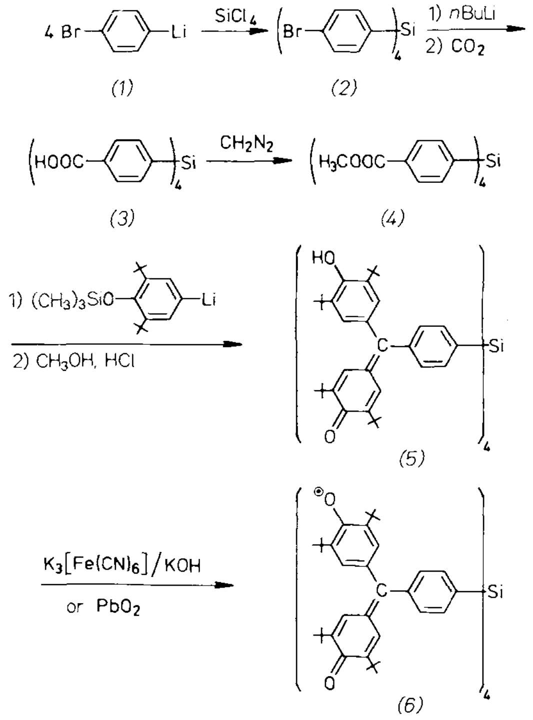
1. If the exchange interaction is large relative to the hyperfine interaction ($|J| \gg |a|$), the number of ESR hyperfine components from the nuclei within the "spin carrier" increase relative to those of the corresponding monoradical.

$$a^{S} = a^{d}/2S \tag{a}$$

Since the separation of the individual ESR lines is accordingly reduced ($a^d$ = coupling constant in the isolated spin carrier (doublet state), $S$ = electron spin quantum number), the total splitting is the same and the resolution of the ESR spectrum becomes poorer. In this connection the ENDOR technique appeared to be promising since it offers a greater resolution compared to ESR spectroscopy.

2. The dipolar interaction of the unpaired electrons—which is measured by the zero field splitting parameter *D*—produces additional relaxation processes, which cause a broadening of the ESR- and ENDOR-lines in liquid solution. As a consequence, the spectral resolution again deteriorates, and according to the theory of ENDOR spectroscopy higher microwave power levels are required[2a]. A tetraradical with *tetrahedral symmetry* should offer two decisive advantages: the exchange interaction is the same between all pairs of spin carriers, hence the formation of a thermally populated quintet state can be assumed and the zero field splitting is roughly zero[3].

The galvinol/galvinoxyl system is a suitable radical type, since the individual oxidation stages, and hence different spin states, can be selectively obtained[4]. The tetrakisgalvinol *(5)* was prepared as follows: reaction of the lithium compound *(1)* with $SiCl_4$, metalation of *(2)* and further reaction with dry-ice yielded the tetracarboxylic acid *(4)*, which was esterified using $CH_2N_2$. The tetraester *(4)* was reacted with (2,6-di-*tert*-butyl-4-lithiophenoxy)trimethylsilane; *(5)* is formed by acidic elimination of the protecting groups[5].



The left side of Figure 1 shows the ESR spectra of the different oxidation states of *(5)*[6]. While the ESR spectrum of the monoradical exhibits the typical quintet pattern of a galvinoxyl radical, the resolution deteriorates with increasing oxidation; the ESR spectrum of the tetraradical *(6)* is completely unresolved.

The ENDOR spectra (Fig. 1, right) can be unequivocally interpreted from the ENDOR resonance condition ($|J| \gg |a|$):

$$\nu_{\text{ENDOR}} = |\nu_n - M_S a^S| \tag{b}$$

($\nu_n$ = free nuclear frequency; $M_S$ = magnetic quantum number of the total electronic spin). It should be noted that the di- and triradical exist in equilibrium with other oxidation states and that, accordingly, lines from other spin states with lower intensity appear in the spectrum[7]. If only the galvinoxyl ring protons, which are viewed as equivalent, are considered, one ENDOR line pair ($M_S = \pm 1/2$) for the monoradical (doublet)[8], three lines ($M_S = \pm 1.0$) for the diradical (triplet), two line-pairs ($M_S = \pm 3/2, \pm 1/2$) for the triradical (quartet), and four equidistant lines ($M_S = \pm 2.0, \pm 1.0$) for the tetraradical (quintet) are expected. It follows from eqs. (a) and (b) that the position of the outermost line-pair is independent of the spin state.

The ENDOR spectrum of the tetraradical *(6)* establishes the presence of a quintet-state molecule. Furthermore, the sample can almost be quantitatively converted into the highest oxidation state. In addition, an electron-nuclear-nuclear triple resonance experiment (TRIPLE)[9] indicates that both line-pairs observed for the galvinoxyl ring-pro-

---

[*] Prof. Dr. H. Kurreck [+], Prof. Dr. W. Harrer, Dr. B. Kirste
Institut für Organische Chemie der Freien Universität
Takustr. 3, D-1000 Berlin 33 (Germany)

[+] Author to whom correspondence should be addressed

[**] This work was supported by the Fonds der Chemischen Industrie and by the Deutsche Forschungsgemeinschaft.

tons result from transitions belonging to the same hyperfine level diagram ($M_S = \pm 2$ and $\pm 1$ in the S = 2 state) (cf. in this context[2b]).

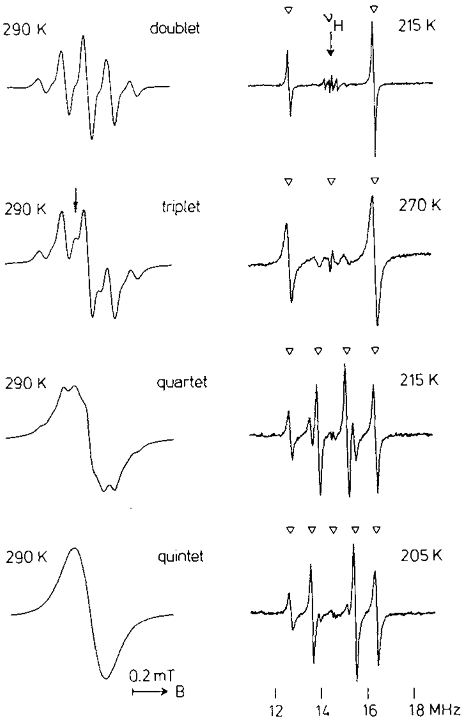


Fig. 1. ESR- (left) and ENDOR-spectra (right) of the different oxidation states of *(5)* in toluene. From top to bottom: mono-, di-, tri- and tetraradical. The symbols (▽) indicate the resonance frequencies calculated for the galvinoxyl ring protons (see also text).

The ENDOR-lines at the free proton frequency ($M_S = 0$), which were predicted for the di- and tetraradical, do not appear. It must, however, be considered that the ESR transitions $|-1\rangle \leftrightarrow |0\rangle$ and $|-0\rangle \leftrightarrow |1\rangle$ are degenerate in liquid solution (averaging of the dipolar coupling by Brownian motion); in consequence, the thermal nuclear spin polarization in the $M_S = 0$ state is not changed by pumping these transitions[10]. If the zero field splitting parameters are different from zero, the ENDOR resonances belonging to the $M_S = 0$ term should show up provided the experiments are performed in a glassy matrix, *e.g.* in toluene at 150 K[2b]. In fact, a $D$ parameter of *ca.* 25 MHz can be estimated from the ESR spectrum of the diradical; consequently, the line at the free proton frequency also appears in the matrix ENDOR spectrum. As can be expected from symmetry considerations the ESR spectrum indicates that its $D$ parameter is too small to be detected. It cannot, however, be exactly zero, since we were also able to detect this ENDOR signal at the free proton frequency for the tetraradical in glassy toluene (or perdeuterotoluene!).

### *Procedure*[11]

*(2):* A solution of 1,4-dibromobenzene (50 g, 0.212 mol) in 200 mL ether is treated within 20 min with 0.212 mol *n*-butyllithium (1.66 M solution in *n*-hexane). After 30 min at 20 °C, a solution of $SiCl_4$ (9 g, 53 mmol) in 15 mL *n*-hexane is slowly (!) added. Addition of 10 mL 50% acetic acid, concentration to dryness, digestion with 50 mL methanol, and filtration yielded 29.4 g crude product, which is purified by dissolving three times in $CH_2Cl_2$ and precipitating with $CH_3OH$; 22.5 g (65%) *(2)*, m.p. 236—239 °C, are produced.

*(4):* A suspension of *(2)* (4 g, 6.13 mmol) in 30 mL of a solution of *n*-butyllithium in *n*-hexane (1.66 M; 50 mmol) is tetrametalated by addition of *N,N,N',N'*-tetramethylethylenediamine (3.56 g, 30.6 mmol) and is finally carboxylated with dry-ice in tetrahydrofuran (THF). After removal of solvent the residue is taken up in water, filtered, acidified and filtered off. Two recrystallizations from methanol/ethyl acetate yield *(3)* (*ca.* 20% yield). *(3)* is esterified with diazomethane, yield 0.56 g (80%) *(4)* after recrystallization from methanol, m.p. 138 °C (lit.[5] 142 °C).

*(5):* A solution of *(4)* (0.5 g, 0.85 mmol) in THF is reacted with (2,6-di-*tert*-butyl-4-lithiophenoxy)trimethylsilane prepared from (2,6-di-*tert*-butyl-4-bromophenoxy)trimethylsilane (5 g, 14 mmol). Crude yield after removal of the trimethylsilyl protecting groups (methanol; 1% HCl) 0.62 g (35%) *(5)*, purification by HPLC and subsequent thin layer chromatography, m.p. 327 °C.

Received: March 26, 1981 [Z 877 IE]
German version: Angew. Chem. *93*, 912 (1981)

CAS Registry numbers:
*(2)*, 18733-98-7; *(3)*, 10256-84-5; *(4)*, 31825-72-6; *(5)*, 79121-01-0; *(6)*, 79121-02-1; 1,4-dibromobenzene, 106-37-6; (2,6 di-*tert*-butyl-4-lithiophenyloxy)trimethylsilane, 79101-69-2

---

[1] a) *F. A. Neugebauer, H. Fischer, R. Bernhardt,* Chem. Ber. *109*, 2389 (1976); b) *E. G. Rozantsev, V. A. Golubev,* Izv. Akad. Nauk SSSR, Ser. Khim. *1965*, 718; c) *E. Wasserman, R. W. Murray, W. A. Yager, A. M. Trozzolo, G. Smolinski,* J. Am. Chem. Soc. *89*, 5076 (1967); *K. Itoh,* Chem. Phys. Lett. *1*, 235 (1967).

[2] a) *B. Kirste, H. Kurreck, W. Lubitz, K. Schubert,* J. Am. Chem. Soc. *100*, 2292 (1978), and literature cited therein; b) *B. Kirste, H. van Willigen, H. Kurreck, K. Möbius, M. Plato, R. Biehl, ibid. 100*, 7505 (1978).

[3] We were unable to observe an ENDOR effect with tetraradicals from the galvinoxyl system with *non-tetrahedral* symmetry, unpublished results.

[4] The di- and triradical states can be prepared by mixing definite amounts of oligogalvinol solution and the solution of the tetraradical.

[5] *(4)* has already been prepared by other routes: *H. Hopff, J. M. Deuber, P. Gallegra, A. Said,* Helv. Chim. Acta *54*, 117 (1971). A general procedure for galvinol synthesis can be found in *W. Harrer, H. Kurreck, J. Reusch, W. Gierke,* Tetrahedron *31*, 625 (1975).

[6] Description of the instrumentation: *H. J. Fey, H. Kurreck, W. Lubitz,* Tetrahedron *33*, 905 (1979).

[7] By suitable positioning of the ESR (arrow in Fig. 1) the appearance of the monoradical-lines in the diradical spectrum was suppressed.

[8] The coupling constants of the monoradical (+3.75, +3.61, +0.54, −0.25, and +0.13 MHz) are comparable with the corresponding values of phenylgalvinoxyl [2a]. For determination of sign (TRIPLE) cf. [9].

[9] *K. Möbius, R. Biehl* in *M. M. Dorio, I. H. Freed:* Multiple Electron Resonance Spectroscopy, Plenum Press, New York 1979, p. 475.

[10] *H. van Willigen, M. Plato, K. Möbius, K.-P. Dinse, H. Kurreck, J. Reusch,* Mol. Phys. *30*, 1359 (1975).

[11] The reaction with organometallic compounds was performed under nitrogen in anhydrous solvents. The spectroscopic data for compound *(5)* are consistent with the suggested structure.

## Stereoisomerization of Aryl-Substituted Cyclopropanes *via* Trimethylene Radical Anions[**]

By *Gernot Boche* and *Helmut Wintermayr*[*]

The *thermal* stereoisomerization of cyclopropanes, which proceeds *via* trimethylene intermediates, is one of the best documented reactions[1a] and, in addition, the *pho-*

---

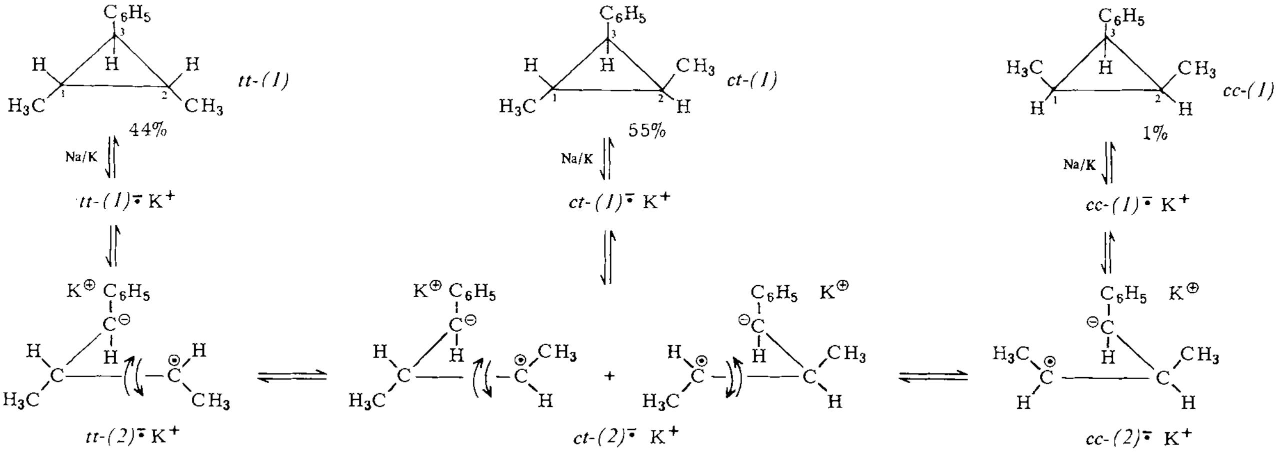
[*] Prof. Dr. G. Boche [+], Dipl.-Chem. H. Wintermayr
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[+] Author to whom correspondence should be addressed. New address:
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

*tochemical* isomerization has also been thoroughly investigated[1b]. We report here on the *electron transfer* (homogeneous: potassium naphthalide ($K^+N^{\cdot-}$); heterogeneous: sodium-potassium alloy (Na/K)) catalyzed reaction. Cyclopropane- and trimethylene-radical anions occur as intermediates.

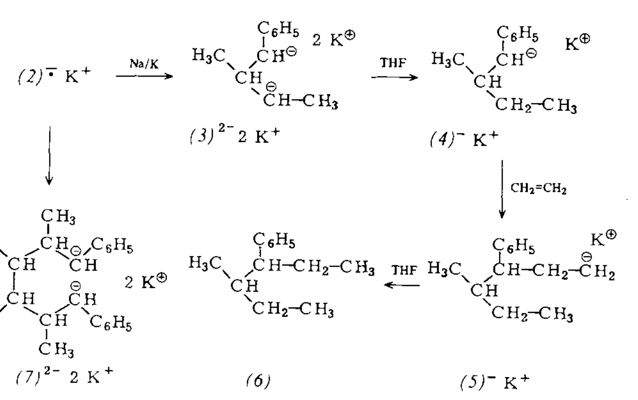
When a mixture of *trans,trans*-1,2-dimethyl-3-phenylcyclopropane *tt-(1)*[2] (146 mg, 1.00 mmol) and Na/K (1 : 1) alloy (621 mg, 20.0 mmol) in 10 mL tetrahydrofuran (THF) is stirred for 16 min at 20 °C, apart from *tt-(1)*, 1,2-*cis,trans*-, and 1,2-*cis,cis*-dimethyl-3-phenylcyclopropane[2], *ct-(1)* and *cc-(1)*, in the ratio 44 : 55 : < 1 are formed in 68% yield (Scheme 1)[3]. Mixtures of *cc-(1)* : *tt-(1)* = 2.47 or 1.71 under similar conditions, produced mixtures having the same ratio, which did not change under continued stirring.



Scheme 1.

This stereoisomerization is considerably different from the *base catalyzed* one conducted by *Closs*[2]: after 17 (!) h at 100 °C (!) a 50 : 1 equilibrium mixture of *tt-(1)* and *cc-(1)* was formed from *cc-(1)* and potassium *tert*-butoxide in dimethyl sulfoxide. Hereby, the intermediate is the benzylic cyclopropyl anion derived from *tt-(1)* and *cc-(1)*.

The formation of *ct-(1)* in the isomerization with Na/K alloy requires bond scission between $C^1C^3$ or $C^2C^3$[4]. This is accomplished by electron transfer from Na/K to form the phenylcyclopropane radical anions $(1)^{\cdot-}K^+$ followed by ring-opening to the trimethylene radical anions $(2)^{\cdot-}K^+$, bond rotation, ring-closure, and retransfer of the electron (Scheme 1), which is corroborated as follows: at long reaction times the yield of *(1)* decreases in favor of three new products. Hence, after 60 h, 16% of $(4)^-K^+$, 47% of *(6)* and 37% of $(7)^{2\cdot-}2K^+$[5] are obtained (Scheme 2).

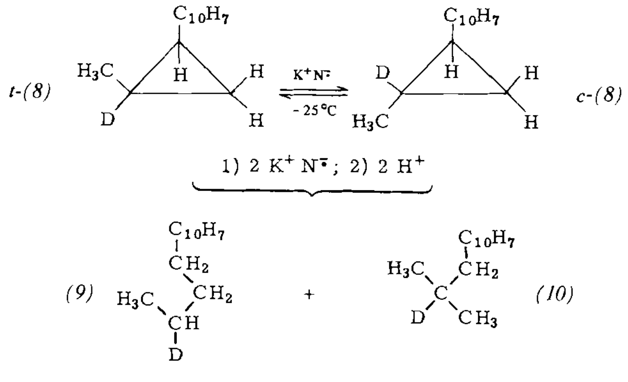


Scheme 2.

$(4)^-K^+$ and *(6)* are formed from the trimethylene radical anions $(2)^{\cdot-}K^+$ *by interaction with Na/K alloy, whereby the dipotassium compound* $(3)^{2-}2K^+$ forms first. The latter compound is spontaneously protonated by THF to the benzylic monoanion $(4)^-K^+$[6,7]. The ethylene[7] thus formed reacts with $(4)^-K^+$, particularly at long reaction times, to give the adduct $(5)^-K^+$, which—by repeated reaction with THF—yields *(6)*[6,8].

$(7)^{2-}2K^+$ is one of three diastereomeric pairs which can be formed by dimerization of the trimethylene radical anions $(2)^{\cdot-}K^+$[9]. Actually, after protonation with methanol—as shown by a gas chromatographic/mass spectroscopic analysis—three "dimers" of mass 294.240 (calc. 294.2348) can be detected; this indicates 1,1-, 1,3-, and 3,3-dimerization processes[10].

If the cyclopropane carries a better electrophore[11a], such as in the cyclopropylnaphthalene *t-(8)*, the stereoisomerization occurs even with the weaker electron transfer agent $K^+N^{\cdot-}$ to give *c-(8)* and *t-(8)* in an 86 : 14 ratio (at −25 °C in 9 h) (Scheme 3). The bimolecular trapping of the intermediate trimethylene radical anion by $K^+N^{\cdot-}$ at 20 °C is also considerably slower than its ring closure; this results from the fact that at this temperature both *c-(8)* and *t-(8)* produce the isomeric deuterium compounds *(9)* and *(10)*[12] in the same ratio (69 : 31).



The reductive cleavage of aryl and acyl substituted cyclopropanes by electron transfer is, above all, well known in protic solvents[11] and *Walborsky*[11h–j], in particular, has pointed out that trimethylene radical anions should occur as intermediates. The reversible formation and dimerization of these species outlined here, establish their existence. Simultaneously, it demonstrates that cyclopropanes of this type can be isomerized under mild conditions[13]; this also occurs with 1-methyl-2-phenyl-, 1,2-dimethyl-1-phenyl-, and 2-methyl-1,1-diphenylcyclopropane, as well as with 2-methyl-spiro[cyclopropane-1,9′-fluorene].

Received: March 16, 1981 [Z 878 IE]
German version: Angew. Chem. *93*, 923 (1981)

CAS Registry numbers:
*tt-(1)*, 25181-26-4; *ct-(1)*, 7653-95-4; *cc-(1)*, 7693-96-5; *tt-(1)*$^{\cdot -}$K$^+$, 79171-33-8; *ct-(1)*$^{\cdot -}$K$^+$, 79171-34-9; *cc-(1)*$^{\cdot -}$K$^+$, 79171-35-0; *(4)*$^-$K$^+$, 79101-71-6; *(6)*, 79101-72-7; *(7)*$^{2-}$2K$^+$, 79121-03-2

---

[1] a) Summary: *J. A. Berson, L. D. Pedersen, B. K. Carpenter*, J. Am. Chem. Soc. *98*, 122 (1976); b) Summary: *S. S. Hixson*, Org. Photochem. *4*, 191 (1979); see also: *H. D. Roth, M. L. M. Schilling*, J. Am. Chem. Soc. *102*, 7958 (1980).

[2] *G. L. Closs, R. A. Moss*, J. Am. Chem. Soc. *86*, 4042 (1964).

[3] Gas chromatographic analysis (SE 30, 1.5 m, 145 °C); error ± 1%.

[4] Deprotonation at $C^1$ and/or at $C^2$ by Na/K alloy, which is faster than at $C^3$, must be excluded. Likewise, bond breaking between $C^1$ and $C^2$ is energetically much more unfavorable, since the trimethylene radical anion formed is not stabilized by the phenyl substituent.

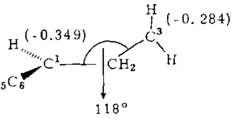
[5] The rate at which the equilibrium *tt-(1)*$\rightleftharpoons$*ct-(1)*$\rightleftharpoons$*cc-(1)* is established and the rate of formation of the secondary products *(4)*$^-$K$^+$, *(6)*, and *(7)*$^{2-}$2K$^+$ is also a function of the stirring rate in these heterogeneous reactions.

[6] 2-Methyl-1-phenylbutane (from the protonation of *(4)*$^-$K$^+$) is identical with the sample described by *D. Dolphin, Z. Muljiani, J. Cheng*, and *R. B. Meyer* (J. Chem. Phys. *58*, 413 (1973)). 3-Methyl-4-phenylhexane *(6)* was synthesized independently; the structure was proven by CH analysis, as well as by mass- and $^1$H-NMR-spectroscopy.

[7] See *e.g. E. Buncel*: Carbanions: Mechanistic and Isotopic Aspects, Elsevier, New York 1975. The spontaneous protonation of tertiary alkylpotassium compounds in THF also excludes the isomerization of the dianion intermediate.

[8] A similar reaction of a benzyl anion with ethylene from THF has recently been reported: *M. Schlosser, P. Schneider*, Helv. Chim. Acta *63*, 2404 (1980). *G. Decher* and *W. E. Russey*, Juniata College, Huntington, Pennsylvania 16652, USA are thanked for a compilation of literature on closely related reactions.

[9] The description of the trimethylene radical anion *(2)*$^{\cdot -}$K$^+$ shown in Scheme 1 only uses one of the two mesomeric structures. A MNDO study (Dr. *H. U. Wagner*, Universität München, unpublished results) indicates that the 1-phenyltrimethylene radical anion has a 0.90-arrangement and carries a considerable negative charge not only on $C^1$ but also on $C^3$:



[10] Prof. *G. Spiteller*, Universität Bayreuth, is thanked for recording and interpreting the spectra.

[11] a) *L. L. Miller, L. J. Jacoby*, J. Am. Chem. Soc. *91*, 1130 (1969); b) *S. W. Staley, J. J. Rocchio, ibid. 91*, 1565 (1969); c) *O. M. Nefedov, N. N. Novitskaya, A. D. Petrov*, Dokl. Akad. Nauk SSSR *152*, 629 (1963); d) *T. Norin*, Acta Chem. Scand. *19*, 1289 (1965); e) *M. G. Dauben, E. I. Deviny*, J. Org. Chem. *31*, 3794 (1966); f) *H. O. House, C. J. Blankley, ibid. 33*, 47 (1968); g) *H. E. Zimmerman, K. G. Hancock, G. C. Licke*, J. Am. Chem. Soc. *90*, 4892 (1968); h) *H. M. Walborsky, J. B. Pierce*, J. Org. Chem. *33*, 4102 (1968); i) *H. M. Walborsky, M. S. Aronoff, M. F. Schulman, ibid. 36*, 1036 (1971); j) Prof. *H. M. Walborsky* has made available to us on June 22, 1981 the paper in print *H. M. Walborsky, E. J. Powers*, Cyclopropanes. Part XLI. Electron Transfer From Lithium Metal Surfaces to (±)- and (−)-(*S*)-1-fluoro-1-methyl-2,2-diphenylcyclopropane, Isr. J. Chem. The chemistry described herein goes back to *E. J. Powers*, Dissertation, Florida State University 1969. We are very grateful to Professor *Walborsky* for informing us about this work.

[12] This is in contrast to an observation made by *Staley* [11b], who in the reduction of *cis*-1-methyl- and *trans*-1-methyl-2-phenylcyclopropane with lithium, in ammonia, obtained the corresponding cleavage products in markedly different ratios.

[13] Phenyl cyclopropanes isomerize *thermally* at *ca.* 300 °C [1a].

# Nickel-Induced Coupling and Cleavage of CC-Bonds

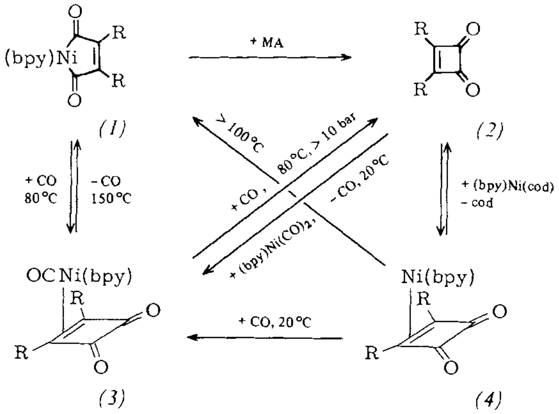
By *Heinz Hoberg* and *Antonio Herrera*[*]

Nickelacyclopentenediones *(1)*, which yield cyclobutenedione derivatives with maleic anhydride (MA) at 20 °C *via* a CC, coupling reaction, are formed from 2,2′-bipyridine (bpy)-stabilized nickel(0) compounds, carbon monoxide, and disubstituted alkynes (R = alkyl, aryl)[1]. In order to gain a detailed insight into the CC-coupling step *(1)*→*(2)* we used ligands other than MA for the reductive elimination ($Ni^{2+} \rightarrow Ni^0$).

Using CO as the reducing agent, an intermediate species could be isolated and hence the CC-coupling and -cleavage reactions rendered reversible.

A solution of *(1)* ($R = C_6H_5$) in toluene at 80 °C first takes up an equivalent of CO, whereby the carbonyl C atoms couple. Compound *(3)* is formed, in which the complex-bound *(2)* is present.

*(2)* is only liberated under a higher CO partial pressure (10 bar) at 80 °C, and simultaneously forms (bpy)Ni(CO)$_2$ and, to a lesser extent, Ni(CO)$_4$.



*(3)* could also be obtained by reaction of *(2)* with (bpy)Ni(CO)$_2$ by CO cleavage at 20 °C, and from *(4)* by reaction with CO. *(4)* is formed from the reaction of *(2)* with (bpy)Ni(cod), (cod = 1,5-cyclooctadiene) (Scheme 1).

*(3)* crystallizes in red leaflets and is diamagnetic. The mass spectrum only contains the fragment ions *m/z* 156 (bpy), 178 (tolan) and 234 *(2)*. The IR spectrum (KBr) shows characteristic bands at 2000 cm$^{-1}$ (Ni—CO) and in the $>$C=O region at 1680 and 1660 cm$^{-1}$. Hydrolysis (2 N $H_2SO_4$, 20 °C) yields *(2)*.

The CC-coupling *(1)*→*(3)* is reversible: upon heating to *ca.* 150 °C, the complex-bound CO cleaves off. Nickelacyclopentene is re-formed in an oxidative addition reaction ($Ni^0 \rightarrow Ni^{2+}$ transition). *(1)* is also formed from the CO-free *(4)* in 3 h at 100 °C.

The X-ray structure analysis[2] shows that the (CO)Ni(bpy) fragment in *(3)* is bonded to the CC double bond of the system *(2)* in such a way that the bpy lies above the carbonyl groups, whereas the CO ligand lies on the same side as the phenyl moieties (Fig. 1).

## *Procedure*

*(3)* from *(1)*: *(1)* (4.04 g, 8.99 mmol) ($R = C_6H_5$[1]) is suspended in 50 mL of toluene and takes up 200 mL (9.0

---

[*] Prof. Dr. H. Hoberg, Dr. A. Herrera
Max-Planck-Institut für Kohlenforschung
Postfach 01 13 25, D-4330 Mülheim an der Ruhr 1 (Germany)

mmol) of CO at 80 °C and 1 bar within 6 h, thereby forming a red solution. The red crystals, which precipitate after 48 h at room temperature, are filtered off and dried. Yield: 1.68 g (39%) *(3)*.

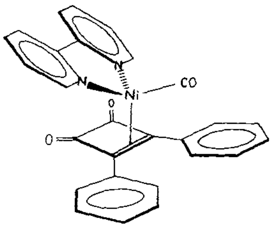


Fig. 1. Structure of *(3)* in the crystal.

*(3)* from *(2)* and (bpy)Ni(CO)$_2$: A solution of *(2)*[1] (1.1 g, 4.7 mmol) in 20 mL tetrahydrofuran (THF) is dropped into a solution of (bpy)Ni(CO)$_2$[3] (1.26 g, 4.7 mmol) in 30 mL of THF at room temperature. The red-violet solution gradually turns red-brown, whereby a precipitate is thrown down with simultaneous evolution of gas. 95 mL (4.2 mmol) of CO is collected within 6 h, and the precipitate is filtered off and dried. Yield: 1.78 g (80%) *(3)*.

*(1)* from *(3)*: *(3)* (1.5 g, 3.2 mmol) is suspended in 50 mL of decalin and heated to 150 °C, whereby evolution of gas is observed. 65 mL (2.9 mmol) of CO is collected within *ca.* 6 h. The precipitate is filtered-off and dried. Yield: 1.34 g (95%) *(1)*.

*(4)* from *(2)*: *(2)*[1] (1.3 g, 5.5 mmol) in 20 mL of THF is dropped into a solution of (bpy)Ni(cod)[4] (1.8 g, 5.5 mmol) in 50 mL of THF. After 24 h the crystals formed are filtered off and dried. Yield: 2.24 g (91%) *(4)*.

*(3)* from *(4)*: A suspension of *(4)* (1.3 g, 2.9 mmol) in 50 mL of toluene takes up 25 mL of CO at 1 bar within 24 h, whereby a solution is formed. The crystals formed after *ca.* 6 d at −20 °C are filtered off and dried. Yield: 0.48 g (35%) *(3)*.

Received: March 17, 1981 [Z 879 IE]
German version: Angew. Chem. *93*, 924 (1981)

CAS Registry numbers:
*(1)*, 75507-29-8; *(2)*, 24234-76-2; *(3)*, 79121-09-8; *(4)*, 79121-10-1; (bpy)Ni(CO)$_2$, 14917-14-7; (bpy)Ni(cod), 55425-72-4

---

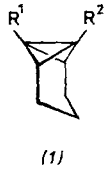
[1] *H. Hoberg, A. Herrera*, Angew. Chem. *92*, 951 (1980); Angew. Chem. Int. Ed. Engl. *19*, 927 (1980).
[2] *C. Krüger, Y.-H. Tsay*, unpublished results.
[3] *E. Zahn*, Dissertation, Technische Hochschule München 1959.
[4] *E. Dinjus, J. Gorski, H. Walther*, Z. Anorg. Chemie *422*, 75 (1976).

---

# 1,2,3-Cycloheptatriene by Isomerization of Tricyclo[4.1.0.0$^{2,7}$]-hept-1(7)-ene[**]

By *Hans-Georg Zoch, Günter Szeimies, Roland Römer,* and *Robert Schmitt*[*]

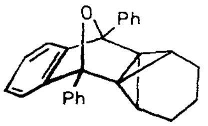
It has been shown by competition experiments that the halides *(1a–c)* react with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −20 °C to give free tricyclo[4.1.0.0$^{2,7}$]hept-1(7)-ene *(2)*[1]. We have now found that *(2)* is also generated by the elimination method developed by *Chan* and *Massuda*[2] on reaction of *(1e)*[3] and potassium fluoride in dimethyl sulfoxide (DMSO) at 55 °C. In the presence of four equivalents of diphenylisobenzofuran, *(2)* could be trapped up to 56% as the already well-known Diels-Alder adduct *(3)*[4]. Formation of the diene *(4)* (12%)[5] in this reaction was unexpected. Reaction of *(1e)*, KF and four equivalents each of anthracene or 9-methoxyanthracene (MOA) in DMSO at 55 °C proceeded analogously and yielded a mixture of *(5a)*[6] (14%) and *(6a)* (41%) or of *(5b)*[1] (24%) and *(6b)* (48%), respectively.



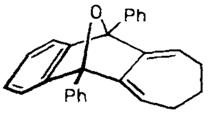
| R$^1$ | Cl | Br | I | Si(CH$_3$)$_3$ | Si(CH$_3$)$_3$ | OC(CH$_3$)$_3$ |
|---|---|---|---|---|---|---|
| R$^2$ | H | H | H | H | Br | H |
| | *(a)* | *(b)* | *(c)* | *(d)* | *(e)* | *(f)* |

*(1)*

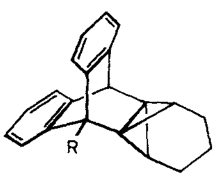
*(2)*



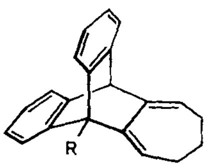
*(3)*



*(4)*



*(5)*



*(6)*

*(a)*, R = H
*(b)*, R = OCH$_3$

*(7)*

Since the dienes *(4)* and *(6)* are not products of the thermal isomerization[4,6] of the propellanes *(3)* and *(5)*, and since the latter are not converted into *(4)* and *(6)* under the reaction conditions used[7] these products must have been formed during the reaction itself. The structure of these dienes would suggest that their precursor is the 1,2,3-cycloheptatriene *(7)*, which is generated according to Scheme 1 by thermal rearrangement of *(2)* and is trapped as the Diels-Alder adduct.

$$\begin{tikzcd}
(1e) \arrow[r, "KF", "DMSO"'] & (2) \arrow[r, "MOA"] \arrow[d] & (5b) \\
& (7) \arrow[r, "MOA"] & (6b)
\end{tikzcd}$$

Scheme 1.

On lowering the concentration of MOA, the yield of *(5b)* should decrease, that of *(6b)* increase. This is in fact the case: The reaction of *(1e)*, KF, and three, two or one molar equivalent(s) of MOA in DMSO at 55 °C afforded *(5b)*/*(6b)*-mixtures of the composition 15% and 54%, 12% and 60%, and 8% and 66%, respectively.

The extent of the rearrangement *(2)*→*(7)* not only depends on the nature and concentration of the trapping agent but also strongly on the temperature. Thus reaction of *(1e)* and KF with tetraphenylcyclopentadienone or 2,5-dimethylfuran in DMSO at 100 °C afforded only the adducts *(8)* and *(9)* (30% and 38%, respectively). Our earlier works, in which *(2)* was formed by elimination of HCl

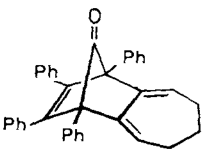
---

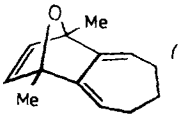
[*] Prof. Dr. G. Szeimies, Dipl.-Chem. H.-G. Zoch, Dipl.-Chem. R. Römer, cand. chem. R. Schmitt
Institut für Organische Chemie der Universität
Karlstr. 23, D-8000 München 2 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

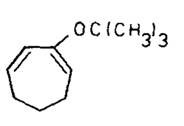
from *(1a)* with LDA at −20 °C in THF, furnished no evidence for the rearrangement *(2)*→*(7)*. However, this isomerization can also be detected when *(1a)* is used as starting material: Thus, on reaction of *(1a)* with 6 equivalents of potassium *tert*-butoxide in THF at 35 °C, the enol ether *(10)* is obtained in 44% yield. Its formation can be explained in terms of the rearrangement *(2)*→*(7)* and subsequent addition of *tert*-butoxide to the reactive double bond C2—C3 of *(7)*. On addition of anthracene to the system *(1a)*/KO-*t*Bu/THF and elevation of the temperature to 65 °C, *(6a)* is formed as well as *(5a)* and *(10)*[8].

*(8)*

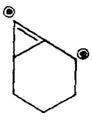




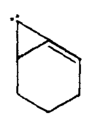
*(9)*



*(10)*



*(11)*



*(12)*

The rearrangement *(2)*→*(7)*, in which two bonds on opposite sides of the bicyclo[1.1.0]but-1(3)-ene moiety in *(2)* are broken, is forbidden as a synchronous reaction according to the Woodward-Hoffmann rules[9]. A stepwise isomerization of *(2)* to *(7)* with the diradical *(11)* or the carbene *(12)* as an intermediate is therefore not ruled out.

Table 1. NMR data (δ values, in CDCl$_3$) of the adducts *(4)*, *(6)*, *(8)*, *(9)*, and *(10)*.

| | |
|---|---|
| *(4)* | $^{1}$H-NMR: 1.52—1.90 (m, 2H), 2.02—2.41 (m, 4H), 5.82 (t, $J$=4.5 Hz, 2H), 6.98—8.03 (m, 14H). $^{13}$C-NMR: 24.4 (t), 30.7 (t), 89.6 (s), 119.6 (d), 124.3 (d), 126.6 (d), 127.0 (d), 127.8 (d), 128.3 (d), 136.0 (s), 140.1 (s), 147.0 (s) |
| *(6a)* | $^{1}$H-NMR: 1.49—1.90 (m, 2H), 2.00—2.44 (m, 4H), 4.67 (s, 2H), 5.96 (t, $J$=4.5 Hz, 2H), 7.00—7.40 (m, 8H). $^{13}$C-NMR: 24.0 (t), 31.0 (t), 57.6 (d), 122.9 (d), 125.8 (d), 126.5 (d), 136.4 (s), 142.9 (s) |
| *(6b)* | $^{1}$H-NMR: 1.37—1.83 (m, 2H), 1.93—2.42 (m, 4H), 4.03 (s, 3H), 4.51 (s, 1H), 5.75 (t, $J$=4.5 Hz, 1H), 6.15 (t, $J$=4.5 Hz, 1H), 6.87—7.52 (m, 8H). $^{13}$C-NMR: 24.3 (t), 30.3 (t), 31.0 (t), 56.7 (q), 56.8 (d), 86.8 (s), 121.0 (d), 122.6 (d), 124.6 (d), 125.4 (d), 125.8 (d), 126.0 (d), 136.0 (s), 136.2 (s), 141.6 (s) |
| *(8)* | $^{1}$H-NMR: 1.72—2.16 (m, 2H), 2.23—2.67 (m, 4H), 5.97 (t, $J$=4.5 Hz, 2H), 6.80—7.41 (m, 20H). $^{13}$C-NMR: 24.6 (t), 31.3 (t), 67.8 (s), 126.7 (d), 126.8 (d), 127.2 (d), 127.5 (d), 127.7 (d), 129.7 (d), 130.6 (d), 132.8 (s), 135.4 (s), 138.5 (s), 143.8 (s), 201.1 (s) |
| *(9)* | $^{1}$H-NMR: 1.55 (s, 6H), 1.67—1.97 (m, 2H), 2.12—2.50 (m, 4H), 5.63 (t, $J$=4.5 Hz, 2H), 6.09 (s, 2H) |
| *(10)* | $^{1}$H-NMR: 1.28 (s, 9H), 1.41—2.07 (m, 2H), 2.07—2.53 (m, 4H), 5.13—5.75 (m, 3H). $^{13}$C-NMR: 24.5 (t), 29.1 (q), 31.3 (t), 32.4 (t), 77.6 (s), 109.1 (d), 123.0 (d), 129.0 (d), 158.7 (s) |

Received: February 2, 1981 [Z 860 IE]
German version: Angew. Chem. *93*, 894 (1981)

CAS Registry numbers:
*(1a)*, 63846-84-4; *(1e)*, 78986-48-8; *(2)*, 78365-77-2; *(3)*, 71794-78-0; *(4)*, 18209-01-3; *(5a)*, 67629-46-3; *(5b)*, 78379-94-9; *(6a)*, 78986-49-9; *(6b)*, 79005-30-4; *(7)*, 79005-31-5; *(8)*, 78986-50-2; *(9)*, 78986-51-3; *(10)*, 78986-52-4; diphenylisobenzofuran, 5471-63-6; anthracene, 120-12-7; 9-methoxyanthracene, 2395-96-2; tetraphenylcyclopentadienone, 479-33-4; 2,5-dimethylfuran, 625-86-5

---

[1] *U. Szeimies-Seebach, A. Schöffer, R. Römer, G. Szeimies*, Chem. Ber. *114*, 1767 (1981).

[2] *T. H. Chan, D. Massuda*, J. Am. Chem. Soc. *99*, 936 (1977).

[3] *(1e)* was synthesized from *(1d)* (*R. T. Taylor, L. A. Paquette*, J. Org. Chem. *43*, 242 (1978)) *via* metalation at position 7 by *n*-butyllithium and reaction of the organometallic intermediate with *p*-toluenesulfonyl bromide (*G. Szeimies, F. Philipp, O. Baumgärtel, J. Harnisch*, Tetrahedron Lett. *1977*, 2135).

[4] *U. Szeimies-Seebach, G. Szeimies, M. Van Meerssche, G. Germain, J.-P. Declercq*, Nouv. J. Chim. *3*, 357 (1979).

[5] *G. Wittig, J. Meske-Schüller*, Justus Liebigs Ann. Chem. *711*, 76 (1968).

[6] *U. Szeimies-Seebach, G. Szeimies*, J. Am. Chem. Soc. *100*, 3966 (1978).

[7] If the adduct *(5b)* is included in the reaction of *(1e)*, KF and anthracene, then no *(6b)* can be detected among the end products *(5a)*, *(6a)* and *(5b)*. Reaction of *(1e)*, KF and MOA in presence of *(5a)* leads to an analogous result.

[8] *(10)* cannot be formed by addition of KO-*t*Bu to *(2)* and subsequent isomerization of *(1f)* to *(10)*: On increasing the anthracene concentration in the system *(1a)*/KO-*t*Bu/anthracene/THF (35 °C), the yield of *(5a)* increases, whereas that of *(10)* decreases. On the other hand, there is no change in the yield of *(5a)* or of *(10)* on variation of the KO-*t*Bu concentration. Hence the two trapping agents do not compete for the same intermediate.

[9] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 2045 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).

# Aldehydes by Formylation of Grignard or Organolithium Reagents with *N*-Formylpiperidine[**]

By *George A. Olah* and *Massoud Arvanaghi*[*]

After having developed methods for electrophilic formylation with formyl fluoride and formic anhydride[1], we turned our attention to nucleophilic formylation *via* Grignard reagents or organolithium reagents, a type of reaction which has represented a long standing challenge[2]. Formyl fluoride reacts with these reagents to give formylated products, but the reaction is not satisfactory and necessitates the use of difficultly available reagents.

In 1976, *Rathke et al.* reported the reaction of (dichloromethyl)diisopropoxyborane with organolithium or organomagnesium reagents[3]; subsequent oxidation with $H_2O_2$ yielded aldehydes. However, the reaction involves four steps, must be carried out in boiling tetrahydrofuran, and only gives low yields of aldehydes.

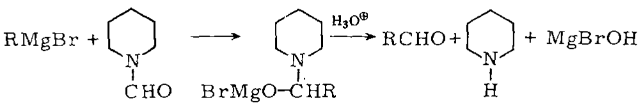
More recently, *Comins* and *Meyers* reported the use of 2-(*N*-methyl-*N*-formyl)aminopyridine[4] as a formylating agent in similar reactions. The presence of the additional ligand (pyridyl nitrogen) and the ready formation of a six-membered chelate ring was considered to prohibit the release of the aldehyde under the reaction conditions, thus protecting it from further reaction with the organometallic reagent.

We report here on a highly efficient and simple method for the formylation of Grignard or organolithium reagents using readily available and inexpensive *N*-formylpiperidine. In ether or hydrocarbon solvents at room temperature *N*-formylpiperidine reacts with aryl-, alkyl-, vinyl- and ethynyllithium or Grignard compounds and results in formation, upon acidic work-up, of the corresponding pure aldehydes in excellent yields (Table 1). None of the earlier methods show this general utility.

---

[*] Prof. Dr. G. A. Olah, Mr. M. Arvanaghi
Hydrocarbon Research Institute and Department of Chemistry
University of Southern California
University Park, Los Angeles, CA 90007 (USA)

[**] Synthetic Methods and Reactions, Part 102. This work was supported by the National Institute of Health and the National Science Foundation, and by the Reilly Tar & Chemical Corporation with gifts of *N*-formylpiperidine. *G. A. O.* thanks the Alexander von Humboldt Foundation for a Senior U. S. Scientist Award and Prof. *P. v. R. Schleyer* for his hospitality.—Part 101: *G. A. Olah, S. C. Narang, L. D. Field, R. Karpeles*, J. Org. Chem., in press.



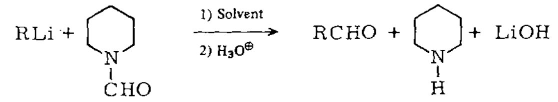


Table 1. Aldehydes by reaction of Grignard and organolithium compounds with *N*-formylpiperidine.

| R—MgX or R—Li | Yield [%][a] | Solvent | M.p. [°C] or B.p. [°C/torr] Found | Ref. [5] |
|---|---|---|---|---|
| $C_6H_5$—MgBr | 96 | Ether or THF | 63—64/10 | 179/751 |
| $C_6H_5CH_2$—MgCl | 89 | | 76—78/10 | 88/18 |
| 1-Naphthyl-MgBr | 94 | | 142/6 | 156/19 |
| 9-Phenanthryl-MgBr | 97 | | 108.4 | 103 |
| $C_6H_5C{\equiv}MgI$ | 85 | | 65/0.1 | 65/0.1 |
| $C_6H_5CH{=}CH$—MgBr | 86 | | 85/2 | 130/20 |
| *c*-$C_3H_5$—MgBr | 80 | | 101—102/760 | 97—100/740 [6] |
| *c*-$C_5H_9$—MgBr | 72 | | 73—76/100 | 41—42/18 [7] |
| 2-Norbornyl-MgBr | 76 [b] | | 52/7 | 70—72/22 [8] |
| *sec*-Butyl-Li | 77 | *n*-Hexane | 91—94/760 | 90—92/760 |
| *n*-Butyl-Li | 83 | *n*-Hexane | 101/760 | 102.5—103/760 |
| *c*-$C_3H_5$—Li | 75 | Ether | 96—98/740 | 97—100/740 [6] |
| $C_6H_5$—Li | 94 | Benzene | 63—64/10 | 179/751 |
| $C_6H_5C{\equiv}C$—Li | 94<br>93 | *n*-Hexane<br>Ether | 65/0.1 | 65/0.1 |

[a] Yields of aldehydes refer to distilled or recrystallized products; they gave IR and $^1$H-NMR spectra which were identical with those of the authentic compounds. [b] Starting with pure *exo*-norbornyl bromide produces a mixture of *exo*- and *endo*-norbornyl carbaldehyde (3 : 1), which was characterized by $^1$H-NMR spectroscopy.

Piperidine can, if necessary, be easily recovered; it can also be recycled after carbonylation with CO, a fact that can be of importance in reactions on a large-scale.

Since in this system there is no additional ligand group available for chelate formation we suggest that the chelating effect suggested in the case of 2-(*N*-methyl-*N*-formyl)aminopyridine is not a crucial one and perhaps even does not occur.

The formylation of organolithium and Grignard reagents can thus be carried out easily and under mild conditions with inexpensive and readily available reagents.

*Procedure:*

A) Formylation of Grignard compounds: A solution of *N*-formylpiperidine (10 mmol) in diethyl ether (10 mL) is slowly added during 2 min to a stirred solution of freshly prepared Grignard reagent (10 mmol) in either dry diethyl ether or tetrahydrofuran (15 mL), cooled to 0 °C. An exothermic reaction takes place. The reaction mixture is stirred for a further 15 min at room temperature, and then it is quenched by 3 N hydrochloric acid, until the solution becomes acidic. After extraction with diethyl ether, the ethereal solution is washed successively with water, with saturated $NaHCO_3$, and with saturated NaCl solution, and is then dried over anhydrous $Na_2SO_4$. Removal of the solvent affords the corresponding aldehyde in almost pure form, which can be further purified by either distillation or crystallization.

B) Formylation of organolithium compounds: As described under A) a freshly prepared solution of the organolithium compound (10 mmol) in the appropriate solvent (see Table 1), (10 ml) is treated with a suspension or an ethereal solution of *N*-formylpiperidine (15 mL). The reaction is moderately exothermic. The solution is stirred for an additional 10 min, and then worked up following the procedure described under A).

Received: January 30, 1981 [Z 863 IE]
German version: Angew. Chem. *93*, 925 (1981)

CAS Registry numbers:
*N*-formylpiperidine, 2591-86-8; piperidine, 110-89-4; 1-naphthaldehyde, 66-77-3; 9-phenanthraldehyde, 4707-71-5; *endo*-2-norbornaldehyde, 3574-54-7; *exo*-2-norbornaldehyde, 3574-55-8; 1-naphthyl-Br, 90-11-0; 9-phenanthryl-Br, 573-17-1; *endo*-2-norbornyl-Br, 13237-87-1; *exo*-2-norbornyl-Br, 2534-77-2; *sec*-butyl-Li, 598-30-1; *n*-butyl-Li, 109-72-8; *sec*-butyl-CHO, 96-17-3; *n*-butyl-CHO, 110-62-3; $C_6H_5Br$, 108-86-1; $C_6H_5CH_2Cl$, 100-44-7; $C_6H_5C{\equiv}CI$, 932-88-7; $C_6H_5CH{=}CHBr$, 103-64-0; *c*-$C_3H_5Br$, 4333-56-6; *c*-$C_5H_9Br$, 137-43-9; *c*-$C_3H_5Li$, 3002-94-6; $C_6H_5Li$, 591-51-5; $C_6H_5C{\equiv}CLi$, 4440-01-1; $C_6H_5CHO$, 100-52-7; $C_6H_5CH_2CHO$, 122-78-1; $C_6H_5C{\equiv}CCHO$, 2579-22-8; $C_6H_5CH{=}CHCHO$, 104-55-2; *c*-$C_3H_5CHO$, 1489-69-6; *c*-$C_5H_9CHO$, 872-53-7

---

[1] a) *G. A. Olah, Y. D. Vankar, M. Arvanaghi, J. Sommer,* Angew. Chem. *91,* 649 (1979); Angew. Chem. Int. Ed. Engl. *18,* 614 (1979); b) *G. A. Olah, S. J. Kuhn,* Chem. Ber. *89,* 2211 (1956); J. Am. Chem. Soc. *82,* 2380 (1960).

[2] *F. Sato, K. Oguro, H. Watanabe, M. Sato,* Tetrahedron Lett. *1980,* 2869.

[3] *M. W. Rathke, E. Chao, G. Wu,* J. Organomet. Chem. *122,* 145 (1976); see also: *D. S. Matteson, D. Majumdar,* J. Am. Chem. Soc. *102,* 7588 (1980).

[4] *D. L. Comins, A. I. Meyers,* Synthesis *1978,* 403, and references cited therein; *A. I. Meyers, D. L. Comins,* Tetrahedron Lett. *1978,* 5179.

[5] Dictionary of Organic Compounds, Oxford University Press, New York 1965.

[6] *H. C. Brown, A. Tsukamoto,* J. Am. Chem. Soc. *83,* 2016 (1961).

[7] *S. M. Naqvi, J. P. Horwitz, R. Filler,* J. Am. Chem. Soc. *79,* 6283 (1957).

[8] Handbook of Chemistry and Physics, 57th edit., The Chemical Rubber Co., Cleveland 1976—77.

## Cyclobutanone and Cyclobutenone Derivatives by Reaction of Tertiary Amides with Alkenes or Alkynes[**]

By *Jean-Bernard Falmagne, José Escudero, Safia Taleb-Sahraoui,* and *Léon Ghosez*[*]

*Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday*

The utility of *N,N*-dialkyl-*N*-alkylideneammonium (keteneiminium) salts for the synthesis of four-membered rings has been illustrated by the facile cycloadditions of tetramethylketeneiminium salts to alkenes[1a] and alkynes[1b]. However, the method still suffers from an important limitation: whereas "keto" keteneiminium salts generated from α-halo enamines[2] and Lewis acids always cycloadd, "aldo" keteneiminium salts often react faster with the α-halo enamines from which they are formed than with an alkenic or alkynic partner[3]. This limitation should not occur with *non-nucleophilic precursors* of the keteneiminium salts: we anticipated that 1-dialkylaminoalkenyl trifluoromethanesulfonates *(5)* would fulfill this purpose.

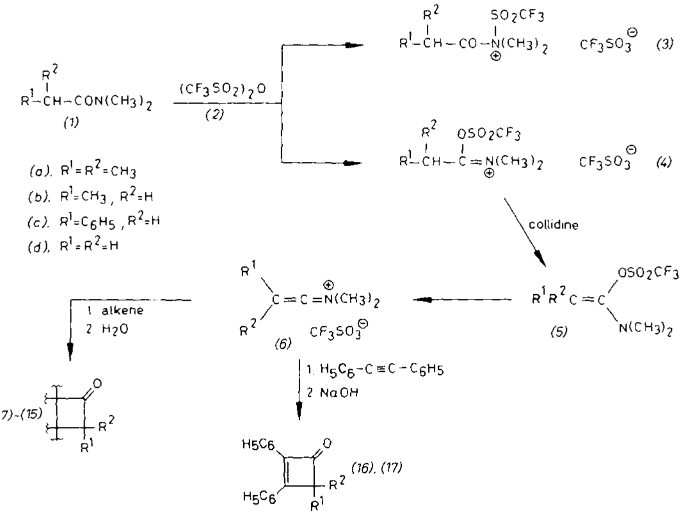
The acylation of tertiary amides *(1)* with trifluoromethanesulfonic anhydride *(2)* was found to give a mixture of *O*-acylated (major) *(4)* and *N*-acylated (minor) *(3)* products. The reaction mixture from *(1a)* and *(2)*, for example, showed two pairs of singlets for the protons of the

---

[*] Prof. Dr. L. Ghosez, Lic. J. B. Falmagne, Lic. J. Escudero,
Lic. S. Taleb-Sahraoui
Laboratoire de Chimie Organique de Synthèse
Université Catholique de Louvain
Place L. Pasteur, B-1348 Louvain-La-Neuve (Belgium)

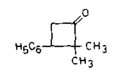
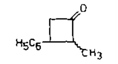
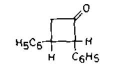
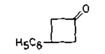
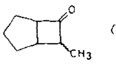
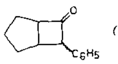
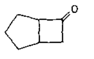
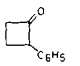
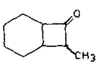
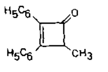
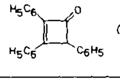
[**] This work was supported by the "Institut pour l'Encouragement de la Recherche Scientifique", the "Administration Générale pour la Coopération au Développement" and the "Service de Programmation de la Politique Scientifique" (Contrat 79/84-13).

$N(CH_3)_3$ groups ($\delta = 3.28$ and 3.37 as well as 3.63 and 3.8) in the ratio 1:4. The most intense low-field signals can be assigned to the *O*-acylated product *(4)*, whereas the high-field signals are most probably due to *(3)*. On hydrolysis, the educt *(1a)* was quantitatively regenerated from the mixture.



When the acylation of *(1)* with *(2)* was conducted in the presence of collidine and an olefin, [2+2] cycloadducts were formed which were directly hydrolyzed to the corresponding cyclobutanones *(7)*–*(15)* (Table 1)[4]. We propose that collidine converts the *O*-acylated intermediates *(4)* into 1-dimethylaminoalkenyl trifluoromethylsulfonates *(5)* which directly ionize to the corresponding keteneiminium salts. Indeed we found no spectroscopic evidence for the presence of substantial amounts of *(5)* while, in certain cases, the presence of *(6)* could be inferred from an IR band around 2020 cm$^{-1}$.

Table 1. Preparation of cyclobutanones and cyclobutenones by reaction of *(1)* with alkenes or alkynes.

| Educts | Products | | Yields [%] [a] | IR ($CCl_4$) [cm$^{-1}$] |
|---|---|---|---|---|
| Styrene + *(1a)* |  | *(7)* | 70 | 1780 |
| Styrene + *(1b)* |  | *(8)* | 60<br>(*cis* + *trans*) | 1785—1790 |
| Styrene + *(1c)* |  | *(9)* | 65 | 1785 |
| Styrene + *(1d)* |  | *(10)* | 77 | 1795 |
| Cyclopentene + *(1b)* |  | *(11)* | 72<br>(2 isomers) | 1760 [b] |
| Cyclopentene + *(1c)* |  | *(12)* | 80 | 1775 |
| Cyclopentene + *(1d)* |  | *(13)* | 50 | 1780 |
| Ethylene + *(1c)* |  | *(14)* | 35 | 1785 [c] |
| Cyclohexene + *(1b)* |  | *(15)* | 48<br>(2 isomers) | 1780 |
| Diphenylacetylene + *(1b)* |  | *(16)* | 80 | 1760 |
| Diphenylacetylene + *(1c)* |  | *(17)* | 62 | 1759 |

[a] The yield was not optimized. [b] In $CHCl_3$. [c] In $CH_2Cl_2$.

Under these conditions, both "aldo" and "keto" keteneiminium salts *(6)* reacted smoothly with olefins. The method also enables the cyclobutenones *(16)* and *(17)* to be prepared from *(1)* and diphenylacetylene. Yields of pure products are generally good. In this respect, the compounds *(6)* are superior to the corresponding ketenes which react only sluggishly with unactivated alkenes or alkynes.

The method described here is thus in general highly suitable for the synthesis of cyclobutanones and cyclobutenones from readily available educts.

### *Experimental*

A 100 mL round-bottomed flask fitted with gas inlet (dry argon atmosphere), dropping funnel and reflux condenser connected to a sulfuric acid trap, is charged with *(1b)* (252 mg, 2.5 mmol), collidine (367 mg, 3 mmol), cyclohexene (4 mL) and $CHCl_3$ (10 mL). A solution of *(2)* (0.5 mL, 3 mmol) in 20 mL of $CHCl_3$ is added to the refluxing mixture over a period of 24 h. Evaporation of the solvent leaves an oil which is washed with ether (3 × 20 mL), and then hydrolyzed overnight in a two phase system (20 mL $CH_2Cl_2$ + 20 mL $H_2O$). Evaporation of $CH_2Cl_2$ and extraction of the aqueous phase with $CCl_4$ gives *(15)* which is chromatographed on silica gel (ethylacetate/petroleum ether 1:5). Yield: 165 mg (48%).

Received: May 4, 1981 [Z 865 IE]
German version: Angew. Chem. *93*, 926 (1981)

CAS Registry numbers:
*(1a)*, 21678-37-5; *(1b)*, 758-96-3; *(1c)*, 18925-69-4; *(1d)*, 127-19-5; *(7)*, 4056-87-5; *cis-(8)*, 79028-17-4; *trans-(8)*, 79028-18-5; *(9)*, 79028-19-6; *(10)*, 52784-31-3; *(11)* isomer 1, 54276-00-5; *(11)* isomer 2, 54235-95-9; *(12)*, 73788-97-3; *(13)*, 13756-54-2; *(14)*, 42436-86-2; *(15)*, 63903-17-3; *(16)*, 79028-20-9; *(17)*, 69490-60-4; styrene, 100-42-5; cyclopentene, 142-29-0; ethylene, 74-85-1; cyclohexene, 110-83-8; diphenylacetylene, 501-65-5

---

[1] a) *J. Marchand-Brynaert, L. Ghosez*, J. Amer. Chem. Soc. 1972, *94*, 2870; *A. Sidani, J. Marchand-Brynaert, L. Ghosez*, Angew. Chem. *86*, 272 (1974); Angew. Chem. Int. Ed. Engl. *13*, 267 (1974); *H.-G. Heine, W. Hartmann, ibid. 93*, 805 (1981); *20*, 782 (1981); *C. Hoornaert, A. M. Frisque-Hesbain, L. Ghosez, ibid. 87*, 552 (1975); *14*, 569 (1975).

[2] *L. Ghosez, J. Marchand-Brynaert*, Adv. Org. Chem. *9*, 421 (1976); *L. Ghosez, M. J. O'Donnell* in *A. P. Marchand, R. E. Lehr:* Pericyclic Reactions Vol. 2, Academic Press, New York 1977.

[3] *M. Houtekie, M. Demuylder, L. Ghosez*, unpublished results.

[4] All the new compounds gave correct analyses and characteristic spectra.

## Anionic Cycloaddition on Electron-Deficient Alkynes—Synthesis and Stereochemistry of 3-Pyrroline-3-carboxylic Acid *N,N*-Dimethylamides

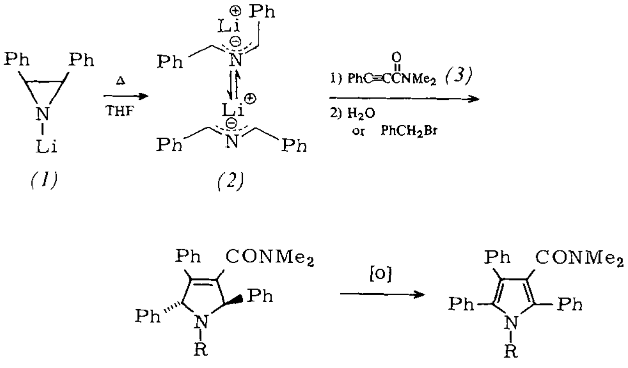
By *Liliane Vo Quang, Henri Gaessler*, and *Yen Vo Quang*[*]

1,3-Diphenyl-2-azaallyllithium *(2)*[1] reacts with alkynes to give quantitative yields of 3-pyrrolines[2]. Studying the

---

[*] Dr. Y. Vo Quang, Dipl.-Ing. H. Gaessler, Dr. L. Vo Quang
Laboratoire de Recherches de Chimie Organique
Ecole Nationale Supérieure de Chimie de Paris
11, rue Pierre-et-Marie-Curie, 75231 Paris Cedex 05 (France)

generality of this anionic polar cycloaddition with activated triple bonds, we have now found that reaction of *(2)* with phenylpropiolic acid *N,N*-dimethylamide *(3)* affords 2,4,5-triphenyl-3-pyrroline-3-carboxylic acid *N,N*-dimethylamide *(4a)*, thus indicating that electron-withdrawing groups are not unsuitable[3] for anionic cycloaddition.



*(1)* *(2)*

*(4a)*, R = H
*(4b)*, R = $CH_2Ph$

*(5a)*, R = H
*(5b)*, R = $CH_2Ph$

Ring opening of *N*-lithiated *cis*-2,3-diphenylaziridine *(1)*[1] occurs easily in boiling tetrahydrofuran under argon atmosphere. The anion *(2)* which is formed can be trapped at −70 °C by slow addition of an equimolar amount of the alkyne *(3)*. After complete conversion (5 h, monitored NMR spectroscopically), the pyrroline *(4a)*[4] can be isolated from the hydrolyzed mixture in 46% yield. *(4a)* is very readily oxidized by air to its corresponding pyrrole derivative *(5a)*, partially during subsequent work-up at room temperature in either day-light or darkness, and completely in a chloroform solution in a few hours. From the mixture of cycloadducts, the pyrrole *(5a)* (22% yield) and a polymeric pyrrole (20% yield, mass spectrometric confirmation) are also isolated.

Using the method of *Hill* and *Chan*[5] it could be shown that the 3-pyrroline *(4a)* is *trans*-configurated with respect to C-2 and C-5: as a result of the lack of a plane of symmetry in identically α,α'-*trans*-disubstituted heterocyclic amines, the methylene protons of their *N*-benzyl derivatives are stereochemically and magnetically non-equivalent. The same observation was made in the case of 1,3-isoindolinedicarboxylic acid dimethyl ester[6].

When treated with an equimolar amount of benzyl bromide before hydrolysis, the crude cycloadduct mixture affords 1-benzyl-2,4,5-triphenyl-3-pyrroline-3-carboxylic acid *N,N*-dimethylamide *(4b)* in 20% yield, which is rapidly oxidized by air to the corresponding pyrrole *(5b)*. Its $^1$H-NMR spectrum shows unambiguously a stereochemically pure *trans*-2,5 configuration *(4b)* (Table 1). The large values observed for $J_{2,5}$ coupling constants in *(4a)* and *(4b)* are noteworthy, and are of the same order of magnitude as those previously reported for compounds of this type[7].

Table 1. $^1$H-NMR data of *(4)* and *(5)* (δ values, referred to TMS).

| Cpd. | R | H-2 | H-5 | $NMe_2$ | Solvent |
|---|---|---|---|---|---|
| *(4a)* | 2.40(s) | 5.84(s) | 5.84(s) | 2.15(s), 2.70(s) | $CDCl_3$ |
| | 2.40(s) | 5.74(d)[a] | 5.88(d)[a] | 1.87(s), 2.46(s) | $C_6D_6$ |
| *(4b)* | 3.82(d), 3.34(d)[b] | 5.62(d)[a] | 5.56(d)[a] | 2.34(s), 2.69(s) | $C_6D_6$ |
| *(5a)* | 9.4(s) | — | — | 2.52(s), 2.82(s) | $CDCl_3$ |
| *(5b)* | 5.11(s) | — | — | 2.55(s), 2.79(s) | $CDCl_3$ |

[a] $J_{2,5} = 5.6$ Hz. [b] $J = 14.2$ Hz.

The present synthetic procedure should be valuable in the stereospecific preparation of substituted 3-pyrrolines which are relatively rare in spite of the promising biological properties of some representative examples[8]. Using this procedure we have also prepared 3-diphenylphosphino-2,4,5-triphenyl-3-pyrroline (31% yield; $^1$H-NMR: $\delta = 5.72$ (d, H-2), 5.24 (d, H-5; $J_{2,5} = 4.5$ Hz)).

Received: December 22, 1980 [Z 875 IE]
German version: Angew. Chem. *93*, 922 (1981)

CAS Registry numbers:
*(1)*, 37019-82-2; *(3)*, 26218-50-8; *(4a)*, 79084-04-1; *(4b)*, 79084-05-2; *(5a)*, 79084-06-3; *(5b)*, 79084-07-4; 3-diphenylphosphino-2,4,5-triphenyl-3-pyrroline, 79084-08-5

---

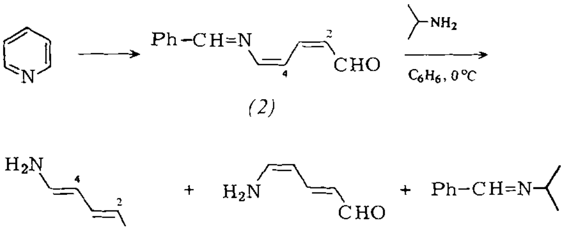
[1] *T. Kauffmann*, Angew. Chem. *86*, 715 (1974); Angew. Chem. Int. Ed. Engl. *13*, 627 (1974), and references cited therein.
[2] *L. Vo Quang, Y. Vo Quang*, Tetrahedron Lett. *1978*, 4679.
[3] a) *T. Kauffmann, H. Ahlers, A. Hamsen, H. Schulz, H.-J. Tilhard, A. Vahrenhorst*, Angew. Chem. *89*, 107 (1977); Angew. Chem. Int. Ed. Engl. *16*, 119 (1977); b) *S. Sinbandhit, J. Hamelin*, J. Chem. Soc. Chem. Commun. *1977*, 768.
[4] All compounds gave characteristic spectra.
[5] *R. K. Hill, T. Chan*, Tetrahedron *21*, 2015 (1965).
[6] *G. Cignarella, A. Vigevani*, Gazz. Chim. Ital. *98*, 1474 (1968).
[7] *T. J. Batterham, N. V. Riggs, A. V. Robertson, W. R. J. Simpson*, Aust. J. Chem. *22*, 725 (1969).
[8] *A. R. Mattocks*, J. Chem. Soc. Perkin Trans. I *1978*, 896.

---

## (*E,E*)-5-Amino-2,4-pentadienal: The First Preparative Synthesis of Hydrolyzed Pyridine

By *Dieter Reinehr* and *Tammo Winkler*[*]

5-Amino-2,4-pentadienal *(1)*, the parent compound of a preparatively important class of compounds[1], has so far never been isolated. *(1)* is formed during the photohydrolysis of pyridine[2a]; it is rather unstable[1] and readily loses water to give pyridine again. *(1)* has been characterized only by its UV spectrum and by trapping reactions[2]. We report here on a simple synthesis of *(1)*, its isolation as a crystalline compound, and on its spectroscopic properties.



*(2)*

*(1a)* *(1b)* *(3)*

Reaction of isopropylamine with the 7-phenyl-6-aza-2,4,6-heptatrienal *(2)*, which is readily accessible from pyridine[3], affords *(1)* in 62% yield. The amine *(1)* is formally replaced by isopropylamine; *(1)* precipitates as yellow crystals which rapidly turn brownish at room temperature and on exposure to air. *N*-Benzylideneisopropylamine *(3)* was isolated from the mother liquor in 58% yield.

*(2)*[3] and *(3)* were characterized by their $^1$H-NMR and IR spectra and elemental analyses and, in the case of *(1)* also by its $^{13}$C-NMR, UV, and mass spectra (Table 1). The UV data of *(1)* are consistent with those of the photohydrolysis product of pyridine[2a]. The absorption maximum of a

---

[*] Dr. D. Reinehr, Dr. T. Winkler
Ciba-Geigy AG, CH-4002 Basel (Switzerland)

solution of *(1)* in acidic methanol appears at 339 nm, while the photohydrolysis product absorbs at 340 nm in acid media[2a]. This small difference allows no conclusions about the configuration of the double bond in the photohydrolysis product, as the difference for the *E,E*- and *Z,Z*-isomers of 2,4-hexadienoic acid[4] is also only 5 nm. According to its $^1$H-NMR spectrum, *(1)* is present mainly in the *E,E*-configuration [*(1a)* $J_{2,3}=14$, $J_{4,5}=12$ Hz; cf. analogous dialkylamino compounds[5]]. The 2*E*,4*Z*-compound *(1b)* ($J_{2,3}=14.5$, $J_{4,5}=8$ Hz) is detectable as minor component (5%). Since *(2)* has 2*Z*,4*Z*-configuration[3] ($J_{2,3}=11.5$, $J_{4,5}=7.5$ Hz), an isomerization into the thermodynamically more stable[1] *E,E*-configuration must have taken place during the reaction. This, and the low solubility of *(1)* in benzene, make its isolation possible. Hence this interesting and synthetically important compound[1] is easily accessible.

Table 1. Spectroscopic data of *(1)*.

UV ($CH_3OH$, 0.02 N HCl): $\lambda_{max}=339$ nm ($\varepsilon=34400$)
IR ($CH_2Cl_2$): $\nu=3510$, 3408, 1630, 1605 cm$^{-1}$
$^1$H-NMR ($(CD_3)_2SO$) *(1a)*: $\delta=9.13$ (d, $J_{1,2}=8.5$ Hz, 1-H), 7.21 (dd, $J_{2,3}=14$, $J_{3,4}=12$, 3-H), 7.06 (broad q, $J_{4,5}=12$, $J_{5,NH}=11$, 5-H), 6.92 (broad d, $J_{5,NH}=11$, $NH_2$), 5.55 (dd, $J_{2,3}=14$, $J_{1,2}=8.5$, 2-H), 5.45 (t, $J_{3,4}=J_{4,5}=12$, 4-H)
*(1b)*: $\delta=9.25$ (d, $J_{1,2}=8.5$, 1-H), 7.75 (dd, $J_{2,3}=14.5$, $J_{3,4}=12.5$, 3-H), 6.57 (dt, $J_{5,NH}=11.5$, $J_{4,5}=8$, 5-H), 5.66 (dd, $J_{2,3}=14.5$, $J_{1,2}=8.5$, 2-H), 4.90 (dd, $J_{3,4}=12.5$, $J_{4,5}=8$, 4-H)
$^{13}$C-NMR ($(CD_3)_2SO$) *(1a)*: $\delta=190.7$ (C-1), 158.2 (C-3, assignment by selective decoupling of 3-H), 152.3 (C-5), 117.2 (C-2), 99.4 (C-4)
*(1b)*: $\delta=191.5$ (C-1), 150.3 (C-3), 146.1 (C-5), 120.2 (C-2), 94.7 (C-4)
MS $m/z$ 97 (*M*), 79 ($M-H_2O$)

### *Procedure*

Isopropylamine (1.82 g, 0.03 mol) is added slowly with ice-cooling to a solution of *(2)*[3] (3.8 g, 0.02 mol) in benzene (6 mL). After 1 h the yellow precipitate which is formed is filtered off, washed with benzene, and dried. Yield 1.24 g (62%) canary-yellow crystals of *(1)*, m.p. 140 °C (dec.).

Received: February 27, 1981 [Z 876 IE]
German version: Angew. Chem. *93*, 911 (1981)

CAS Registry numbers:
*(1a)*, 79101-67-0; *(1b)*, 79101-68-1; *(2)*, 19946-76-0; *(3)*, 6852-56-8; Isopropylamine, 75-81-0

---

[1] *J. Becher*, Synthesis *1980*, 589.
[2] a) *J. Joussot-Dubien, J. Houdard-Pereyre*, Bull. Soc. Chim. Fr. *1969*, 2619, and references cited therein; b) *K. E. Wilzbach, D. J. Rausch*, J. Am. Chem. Soc. *92*, 2178 (1970); *O. Traverso, V. Carassiti, R. Portanova, P. A. Vigato*, Inorg. Chim. Acta *9*, 227 (1974).
[3] *R. Kuhn, E. Teller*, Justus Liebigs Ann. Chem. *715*, 106 (1968).
[4] *J. L. H. Allan, E. R. H. Jones, M. C. Whiting*, J. Chem. Soc. *1955*, 1862.
[5] *M. Martin, G. Martin*, C. R. Acad. Sci. *256*, 403 (1963); *L. Finsen, J. Becher, O. Buchardt, R. R. Koganty*, Acta Chem. Scand. *B34*, 513 (1980), and references cited therein.

## Oxidation of Isatins to Anthranilic Acid Esters

By *Gernot Reissenweber* and *Dietrich Mangold*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

The regiospecific Baeyer-Villiger oxidation of isatins by aqueous hydrogen peroxide in glacial acetic acid leads to isatoic anhydrides and with potassium peroxodisulfate in sulfuric acid to 2,3-dioxo-1,4-benzoxazines[1]. The oxidation of isatins by hydrogen peroxide in aqueous alkali metal hydroxides to anthranilic acids has long been used as a preparative route to anthranilic acid derivatives, which are otherwise only accessible with difficulty[2].

We have now found that methyl anthranilates *(2)* can be prepared directly in good yields *via* an exothermic process involving the reaction of isatins *(1)* in methanol with 30 to 50% hydrogen peroxide and sodium methoxide. Their purity after extractive work-up is greater than 96%. The only by-products are the corresponding anthranilic acids (Table 1). Variously substituted methyl anthranilates, which until now have only been accessible indirectly *via* isatoic anhydrides, can therefore be prepared using aniline derivatives as starting materials *via* the readily accessible isatin derivatives[2,3].

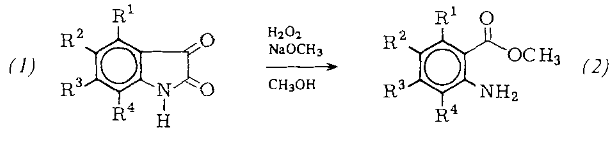


Table 1. Examples for the synthesis of methyl anthranilate esters *(2)* from isatins *(1)* [a].

|  | $R^1$ | $R^2$ | $R^3$ | $R^4$ | *(2)* Yield [%] | B. p. [°C] $n_D^{20}$ |
|---|---|---|---|---|---|---|
| *a* | H | H | H | H | 82 | 1.5818<br>1.5820 [4] |
| *b* | H | H | H | $CH_3$ | 78 | 1.5743 |
| *c* | H | H | H | $CF_3$ | 74 | 1.5042 |
| *d* | H | Cl | H | Cl | 80 | 62—63<br>63—64 [5] |
| *e* | H | Br | H | H | 76 | 73—74<br>74 [5] |
| *f* | H | H | Cl | H | 76 | 69—70 |
| *g* | H | Cl | H | $CH_3$ | 78 | 40—42 |
| *h* | H | H | $CH_3$ | H | 79 | 40 |
| *i* | $CH_3$ | H | H | $CH_3$ | 68 | 34—36 |

[a] All the compounds gave correct elemental analyses as well as satisfactorily IR- and NMR-spectra.

In contrast to the oxidation of isatins *(1)* in aqueous alkali media, the reaction in methanol/sodium methoxide proceeds, based on the results of our investigations, *via* deprotonated isatoic anhydrides *(4)*, which immediately react to the esters *(2)*. There are two possible modes of formation of *(3)*: Route *A* (the water stems from aqueous hydrogen peroxide) and Route *B*.

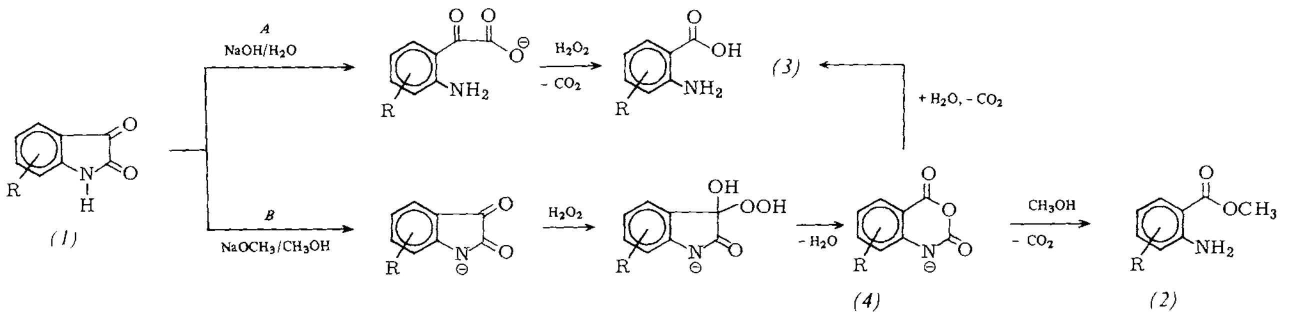
Furthermore, the reaction is not only limited to the preparation of the methyl esters *(2)*. With ethanol/sodium ethoxide, the ethyl esters can be prepared in equally high yields. A further example: using 1-butanol with sodium hydride as base, *n*-butyl-3-methylanthranilate is formed from *(1b)* in 60% yield.

### *Procedure*[6]

*(1)* (1 mol) is suspended in 1500 mL of methanol. After addition of sodium methoxide (1.5 mol, 30% sodium methoxide solution), hydrogen peroxide (1.2 mol, 50% aqueous solution) is dropped into the cooled mixture (0—10 °C), whereby the initially dark violet solution becomes colorless. The mixture is stirred for 30 min at room temper-

---

[*] Dr. G. Reissenweber [+], Dr. D. Mangold
BASF Aktiengesellschaft, Hauptlaboratorium, D-ZHP-B9
D-6700 Ludwigshafen (Germany)
[+] Author to whom correspondence should be addressed.



ature, the solvent evaporated off, and water added to the residue, which is then extracted with dichloromethane.

Received: April 2, 1981 [Z 881 IE]
German version: Angew. Chem. *93*, 914 (1981)

CAS Registry numbers:
*(1a)*, 91-56-5; *(1b)*, 1127-59-9; *(1c)*, 391-12-8; *(1d)*, 6374-92-1; *(1e)*, 87-48-9; *(1f)*, 6341-92-0; *(1g)*, 14389-06-1; *(1h)*, 1128-47-8; *(1i)*, 15540-90-6; *(2a)*, 134-20-3; *(2b)*, 22223-49-0; *(2c)*, 64321-95-5; *(2d)*, 52727-62-5; *(2e)*, 52727-57-8; *(2f)*, 5900-58-3; *(2g)*, 79101-83-0; *(2h)*, 18595-17-0; *(2i)*, 27023-00-3; 3-methylanthranilic *n*-butyl ester 79101-94-1

---

[1] *G. Reissenweber, D. Mangold*, Angew. Chem. *92*, 196 (1980); Angew. Chem. Int. Ed. Engl. *19*, 222 (1980).

[2] *Houben-Weyl:* Methoden der organischen Chemie, Bd. 7/4, Thieme, Stuttgart 1968, S. 5.

[3] *G. M. Coppola*, Synthesis *1980*, 505.

[4] Handbook of Chemistry and Physics, 55th edition, CRC Press, Cleveland 1974.

[5] *M. P. Freundler*, Bull. Soc. Chim. Fr. [4] *9*, 605 (1911).

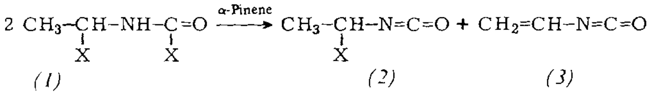
[6] *G. Reissenweber, D. Mangold*, DOS 3001579 (1980), BASF.

# Vinyl Isocyanate by Thermal Dehydrohalogenation of 1-Haloethylcarbamoyl Halides with α-Pinene

By *Karl-Heinz König, Karl-Heinz Feuerherd, Volker M. Schwendemann*, and *Heinz-Günter Oeser*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

Numerous synthetic routes to vinyl isocyanate *(3)* are known[1]. We have recently synthesized 1-haloethylcarbamoyl halides *(1)* by addition of hydrogen halides to vinyl isocyanate[2], as well as by the halogenation of ethyl isocyanate or ethylcarbamoyl halides[3]. *(1)* shows the tendency to liquefy at room temperature and evolves hydrogen halides. Cleavage of hydrogen halide at room temperature certainly leads at first to 1-haloethyl isocyanate *(2)*. Since, however, considerable amounts of polymeric material are produced in this reaction, presumably at least partial double dehydrohalogenation of *(1)* to the readily polymerizable vinyl isocyanate *(3)* occurs. We have now found that *(1)* and α-pinene react to give a mixture of vinyl isocyanate *(3)* and the, until now unknown, 1-haloethyl isocyanate *(2)*.

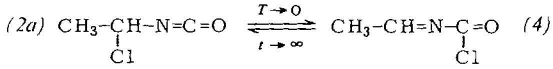


$$2\ \mathrm{CH_3{-}\underset{X}{CH}{-}NH{-}\underset{X}{C}{=}O} \xrightarrow{\alpha\text{-Pinene}} \mathrm{CH_3{-}\underset{X}{CH}{-}N{=}C{=}O} + \mathrm{CH_2{=}CH{-}N{=}C{=}O}$$

*(1)* *(2)* *(3)*

*(a)*, X = Cl; *(b)*, X = Br

With the chloro compound *(1a)*, the fraction of vinyl isocyanate *(3)* in the product mixture of *(2a)* and *(3)* depends on the reaction time. This indicates a mechanism involving intermediates, whereby it can be assumed that a chlorotropic equilibrium between the α-chloroisocyanate *(2a)* and the *N*-alkylidenecarbamoyl chloride *(4)* is involved[4, 5].



$$(2a)\quad \mathrm{CH_3{-}\underset{Cl}{CH}{-}N{=}C{=}O} \underset{t\to\infty}{\overset{T\to 0}{\rightleftharpoons}} \mathrm{CH_3{-}CH{=}N{-}\underset{Cl}{C}{=}O}\quad (4)$$

The formation of vinyl isocyanate *(3)* indicates an azavinylogous dehydrohalogenation of the carbamoyl chloride *(4)*; the position of the equilibrium *(2a)*⇌*(4)* could prevent the rapid formation of vinyl isocyanate *(3)*. In similar chlorotropic equilibria shifts in favor of the α-chloroisocyanate form are known at higher temperatures[4].

*Procedure*

*(2a)* and *(3a)* from *(1a)*: *(1a)* (160 g, 1.13 mol) and α-pinene (537 g, 3.9 mol) were stirred for 2 h while the temperature was increased from 24 to 105 °C; the product mixture was continually distilled out. Total yield 27.6 g (23%). *(2a)* and 34.6 g (44%) *(3)* were purified by preparative gas chromatography[6].

*(3)* from *(1a)*: A mixture of *(1a)* (525 g, 3.7 mol) and α-pinene (1770 g, 13 mol) were heated from 25 to 155 °C over 6.5 h in a stirred flask fitted with a 25 cm packed column and NORMAG distillation head. A distillate of the product was simultaneously collected at reflux ratios of 1 : 15 to 1 : 20; yield 155.5 g (61%) *(3)* with < 1% *(2a)*.

*(3)* from *(1b)*: A mixture of *(1b)* (231 g, 1 mol) and α-pinene (475 g, 3.5 mol) were heated from 23 to 120 °C over 1.5 h in a stirred flask. *(3)* (61.5 g, 89%) in 90% purity was obtained by distillation.

Received: June 3, 1980 [Z 883 IE]
German version: Angew. Chem. *93*, 915 (1981)

CAS Registry numbers:
*(1a)*, 70008-75-2; *(1b)*, 72866-46-7; *(2a)*, 72866-60-5; *(3)*, 3555-94-0; *(4)*, 72866-59-2; α-pinene, 80-56-8

---

[*] Dr. K.-H. König, Dr. K.-H. Feuerherd, Dr. V. M. Schwendemann, Dr. H.-G. Oeser
BASF Aktiengesellschaft, Hauptlaboratorium
D-6700 Ludwigshafen (Germany)

[1] a) *M. Sato*, J. Org. Chem. *26*, 770 (1961); b) *D. H. Heinert*, DBP 1932811 (1969); c) *K.-H. König, Ch. Reitel, D. Mangold, K.-H. Feuerherd, H.-G. Oeser*, Angew. Chem. *91*, 334 (1979); Angew. Chem. Int. Ed. Engl. *18*, 319 (1979).

[2] *K.-H. König, Ch. Reitel, K.-H. Feuerherd*, Angew. Chem. *92*, 197 (1980); Angew. Chem. Int. Ed. Engl. *19*, 201 (1980).

[3] Halogenation of ethyl isocyanate: *K.-H. König, K.-H. Feuerherd, V. M. Schwendemann, H.-G. Oeser*, unpublished results.

[4] *L. J. Samarai, V. J. Gorbatenko, J. E. Boldeskul, V. P. Luk'yanchuk*, Zh. Org. Khim. *12*, 547 (1976).

[5] *H. Holtschmidt*, Angew. Chem. *74*, 848 (1962); Angew. Chem. Int. Ed. Engl. *1*, 632 (1962).

[6] *(2a)*: b.p. = 92 °C; $^1$H-NMR (CDCl$_3$): $\delta$ = 1.8 (d, 3H), 5.4 (q, 1H); IR: 3100 w, 2990 w, 2250 s, 1775 w, 1440 m, 1380 m, 1335 m, 1250 m, 1100 m, 1070 s, 1000 m, 820 s, 740 m, 650 s cm$^{-1}$. *(3)*: b.p. = 38.3 °C (Lit. [1c]: 38.5 °C); $^1$H-NMR (CDCl$_3$): 5.35 (dd, 1H), 5.9 (d, 1H), 6.15 (d, 1H).

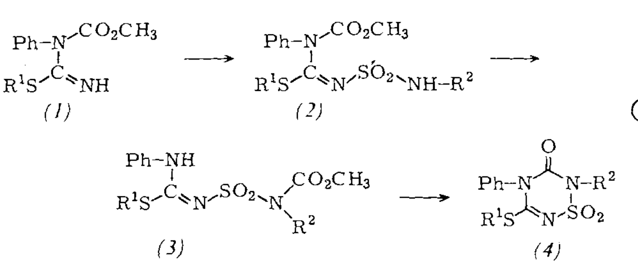
# Thiatriazinones *via* a Novel 1,5-Carboxylic Ester Shift

By *Rolf-Dieter Acker*, *Gerhard Hamprecht*, and *Erich Hädicke*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

Heterocycles with N—$SO_2$—N substructures show a wide range of biological activity[1,2]. The combination of the uracil ring with the sulfonamide element leads to thiatriazinone structures whose synthesis is interesting because of their potential biological activity. A route to the novel 2-alkyl-5-(alkylthio)-4-phenyl-2*H*-1,2,4,6-thiatriazin-3-(4*H*)-one 1,1-dioxides *(4)* was accomplished *via* an unusual 1,5-carboxylic ester shift.

The educts used were the *N*-carboxymethyl-*N*-phenylisothioureas *(1)*[3], which can be readily converted into the sulfamides *(2)* by the action of *N*-alkylsulfamoyl chlorides[2] (Table 1)[4]. Direct cyclization of *(2)* to *(4)* was not possible; however, under mild conditions (2 N NaOH, 20 °C, 30 min, yield 70—80%) the ester group migrated to the alkyl substituted nitrogen atom to form *(3)*. *(3)* cyclized in aqueous alkali (1—2 N NaOH, 50—90 °C, yield 20—40%, depending on the nature of the substituents) to the thiatriazinones *(4)* (Table 1).



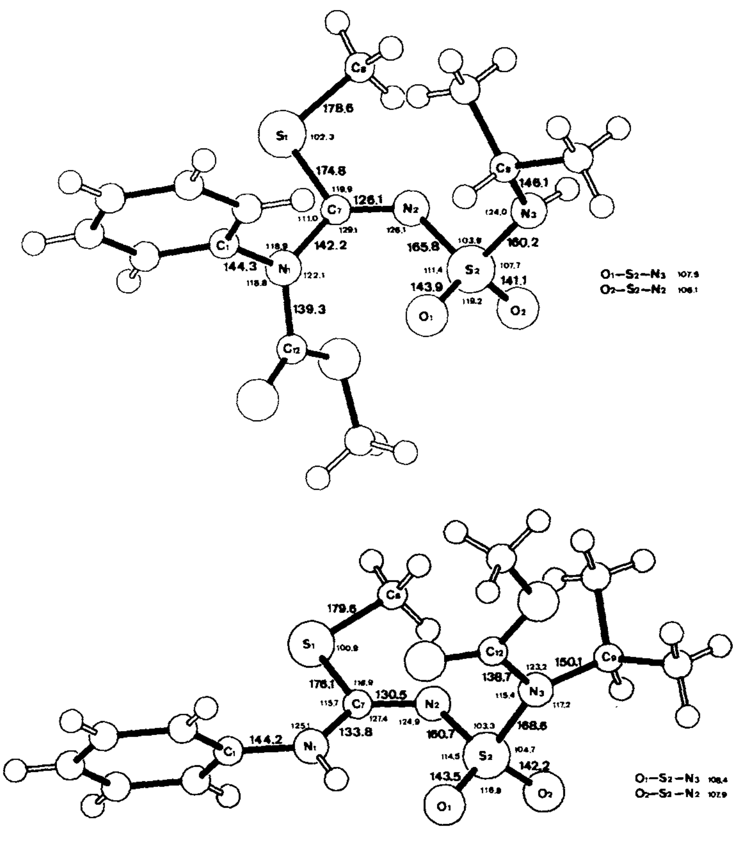


Fig. 1. Molecular structures of *(2a)* (above) and *(3a)* (below) in the crystal. Standard deviations (without hydrogen atoms) 0.2 to 0.7 pm and 0.1 to 0.4° [5].

Table 1. Synthesized products of the type *(1)*—*(4)*.

| | $R^1$ | $R^2$ | *(1)* M.p. [°C] | *(2)* M.p. [°C] | *(3)* M.p. [°C] | *(4)* M.p. [°C] | $^1$H-NMR ($\delta$ value) |
|---|---|---|---|---|---|---|---|
| *a* | $CH_3$ | *i*-$C_3H_7$ | 77—78 | 108—110 | 115—116 | 162—163 | 1.50 (d, 6H), 4.61 (m, 1H), 2.37 (s, 3H), 7.55 (m, 5H) |
| *b* | $CH_3$ | $CH_3$ | | (82—83) [a] | 87—89 | 231—233 | 2.38 (s, 3H), 3.35 (s, 3H), 7.52 (m, 5H) |
| *c* | $C_2H_5$ | *i*-$C_3H_7$ | 74—75 | viscous | [b] | 150—151 | 1.30 (t, 3H), 1.60 (d, 6H), 3.00 (q, 2H), 4.21 (m, 1H), 7.45 (m, 5H) |
| *d* | $C_2H_5$ | $CH_3$ | | 90—91 | 96—98 | 228—230 | 1.29 (t, 3H), 3.00 (q, 2H), 3.35 (s, 3H), 7.50 (m, 5H) |
| *e* | $CH_2$—$C_6H_5$ | *i*-$C_3H_7$ | 98—99 | viscous | 97—99 | 160—161 | 1.55 (d, 6H), 4.15 (s, 2H), 4.73 (m, 1H), 7.25 (m, 10H) |

[a] 4 : 1 mixture of *(3b)* and *(2b)*. [b] Cyclization of *(4c)* commenced at room temperature; *(3c)* was not isolated but could be detected in the reaction mixture.

The surprising rearrangement of *(2)* to *(3)* was confirmed by X-ray structure analyses[5] of *(2a)* and *(3a)* (Fig. 1).

The results of these studies indicate that *(2a)* and *(3a)* have *syn*-configurations (relative to N1—S2) and can readily undergo cyclization. An explanation for selectivity of *(3)* in cyclization reactions is provided by the structural data. The N2—S2—N3 bond lengths in *(2a)* and *(3a)* are considerably different (166 and 160 pm, and 161 and 169 pm, respectively); the marked double bond character of the N1—C7 bond in *(3a)*, relative to that of *(2a)*, is indicated by shortening of this bond from 142 to 134 pm. The different position of the carboxylic ester group causes a shift in the bonding electron density in *(3a)*, which in the N1-to-N3-section of the molecule leads to alternating long and short bonds. This influences the nucleophilicity and increases the acidity at N1. Moreover, the thermolability of the isomer *(2)* in the basic media is presumably important: decomposition of *(2)* begins even at 40 °C.

The $^1$H-NMR spectra are in accord with the molecular geometries of *(2)* and *(3)*. A considerably larger low-field shift of the *N*-alkyl protons in *(3)* relative to those of *(2)* is observed; the same, but less intense effect is observed with *S*-alkyl protons[6].

The structural assignment of the thiatriazinones *(4)* is supported not only by the NMR data (significant low-field shift of the *N*-alkyl protons (Table 1), which is comparable to that of previously known thiatriazinones[7]), but also by IR- (*inter alia* an NH-bond is absent) and mass-spectroscopy.

Received: April 8, 1981 [Z 882 IE]
German version: Angew. Chem. *93*, 916 (1981)

---

[*] Dr. R.-D. Acker [+], Dr. G. Hamprecht
BASF Aktiengesellschaft, Hauptlaboratorium, D-ZHP, B1
D-6700 Ludwigshafen (Germany)
Dr. E. Hädicke
BASF-Ammoniaklaboratorium

[+] Author to whom correspondence should be addressed.

CAS Registry numbers:
*(1a)*, 79101-85-2; *(1c)*, 79101-96-3; *(1e)*, 79101-87-4; *(2a)*, 79101-88-5; *(2b)*, 79101-89-6; *(2c)*, 79101-90-9; *(2d)*, 79101-91-0; *(2e)*, 79101-92-1; *(3a)*, 79101-93-2; *(3b)*, 79101-94-3; *(3c)*, 79101-95-4; *(3d)*, 79101-96-5; *(3e)*, 79101-97-6; *(4a)*, 79101-98-7; *(4b)*, 79101-99-8; *(4c)*, 79102-00-4; *(4d)*, 79102-01-5; *(4e)*, 79102-02-6; *N*-methylsulfamic acid, 4112-03-2; *N*-ethylsulfamic acid, 4626-94-2; *N*-benzylsulfamic acid, 46119-69-1

---

[1] a) Review: *A. Lawson, R. B. Tinkler*, Chem. Rev. *70*, 593 (1970); b) *H. Teufel*, US-Pat. 3041366 (1962); Chem. Abstr. *62*, 14705g (1965); c) *W. J. Houlihan*, US-Pat. 3278532 (1964); Chem. Abstr. *65*, P20154c (1965).

[2] *G. Hamprecht, K. H. König, G. Stubenrauch*, Angew. Chem. *93*, 151 (1981); Angew. Chem. Int. Ed. Engl. *20*, 151 (1981).

[3] The compounds *(1)* were prepared by reaction of the corresponding *S*-alkyl-*N*-phenylisothioureas with methyl chloroformate and 1 equiv. of 10 N NaOH in $CH_2Cl_2$.

[4] All the compounds described gave correct elemental analyses and satisfactory IR- and $^1$H-NMR-spectra.

[5] *(2a)*: $P2_1/c$, $a=1044.2(2)$, $b=803.7(2)$, $c=2055.7(4)$ pm, $\beta=91.24(2)°$, $Z=4$, Syntex-P2$_1$ diffractometer, $Cu_{K\alpha}$ irradiation, 1853 observed ($I>2\sigma_I$), non-corrected reflections, $2\theta<115°$, $R=0.043$; *(3a)*: $P1$, $a=894.4(3)$, $b=1066.1(3)$, $c=1106.8(4)$ pm, $\alpha=94.22(3)$, $\beta=92.02(3)$, $\gamma=128.98(3)°$, $Z=2$, Syntex-P2$_1$ diffractometer, $Cu_{K\alpha}$ irradiation, 2040 observed ($I>2\sigma_I$), corrected reflections at $-60$ °C, $2\theta<115°$, $R=0.047$.

[6] Examples: *(2e)*: $\delta=1.20$ (d, 6 H), 3.70 (m, 1 H), 3.75 (s, 3 H), 4.12 (s, 2 H), 7.25 (m, 10 H); *(3e)*: $\delta=1.32$ (d, 6 H), 4.57 (m, 1 H), 3.72 (s, 3 H), 4.30 (s, 2 H), 7.40 (m, 10 H). Dr. *H. Bremser* is thanked for the NMR spectra.

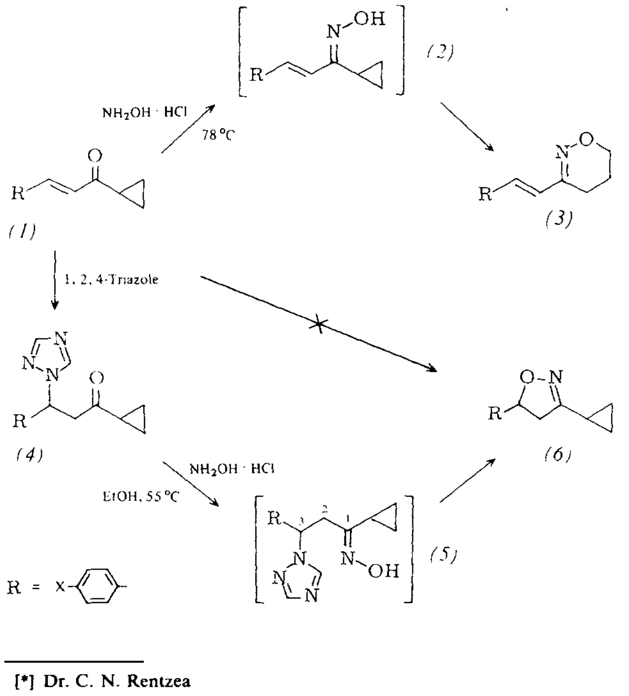
[7] *J. A. Kloek, K. Leschinsky*, J. Org. Chem. *43*, 3824 (1978); *T. Bartholomew, I. T. Kay*, J. Chem. Res. *1977*, 2813.

## 4,5-Dihydroisoxazoles from Cyclopropyl Ketone Oximes[**]

By *Costin N. Rentzea*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

Cyclopropyl styryl ketones *(1)* and the corresponding oximes *(2)* rearrange to 5,6-dihydro-4*H*-1,2-oxazines *(3)* on heating in the presence of hydroxylammonium chloride[1]. Cyclizations of *(1)* or *(2)* to give isoxazole derivatives have not so far been observed under these conditions.



We have, however, been able to prepare the 4,5-dihydroisoxazoles *(6)* in the following way: (i) by addition of 1,2,4-triazole to the double bond of *(1)* to give *(4)*[2] [*(4a)*, X=$CH_3$, m.p. 65 °C; *(4b)*, X=Cl, m.p. 82 °C], and (ii) reaction of the *p*-substituted 1-cyclopropyl-3-phenyl-3-(1,2,4-triazol-1-yl) 1-propanone *(4)* under mild conditions (1 h at 55 °C in ethanol; *(4)*: $NH_2OH\cdot HCl=1:1.5$) to give the corresponding *p*-substituted 3-cyclopropyl-5-phenyl-4,5-dihydroisoxazoles *(6)* (see Table 1).

Table 1. Some data of the dihydroisoxazoles *(6)* obtained from the ketones *(4)*. IR in KBr, $^1$H-NMR in $CDCl_3$, TMS int.

*(6a)*, X=$CH_3$; yield 46%, m.p. 160 °C; $^1$H-NMR: $\delta=0.65$ (s, 2 H), 0.9 (s, 2 H), 1.75 (m, 1 H), 2.25 (s, 3 H), 2.5 (AB system, 2 H), 4.1 (split. d, 1 H), 6.9—7.5 (m, 4 H); IR: 1556, 1248, 976, 945, 808 $cm^{-1}$.
*(6b)*, X=Cl; yield 50%, m.p. 152 °C; $^1$H-NMR: $\delta=0.75$ (s, 2 H), 0.85 (s, 2 H), 1.7 (m, 1 H), 2.6 (AB system, 2 H), 4.05 (split d, 1 H), 7.1—7.5 (m, 4 H); IR: 1482, 1222, 1084, 985, 950, 805 $cm^{-1}$.

During the course of the reaction *(4)*→*(6)* the intermediary oximes *(5)*[3] appear on the thin-layer chromatogram ($CHCl_3$ : acetone = 9 : 1). The triazole ring in *(5)* is protonated even more rapidly than the cyclopropane ring. Hence an extremely good leaving group exists on C-3 which is subsequently readily replaced by the oxime oxygen with formation of the dihydroisoxazole *(6)*.

Received: March 19, 1981 [Z 880 IE]
German version: Angew. Chem. *93*, 913 (1981)

CAS Registry numbers:
*(1a)*, 56105-34-1; *(1b)*, 56105-33-0; *(4a)*, 79084-00-7; *(4b)*, 79084-01-8; *(6a)*, 79084-02-9; *(6b)*, 79084-03-0

---

[1] *C. N. Rentzea*, Angew. Chem. *92*, 195 (1980); Angew. Chem. Int. Ed. Engl. *19*, 199 (1980).

[2] *R. H. Wiley, N. R. Smith, D. M. Johnson, J. Moffat*, J. Am. Chem. Soc. *77*, 2572 (1955); *C. N. Rentzea, E. H. Pommer, B. Zeeh*, DOS 2634511 (1977), BASF; Chem. Abstr. *88*, 165478s (1978).

[3] *C. N. Rentzea, H. Sauter, B. Zeeh, G. Heilen, J. Jung*, DOS 2842801 (1980), BASF; Chem. Abstr. *93*, 114537f (1980).

---

[*] Dr. C. N. Rentzea
BASF Aktiengesellschaft, Hauptlaboratorium,
D-6700 Ludwigshafen (Germany)

[**] Oximes, Part 2.—Part 1: [1].

## Base Catalyzed Asymmetric Induction of the Reaction of Methyl(phenyl)ketene with 1-Phenylethanol: Method of Obtaining Hydratropic Acid in High Enantiomeric Purity

By *Joachim Jähme* and *Christoph Rüchardt*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

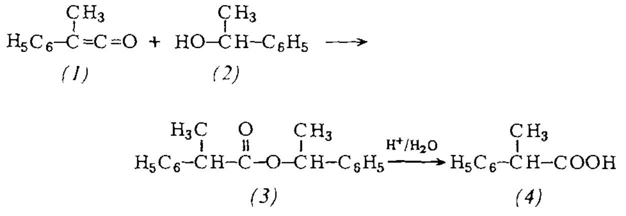
Chiral, secondary alcohols can react stereoselectively with non-symmetrically substituted ketenes to yield esters[1,2]. Asymmetric induction also occurs if the ketene is reacted with methanol or other achiral alcohols, catalyzed by chiral tertiary amines such as acetyl quinine[2,3].

We now report on the stereoselective formation of the 1-phenylethyl hydratropate ester *(3)* from methyl(phenyl)ketene *(1)* and 1-phenylethanol *(2)*, and on the novel drastic increase in the stereoselectivity caused by addition of achiral bases such as pyridine and 1,4-diazabicyclo[2.2.2]octane. This discovery enables hydratropic acid *(4)* to be obtained in high enantiomeric purity.

(*S*)-(–)-*(2)* or *rac-(2)* and the base were dissolved in toluene or ether under an argon atmosphere in one limb of a

---

[*] Prof. Dr. C. Rüchardt, Dipl.-Chem. J. Jähme
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)



$$H_5C_6-\overset{\overset{CH_3}{|}}{C}=C=O + HO-\overset{\overset{CH_3}{|}}{C}H-C_6H_5 \longrightarrow$$

*(1)* *(2)*

$$H_5C_6-\overset{\overset{H_3C}{|}}{C}H-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{CH_3}{|}}{C}H-C_6H_5 \xrightarrow{H^+/H_2O} H_5C_6-\overset{\overset{CH_3}{|}}{C}H-COOH$$

*(3)* *(4)*

Schlenck tube, the other limb of which contained a solution of *(1)* in the same solvent. The Schlenck tube was thermostated and the solutions rapidly mixed until *(1)* was decolorized. After concentration *in vacuo* the diastereomeric ratio of the ester *(3)* was determined by GC (4 m, 1% Reoplex 400 on Chromosorb W/HP, 80—100 mesh, 150 °C)[4].

Table 1. Diastereomeric ratio of ester *(3)* in the reaction of methylphenylketene *(1)* with racemic 1-phenylethanol *(2)* in toluene, with or without addition of base.

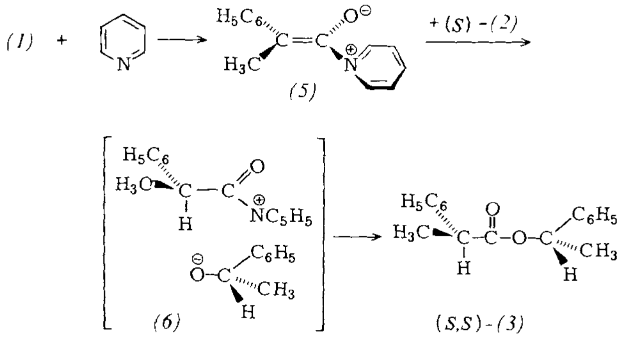
| Expt. No. | $c_0$ *(2)* [mol/L] | Base [a] | *(1)*:*(2)*:Base Mol-ratio | *T* [°C] | *(3)* *threo*:*erythro* [b] |
|---|---|---|---|---|---|
| 1 | 1.0 | — | 1:50 | 25 | 71:29 |
| 2 | 0.2 | — | 1:40 | 25 | 60:40 |
| 3 | 1.0 | — | 1:10 | 25 | 63:37 |
| 4 | 1.0 | Py | 1:10:5 | 25 | 84:16 |
| 5 | 1.0 | Py | 1:10:1 | 25 | 84:16 |
| 6 | 1.0 | Py | 1:10:1 [c] | 25 | 84:16 |
| 7 | 1.0 | Py | 1:10:0.1 | 25 | 82:18 |
| 8 | 1.0 | Py | 1:1:1 | 25 | 83:17 |
| 9 | 0.1 | Py | 1:1:1 | 25 | 84:16 |
| 10 | 0.1 | Py | 1:1:0.6 | 25 | 87:13 |
| 11 | 0.1 | Py | 1:1:0.1 | 25 | 86:14 |
| 12 | 0.1 | Py | 1:10:1 | 25 | 81:19 |
| 13 | 0.1 | Py | 1:1:1 | −40 | 89:11 |
| 14 [d] | 0.1 | Py | 1:1:1 | −40 | 88:12 |
| 15 | 0.1 | Py | 1:1:1 [c] | −40 | 90:10 |
| 16 | 0.1 | Py | 1:1:1 [c] | −80 | 91:9 |
| 17 | 0.1 | Py | 1:10:20 | −40 | 90:10 |
| 18 [d] | 0.1 | Py | 1:10:20 | −40 | 89:11 |
| 19 | 0.1 | DABCO | 1:1:1 | −40 | 90:10 |
| 20 | 0.1 | 4-Pic | 1:1:1 | −40 | 89:11 |
| 21 | 0.1 | NEt₃ | 1:1:1 | −40 | 86:14 |
| 22 | 0.1 | DMA | 1:1:1 | −40 | 76:24 |
| 23 | 0.1 | DIEA | 1:1:1 | −40 | 72:28 |
| 24 | 0.1 | 2,6-Lu | 1:1:1 | −40 | 66:34 |
| 25 | 0.1 | DMPP | 1:1:1 | −40 | 60:40 |
| 26 | 0.1 [e] | Py | 1:1:1 | −40 | 88:12 |
| 27 | 0.1 [e] | Py | 1:10:20 | −40 | 87:13 |
| 28 [d] | 0.1 [e] | Py | 1:10:20 | −40 | 87:13 |

[a] Py = Pyridine; DABCO = 1,4-Diazabicyclo[2.2.2]octane; 4-Pic = 4-Picoline; $NEt_3$ = Triethylamine; DMA = *N,N*-Dimethylaniline; DIEA = Diisopropyl(ethyl)amine; 2,6-Lu = 2,6-Lutidine; DMPP = Dimethyl(phenyl)phosphane. [b] (*R,R*)+(*S,S*):(*R,S*)+(*S,R*). [c] Inverse reaction conditions: base and *(1)* were mixed and then treated with *(2)*. [d] Experiment with (*S*)-(−)-*(2)*. [e] Experiment in diethyl ether.

The results are shown in Table 1. In all cases, the *threo*-diastereomer [(*S,S*)- and/or (*R,R*)-configuration] is formed in higher yield than the *erythro*-compound [(*R,S*)- and/or (*S,R*)-diastereomer].

Whereas the stereoselectivity of the non-catalyzed reaction of *(1)* and *(2)* is dependent both on the initial concentrations (experiments 1 and 2) and on the ratio of *(1)*:*(2)* (experiments 1 and 3), it was only slightly influenced by the same parameters under pyridine catalysis, which also has a large rate enhancing effect (cf. experiments 8 and 9, 5 and 12). The diastereomeric ratio of *(3)* hardly changed when the reaction was conducted under inverse conditions (cf. experiments 5 and 6, as well as 13 and 15) or when a deficiency of base was used. The reaction proceeded more selectively at low temperatures (experiments 13—18) than at 25 °C; changing the solvent from toluene to ether (experiments 26—28) has no marked influence. Use of (*S*)-(−)-*(2)* results in the same diastereomeric ratio as found with racemic *(2)* (cf. experiments 13 and 14, 17 and 18 as well as 27 and 28). The stereoselectivity depends largely on the catalytic base (experiments 19—25). In nitrogen bases, bulky groups and low basicity can be recognized as factors which reduce the selectivity. The use of dimethyl(phenyl)-phosphane as base leads to low selectivity.

When the reaction of (*S*)-(−)-*(2)* ($c_0$ = 0.064 mol/L) with *(1)* and pyridine was conducted in toluene in the molar ratio 1:1:1.1 at 0 °C, the diastereomeric mixture of *(3)* was isolated in 77% yield (by GC (*S,S*):(*R,S*) = 88:12), from which the pure (*S,S*)-diastereomer *(3)* was obtained by one recrystallization from *n*-pentane. Hydrolysis of the crude product with conc. HCl yielded (*S*)-(+)-hydratropic acid (*S*)-(+)-*(4)* with $[\alpha]_D^{22}$ (acetone) + 69.9[5]. This corresponds to 73.2% optical purity, or to an enantiomeric ratio of 87:13 which is in accord with the results in Table 1. Since (*S*)-(−)-1-phenylethanol *(2)* can be reisolated, it serves merely as an optically active auxiliary agent: hydratropic acid can be obtained in this way in high enantiomeric purity by a single recrystallization from *(3)*. In addition, the isolation of the unstable ketene *(1)* can be avoided if it is prepared *in situ* from hydratropaoyl chloride and triethylamine in toluene (molar ratio 1:1, 2 h, 25 °C), and then treated with pyridine and (*S*)-*(2)* (molar ratio 1:1:1) at 0 °C. After 1 h, 59% *(3)* in the diastereomeric ratio (*S,S*):(*R,S*) = 79:21 was isolated.



The fact that almost the same stereoselectivity was obtained with racemic 1-phenylethanol *(2)* as with optically active *(2)*, suggests that the transfer of the proton and the alcoholate to one molecule of ketene *(1)* proceeds from one and the same molecule *(2)* and, hence, that the proton transfer is the descisive enantioselective step. We assume that an enolbetaine, which presumably has the configuration *(5)*, is initially formed from *(1)* and pyridine. This takes over a proton from (*S*)-*(2)* preferentially "from below", forming the ion-pair *(6)*, which by analogy to ion-recombination is acylated to *(3)* in a fast consecutive step. Even in the polar solvent ether dissociation of the ion-pair *(6)* apparently does not compete; in the reaction of *rac-(2)* this ion pair dissociation would lead to a change in stereoselectivity[6] because the acylation step would then be selectivity determining. At present we are investigating the scope of the application of this method and the possibility of applying the principle of stereoselective proton transfer[8] to other molecules.

Received: March 10, 1980;
supplemented: July 5, 1981 [Z 885 IE]
German version: Angew. Chem. 93, 919 (1981)

CAS Registry numbers:
*(1)*, 3156-07-8; *(S)-(2)*, 1445-91-6; *(±)-(2)*, 13323-81-4; *(R,R)-(3)*, 79121-13-4; *(R,S)-(3)*, 79121-14-5; *(S,R)-(3)*, 79121-15-6; *(S,S)-(3)*, 79121-16-7; *(S)-(4)*, 7782-24-3

---

[1] a) *E. Anders, E. Ruch, I. Ugi*, Angew. Chem. *85*, 16 (1973); Angew. Chem. Int. Ed. Engl. *12*, 25 (1973); b) see also *H. Pracejus*, Justus Liebigs Ann. Chem. *634*, 23 (1960).

[2] *H. Pracejus*, Fortschr. Chem. Forsch. *8*, 493 (1967).

[3] a) *H. Pracejus, G. Kohl*, Justus Liebigs Ann. Chem. *722*, 1 (1969); b) *H. Pracejus, ibid. 634*, 9 (1960); c) *T. Yamashita, H. Yasueda, Y. Miyauchi, N. Nakamura*, Bull. Chem. Soc. Jpn. *50*, 1532 (1977); *T. Yamashita, H. Yasueda, N. Nakamura, ibid. 52*, 2165 (1979).

[4] Diastereomeric ratios of >9 : 1 cannot readily be differenciated using this method.

[5] (*R*)-(−)-Hydratropic acid has the maximum rotation $[\alpha]_D^{25}$ −95.5 ($c$ = 1.5, acetone); *A. Fredga*, Ark. Kemi *7*, 241 (1955).

[6] The alternative interpretation [7] of the results, that racemic *N*-(2-phenylpropionyl)pyridinium ions are formed from *(4)* in an equilibrium reaction with subsequent acylation of *(2)*, is currently being investigated.

[7] Prof. *J. Kampmeier* is thanked for this suggestion.

[8] See *e.g. H. Matsushita, M. Noguchi, M. Saburi, S. Yoshikawa*, Bull. Chem. Soc. Jpn. *48*, 3715 (1975); *L. Duhamel*, C. R. Acad. Sci. *C 282*, 125 (1976).

# Experimental Electron Density Determination of a Dimetallacyclopropane-Type μ-Methylene Complex[**]

By *Dore Augusto Clemente, Bernard Rees, Giuliano Bandoli, Marina Cingi Biagini, Barbara Reiter,* and *Wolfgang A. Herrmann*[*]

There is now firm evidence that bridging methylene units play a pivotal role in the metal surface catalyzed gas-phase decomposition of diazomethane; even more importantly, reactive μ-methylene surface complexes appear to dominate the mechanism of the Fischer-Tropsch synthesis[1,2]. *Hofmann et al.*[3a,b] and *Lichtenberger et al.*[3c] have presented detailed MO calculations, according to which the methylene bridge carbon atoms carries a high negative charge.

In order to substantiate this prediction, we have now carried out an experimental X-ray diffraction electron density determination of the prototype dimetallacyclopropane compound *(1)* first prepared by us in 1975[4].

The molecule *(1)* (Fig. 1, Table 1) consists of two equivalent fragments related by a $C_2$ axis passing through the C(3) atom and the middle of Mn—Mn. Each cyclopentadienyl ring is planar within experimental accuracy, and is situated on one side of the dimetallacyclopropane plane, while the carbonyl atoms C(1) and C(2) lie on the other side at 120 and 137 pm, respectively, from this plane. The angles C(1)—Mn—$C_c$, C(2)—Mn—$C_c$, C(3)—Mn—$C_c$ are practically identical (122.0, 121.3 and 121.0°, respectively),

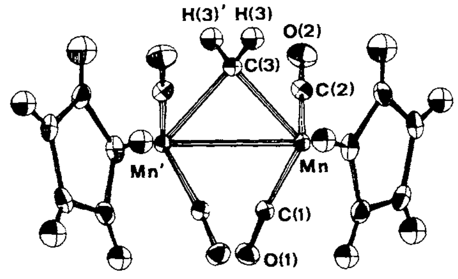


Fig. 1. Molecular Structure of μ-Methylene-bis[dicarbonyl($\eta^5$-cyclopentadienyl)manganese] *(Mn—Mn)* at 130°K. Two crystals were cut into spheres of 0.28 and 0.33±0.02 mm diameter, covered with Loctite®, and sealed in a Lindeman glass capillary. Low-temperature X-ray diffraction data were collected on a Philips PW-1100 diffractometer ($Mo_{K\alpha}$ radiation, Leyboldt Heraeus NCD-1 cooling device). The temperature at the crystal (Chromel/Alumel thermocouple) was maintained at 130°K by means of a stream of $N_2$ gas; space group Pccn, unit cell parameters $a$ = 716.1(4), $b$ = 1517.7(6), and $c$ = 1270.3(6) pm (mean of two crystals). *Ca.* 7500 and 14000 reflections were measured with the two spherical crystals, respectively (for the second, at least two symmetry equivalents for each reflection), and averaged to 6986 independent reflections. The intensities, corrected for Lorentz, polarization and absorption effects, were correlated with each other using least-squares techniques. The structure was solved by repeated Fourier and Patterson syntheses and refined by least-squares methods, using the 4283 reflections with $I \geq 3\sigma(I)$; positional and thermal parameters were refined for all atoms (isotropic parameters only for H atoms); a secondary isotropic extinction dominated by mosaic spread with a Lorentzian distribution function was assumed, but the corresponding $g$ parameter proved to be very small and was later disregarded. Final $R$ values for the full set of data: $R(F)$ = 0.040, $R(F^2)$ = 0.059, and $S(F^2)$ = 1.89.

Table 1. Selected Bond Distances [pm] and Angles [°] of *(1)* [a].

| | | | |
|---|---|---|---|
| Mn—Mn' | 279.9(0) | Mn—C(3)—Mn' | 87.4(1) |
| Mn—C(1) | 179.3(1) | C(3)—Mn—Mn' | 46.3(0.5) |
| Mn—C(2) | 177.8(1) | C(1)—Mn—Mn' | 80.2(0.5) |
| Mn—C(3) | 202.6(1) | C(2)—Mn—Mn' | 106.5(0.5) |
| Mn—$C_{Cp}$ [b] | 216.1 | C(1)—Mn—C(2) | 86.5(0.5) |
| Mn—$C_c$ | 179.4 | C(1)—Mn—C(3) | 113.8(0.5) |
| C(1)—O(1) | 116.0(2) | C(2)—Mn—C(3) | 77.6(0.5) |
| C(2)—O(2) | 115.3(2) | Mn—C(1)—O(1) | 172.8(1) |
| C(3)—H(3) | 93(2) | Mn—C(2)—O(2) | 178.9(1) |
| $C_{Cp}$—$C_{Cp}$ [b] | 141.7 | H(3)—C(3)—H(3)' | 108.8(1.5) |
| $C_{Cp}$—$H_{Cp}$ [b] | 94 | $C_{Cp}$—$C_{Cp}$—$C_{Cp}$ [b] | 108.0 |

[a] Uncorrected for thermal motions; $C_c$ denotes the centroid of the π-bonded cyclopentadienyl ligands (Cp). [b] Average value.

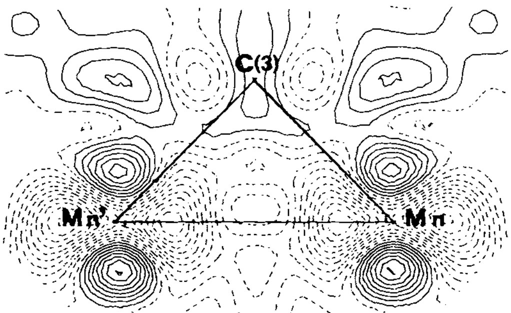


Fig. 2. Section of the *X—X* deformation density through the dimetallacyclopropane plane (Mn—C(3)—Mn'). Contour interval: 0.1 eÅ$^{-3}$. Dashed contours for negative deformation density. Resolution: $2\sin\vartheta_{max}/\lambda$ = 1.41 Å$^{-1}$ ($\theta_{max}$ = 30°). The average standard deviation of the *X—X* deformation density is 0.07 eÅ$^{-3}$.

---

[*] Dr. D. A. Clemente [+], Dr. B. Rees
Institut de Chimie, Université Louis Pasteur,
Laboratoire de Cristallochimie et Chimie Structurale
F-67070 Strasbourg-Cédex (France)

Dr. G. Bandoli, Prof. Dr. M. Cingi Biagini
Istituto di Chimica Generale ed Inorganica
Via M. d'Azeglio 85, I-43100 Parma (Italy)

Prof. Dr. W. A. Herrmann, B. Reiter
Institut für Anorganische Chemie der Universität
Universitätstrasse 31, D-8400 Regensburg 1 (Germany)

[+] Present address: Istituto di Chimica e Tecnologia dei Radioelementi C.N.R.
Corso Stati Uniti, I-35100 Padova (Italy)

[**] Transition-Metal-Methylene Complexes, Part 21. This work was supported by CNR Grant No. 780.176.803 and the Deutsche Forschungsgemeinschaft.—Part 20: *Ch. Bauer, W. A. Herrmann*, J. Organometal. Chem. *209*, C 13 (1981).

while the angle Mn—Mn′—$C_c$ is 126.7°. Thus, the overall geometry very much resembles that of the related $(\eta^5\text{-}C_5H_5)Mn(CO)_3$ compound[5].

To ascertain if there is an accumulation of electron density between the two metal centers or whether the two mononuclear fragments are bonded *via* multicentered linkages between the metal atoms and the methylene bridge[3c], we have calculated a preliminary *X*—*X* deformation density map in the Mn—C(3)—Mn′ plane (Fig. 2). The subset consisting of low order *(LO)* reflections up to $\sin\vartheta/\lambda = 0.71$ Å$^{-1}$ ($\vartheta_{max} = 30°$) was used in the calculations of deformation densities computed with the Fourier coefficients $\Delta F = F_0(LO) - F_c(HO)$; the atomic parameters of the structural model used in the calculation of $F_c(HO)$ ($HO$ = high order) were obtained from high-order ($30° < \vartheta < 50°$) refinement. Interestingly, the deformation density map shows no accumulation of density along the Mn—Mn′ vector — being near to zero ($-0.02$ eÅ$^{-3}$) between the Mn atoms, in contrast to quantum chemical calculations which indicate direct bonding interactions between the two metal atoms of dimetallacyclopropane-type frameworks[3,6]. This is quite analogous to the observation made for $Mn_2(CO)_{10}$[7] and is probably related to insufficient overlap of the corresponding metal orbitals in a long metal-metal bond[8]. On the other hand, a significant charge gradient is found along the Mn—C(3) bond, with a region of charge accumulation close to the bridging carbon atom. In this respect the $CH_2$-bridged compound *(1)* hardly differs from the CO-bridged compound $(\mu\text{-}CO)_2[(\eta^5\text{-}C_5H_5)Fe(CO)]_2$[9], except that in *(1)* the charge accumulation in the carbon lone pair region appears smaller. A possible explanation is that the position of C(3) determined by least-squares refinement does not coincide exactly with the actual position of this atom. By way of contrast, a smaller shift is expected for a carbonyl bridge, the "lone pair" charge accumulation being compensated by the strong charge accumulation on the CO bond.

The finding that the methylene carbon is situated in a region of high charge density is in accord with earlier MO calculations and is also consistent with NMR results on dimetallacyclopropanes[1]. An effective charge transfer from the metal center to the methylene ligands is evident from parameter-free Fenske-Hall calculations which yield a methylene carbon atomic charge of $-0.526$ eÅ$^{-3}$[3c]; a similar value ($-0.78$ eÅ$^{-3}$) results from a SCCCMO treatment of *(1)*[6]. The latter method attributes a charge of $-0.92$ eÅ$^{-3}$ to the entire $CH_2$ fragment. These results, and those obtained from the EHMO analysis performed by *Hofmann*[3a,b], appear quite consonant and emphasize that nucleophilic reactions at the methylene bridge must come to the fore unless the reactivity of these systems is governed by the nature of the metal-metal bond itself[10].

Received: February 11, 1981 [Z 886 IE]
German version: Angew. Chem. *93*, 920 (1981)

CAS Registry number:
*(1)*, 57603-41-5

---

[1] Reviews: a) *W. A. Herrmann*, Angew. Chem. *90*, 855 (1978); Angew. Chem. Int. Ed. Engl. *17*, 800 (1978); b) Advan. Organometal. Chem., in press; c) Pure Appl. Chem., in press.

[2] *R. C. Brady III, R. Pettit*, J. Am. Chem. Soc. *102*, 6181 (1980); cf. [1b].

[3] a) *P. Hofmann*, Angew. Chem. *91*, 591 (1979); Angew. Chem. Int. Ed. Engl. *18*, 554 (1979); b) *A. R. Pinhas, T. A. Albright, P. Hofmann, R. Hoffmann*, Helv. Chim. Acta *63*, 29 (1980); c) *D. Calabro, D. L. Lichtenberger, W. A. Herrmann*, J. Am. Chem. Soc., in press.

[4] *W. A. Herrmann, B. Reiter, H. Biersack*, J. Organometal. Chem. *97*, 245 (1975).

[5] Cf. *M. Creswick, I. Bernal, W. A. Herrmann*, J. Organometal. Chem. *172*, C39 (1979). *M. Creswick, I. Bernal, B. Reiter, W. A. Herrmann*, Inorg. Chem., and references cited therein, in press.

[6] *D. Ajò, M. Casarin, G. Granozzi, I. Fjagalà*, XIII Cong. Naz. Chim. Inorg., Camerino (Italy) 1980, Abstract C15 (CNDO calculation).— SCCCMO calculations: *D. A. Clemente, B. Rees*, unpublished results 1980.

[7] *M. Martin, B. Rees, A. Mitschler*, Acta Crystallogr., in press.

[8] The lack of charge density accumulation on the Mn—Mn bond is most probably associated with the small value of the metal 3d density at the center of the bond. Assuming for example a bonding orbital of the form $(2+2S)^{-1/2}(d+d')$, where $S$ is the overlap between the orbitals $d$ and $d'$ centered on the two metals, the density associated with this at the midpoint would be $4(1+S)^{-1}d^2$ and the deformation density with five 3d electrons of the Mn atom: $2\frac{1-S}{1+S}d^2$. This is only of the order of 0.03 eÅ$^{-3}$. There is also circumstantial NMR evidence for M—M bonds in complexes of this type [1b, c].

[9] *A. Mitschler, B. Rees, M. S. Lehann*, J. Am. Chem. Soc. *100*, 3390 (1978).

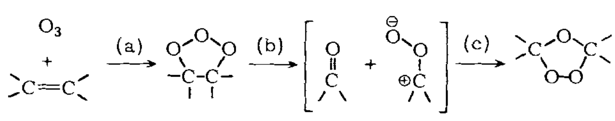
[10] See, for example: a) *W. A. Herrmann, J. Plank, E. Guggolz, M. L. Ziegler*, Angew. Chem. *92*, 660 (1980); Angew. Chem. Int. Ed. Engl. *19*, 651 (1980); b) *W. A. Herrmann, J. Plank, D. Riedel, M. L. Ziegler, K. Weidenhammer, E. Guggolz, B. Balbach*, J. Am. Chem. Soc. *103*, 63 (1981); c) *M. B. Hursthouse, R. A. Jones, K. M. Abdul Malik, G. Wilkinson*, J. Am. Chem. Soc. *101*, 4128 (1979); d) *P. A. Dimas, E. N. Duesler, R. J. Lawson, J. R. Shapley*, J. Am. Chem. Soc. *102*, 7787 (1980).

---

## Stereochemistry of the Ozonolysis of Alkenes: Ozonide- *versus* Carbonyl Oxide-Control

By *Dieter Cremer*[*]

The reaction of ozone with alkenes in non-polar, aprotic solvents essentially proceeds according to the three-step mechanism proposed by *Criegee*[1], namely: (a) formation of primary ozonide *(1)*, (b) decomposition of *(1)* to aldehyde *(2)* and carbonyl oxide *(3)*, (c) recombination of the decomposition products to give the final ozonide *(4)*.



*(1)* *(2)* *(3)* *(4)*

Of particular interest is the reaction step (b), whose energetics and stereochemistry could hitherto not be investigated because of the instability of *(1)* and *(3)*. Whereas *(1)* and *(4)* are each formed in a strongly exothermic reaction, the sign of the energy of reaction step (b) depends upon

Table 1. *Ab-initio* energies of reaction (in kcal/mol) calculated for the ozonolysis of alkenes [a].

| Reaction step | Ethene | Propene | 2-Butene *trans* | 2-Butene *cis* |
|---|---|---|---|---|
| (a) | −49.2 | − 50.5 | − 50.7 | − 51.2 |
| (b) | 13.7 | 6.4 [b] | 1.2 | − 0.2 |
| (c) | −63.1 | − 58.3 | − 55.9 | − 55.1 |
| (a + b + c) | −98.6 | −102.4 | −105.3 | −106.5 |

[a] Correlation-corrected calculations with augmented 6-31G* basis according to the Møller-Plesset perturbation method (2nd order). The absolute energies for the parent compounds are: −224.87683 (ozone), −78.29431 (ethene), −303.34952 *(1)*, −114.17494 *(2)*, −189.05283 *(3)*, −303.32834 Hartree *(4)*. The alkyl effects were calculated according to the Hartree-Fock method. [b] Calculated for the formation of methylcarbonyl oxide and formaldehyde. The formation of acetaldehyde and carbonyl oxide is 2.3 kcal/mol more endothermic.

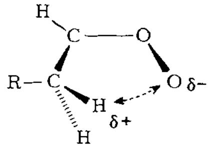
---

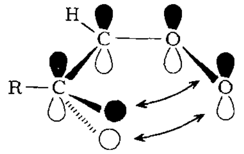
[*] Priv.-Doz. Dr. D. Cremer
Lehrstuhl für Theoretische Chemie
Greinstrasse 4, D-5000 Köln 41 (Germany)

the substituents at the alkene double bond. *Ab initio* calculations (Table 1) show that step (b) in the ozonolysis of ethene proceeds endothermally. The endothermic character of step (b) decreases on going to propene and 2-butene; in the case of 2,5-dimethyl-3-hexene, step (b) is distinctly exothermic[2]. The change in energy of reaction results from the different stabilization of *(1)*, *(2)* and *(3)* by alkyl groups[3-5].

If one assumes, in accord with the Hammond postulate[6], that the transition state is influenced by the product in endothermic reactions but by the educt in the case of exothermic reactions, then two alternatives can be distinguished for reaction step (b).

1) In the case of lower alkenes (ethene, propene, 2-butene) the stereochemistry of step (b) is essentially determined by the electronic properties of the carbonyl oxide that is formed. Quantum-chemical calculations on alkylcarbonyl oxides[4] show that, despite apparently unfavorable repulsion, the *syn*-isomers are 3—4 kcal/mol more stable than the corresponding *anti*-forms. This is ascribed to the attraction between a negatively charged terminal oxygen and positively charged H-atoms of the alkyl substituents. Through space π-bonding interactions (formation of a homoaromatic 6π-system) also contribute to stabilization of the *syn*-form[4].





This effect should also play a role in the transition state of step (b) and should lead—irrespective of the configuration of *(1)*—to preferred formation of *syn-(3)*.

2) In the case of higher alkenes the conformational properties of the primary ozonide *(1)* determine the stereochemistry of step (b). The rules put forward by *Bailey et al.*[7] and *Kuczkowski et al.*[8] can be applied, namely *cis-(1)* preferably decomposes to *anti-(3)*, *trans-(1)* preferably to *syn-(3)*.

According to experimental[1,7,8] and theoretical findings[2] the following statements can be made about the stereochemistry of steps (a) and (c): The formation of *(1)* proceeds stereochemically with retention of the alkene configuration. The final ozonide *(4)*, on the other hand, is formed stereoselectively, *syn-(3)* being preferably incorporated in *trans-(4)*, *anti-(3)* preferably in *cis-(4)*.

The proportion of *cis-* and *trans-(4)* in the product mixture of the ozonolysis is substantially influenced by the stereochemistry of step (b). In the case of "carbonyl oxide-control" (ozonolysis of lower alkenes) predominantly *trans-(4)* is formed—irrespective of the configuration of the alkene[9]. In the case of "ozonide-control" (ozonolysis of higher alkenes) the *cis(trans)*-configuration of the alkene is essentially transferred to the final ozonide *(4)*. These quantum-chemical predictions explain the unusual stereochemistry of the ozonolysis of lower alkenes[1].

Received: February 27, 1981 [Z 868 IE]
German version: Angew. Chem. 93, 934 (1981)

CAS Registry numbers:
Ethene, 74-85-1; propene, 115-07-1; *trans*-2-butene, 624-64-6; *cis*-2-butene 590-18-1

---

[1] *R. Criegee*, Angew. Chem. *87*, 765 (1975); Angew. Chem. Int. Ed. Engl. *14*, 716 (1975); cf. also *P. S. Bailey:* Ozonation in Organic Chemistry, Vol. I, Olefinic Compounds, Academic Press, New York 1978.

[2] *D. Cremer*, J. Am. Chem. Soc. *103*, 3619, 3627, 3633 (1981).

[3] *D. Cremer*, J. Chem. Phys. *70*, 1898, 1911, 1928 (1979).

[4] *D. Cremer*, J. Am. Chem. Soc. *101*, 7199 (1979).

[5] According to Hartree-Fock calculations with augmented 6—31G* basis a methyl group stabilizes ethene by 3, the corresponding primary ozonide *(1)* by 4.3, the carbonyl oxide *(3)* by 11.6, formaldehyde by 9.3, and the final ozone *(4)* by 6.8 kcal/mol.

[6] *G. S. Hammond*, J. Am. Chem. Soc. *77*, 334 (1955); cf. also *A. R. Miller, ibid. 100*, 1984 (1978).

[7] *L. Bauld, J. A. Thompson, C. E. Hudson, P. S. Bailey*, J. Am. Chem. Soc. *90*, 1822 (1968); *P. S. Bailey, T. M. Ferrell, ibid. 100*, 899 (1978).

[8] *R. P. Lattimer, R. L. Kuczkowski, C. W. Gillies*, J. Am. Chem. Soc. *96*, 348 (1974).

[9] The formation of *cis*-cross ozonide (3,5-dimethyl-1,2,4-troxolane) in the ozonolysis of propene [8] cannot be explained in this way. Actually, however, only 4% of cross-ozonide has been observed in this reaction.

---

## On the Structure of the Helical N-Terminus in Alamethicin—α-Helix or $3_{10}$-Helix?[**]

By *Thomas Butters, Peter Hütter, Günther Jung, Norbert Pauls, Heribert Schmitt, George M. Sheldrick*, and *Werner Winter*[*]

In lipid bilayer membranes the polypeptide antibiotics alamethicin *(2)*, suzukacillin and trichotoxin form potential-dependent, ion-conducting pores having discrete conductance values[1]. The study of these model systems could possibly contribute to a better understanding of excitation in nerve membranes, if the molecular structure of the pores made up of oligomers were to be known.

CD and $^{13}$C-NMR spectra of the natural peptide antibiotics and of synthetic analogues have revealed a strongly solvent-dependent α-helix content of 20—40%[2]. A structural prerequisite for pore formation and hemolytic action is the presence of a non-helical C-terminal segment of 6 or 7 amino acid residues together with an N-terminus of 10—12 amino acid residues[3]. Alternating sequences, *e.g.* (Aib-Ala)$_n$ containing the conformationally very restrictive α-aminoisobutyric acid form a very stable α-helix dipole on the polypeptide antibiotics, especially in lipophilic environment.

In several recent works it has been suggested that a $3_{10}$-helix could also be present in alamethicin[4]. For example, an X-ray structure analysis of the N-terminal tetrapeptide of *(2)*, Z-Aib-L-Pro-Aib-L-Ala-OMe has shown that this short peptide forms one turn of a $3_{10}$-helix. The X-ray structural data of Tos-(Aib)$_5$-OMe and Z-(Aib)$_5$-O*t*Bu, each with three type-III β-turns[9], seem also to indicate the presence of a $3_{10}$-helix in the antibiotics[4]. On the other hand, on the basis of conformational calculations, *Burgess* and *Leach*[5] designate Aib as an "obligatory α-helicogenic residue".

Since we have previously been unable to obtain useful single crystals of the natural peptide antibiotics, owing to their microheterogeneity, for spectroscopic and X-ray purposes we have synthesized the model *(1)* of the N-terminal alamethicin helix containing eleven amino acid residues[6].

---

[*] Doz. Dr. W. Winter [+], Dipl.-Chem. T. Butters, Dipl.-Chem. P. Hütter, Dipl.-Chem. N. Pauls
Prof. Dr. G. Jung [+], Dipl.-Chem. H. Schmitt
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)
Prof. Dr. G. M. Sheldrick
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[+] Authors to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Helical undecapeptide *(1)*:
Boc-L-Ala$^1$-Aib$^2$-Ala$^3$-Aib$^4$-Ala$^5$-Glu(OBzl)$^6$-Ala$^7$-Aib$^8$-Ala$^9$-Aib$^{10}$-Ala$^{11}$-OMe

Alamethicin *(2)*:
Ac-Aib$^1$-L-Pro$^2$-Aib$^3$-Ala$^4$-Aib$^5$-Ala(or Aib)$^6$-Gln$^7$-Aib$^8$-Val$^9$-Aib$^{10}$-Gly$^{11}$-Leu$^{12}$-Aib$^{13}$-Pro$^{14}$-Val$^{15}$-Aib$^{16}$-Aib$^{17}$-Glu$^{18}$-Gln$^{19}$-Pheol$^{20}$

Aib = α-aminoisobutyric acid (2-methylalanine), Pheol = L-phenylalaninol, Ac = acetyl, Boc = *tert*-butyloxycarbonyl, Bzl = benzyl, Me = methyl

Single crystals of *(1)* could be grown from dichloromethane/hexane, but they disintegrated within seconds in absence of the mother liquor. However, with two "surviving" crystals we were able to collect several data sets with a four-circle diffractometer[7]. After numerous unsuccessfull attempts with the usual program systems, solution of the structure by direct methods ($P2_1$, 90 atoms other than hydrogen) was achieved with a new random phase refinement + E-Fourier recycling program[8]. The present state of the isotropic structure refinement is $R = 0.12$ (4327 reflections with $F \geqslant 3\sigma(F)$, 6 dichloromethane solvent molecules per unit cell).

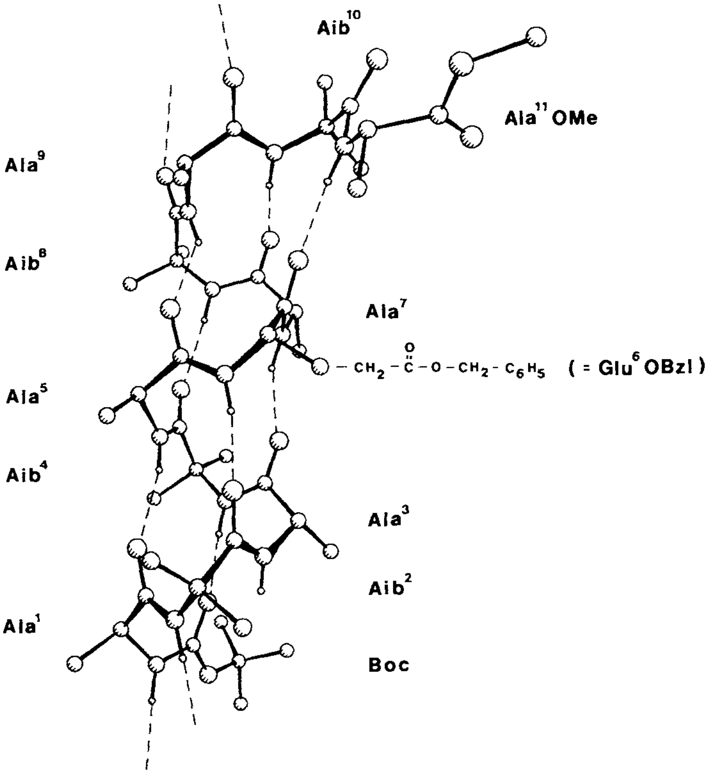


Fig. 1. Perspective view of the peptide skeletal framework of *(1)*. For sake of clarity, the atoms of the Glu$^6$(OBzl) side chain have been omitted. Intra- and intermolecular H-bonding is shown by dotted lines.

Nine of the eleven amino acids of *(1)* are part of an α-helix, only the two C-terminal amino acids Aib$^{10}$ and Ala$^{11}$ are bent away by a β-turn (Fig. 1). The carbonyl groups of Aib$^8$ and Ala$^9$ are thereby situated on the periphery of the molecule and act as acceptors for intermolecular H-bonding with the NH-groups of Ala$^1$ and Aib$^2$ of a neighboring molecule. The α-helices coupled head-to-tail in this way form antiparallel chains.

On the basis of the crystal structure of *(1)* we can assume that no $3_{10}$-, but α-helix conformations are present in the antibiotics alamethicin, suzukacillin and trichotoxin. Only the last three N-terminal amino acids of *(2)*, Ac-Aib$^1$-Pro$^2$-Aib$^3$-, can close the α-helix like a β-turn[2,3].

The CD spectrum of undecapeptide *(1)* in solution showed the typical Cotton effects for a α-helix, and the $^{13}$C-NMR spectrum showed the pronounced magnetic non-equivalence of the geminal Aib-$C_\beta$ atoms due to the helix dipole, which was also observed in the natural peptides and their analogues[2,3,6]. An antiparallel arrangement of the helices of aggregated alamethicin molecules is also possible in the lipid membrane; the opening of an ion-conducting pore could be caused by high local field strengths occurring during an action potential and may include a parallel arrangement of the helices. In experiments with planar lipid membranes, beside the potential-dependent pore formation, an additional but only weak potential-dependent conductivity was observed[1]. This could be explained in terms of aggregates of parallel helices.

Received: March 9, 1981 [Z 871 IE]
German version: Angew. Chem. *93*, 904 (1981)

CAS Registry numbers:
*(1)*, 79083-85-5; *(2)*, 27061-78-5

---

[1] *G. Boheim, H. A. Kolb*, J. Membr. Biol. *38*, 99 (1978), and references cited therein; *B. Sakmann, G. Boheim*, Nature *282*, 336 (1979); *G. Boheim, K. Janko, D. Leibfritz, T. Ooka, W. A. König, G. Jung*, Biochim. Biophys. Acta *433*, 182 (1976); *G. Boheim, G. Irmscher, G. Jung, ibid. 507*, 485 (1978).

[2] *G. Jung, N. Dubischar, D. Leibfritz*, Eur. J. Biochem. *54*, 395 (1975); *W. Mayr, R. Oekonomopulos, G. Jung*, Biopolymers *18*, 425 (1979); *W. Mayr, G. Jung*, Liebigs Ann. Chem. *1980*, 1489; *R. Oekonomopulos, G. Jung*, Biopolymers *19*, 203 (1980).

[3] *G. Jung, H. Brückner, R. Oekonomopulos, G. Boheim, E. Breitmaier, W. A. König* in *E. Gross, J. Meienhofer*: Peptides: Structure and Biological Function, Proc. 6th Am. Pept. Symp. 1978, Pierce Chem. Corp., Rockford 1979, p. 647; *G. Irmscher, G. Jung*, Eur. J. Biochem. *80*, 165 (1977); *H. Brückner, W. A. König, M. Greiner, G. Jung*, Angew. Chem. *91*, 508 (1979); Angew. Chem. Int. Ed. Engl. *18*, 476 (1979).

[4] *N. Shamala, R. Nagaraj, P. Balaram*, Biochem. Biophys. Res. Commun. *79*, 292 (1977); *G. D. Smith, W. L. Duax, E. W. Czerwinski, N. E. Kendrick, G. R. Marshall, F. S. Mathews* in *M. Goodman, J. Meienhofer*: Peptides, Proc. 5th Am. Pept. Symp. 1977, Wiley, New York 1978, p. 277; *N. Shamala, R. Nagaraj, P. Balaram*, J. Chem. Soc. Chem. Commun. *1978*, 996; *E. Benedetti, C. Pedone, C. Toniolo*, Abstr. 16th Eur. Pept. Symp., Copenhagen 1980, p. 150; *R. Nagaraj, N. Shamala, P. Balaram*, J. Am. Chem. Soc. *101*, 16 (1979); see also *B. R. Malcolm*, Biopolymers *16*, 2591 (1977).

[5] *A. W. Burgess, S. J. Leach*, Biopolymers *12*, 2599 (1973).

[6] *H. Schmitt*, Diplomarbeit, Universität Tübingen 1979.

[7] NONIUS CAD4 data sets with $Mo_{K_\alpha}$ as well as $Cu_{K_\alpha}$ radiation (graphite monochromator) at −130 °C (Mo) and room temperature (Cu). The best resolution was achieved with a room-temperature Cu-data set; only these data enabled solution of the phase problem. Figure 1 and the cell constants $a = 10.702(1)$, $b = 24.225(3)$, $c = 13.817(1)$ Å, $\beta = 96.11(6)°$ are also based on this data set.

[8] *G. M. Sheldrick*, 1981, unpublished.

[9] β-Turn (β-bend) is a bend in a peptide chain stabilized by hydrogen bonds.

## Selective Micellar Catalysis with Histidinyl Surfactants of Defined Absolute Configuration[**]

By *John M. Brown, Richard L. Elliott, Colin G. Griggs, Günter Helmchen*, and *Günter Nill*[*]

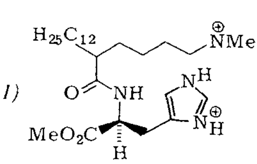
Some time ago[1] it was found that in the presence of micelles of *(1)* the (*S*)-enantiomer of *N*-acetylphenylalanine *p*-

---

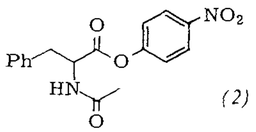
[*] Dr. J. M. Brown, Dr. R. L. Elliott, Dr. C. G. Griggs
Dyson Perrins Laboratory
South Parks Road, Oxford OX1 3QY (England)
Prof. Dr. G. Helmchen, Dr. G. Nill
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] This work was supported by Procter and Gamble, U.K. (partial support for *R. L. E.* and *C. G. G.*) and the Deutsche Forschungsgemeinschaft (Project He 880/6).

nitrophenyl ester *(2)* is hydrolyzed three times faster than the *R*-enantiomer. The absolute configuration at C-5 in *(1)* was unknown and subsequent work[2] has concentrated on varying the histidine moiety. We now report the synthesis of both diastereomers of an analogue of *(1)* and their catalysis of the hydrolysis of the enantiomers of *(2)*.



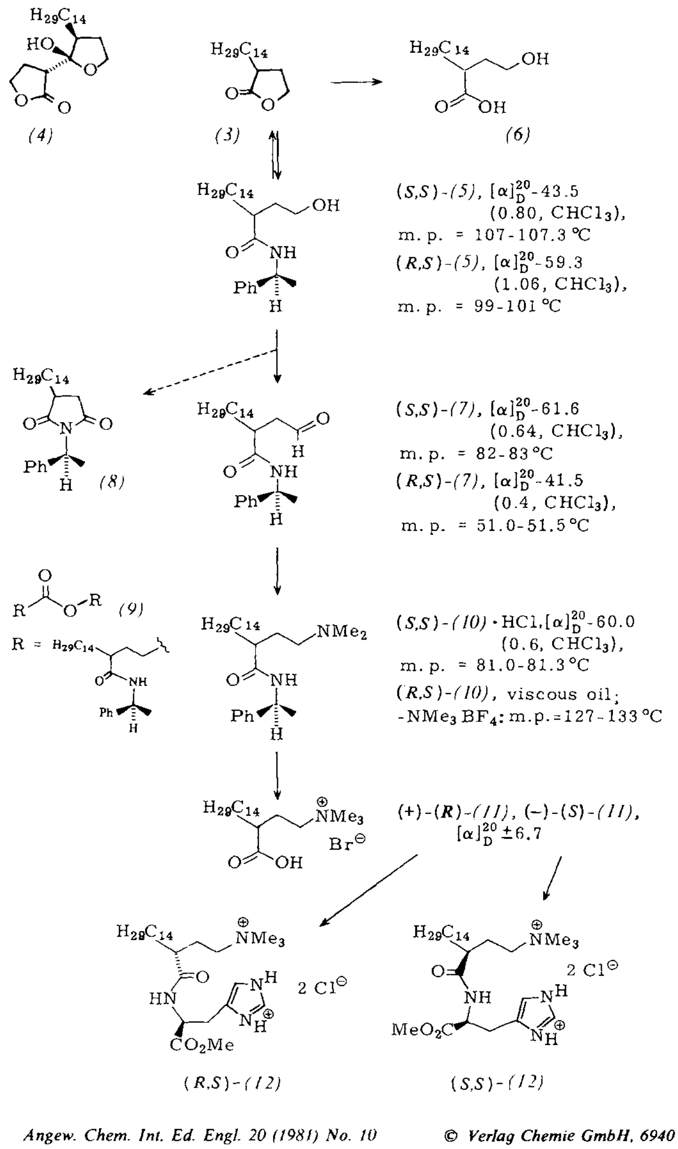
*(1)*



*(2)*

Racemic α-tetradecyl-γ-butyrolactone *(3)* was prepared by alkylation of butyrolactone (lithium diisopropylamide, tetrahydrofuran/hexamethylphosphoric triamide 1 : 1, −40°, $C_{14}H_{29}Br$) and separated from by-product *(4)*[3]. It was efficiently resolved by medium-pressure liquid chromatographic or flash chromatographic[4] separation of the diastereomeric hydroxyamides *(5)* formed by reaction of *(3)* with (−)-(*S*)-α-phenylethylamine and reconversion[5] [(+)-(*S*)-*(3)*: $[\alpha]_D^{20} = +8.17°$ ($c = 10.2$, $CHCl_3$), (−)-(*R*)-*(3)*: $[\alpha]_D^{20} = -8.13$ ($c = 10.0$, $CHCl_3$)]. The absolute configurations are assigned by the resolution method on the basis of many corollaries[5]. All attempts to convert optically pure lactones *(3)* to hydroxycarboxylic acids *(6)* under mild conditions (*e.g.* KOH, MeOH, 0 °C, 30 s) led to partially racemized compounds[6]. Thus the following approach was devised. The diastereomerically pure hydroxyamides *(5)* were oxidized with pyridinium chlorochromate[7] giving the corresponding aldehydes (*R,S*)- and (*S,S*)-*(7)*, purified chromatographically in each case to remove *ca.* 20% of the succinimide *(8)*. Similar results were obtained when $CrO_3$-pyridine was employed but now *(9)* was the major impurity. The tertiary amines (*R,S*)-and (*S,S*)-*(10)* were prepared by reductive amination of the aldehydes [$NaBH_3CN$, $NH(CH_3)_2$][8]. Methylation ($CH_3Br$) and hydrolysis gave rise to the two enantiomeric quaternary ammonium salts *(11)*[9]. The final reaction step was carried out as previously described[1] and gave the diastereomeric histidines (*R,S*)- and (*S,S*)-*(12)* as amorphous solids. These were shown to be chemically and stereochemically pure by $^{13}C$-NMR spectroscopy, with distinct carbonyl resonances (75.47 MHz, $D_2O$, δ(CO), (*R,S*)-*(12)*: 176.2, 171.7, (*S,S*)-*(12)*: 176.5, 172.0).

(*R*)- or (*S*)-*(2)* was allowed to react in aqueous phosphate buffer in the presence of both diastereomeric catalysts *(12)* and the rate profiles thus obtained are recorded in Figure 1. The curves are typical of nucleophilic catalysis in homomicelles[10]. The fastest reaction is shown for the combination (*S,S*)-*(12)* and (*S*)-*(2)*, which is 2.5 times more reactive than (*R*)-*(2)* in the plateau region. Thus, by analogy, the configuration of *(1)* must be (*S,S*). The other diastereomer, (*R,S*)-*(12)*, surprisingly shows opposite selectivity, for (*R*)-*(2)* reacts 1.5 times faster than (*S*)-*(2)* in the plateau region. This requires that the chain is intimately involved in stereochemical control of catalysis, which imposes severe limits on possible models for the reaction transition-state.



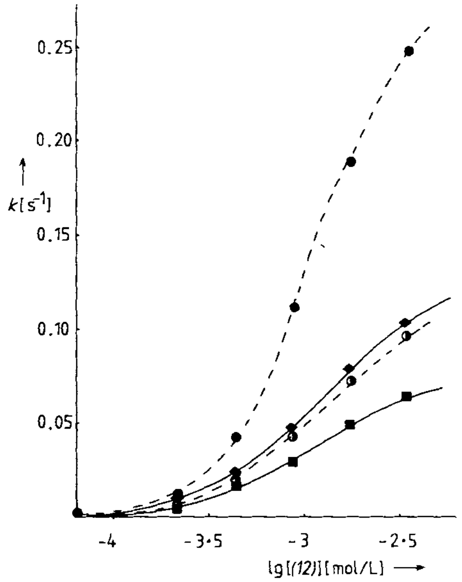


Fig. 1. Rate profile of the hydrolysis of the ester *(2)* catalyzed by *(12)*; pH 7.26±0.04, 0.02 M phosphate buffer, $[(2)] = 5 \times 10^{-5}$M, 0.47 vol.-% acetone in water. ● (*S,S*)-*(12)*, (*S*)-*(2)*; ◑ (*S,S*)-*(12)*, (*R*)-*(2)*; ◆ (*R,S*)-*(12)*, (*R*)-*(2)*; ■ (*R,S*)-*(12)*, (*S*)-*(2)*.

The pH-rate profile (Fig. 2) is equally instructive. In phosphate buffer below pH 8, reaction proceeds predominantly through neutral imidazole nucleophilic catalysis and little variation in stereoselectivity is observed. In borate buffer, where the reactive nucleophile is an imidazolide anion[11], at least in part, reactivities are much less vari-

0570-0833/81/1010-0891 $ 02.50/0

able (Figure 2). This places further constraints on asymmetric catalysis: (a) only the neutral histidine is effective, and (b) phosphate buffer (predominant counterion $HPO_4^{2-}$ at pH 7.5) is more efficacious than borate buffer (predominant counterion $Cl^-$ rather than $H_3BO_4^-$ at pH 9). A model which displays these features is presented by formula *(13)*.

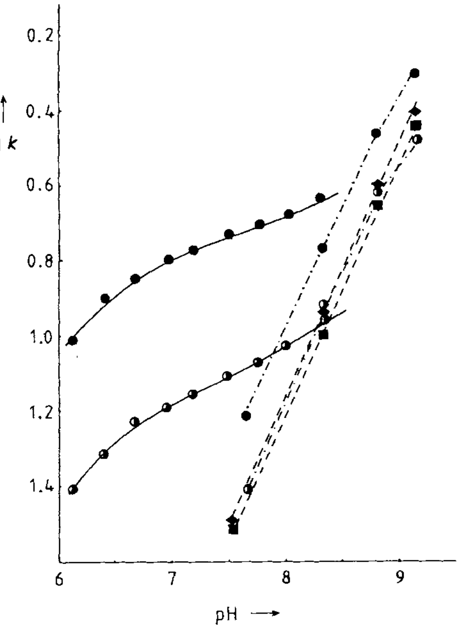
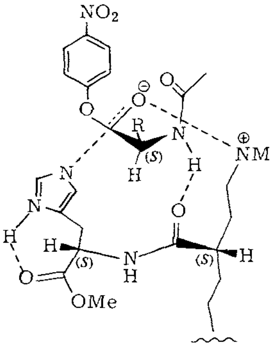


Fig. 2 Dependence of lg *k* on the pH of the solution in the hydrolysis of *(2)* catalyzed by *(12)*; $[(12)] = 1.08 \times 10^{-3}$M, $[(2)] = 5 \times 10^{-5}$M, [buffer] = 0.02 M, 0.47 vol.-% acetone in water; ● (*S*,*S*)-*(12)*, (*S*)-*(2)*, ----- borate buffer; —— phosphate buffer; ■ (*R*,*S*)-*(12)*, (*S*)-*(2)*, — — — borate buffer; ◑ (*S*,*S*)-*(12)*, (*R*)-*(2)*, -·-·- borate buffer, ——— phosphate buffer; ◆ (*R*,*S*)-*(12)*, (*R*)-*(2)*, — — — borate buffer.



*(13)*

Received: February 23, 1981 [Z 873 IE]
German version: Angew. Chem. *93*, 906 (1981)

CAS Registry numbers:
(*R*)-*(2)*, 14009-95-1; (*S*)-*(2)*, 14009-94-0; (±)-*(3)*, 79102-03-7; (*R*)-*(3)*, 79171-36-1; (*S*)-*(3)*, 79171-37-2; *(4)*, 79102-04-8; (*S*,*S*)-*(5)*, 79102-05-9; (*R*,*S*)-*(5)*, 79102-06-0; (*R*,*S*)-*(7)*, 79102-07-1; (*S*,*S*)-*(7)*, 79102-08-2; (*S*,*S*)-*(8)*, 79102-09-3; (*R*,*S*)-*(8)*, 79121-04-3; *(9)*, 79102-10-6; (*S*,*S*)-*(10)* HCl, 79102-11-7; (*R*,*S*)-*(10)* ($NMe_3^+$, $BF_4^-$), 79102-13-9; (*R*)-*(11)*, 79102-14-0; (*S*)-*(11)*, 79102-15-1; (*R*,*S*)-*(12)*, 79102-16-2; (*S*,*S*)-*(12)*, 79102-17-3; (*S*)-α-phenylethylamine, 2627-86-3

---

[1] *J. M. Brown, C. A. Bunton,* J. Chem. Soc. Chem. Commun. *1974*, 969; see also *C. A. Bunton,* Pure Appl. Chem. *49*, 969 (1977); *J. M. Brown:* Further Perspectives in Organic Chemistry, Ciba Found. Ser. *53*, 149 (1978).

[2] *K. Ohkubo, K. Sugahara, K. Yoshinaga, R. Uoeka,* J. Chem. Soc. Chem. Commun. *1980*, 637; *Y. Ihara, ibid. 1978*, 984; J. Chem. Soc. Perkin Trans. II *1980*, 1483; *K. Yamada, H. Shosenji, H. Ihara, Y. Otsubo,* Tetrahedron Lett. *1979*, 2529; *K. Yamada, H. Shosenji, H. Ihara,* Chem. Lett. *1979*, 491.

[3] All new compounds gave correct analyses and characteristic spectra.

[4] *W. C. Still, M. Kahn, A. Mitra,* J. Org. Chem. *43*, 2923 (1979).

[5] *G. Helmchen, G. Nill, D. Flockerzi, M. S. K. Youssef,* Angew. Chem. *91*, 64 (1979); Angew. Chem. Int. Ed. Engl. *18*, 62 (1979); *G. Helmchen, G. Nill, ibid. 91*, 66 (1979) and *18*, 65 (1979).

[6] We have previously commented on the extremely facile racemization of lactones [5]; see also: *A. I. Meyers, Y. Yamamoto, E. D. Mihelich, R. A. Bell,* J. Org. Chem. *45*, 2792 (1980).

[7] *E. J. Corey, J. W. Suggs,* Tetrahedron Lett. *1975*, 2647.

[8] *R. F. Borch, M. D. Bernstein, H. D. Durst,* J. Am. Chem. Soc. *93*, 2897 (1971); *C. F. Lane,* Synthesis *1975*, 135.

[9] Conversion into the respective methyl esters and observation of their $^1$H-NMR spectra (300 MHz, $CDCl_3$) in the presence of $Eu(tfc)_3$ showed them both to be enantiomerically pure.

[10] *W. Tagaki, D. Fukushima, T. Eiki, Y. Yano,* J. Org. Chem. *44*, 555 (1979).

[11] *P. Heitmann, R. Husung-Bublitz, H. J. Zunft,* Tetrahedron *30*, 4137 (1974).

## A Mild and Effective Method for the Reactivation or Maintenance of the Activity of Heterogeneous Catalysts[**]

By *Helmut Tiltscher, Helmut Wolf,* and
*Joachim Schelchshorn*[*]

*Dedicated to Professor Franz Patat on the occasion of his 75th birthday*

There is considerable current interest in investigations of highly compressed fluid mixtures in the critical or supercritical region chiefly due to their significance in new separation processes[1]. The effect of increase of pressure at the supercritical region can change the course of homogeneous and heterogeneous reactions as a result of the drastic change in material properties. Apart from a few, previously reported investigations[2] hardly any systematic studies are known.

By measuring the isomerization of 1-hexene on γ-$Al_2O_3$ with 2-chlorohexane as cocatalyst we found that a catalyst, which was deactivated under gaseous or liquid phase reaction conditions, can be reactivated by increasing the pressure and/or temperature until a supercritical state is reached. The method can be employed in the case of loss of catalytic activity, whether caused by deposition of substances of low volatility, (catalyst 'coking', 'fouling') or by specific compounds ('poisoning'). The deactivation phenomena of the mentioned types can be avoided by applying higher pressures under supercritical reaction conditions at the initial stages of heterogeneous, catalytic conversions.

A continuously operating high pressure apparatus, which allowed kinetic measurements to be made, was used[3]. The main part of the system consists of a novel type of high pressure differential recycle-reactor[4,5].

For the kinetic measurements the high pressure reactor was charged with 7.5 g of a freshly synthesized shell catalyst (γ-$Al_2O_3$/Al-metal, particle diameter: 0.6—0.75 mm, catalytically active specific surface: 4.95 $m^2/g$). As shown in Figure 1a (bottom curve), the theoretically expected degree of conversion of 1-hexene (24%) cannot be achieved

---

[*] Dr. H. Tiltscher, Dipl.-Chem. H. Wolf, Dipl.-Ing. J. Schelchshorn
Institut für Technische Chemie, Lehrstuhl II der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] Chemical Reactions at High Pressures, Part 5. We thank Prof. Dr. *K. Dialer* for his valuable comments and generous support of this work. – Part 4: H. Tiltscher, Y. K. Wang, H. Wolf, High Temperatures - High Pressures *9*, 529 (1977).

with a gaseous reaction phase[6] at 15 bar and 523.2 K after stationary conditions had been established within the reactor (ca. 4 h = four times the mean residence time). The resulting curve is typical of a conversion upon which a deactivation process is superimposed. In the colorless product solution only the hexene isomers 1-hexene, *cis*-2-hexene, *trans*-2-hexene, *trans*-3-hexene could be detected by capillary gas-chromatography, GC/MS, and $^{13}$C-NMR-analytical methods.

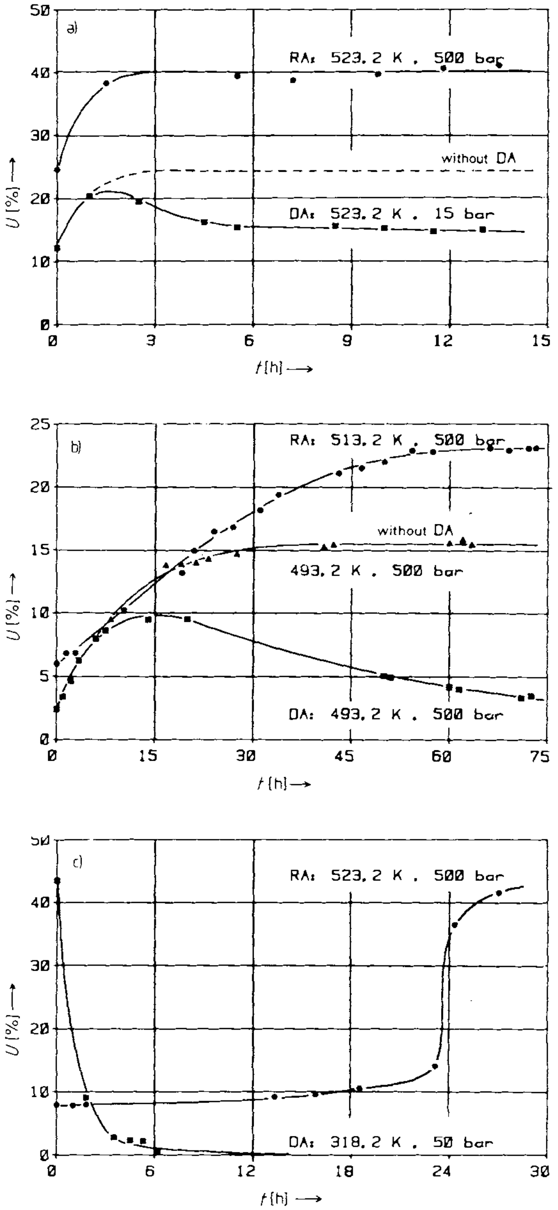


Fig. 1. Isomerization of 1-hexene in the presence of 2-chlorohexane (molar ratio 500:1) on $\gamma$-$Al_2O_3$. Units see text. a) Deactivation (DA) of the catalyst by side reactions, and reactivation (RA) in the supercritical region under gas phase reaction conditions. Residence time $\tau = 1.08 \times 10^5$ s·g/mol. b) Deactivation (DA) of the catalyst by $MoS_2$ under liquid phase reaction conditions and reactivation (RA) under supercritical conditions. Middle: Measurements with reactivated catalyst. Residence time $\tau = 1.89 \times 10^5$ s·g/mol. c) Deactivation (DA) of the catalyst by poisoning of the catalytic active acid sites with pyridine under liquid phase reaction conditions and reactivation (RA) at supercritical conditions. Residence time $\tau = 1.08 \times 10^5$ s·g/mol. $U$ = conversion.

An increase of pressure, at the same temperature, to a value higher than the critical pressure $p_c$, *e.g.* 500 bar, produces an immediate dark brown coloration of the product solution, which gradually brightens again. After the stationary conditions have been re-established, the conversion corresponds to the expected values. As seen in the upper curve even at extremely long reaction times the catalyst does not decay, despite the essentially higher reactivity. The dark brown oily product solutions which were sampled immediately after pressurization, contained, besides the hexene isomers, considerable amounts of oligomers ($C_{12}$ to $C_{30}$). Under gaseous reaction phase conditions, these oligomeric compounds remain on the catalyst surface due to their markedly lower volatility relative to the hexene isomers and finally cause complete coking. After reactivation only a small constant residual amount of hexene-dimers could be detected in the product solution.

Whilst pressurization at a constant temperature of a gaseous reaction phase usually favors sorption processes in heterogeneous catalytic conversions and thus hinders desorption of low volatile compounds, increase of pressure in the supercritical region causes the opposite effect. Distinct influences for practical applications can even be obtained at pressures of 50 to 150 bar. Based on the present kinetic measurements it can be concluded that the applied pressure is the higher, the less volatile the deposited substances and the faster the reactivation should occur.

The advantages of supercritical reaction conditions also apply to catalyst fouling caused by the introduction of compounds of low volatility. Hence, a small amount of finely dispersed $MoS_2$ was introduced into the reactor under liquid phase reaction conditions ($T = 493.2$ K; $p = 500$ bar) again resulted in a conversion-time curve, which is typical for a heterogeneous catalytic reaction with catalyst decay (Fig. 1b, bottom curve). Catalytic activity could not be regained under liquid phase conditions, not even after an extremely long operation period (75 h). By raising the temperature to 513.2 K at the same pressure the supercritical region was reached, resulting in an increase of the degree of conversion (upper curve). Finally the isomerization could be studied under liquid phase conditions by means of the reactivated catalyst, without catalyst decay (middle curve).

The ability of compressed supercritical reaction phases to reactivate poisoned catalysts is shown in Figure 1c. For this purpose, the active acidic sites of the catalyst were initially poisoned at a pressure of 50 bar and a temperature of 318 K by continuous addition of a $6.4 \times 10^{-2}$ M solution of pyridine in 1-hexene over a period of twelve hours. The conversion decreases rapidly as shown by the deactivation curve. At 493.2 K and 500 bar in the liquid phase, the catalyst could not be reactivated even after an extremely long reaction time. Only after a further increase of the temperature to 523.2 K at constant pressure and supercritical conditions had been reached, was a degree of conversion of about 8% achieved; this level increased with time, until the original value was obtained after *ca.* 24 h. A white deposit of pyridinium chloride was isolated from the product solution.

The use of highly compressed supercritical fluid reaction phases for the reactivation of heterogeneous catalysts thus has considerable advantages over the usual methods employed in heterogeneous catalytic syntheses:

1. The reactivation conditions are relatively mild.
2. The reactivation or maintenance of the activity is performed by the fluid reaction phase itself; no other substances have to be added to the reaction system.
3. The reactivation can be easily carried out *in situ*.

4. The heterogeneous catalyst can be used over long working periods with constant catalytic activity.
5. At constant residual catalytic activity, more drastic reaction conditions can be used and higher space-time yields are obtainable.

The heterogeneous catalyst used in our kinetic measurements loses its activity completely within a 14 day period of operation under gaseous reaction conditions (*e.g.* $T = 523.2$ K; $p = 15$ bar). However the experiments described here could be performed with a single catalyst charge without any loss of catalytic activity for a period of four months by periodical reactivation at supercritical conditions. Thus, the ratio of volume of the reactants passed through the catalyst to the volume of the catalyst ($1.2 \times 10^6 : 1$) reached an order of magnitude desirable for many industrial syntheses.

Received: November 17, 1980 [Z 874 IE]
German version: Angew. Chem. *93*, 907 (1981)

CAS Registry numbers:
γ-$Al_2O_3$, 1344-28-1; 1-hexene, 592-41-6

---

[1] Destraction: *G. M. Schneider, E. Stahl, G. Wilke:* Extraction with Super-Critical Gases, Verlag Chemie, Weinheim 1979; *K. Zosel,* Angew. Chem. *90,* 748 (1978); Angew. Chem. Int. Ed. Engl. *17,* 702 (1978); *P. Hubert, O. G. Vitzthum, ibid. 90,* 756 (1978); *17,* 710 (1978); *S. Peter, G. Brunner, ibid. 90,* 794 (1978); *17,* 746 (1978); Supercritical Fluid Chromatography: *E. Klesper, A. H. Corwin, D. A. Turner,* J. Org. Chem. *27,* 700 (1962); *E. Klesper,* Angew. Chem. *90,* 786 (1978); Angew. Chem. Int. Ed. Engl. *17,* 738 (1978); *U. van Wasen, I. Swaid, G. M. Schneider, ibid. 92,* 585 (1980); *19,* 575 (1980).
[2] *F. Patat,* Monatsh. Chem. *77,* 352 (1945).
[3] *H. Tiltscher, J. Schelchshorn, H. Wolf, W. Foag,* unpublished results.
[4] *H. Tiltscher, J. Schelchshorn, H. Wolf, K. Dialer,* Chem. Ing. Tech. *51,* 682 (1979); Ger. Chem. Eng. *2,* 313 (1979); DOS 2832376 (1980).
[5] Manufacturer: Andreas Hofer, Hochdrucktechnik GmbH, Friedrich-Freye-Strasse 59—61, D-4330 Mülheim (Ruhr) (Germany).
[6] Critical data for 1-hexene: $T_c = 504$ K, $p_c = 31.1$ bar; *R. C. Reid, J. M. Prausnitz, T. K. Sherwood:* The Properties of Gases and Liquids, 3. Edition, McGraw-Hill, New York 1977.

---

# Synthesis of Glycopeptides: Selective Carboxy-Deblocking of Completely Protected Glucosylserine Derivatives[**]

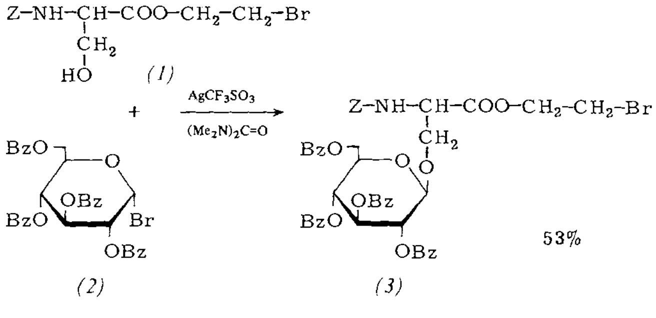
By *Horst Kunz* and *Michael Buchholz*[*]

*Dedicated to Professor Leopold Horner on the occasion of his 70th birthday*

In the glycoproteins of connective tissue and mucins[1a], as also in other physiologically important glycoproteins, *e.g.* in blood-group active sialoglycopeptides of human erythrocytes[1b], the carbohydrate moiety is linked *O*-glycosidically with the protein moiety. In many globulins, *e.g.* in immunoglobulins of the rabbit[2], *O*-glycosidic linkage to serine and to threonine is found in addition to the more frequently met *N*-acetylglucosamine-asparagine linkage. The *O*-glycosidically bound serine and threonine residues are not only sensitive to acid, but are also characteristically unstable towards alkalis: β-elimination of the sugar residue readily occurs[3], with formation of unsaturated amino acid derivatives[1a,4].

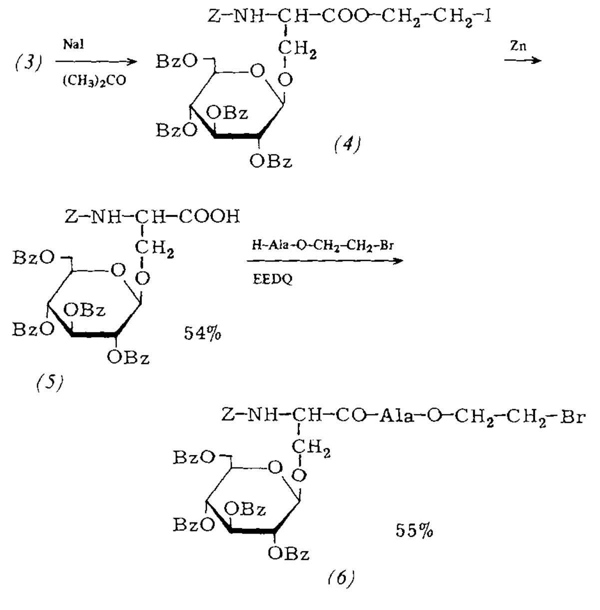
Model compounds such as benzyloxycarbonyl(Z)- or dinitrophenyl(Dnp)-serine and threonine methyl or benzyl esters[5], which have been used to study the β-elimination, are not particularly suitable for a directed glycopeptide synthesis, since selective cleavage of the N- and C-terminal protecting groups cannot be achieved. According to *Garg* and *Jeanloz*[6] predominantly the *O*-glycosidic linkage is cleaved during acidolytic cleavage of the Z-group of glycosyl-Z-serine methyl esters; alkaline hydrolysis likewise proves unsuccessful, since β-elimination leads to decomposition of the glycoside.

We report here the selective deblocking of the C-terminal of glucosyl-Z-serine esters using the 2-bromoethyl ester protecting group[7]. Fundamental for this synthetic pathway is the finding that the Z-serine-2-bromoethyl ester *(1)* reacts with 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide *(2)* according to the "triflate method"[8] to give the fully protected β-glucosyl-Z-serine-2-bromoethyl ester *(3)*[9].



Bz = Benzoyl

Under these conditions the 2-bromoethyl ester is not attacked by $CF_3SO_3Ag$. The only feature which lowered the yield was the partial hydrolysis of the 1-bromo sugar *(2)*. In analogous reactions of the acetobromoglucose with *(1)*, according to either the classical Koenigs-Knorr method with $Ag_2CO_3$ or $Ag_2O$ or to the more recent variants *e.g.* with silver salicylate[10] or with mercury salts, we recorded low yields and several by-products, among which the corresponding ortho ester represented the main part. Position and splitting of the signal of the anomeric proton in the $^1$H-NMR spectrum and the $^{13}$C-NMR signal for C-1



---

[*] Prof. Dr. H. Kunz, Dipl.-Chem. M. Buchholz
Institut für Organische Chemie der Universität
Johann-Joachim-Becher-Weg 18—20, D-6500 Mainz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

($\delta = 101.2$)[11] afford proof of the β-configuration of the glucoside *(3)*. The C-terminal protection of the serine glucoside *(3)* is selectively removed by initially converting the 2-bromoethyl ester with sodium iodide in acetone (60 min, room temperature) into the iodoethyl ester *(4)*, which is then reductively fragmented with zinc (48 h, 40—50 °C) to yield *(5)*[9] in a one-pot procedure.

For the purpose of identification the iodoethyl ester may be isolated. In some experiments educt *(4)* is still found in the heterogeneous mixture after 48 h, irrespective of the quality of the zinc used. The N-terminal protecting group Z is not attacked, nor is the glucosidic bond cleaved; hence this process, which proceeds under neutral conditions, enables selective deblocking of the polyfunctional serine glucoside *(4)* to give the free carboxylic acid *(5)*. Coupling of *(5)* with alanine 2-bromoethyl ester using ethyl 2-ethoxy-1,2-dihydroquinoline-1-carboxylate (EEDQ) affords the glucodipeptide ester *(6)*.

The 2-haloethyl ester accordingly offers a possibility of directed lengthening of the C-terminal of glycopeptides; lengthening of the N-terminals is achieved *via* the selective cleavage of the 2-triphenylphosphonioethoxycarbonyl (Peoc) protecting group[12].

### *Procedure*

*(3)*: A solution of freshly prepared $AgCF_3SO_3$ (5.1 g, 0.02 mol) in anhydrous $CH_2Cl_2$ (10 mL) is treated dropwise at −30 °C under $N_2$ (exclusion of moisture!) with a solution of *(1)*[7] (6.85 g, 0.02 mol), *(2)*[13] (10.6 g, 0.016 mol) and tetramethylurea (2.3 g, 0.02 mol) in anhydrous $CH_2Cl_2$ (30 mL). The mixture is stirred for 2 h at −30 °C and 5 h at room temperature, filtered to remove the precipitated AgBr, and the filtrate is washed with 50 mL each of 0.05 N HCl, $H_2O$, 1% $NaHCO_3$ solution, and finally with water again. After drying over $Na_2SO_4$ and removal of the solvent by evaporation the residue is purified by preparative high-pressure liquid chromatography (petroleum ether/ethyl acetate, 2 : 1). Yield 7.8 g (53%) of the analytically pure amorphous solid *(3)*, $[\alpha]_D^{20} = +18.2$ ($c = 2.4$, $CHCl_3$).

*(4)*: A solution of *(3)* (0.5 g, 0.54 mmol) in anhydrous acetone (5 ml) is treated with NaI (0.3 g, 2 mmol) and the mixture stirred for *ca.* 1 h at room temperature. (The separation of NaBr is then complete.) Zinc powder (0.26 g, 4 mmol), freshly treated with HCl and dried, is then added to the mixture, which is stirred at 40—50 °C until no more *(3)* can be detected in the thin layer chromatogram (toluene/ethanol (9 : 1), silica gel 60) (*ca.* 48 h). After filtration and evaporation to dryness the residue is taken up in $CHCl_3$ (20 mL), filtered again, and the organic phase is washed with 10 mL each of 0.05 N HCl, 10% $Na_2S_2O_3$ solution and $H_2O$. After drying over $Na_2SO_4$ the solution is evaporated to dryness under reduced pressure and the residue is taken up in toluene/ethanol (9 : 1) and filtered through a short column of silica gel 60. The free acid *(4)* is eluted with ethanol. 0.24 g (54%) of *(4)* is obtained as analytically pure amorphous solid; $[\alpha]_D^{20} = +7.8°$ ($c = 2.37$, $CHCl_3$).

Received: May 4, 1981 [Z 884a IE]
German version: Angew. Chem. *93*, 917 (1981)

CAS Registry numbers:
*(1)*, 79134-70-6; *(2)*, 14218-11-2; *(3)*, 79134-71-7; *(4)*, 79121-22-5; *(5)*, 79121-23-6; *(6)*, 79121-24-7; H-Ala-$OCH_2CH_2Br$, 71283-20-0

---

[1] *A. Neuberger, A. Gottschalk, R. D. Marshall, R. G. Spiro, U. Lindahl, L. Rodén* in *A. Gottschalk*: Glycoproteins, Elsevier, Amsterdam 1972, p. 450ff. and p. 491ff.; b) *G. F. Springer, H. J. Yang, D. Grohlich* in *R. Schauer, P. Boer, E. Buddecke, M. F. Kramer, J. F. G. Vliegenhart, H. Wiegandt*: Glycoconjugates, Thieme, Stuttgart 1979.
[2] *D. S. Smyth, S. Utsumi*, Nature *216*, 332 (1967).
[3] *R. Kuhn, J. Löw*, Chem. Ber. *74*, 219 (1941).
[4] *B. Anderson, P. Hoffman, K. Meyer*, Biochim. Biophys. Acta *74*, 309 (1963).
[5] a) *J. R. Vercellotti, N. Nienhaber, C. J. Chang*, Carbohydr. Res. *13*, 63 (1970), and references cited therein; b) *E. Rüde, M. Meyer-Delius, ibid. 8*, 219 (1968).
[6] *H. G. Garg, R. W. Jeanloz*, Carbohydr. Res. *52*, 246 (1976).
[7] *H. Kunz, M. Buchholz*, Chem. Ber. *112*, 2145 (1979).
[8] a) *S. Hanessian, J. Banoub*, Carbohydr. Res. *53*, C13 (1977); b) *J. Banoub, D. R. Bundle*, Can. J. Chem. *57*, 2091 (1979); c) *B. Erbing, B. Lindberg, T. Norberg*, Acta Chem. Scand. *B32*, 308 (1978); d) *P. Garegg, T. Norberg*, Acta Chem. Scand. *B33*, 116 (1979).
[9] *(3)* and *(5)* gave satisfactory analyses and characteristic spectra.
[10] *G. Wulff, G. Röhle*, Chem. Ber. *105*, 1097 (1972).
[11] *J. M. Lacombe, A. A. Pavia, G. M. Roucheville*, Can. J. Chem. *59*, 473 (1981).
[12] *H. Kunz, H. Kauth*, Angew. Chem. *93*, 918 (1981); Angew. Chem. Int. Ed. Engl. *20*, 895 (1981).
[13] *R. K. Ness, H. G. Fletcher, C. S. Hudson*, J. Am. Chem. Soc. *72*, 2200 (1950).

---

## Synthesis of Glycopeptides: Selective Amino-Deblocking of 2-Phosphonioethoxycarbonyl-Protected Asparagine *N*-Acetylglucosamine Moieties[**]

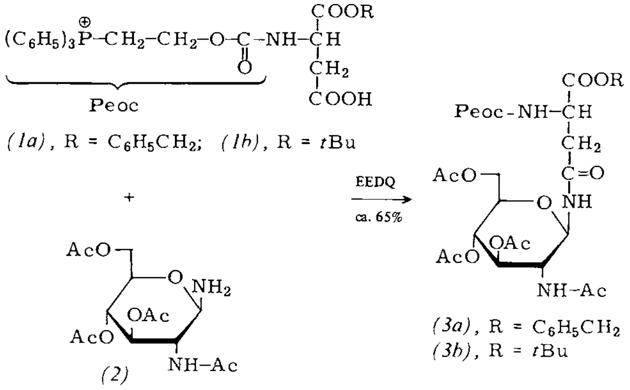
By *Horst Kunz* and *Hermann Kauth*[*]

*Dedicated to Professor Leopold Horner on the occasion of his 70th birthday*

Glycoproteins[1] have important biological functions. Unlike in peptide synthesis, in the synthesis of glycopeptides the functional groups of the carbohydrate moieties must also be taken into consideration. The reactions are rendered difficult by the glycosidic bond between the carbohydrate and the peptide moieties, since this bond is sensitive to acids, thus making the acid-cleavable protecting groups used in peptide synthesis unsuitable[2].

Therefore we have used the base-sensitive 2-triphenylphosphonioethoxycarbonyl(Peoc) protecting group[3] for amino-blocking of *N*-glycosidically bonded asparagine moieties. The *N*-glycosidic linkage is more stable than the *O*-glycosidic bond, both towards acids as well as bases[1,4]; thus these compounds are suitable for model experiments.

For preparation of the glycosylamines *(3a)* and *(3b)* *N*-Peoc aspartic acid α-benzyl- or *tert*-butyl-ester is allowed



*(1a)*, R = $C_6H_5CH_2$; *(1b)*, R = *t*Bu

*(2)*

*(3a)*, R = $C_6H_5CH_2$
*(3b)*, R = *t*Bu

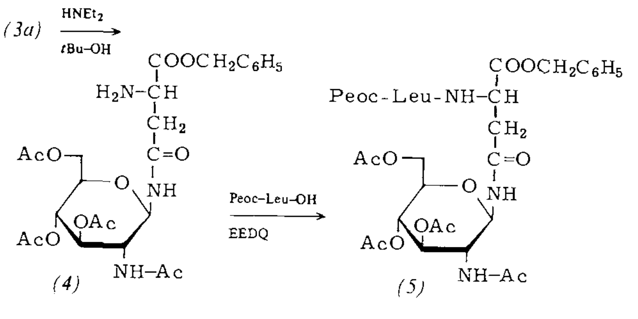
---

[*] Prof. Dr. H. Kunz, Dipl.-Chem. H. Kauth
Institut für Organische Chemie der Universität
Johann-Joachim-Becher-Weg 18—20, D-6500 Mainz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

to react with 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosylamine *(2)*[4a,6] in the presence of ethyl 2-ethoxy-1,2-dihydroquinoline-1-carboxylate (EEDQ)[5].

The structure of *(3a)* and *(3b)* is confirmed by IR and $^1$H-NMR spectroscopy. The selective cleavage of the Peoc-protecting group proceeds quite smoothly in a *ca.* 5% solution of diethylamine in *tert*-butyl alcohol.



After 30 minutes at room temperature, *(3a)* affords the crystalline deblocked benzyl 4-*N*-glycosylasparaginate *(4)* in 67% yield. Under these conditions the primary ester at C-6 of the glucosamine is not attacked.

In the case of glycosyl peptides the Peoc-protecting group has three advantages in comparison to the frequently employed benzyloxycarbonyl (Z)-moiety:

1) In the case of a Z-protected compound analogous to *(3a)*, the hydrogenolysis leads to unselective deblocking of the *N*- and *C*-terminals[7a].

2) During the basic cleavage of the benzyl ester in the presence of the Z-group the *O*-acetyl groups are removed[4a]. At the same time there is the likelihood of rearrangement in the asparagine moiety—as is also likely under acid conditions[7].

3) *N*-Glycoside coupling *via* Z-aspartic anhydride and hence separation of the desired 4-amide from the 1-amide of the aspartic acid formed in the same way can thus be avoided[8].

In the case of *(3a)*, not only selective cleavage of the Peoc-protecting group is possible but also hydrogenolytic deblocking of the C-terminal with intact ester groups on the carbohydrate moiety.

The peptide chain can be elongated on the free amino group of *(4)*; thus, with Peoc-leucine[3], *e.g.* in dichloromethane in the presence of EEDQ, the Peoc-glycodipeptide ester *(5)* can be synthesized in *ca.* 60% yield.

## *Experimental*

*(3a)*: To a solution of *(1a)*[3] (6.7 g, 12 mmol) in anhydrous $CHCl_3$ (80 ml) cooled to −10 to −5 °C are added first a solution of *(2)* (4.2 g, 12 mmol), likewise cooled to −10 to −5 °C, and then solid EEDQ (3.26 g, 13.2 mmol). The mixture is stirred overnight and allowed to warm to room temperature. The solution is then washed three times each with 50 ml 0.5 N HCl and with $H_2O$, and dried over $Na_2SO_4$; after removal of the solvent under reduced pressure, the crude product is chromatographed on 300 g of silanated silica gel, 70—230 mesh (Merck), with chloroform/methanol (25 : 1). Yield 7.2 g (65%), amorphous, decomp.: 100—110 °C.

*(4)*: A solution of *(3a)* (6 g, 6.5 mmol) in *tert*-butyl alcohol (150 ml) is treated with a 20% solution of diethylamine in *tert*-butyl alcohol and the mixture stirred for 30 min at room temperature. After removal of the solvent under reduced pressure the residue is taken up in 100 mL of $CH_2Cl_2$, washed three times with 50 ml of water and dried over $Na_2SO_4$. Renewed evaporation of the solvent and recrystallization from chloroform/ether affords 2.4 g (67%) of crystalline, analytically pure *(4)*, m.p. 149—150 °C (dec.).

Received: March 20, 1981 [Z 884b IE]
German version: Angew. Chem. *93*, 918 (1981)

CAS Registry numbers:
*(1a)*, 79134-86-4; *(1b)*, 79134-87-5; *(2)*, 4515-24-6; *(3a)*, 79134-88-6; *(3b)*, 79134-89-7; *(4)*, 79134-90-0; *(5)*, 79134-91-1; Peoc-Leu-OH, 73951-87-8

---

[1] *A. Gottschalk:* Glycoproteins, 2nd edit., Elsevier, Amsterdam 1972.
[2] Cf. a) *H. G. Garg, R. W. Jeanloz,* Carbohydr. Res. *52,* 246 (1976); b) *ibid. 70,* 47 (1979).
[3] *H. Kunz,* Chem. Ber. *109,* 2670 (1976); Angew. Chem. *90,* 63 (1978); Angew. Chem. Int. Ed. Engl. *17,* 67 (1978).
[4] a) *G. S. Marks, R. D. Marshall, A. Neuberger,* Biochem. J. *87,* 274 (1963); b) *A. Neuberger, ibid. 32,* 1435 (1938).
[5] a) *D. Belleau, G. Malek,* J. Am. Chem. Soc. *90,* 1651 (1968); b) *D. Dunstan, L. Hough,* Carbohydr. Res. *23,* 17 (1972).
[6] *C. H. Bolton, R. W. Jeanloz,* J. Org. Chem. *28,* 3228 (1963).
[7] a) *A. Yamamoto, C. Miyashita, H. Tsukamoto,* Chem. Pharm. Bull. *13,* 1041 (1965); b) *A. R. Battery, J. C. Robinson,* J. Chem. Soc. *1955,* 259.
[8] *H. G. Garg, R. W. Jeanloz,* Carbohydr. Res. *23,* 437 (1972).

# BOOK REVIEWS

**Analytiker Taschenbuch. Band 1.** (Analytical Pocketbook. Vol. 1). Edited *H. Kienitz, R. Bock, W. Fresenius, W. Huber* and *G. Tölg.* Springer-Verlag, Berlin 1980. vii, 439 pp., bound, DM 78.00.

If, as is planned, a volume of the "Analytiker Taschenbuch" actually appears every two years, the analytical community can truly congratulate itself, particularly if the high level of the publications can be maintained. The great novelty value lies in that apart from the subdivision into Fundamentals, Methods, and Applications there is no scheme of structure and treatment laid down beforehand and references are made to current needs. The editors have been able to secure the services of well-known and excellent authors and to achieve a high standard.

In the Fundamentals, the chapter on sampling, data processing, and evaluation methods must be specially singled out. The Methods section is particularly valuable because of the clear nomenclature in electrochemical processes, corresponding to the IUPAC rules, the exhaustive tables for gas chromatography, and—for the air-monitoring environmental analyst—a summary of the testing tubes available for monitoring working premises and for industrial gas analyses. Also noted with pleasure is the introduction to chiroptical methods and, particularly, the table of Cotton effects covering many examples.

It is likewise appropriate to mention the valuable hints on sources of error in measurements with ion-selective electrodes. Of modern physical methods of analysis, a very good chapter on X-ray spectral analysis in SEM has been included. The methodological part is completed by a contribution on surface analysis, which—with the exception of the now widely used ATR-FT-IR methods—gives an excellent review of this important field.

The third part, dealing with application techniques, begins with a relatively new but increasingly important field, enzymatic analysis, and shows how widespread the direct determination of various substances with comparatively specific enzymes in the presence of complex mixtures has already become. Since there is no doubt about the extreme importance of the determination of mycotoxins, and especially aflatoxins, the corresponding contribution, made more valuable by the schemes of analysis, is greatly welcomed. It will prove particularly valuable for the foodstuffs and feedstuffs researcher. The qualitative investigation of dyestuffs as such and on the fiber has undoubted practical importance.

Methods of detecting and determining environmentally relevant products and compounds are now in constant demand, and this has been taken into account. Thus, in addition to methods for the detection of narcotics and dopes, the determination of mercury compounds (including organomercury compounds) in water and the analysis of plutonium are given.

Summarizing, volume 1 of the pocketbook is indeed heterogeneous. It is also very informative and up to date, and the chemists and analysts not dealing directly with the individual subject fields now have at their disposal a very valuable guide.

*Hanns Malissa* [NB 548 IE]

**X-Ray Analysis and the Structure of Organic Molecules.** By *J. D. Dunitz.* Cornell University Press, Ithaca 1979, 528 pp., bound, £ 33.00.

*Dunitz*'s monograph is based on a series of lectures and is therefore very personal in style and presentation. For this reason alone, it is worth reading. This naturally also applies to its contents, which are organized in two large sections, crystal structure analysis (I) and molecular structures (II), relieved by historical observations on the development of X-ray structure analysis. Diffraction, symmetry, methods of structure determination, refinement processes, and above all treatment of the results are dealt with in Part I. The direct juxtaposition of theory and practise, instead of a chronological exposition, is particularly successful. The detailed examples thus make the material understandable even to readers with little mathematical training. Part II is not just a compilation of results, but begins with a unique reference to the aspects decisive for the chemist that can be demonstrated from the wealth of known molecular structures. The sections on structural analysis and chemistry, electron density in molecules, topological limitations in cyclic systems, and treatment of conformations with symmetry groups open up a fascinating field of molecular events far beyond that achievable by drawings of molecules and statements of distances.

The book may be recommended most heartily to anyone who would like to know how molecular structures are determined and what can be deduced from them apart from their topology. The author is evidently a great admirer of the method and its results. The reviewer would agree that "cooking" is not the only way to bring chemically relevant knowledge to light.

*Hans Georg von Schnering* [NB 549 IE]

## Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**The Heterocyclic Chemistry of Phosphorus. Systems Based on the Phosphorus-Carbon Bond.** By *L. D. Quin.* John Wiley & Sons, Chichester 1981. xiii, 434 pp., bound £ 27.05.—ISBN 0-471-06461-0

**The Inorganic Chemistry of Biological Processes.** By *M. N. Hughes.* John Wiley & Sons, Chichester 1981. 2nd edit. ix, 338 pp., bound, £ 9.90.—ISBN 0-471-27815-7

**Annual Reports on Fermentation Processes.** Vol. 4. Edited by *G. T. Tsao.* Academic Press, New York 1980. xiv, 319 pp., bound, $ 28.50.—ISBN 0-12-040304-8

**Chromatographic Science Series. Vol. 14.** Introduction to Analytical Gas Chromatography. History, Principles, and Practice. By *J. A. Perry.* Marcel Dekker, Basel 1981. xviii, 426 pp., bound, SFr. 74.00.—ISBN 0-8247-1537-3

**Electron Spin Resonance.** Vol. 6. Senior Reporter: *P. B. Ayscough.* The Royal Society of Chemistry, London 1981. xiii, 359 pp., bound, £ 49.00.—ISBN 0-85186-810-0.—A volume in the series "Specialist Periodical Reports"

**Pergamon Series in Analytical Chemistry. Vol. 1.** An Introduction to Chemical Equilibrium and Kinetics. By *L. Meites.* Pergamon Press, New York 1981. xiii, 549 pp., bound, $ 19.95.—ISBN 0-08-023803-3

**Advances in Heterocyclic Chemistry.** Vol. 27. Edited by *A. R. Katritzky* and *A. J. Boulton.* Academic Press, New York 1980. ix, 331 pp., bound, $ 49.50.—ISBN 0-12-020627-7

**Analytical Sciences Monographs No. 8.** The Sampling of Bulk Materials. By *R. Smith* and *G. V. James.* The Society of Chemistry, London 1981. viii, 191 pp., bound, £ 16.50.—ISBN 0-85186-810-X

**Molecular Interactions.** Vol. 2. Edited by *H. Ratajczak* and *W. J. Orville-Thomas.* John Wiley & Sons, Chichester 1981. xxiii, 627 pp., bound, £ 39.00.—ISBN 0-471-27681-2

**The Chemistry of Functional Groups.** The Chemistry of the Sulphonium Group. Part 1 and 2. Edited by *C. J. M. Stirling.* John Wiley & Sons, Chichester 1981. xiv, 847 pp.,

**Grundlagen der Verfahrenstechnik und chemischen Technologie.** Modellierung von Phasengleichgewichten als Grundlage von Stofftrennprozessen. Edited by *K. Hartmann, W. Schirmer,* and *M. G. Slinko.* Academie-Verlag, Berlin 1981. xviii, 419 pp., bound, DM 87.00

**Pharmazeutische Biologie I.** By *H. Kating* and *S.-W. Breckle.* Thieme Verlag, Stuttgart 1981. 2nd edit. 504 pp., bound, DM 33.00.—ISBN 3-13-548102-6

**N-Nitrosoverbindungen in Nahrung und Umwelt.** Eigenschaften, Bildungswege, Nachweisverfahren und Vorkommen. Edited by *G. Eisenbrand.* Wissenschaftliche Verlagsgesellschaft, Stuttgart 1981. x, 134 pp., bound, DM 40.00

**Pareys Studientexte 27. Grundlagen der Zellbiologie.** Struktur, Moleküle, Stoffwechsel—Ein Lernprogramm. By *W. K. Stephenson.* Verlag Paul Parey, Berlin 1980. 238 pp., bound, DM 29.00.—ISBN 3-489-60634-5

**Adsorption of Microorganisms to Surfaces.** Edited by *G. Bitton* and *K. C. Marshall.* John Wiley & Sons, New York 1980. x, 439 pp., bound.—ISBN 0-471-03157-7

**Monitoring for Drug Safety.** Edited by *W. H. W. Inman.* MTP Press, Lancaster 1980. xxv, 673 pp., bound, £ 24.95.—ISBN 0-85200-234-3

**Weissberger: Techniques of Chemistry. Vol. IX.** Chemical Experimentation under Extreme Conditions. Edited by *B. W. Rossiter.* John Wiley & Sons, Chichester 1980. x, 369 pp., bound, £ 15.80.—ISBN 0-471-93269-8

**Messen, Steuern und Regeln in der Chemischen Technik.** Betriebsmesstechnik I. Edited by *J. Hengstenberg, B. Sturm,* and *O. Winkler.* Springer-Verlag, Heidelberg 1980. xvii, 788 pp., bound, DM 298.00.—ISBN 3-540-08672-2

**Umweltschutz.** Technologie—Ökologie. By *W. J. Fleischhauer, K.-R. Meis,* and *F.-H. Schwartz.* Vieweg Verlag, Wiesbaden 1980. viii, 171 pp., bound, DM 24.80.—ISBN 3-528-04167-6

**Studies in Organic Chemistry, Vol. 9.** Kinetics Applied to Organic Reactions. Von *W. Drenth* und *H. Kwart.* Marcel Dekker, Base. 1980. ix, 207 pp., bound, SFr. 41.00.—ISBN 0-8247-6889-2

**Reactivity and Structure—Concepts in Organic Chemistry 10.** Organic Synthesis with Palladium Compounds. By *J. Tsuji.* Springer-Verlag, Heidelberg 1980. xii, 206 pp., bound, DM 98.00.—ISBN 3-540-09767-8

**Laser-Induced Chemical Processes.** Edited by *J. I. Steinfeld.* Plenum Press, New York 1981. xii, 276 pp., bound, $ 32.50.—ISBN 0-306-40587-3

**Burger's Medicinal Chemistry. Part I.** 4th edit. The Basis of Medicinal Chemistry. Edited by *M. E. Wolff.* John Wiley & Sons, Chichester 1980. x, 497 pp., bound, £ 18.00.—ISBN 0-471-01570-9

**Gmelin Handbuch der Anorganischen Chemie.** Springer-Verlag, Berlin 1980. 8th edit.
Sc, Y, La—Lu—Seltenerdelemente. Teil A: Geschichtliches. Vorkommen. Lieferung 3: Y, La und Lanthanide: Kosmochemie. xiv, 180 pp., bound, DM 421.00.—ISBN 3-540-93410-3
Sc, Y, La—Lu—Rare Earth Elements. Part D 1: Coordination Compounds. xiv, 256 pp., bound, DM 587.00.—ISBN 3-540-93407-3
U—Uran. Ergänzungsband. Teil C: Verbindungen. Lieferung 8: Verbindungen mit Fluor. xxxii, 301 pp., bound, DM 687.00.—ISBN 3-540-93406-5

**Gespräche mit Chemikern.** Published by Bayer AG, Leverkusen 1980. 103 pp., bound, DM 16.00

**Thermal Electrocyclic Reactions.** Vol. 43. By *E. N. Marvell.* Academic Press, New York 1980. ix, 422 pp., bound, $ 51.00.—ISBN 0-12-476250-6

**Anorganische Chemie. Band 1 and Band 2.** By *L. Kolditz.* VEB Deutscher Verlag der Wissenschaften, Berlin 1980. xxi, 950 pp., bound, DM 61.00

**Arbeitsmedizin und Gesundheitsschutz.** Werksärztliche Erfahrungen der BASF Aktiengesellschaft 1866 bis 1980. Published by BASF Aktiengesellschaft. Verlag Wissenschaft und Politik, Köln 1980. 370 pp., bound, DM 40.00.—ISBN 3-8046-8577-3

**Origin and Chemistry of Petroleum.** Edited by *G. Atkinson* and *J. J. Zuckerman.* Pergamon Press, New York 1981. ix, 116 pp., bound, $ 30.00.—ISBN 0-08-026179-5

**Chromatographic Methods.** Comparisons of Fused Silica and Other Glass Columns in Gas Chromatography. By *W. G. Jennings.* Hüthig Verlag, Heidelberg 1981. 80 pp., bound, DM 38.00.—ISBN 3-7785-0729-X

---

**Editorial office:** Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 602-1, Telex 465516 vchwh d.

**Editor:** *O. Smrekar,* **Translation Editors:** *I. G. Neil* and *A. Stimson.*

**Publishers:** Verlag Chemie GmbH. (Managing Director *Dr. Helmut Grünewald*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany, Telephone Weinheim (06201) 602-1, Telex 465516 vchwh d.

ANGEWANDTE
CHEMIE

Volume 20 · Number 11
November 1981
Pages 899-990

International Edition in English

# Hybrid Orbitals and Their Applications in Structural Chemistry

By Werner A. Bingel and Wolfgang Lüttke[*]

*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

A uniform, systematic, and complete review is given on s-p hybrid orbitals with which a central atom Z enters into $\sigma$ bonds with two to four ligands L. All possible cases of symmetry are treated: in four-coordination from $T_d$ symmetry in $ZL_4$ molecules to the asymmetric case of four different ligands; in three-coordination from $D_{3h}$ symmetry in $ZL_3$ molecules to $C_s$ symmetry for $ZLL'L''$ molecules. For some cases the formulas are given for the first time. In this connection it is shown that the most general $sp^3$ and $sp^2$ hybrids still contain three and two free parameters, respectively. The appearance of hybrid orbitals on changing from a *"delocalized"* to a *"localized"* description of the bonding situation is illustrated with examples. Finally, possible applications in the description of the bonding relationships of molecules and the interpretation of the results of spectroscopic methods for the determination of molecular structure are indicated and likewise illustrated by examples.

## 1. Introduction

The s-p hybrid orbitals with which a central atom Z binds two, three, or four *identical* ligand atoms L should be known to any chemist. Diagrams of their spatial arrangement, often together with formulas by which they are expressed through the s and the three p atomic orbitals (AO's) of the central atom Z, are nowadays given in many introductory textbooks of general, inorganic, and organic chemistry[1]. These are the well-known *special digonal* or sp, *trigonal* or $sp^2$, and *tetrahedral* or $sp^3$ hybrid AO's, introduced already in 1928 by *Pauling* to explain the directed valence in linear $ZL_2$, planar $ZL_3$, and tetrahedral $ZL_4$ molecules[2].

These orbitals are called *special* because the *valence* or *interorbital* angles[3] are all equal and have the special values of 180°, 120°, and 109.5°, respectively. Since at the same time the percentage s or p character is also fixed (see below), these special hybrids contain *no other free parameters* of any kind. They are also characterized by the fact that for reasons of symmetry their bond *and* valence angles[3] must coincide.

If, on the other hand, the central atom Z binds *different* ligands, L, L', L'', *etc.*, the bond angles will deviate from these special values to a greater or lesser extent, depending on the nature of the ligands in question. Consequently, *more general* hybrid orbitals are now needed, in which the parameters (valence angle and s or p character) are—within certain limits—still freely variable to be able to adapt them to the particular molecule.

Several of such hybrid orbitals for planar $ZL_2L'$ molecules such as $F_2C{=}O$ or pyramidal $ZL_3L'$ molecules such as $CH_3Cl$ can indeed be found scattered among the literature of the 'thirties to 'fifties[4-6,88].

---

[*] Prof. Dr. W. A. Bingel
Lehrstuhl für Theoretische Chemie der Universität
Tammannstrasse 6, D-3400 Göttingen (Germany)
Prof. Dr. W. Lüttke
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

0570-0833/81/1111-0899 $ 02.50/0

What is still lacking is a *coherent* and *comprehensive* account, and this is the aim of the present review.

In the second section the formulas for arbitrary hybrids with s and p orbitals will be summarized, including the auxiliary conditions that the parameters appearing in the hybrid orbitals must satisfy. It will be shown that the *most general* $sp^3$ orbitals, which contain the maximum possible number of still *freely variable* parameters, have not been known before. They are therefore given for the first time in Sections 2.1—2.11; here also are given, for the sake of completeness, results for the *most general* sp and $sp^2$ hybrid orbitals, which are already well known. A review of all possible cases (with examples) is given in Table 1 (Section 2).

To clarify the concepts, it may be mentioned at this point that, for example, the designation $sp^2$ does not indicate, as is often incorrectly done, only the three special *trigonal* hybrid orbitals, but also those three general hybrid orbitals, for the construction of which a total of one s and two p AO's are used. The distribution of, for example, the s AO's over the three hybrid orbitals is *uniform* in the *special* case (with 33% each), but it is *nonuniform* in the *general* case[7].

The hybrid AO's of Z discussed here are necessary for the formation of localized Z—L σ-bonds with the ligands L. In addition, of course, π-bonds (localized or delocalized) between Z and its ligands can also be formed, provided that suitable orbitals and valence electrons are still available in both the central atom and its ligands.

In addition, one or more σ-bonds between Z and the ligands L can be replaced by lone or "free" electron pairs E on Z. Thus, the hybrid AO's of $ZL_2L'_2$ molecules can naturally also be used for the bonds in $ZL_2E_2$ molecules such as $H_2O$, those of $ZL_3L'$ molecules can similarly be used for $ZL_3E$ molecules such as $NH_3$, and so on.

The reader may well ask whether in present-day quantum chemistry hybrid orbitals are still of such importance that an article devoted to this rather special subject is justified. Hybrid orbitals play an important role as basis functions in molecular calculations by the "valence bond" or VB method[8-10]. However, in the MO methods used almost exclusively today they are not normally used as basis orbitals; the molecular orbitals or MO's so obtained are, rather, expressed in terms of unhybridized atomic orbitals or AO's of the atoms involved. These MO's are *delocalized, i.e.* they extend over the whole molecule, even in the case of *saturated* compounds. If, however, the results of such calculations are to be brought into harmony with the usual chemical ideas, the MO's must be *localized* by a suitable transformation[11-14] (see below). In this way, by analogy with the valence bonds of the chemist, we obtain localized two-center MO's which are now expressed in terms of hybrid AO's of the neighboring atomic centers, together with localized one-center hybrid orbitals for the "lone" or "free" electron pairs. This localization can in general be carried out just for *those* molecules whose bond situation is described by the chemist by means of a *single* valence-bond formula.

The fact that in such cases the localized and the delocalized descriptions are almost completely *equivalent* was recognized even in the early period of theoretical chemistry, but the reason *why* this is so does not appear to be generally known to this day. Consequently, an attempt will be made using simple examples to make this equivalence at least *plausible.* More far-reaching presentations of this problem can be found in the literature of theoretical chemistry[15,16].

### 1.1. Localization of Orbitals

As the first example, let us consider the nitrogen molecule N≡N; here the chemist expects to find the following *localized* orbitals: 1) For each of the two K shells one 1s AO for each of the two atoms; 2) two hybrid AO's for the two "free" electron pairs; 3) one σ and two π MO's which together describe the triple bond. This gives the following MO configuration (the exponent 2 shows the *double occupation* of each orbital):

$$(1s_a)^2(1s_b)^2(n_a)^2(n_b)^2\sigma^2\pi_x^2\pi_y^2 \tag{1}$$

On the other hand, an MO calculation gives a different, more *delocalized* description by so-called "canonical" MO's, which are *all* two-centered:

$$(1\sigma_g)^2(1\sigma_u)^2(2\sigma_g)^2(2\sigma_u)^2\pi_x^2\pi_y^2(3\sigma_g)^2 \tag{2}$$

Nevertheless, all chemical properties of the $N_2$ molecule are described by (1) or (2) in a completely *equivalent manner.* For example, let us consider the contribution of the two lowest-energy orbitals to the *electron density.* In the delocalized description (2), the orbitals are given to a good approximation by the LCAO forms

$$\begin{aligned} 1\sigma_g &= (2)^{-1/2}\cdot(1s_a + 1s_b) \\ 1\sigma_u &= (2)^{-1/2}\cdot(1s_a - 1s_b) \end{aligned} \tag{3}$$

and their contribution to the electron density is twice the sum of the squares

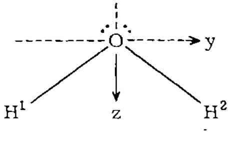
$$\Delta\rho = 2(1\sigma_g^2 + 1\sigma_u^2) \tag{4}$$

By substituting Eq. (3) in Eq. (4) and using the algebraic identity $(a+b)^2+(a-b)^2=2a^2+2b^2$, it is found that the contribution (4) is identical with

$$\Delta\rho = 2(1s_a^2 + 1s_b^2) \tag{5}$$

However, this is precisely the part of the charge density $\rho$ that the two K-shells of (1) contribute to $\rho$. It can also be shown for the remaining orbitals of Eqs. (1) and (2) that they can be converted into one another by a generalization of the transformation equations (3) in such a way that *their* contribution to the charge density is also the same for both pictures.

As a second example, consider the water molecule. The *localized* description corresponding to the valence-bond formula



(6)

is described by the MO configuration

$$(1s_0)^2(b_1)^2(b_2)^2(n_1)^2(n_2)^2 \tag{7}$$

in which $b_1$ and $b_2$ are the two-center orbitals of the two OH bonds and $n_1$ and $n_2$ are the one-center hybrid orbitals for the two lone electron pairs on the O atom.

An SCF-MO calculation, on the other hand, gives five doubly occupied MO's which belong to one of the four symmetry types of the symmetry group $C_{2v}$ of (6), which, instead of (7), leads to the MO configuration

$$(1a_1)^2(2a_1)^2(1b_2)^2(3a_1)^2(1b_1)^2 \tag{8}$$

In a so-called "minimal" AO basis these canonical MO's have the LCAO forms

$$1a_1 \approx 1s_0 \tag{9a}$$
$$na_1 = \alpha_n \cdot 2s_0 + \beta_n \cdot 2p_z + \gamma_n \cdot (1s_1 + 1s_2) \qquad n = 2, 3 \tag{9b}$$
$$1b_2 = \delta \cdot 2p_y + \varepsilon(1s_1 - 1s_2) \tag{9c}$$
$$1b_1 = 2p_x \tag{9d}$$

The lowest-energy $1a_1$ MO is, according to (9a), to a good approximation identical with the 1s orbital of the oxygen atom, and the $1b_1$ MO is, for reasons of symmetry, *exactly* identical with the $2p_x$ AO of the O atom which is oriented perpendicularly to the plane of the molecule [cf. Eq. (6)]. According to Eqs. (9b, c), on the other hand, the remaining three MO's are *completely delocalized, i.e.* they extend over all three atoms. By means of a transformation generalizing Eq. (3), however, these three MO's together with the $1b_1$ "MO" of Eq. (9d) can be replaced by four *substantially localized* MO's, which are *almost* identical with the four "highest" MO's of the localized description (7). More accurately, one obtains in this way one of the OH bonding orbitals in the form

$$B_1 = (\alpha h_1 + \beta 1s_1) + \gamma 1s_2 \tag{10}$$

and an equivalent orbital for the other OH bond ($B_2$), which follows from Eq. (10) by the interchange $1 \leftrightarrow 2$, as well as two one-center hybrid AO's $N_1$ and $N_2$ for the two lone electron pairs. The limitation "almost" shows up in a comparison of $B_1$ and $b_1$: 1) The *hybrid* AO $h_1$ in Eq. (10) deviates somewhat from the direction of the $OH^1$ bond, *i.e.* the interorbital or valence angle is, in general, not identical with the bond angle $\sphericalangle H^1OH^2$ ("bent" bonds, see below), and 2) $B_1$ is not *completely* localized in the $OH^1$ bond; an—albeit smaller—*"localization defect"* exists, which is expressed by a value of the coefficient $\gamma$ for the "false" H orbital in Eq. (10) that is small but does not vanish.

If these, generally small, corrections are ignored, then in this example the localized and delocalized descriptions of the bond situation are again completely equivalent.

Passing from the special to the general, it can be said that this equivalence is valid for all states—not necessarily ground states—of molecules with an even number of electrons and closed shells, *i.e.* purely doubly-occupied MO's that can be described by a *single* valence-structural formula. If the double occupation of the delocalized MO's in such molecules is partially lost by ionization or excitation of an electron, a localized description is generally no longer possible for the states of the resulting molecular ion or excited molecule. An example of this is the ESCA spectrum of $H_2O$[17]. In the three states of $H_2O^+$ that arise through the ionization of an electron from one of the three delocalized MO's $2a_1$, $1b_2$, and $3a_1$ of (8), a transformation to localized MO's of $H_2O^+$ can no longer be performed. The reason can be illustrated more simply with the state of $N_2^+$ that corresponds to the 1s "peak" in the ESCA spectrum of $N_2$[17]. Here ionization takes place from one of the two lowest MO's of (2) which have very similar energies (separation $\approx 0.1$ eV). The resulting highly-excited $N_2^+$ is then in one of the states

$$(1\sigma_g)^1(1\sigma_u)^2 \cdots {}^2\Sigma_g^+ \tag{11}$$

or

$$(1\sigma_g)^2(1\sigma_u)^1 \cdots {}^2\Sigma_u^+ \tag{12}$$

with the following contributions to the electron density for (11) and (12), respectively:

$$\begin{aligned} \Delta\rho &= 2 \cdot 1\sigma_g^2 + 1 \cdot 1\sigma_u^2 \\ \Delta\rho &= 1 \cdot 1\sigma_g^2 + 2 \cdot 1\sigma_u^2 \end{aligned} \tag{13}$$

The same simple substitution that led from Eq. (4) to Eq. (5) for neutral $N_2$ now gives

$$\Delta\rho = 1s_a^2 + 1s_b^2 + 1\sigma_u^2 \quad \text{and} \quad 1s_a^2 + 1s_b^2 + 1\sigma_g^2 \tag{14}$$

*i.e.* two electrons are localized in the now *singly*-occupied K-shells, while in both cases the third occupies a delocalized two-center MO. This state of affairs can also be explained by valence bond formulas: the two states (11) and (12) of $N_2^+$ can no longer be described by a single valence structure. Rather, there are *two* structures (*A*) and (*B*) with only one electron in one of the two K-shells:

$$(A) \quad \overset{+}{N}\equiv N \qquad N\equiv\overset{+}{N} \quad (B)$$

The "resonance" or mesomerism between these two structures then leads to the VB wave functions $(A)+(B)$ and $(A)-(B)$, which correspond to (11) and (12), respectively.

This digression on the relationship between delocalized and localized descriptions of chemical bonds in molecules will also serve as an illustration of the above-mentioned necessary occurrence of hybrid orbitals on localization. Consequently, even in present-day quantum-chemical calculations hybrid AO's have a firm place because they allow their interpretation in a language with which the chemist is familiar.

In addition to this, hybrid AO's are used in the interpretation of the results of spectroscopic methods of *structure determination:* in NMR spectroscopy, the percentage s character of the hybrid orbitals of the bonds concerned is deduced from measured CH and CC coupling constants[18]; bond angles and the percentage ionic character of bonds are determined from measured nuclear quadrupole coupling constants using hybrid orbitals[19]. Hybrid orbitals are also involved in the discussion of bond lengths[20], force constants, and dipole moments[21], and of other molecular constants.

While it is true that the relationships between experimentally measured values and theoretical bond quantities that are used in these cases have often only an approximate validity, they are the only possible means of interpretation in all those cases—and they are the overwhelming majority—in which a direct quantum-mechanical *ab-initio* calculation of these measured values with sufficient accuracy is still impossible. These applications will be discussed in closer detail in Section 3.

### 1.2. Construction of s-p Hybrid Orbitals

The central atom Z makes available its s orbital and the three p orbitals of its valence shell. The three real and normalized p AO's

$$p_x = R(r)\frac{x}{r}, \quad p_y = R(r)\frac{y}{r}, \quad p_z = R(r)\frac{z}{r} \tag{15}$$

are transformed under rotations like unit vectors in the three axial directions. Consequently, the $p_i$ orbital, whose axis of symmetry coincides with an arbitrary *valence direction i* described by the unit vector $\boldsymbol{n}_i$, can be written as

$$p_i = \boldsymbol{p}\cdot\boldsymbol{n}_i = \frac{R(r)}{r}\,\boldsymbol{r}\cdot\boldsymbol{n}_i \qquad \boldsymbol{p} = (p_x, p_y, p_z) \tag{16}$$

*i.e.* as the scalar product of $\boldsymbol{n}_i$ with the "vector" $\boldsymbol{p}$. In Figure 1, this construction is illustrated for the special case of a p orbital lying in the xy plane.

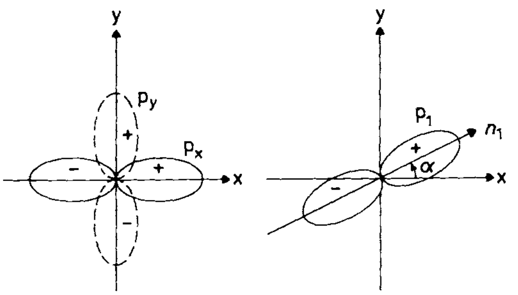


Fig. 1. p-Orbital in the xy plane with its valence direction $\boldsymbol{n}$ forming the angle $\alpha$ with the x axis. Here Eq. (16) has the special form $p = p_x\cos\alpha + p_y\sin\alpha$.

An s-p hybrid in direction $i$ is then of the form

$$h_i = (s + \lambda_i p_i)/\sqrt{1+\lambda_i^2} \tag{17}$$

with the *hybridization parameter* $\lambda_i \geqslant 0$[22], the s contribution $1/(1+\lambda_i^2)$, and the p contribution $\lambda_i^2/(1+\lambda_i^2)$[23]. The square root normalizes $h_i$ to 1. The smallest possible value $\lambda_i = 0$ gives the pure s orbital, and $\lambda_i = \infty$ gives the pure, *i.e.* unhybridized, p orbital. In this way, four hybrid AO's (17) with four different valence directions ($i = 1, 2, 3, 4$) can be formed from one s and three p AO's.

If the central atom Z is imagined to be at the center of a unit sphere, the tips of the four valence direction vectors $n_i$ whose origin is at Z lie on this sphere and form the corners of a spherical quadrilateral.

The angle between the valence directions $i$ and $j$ is the valence angle $\theta_{ij}$, which can be represented by a side or diagonal of this spherical quadrilateral (Fig. 2).

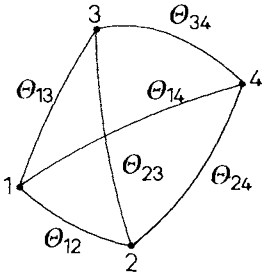


Fig. 2. The spherical quadrilateral formed by the four valence directions $i$ and the six valence, *i.e.* interorbital, angles $\theta_{ij}$.

Of the four hybrid AO's $h_i$ in (17) we must demand that they—just like the unhybridized s and p AO's—are *orthogonal* to one another, *i.e.* that the integral over the whole of space vanishes

$$\iiint h_i h_j \,dx\,dy\,dz = 0 \quad \text{for all} \quad i \neq j \tag{18}$$

Because of (17) and the normalization of the AO's it follows from this that

$$1 + \lambda_i\lambda_j \iiint p_i p_j \,dx\,dy\,dz = 0 \quad \text{for all} \quad i \neq j \tag{19}$$

The integral in Eq. (19) is equal to $\cos\theta_{ij}$, which follows from Eq. (16). In this way one obtains the *six* orthogonality relations (abbreviated to OR)

$$\cos\theta_{ij} = -1/\lambda_i\lambda_j \quad \text{for all} \quad i \neq j \tag{20}$$

Two further auxiliary conditions are obtained from the requirement that the sum of all the s contributions and the sum of all the p contributions in the four hybrid AO's must add up to 1 and 3, respectively [Eq. (21a, b)].

$$\sum_{i=1}^{4} \frac{1}{1+\lambda_i^2} = 1 \tag{21a}$$

$$\sum_{i=1}^{4} \frac{\lambda_i^2}{1+\lambda_i^2} = 3 \tag{21b}$$

A preliminary assessment might be made in the following way: There are six $\theta$ values and four $\lambda$ values, *i.e.* a total of ten parameters. But these parameters must satisfy the six OR's of Eq. (20) and the two conditions of Eqs. (21a and b). Thus, 10—6—2 or 2 independent parameters should remain.

This reasoning is erroneous in several respects: in the first place, even a *general* spherical quadrilateral (Fig. 2) is determined not by six but by only five parameters: the four sides and one diagonal in Figure 2 are sufficient to fix the second diagonal. In the second place, even in a molecule ZLL′L″L‴ with four different ligands there are not five but only three independent valence angles $\theta_{ij}$. The special form of the OR's of Eq. (20) means in fact that *van Vleck*'s identity[4]

$$\cos\theta_{12}\cos\theta_{34} = \cos\theta_{13}\cos\theta_{24} = \cos\theta_{14}\cos\theta_{23} = (\lambda_1\lambda_2\lambda_3\lambda_4)^{-1} \tag{22}$$

must be satisfied. This condition represents *two* additional constraints on the valence angles $\theta_{ij}$, which explains the above reduction from five to three.

On the other hand, there are likewise not $4-2=2$ independent values for $\lambda$ but again three of them. The two auxiliary conditions (21a, b) are in fact not independent of each other. When one holds, the other is automatically satisfied too, as may be easily verified.

If it is now possible to determine, on the one hand, from three mutually independent valence angles $\theta$ the remaining three angles and all values for $\lambda$ and, on the other hand, when three independent values for $\lambda$ are specified to determine the fourth and all six angles $\theta$, the *most general* $sp^3$ hybrid orbitals should contain *three independent* parameters in each case. The fact that this is actually so will be shown in Section 2.1.

In addition to the equations (20) to (22), the hybridization parameters $\lambda_i$ must also satisfy the following *inequalities*

$$\lambda_i \geq 0 \quad \text{for all} \quad i \tag{23}$$

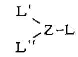
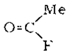
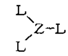
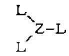
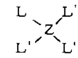
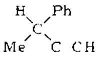
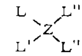
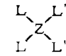
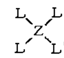
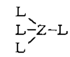
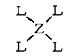
$$\lambda_i \lambda_j \geq 1 \quad \text{for all pairs} \quad i,j \quad \text{with } i \neq j \tag{24}$$

Inequality (23) has already been introduced before as a convention[22]. Inequality (24) follows from Eq. (20), since the cosines of real angles $\theta$ can only assume values between $-1$ and $+1$. This limits the permissible values of $\lambda$ to certain intervals of the positive $\lambda$-axis. Finally, it follows from Eqs. (20) and (24) that $\cos\theta_{ij}$ must be negative and therefore the valence angle $\theta_{ij}$ must be $\geq 90°$.

Knowing the above relationships, we will now in the following sections derive the most general hybrids and their special cases.

All the possible cases so arising are summarized in Table 1.

Table 1. Summary of all possible cases of hybridization with the numbers of *independent* bond angles ($\alpha$), valence angles ($\alpha^{\text{val.}}$), and hybridization parameters ($\lambda$).

| Hybridization | Case [b] | Symmetry | Molecule | No. of independent values for $\alpha$ | $\alpha^{\text{val.}}$ | $\lambda$ | Examples |
|---|---|---|---|---|---|---|---|
| sp | 1 | $C_{\infty v}$ | LZL′ | 0 | 0 | 1 | OCS, $N_2O$, HCN |
| | 2 | $D_{\infty h}$ | LZL | 0 | 0 | 0 | OCO, $N_3^-$ |
| $sp^2$ | 3 | $C_s$ |  | 2 | 2 | 2 |  |
| | 4 | $C_{2v}$ |  | 1 | 1 | 1 | $H_2C$ $CH_2$, $H_2C$ ·O |
| | 5 | $D_{3h}$ |  | 0 | 0 | 0 | $CO_3^{2-}$, $BF_3$ |
| $sp^3$ | 6 | $C_1$ |  | 5 | 3 | 3 |  |
| | 7 [a] | $C_1$ |  | 4 | 3 | 3 | ? |
| | 8 | $C_s$ |  | 3 | 2 | 2 | $CH_2ClBr$ |
| | 9 | $C_{2v}$ |  | 2 | 1 | 1 | $CH_2Cl_2$ |
| | 10 | $C_{3v}$ |  | 1 | 1 | 1 | $CH_3Cl$ |
| | 11 | $T_d$ |  | 0 | 0 | 0 | $CH_4$, $NH_4^+$, $C(Me)_4$ |

[a] In this (hypothetical?) case the dihedral angle between the LZL‴ and the L′ZL″ planes is 90°. [b] The designations of the cases correspond to the appropriate paragraphs of Section 2.

## 2. Types of Hybrid Orbitals

### 2.1. The Most General Digonal sp Hybrid Orbitals of Symmetry $C_{\infty v}$

The form of two *general, i.e.* nonequivalent collinear hybrids has been known for a long time[2]. The hybrid orbital

$$h_1 = (s + \lambda_1 p_z)/\sqrt{1+\lambda_1^2} \tag{25a}$$

*i.e.* $p_1 = p_z$, is complemented by the so-called "ortho-hybrid" with $p_2 = -p_1$ and $\lambda_2 = 1/\lambda_1$ (only *one* free parameter)

$$h_2 = (\lambda_1 s - p_z)/\sqrt{1+\lambda_1^2} \tag{25b}$$

in such a way that the s and p contributions of the two each add up to 1. The two p AO's of the central atom Z that have not yet been involved, $h_3 = p_x$ and $h_4 = p_y$, are still available for the formation of π-bonds with the two ligands in linear LZL′ molecules such as, *e.g.*, OCS. It may be shown that because $\lambda_3=\lambda_4=\infty$ for the pure p AO's (see Section 1.2), the six OR's [Eq. (20)], the two auxiliary conditions (21a, b), and the inequalities (23) and (24) are all satisfied. Thus, with the linear arrangement present here the valence angles in Eqs. (20) and (22) are $\theta_{12}=180°$ and $\theta_{ij}=90°$ for all other pairs.

### 2.2. Special Digonal sp Hybrid Orbitals of Symmetry $D_{\infty h}$

With two *identical* ligands, as in the $CO_2$ molecule, the symmetry group rises to $D_{\infty h}$, and the two hybrid AO's (25a, b) must become *equivalent, i.e.* $\lambda_1=1/\lambda_1$ or $\lambda_1^2=1$, which, in view of Eq. (23), has the consequence $\lambda_1=+1$. In this way we obtain

$$\mathrm{di}_1=\frac{1}{\sqrt{2}}(s+p_z) \tag{26a}$$

$$\mathrm{di}_2=\frac{1}{\sqrt{2}}(s-p_z) \tag{26b}$$

### 2.3. The Most General $sp^2$ Hybrid Orbitals of Symmetry $C_s$

They occur in planar molecules with *three different* ligands (ZLL′L″). The three hybrid AO's in the x,y plane (Fig. 3a) are all of the form of Eq. (17); and in addition $h_4=p_z$, *i.e.* $\lambda_4=\infty$ (see Section 2.1). Consequently, the three OR's

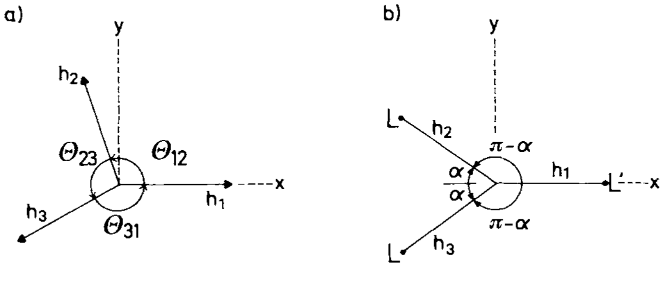


Fig. 3. a) The three most general planar $sp^2$ hybrids with $C_s$ symmetry. b) Special $sp^2$ hybrids for $L_2ZL'$ molecules with $C_{2v}$ symmetry.

$$\cos\theta_{i4}=0,\quad i=1,2,3$$

just like the *Van Vleck* identity [Eq. (22)], are satisfied automatically. Of the remaining three OR's

$$\cos\theta_{12}=-1/\lambda_1\lambda_2 \tag{27a}$$
$$\cos\theta_{23}=-1/\lambda_2\lambda_3 \tag{27b}$$
$$\cos\theta_{31}=-1/\lambda_3\lambda_1 \tag{27c}$$

only two are independent, since

$$\theta_{12}+\theta_{23}+\theta_{31}=360°.$$

Because $\lambda_4=\infty$, the conditions (21a, b) now take the form

$$\sum_{i=1}^{3}\frac{1}{1+\lambda_i^2}=1\qquad\sum_{i=1}^{3}\frac{\lambda_i^2}{1+\lambda_i^2}=2 \tag{28a, b}$$

We therefore have only *two* independent hybridization parameters, *e.g.* $\lambda_1$ and $\lambda_2$. If these are given initially, the three valence angles are determined from Eqs. (27a–c).

If, conversely, two independent valence angles $\theta$ are known, the three $\lambda$ values can be determined from the expressions[24]:

$$\lambda_1^2=-\cos\theta_{23}/\cos\theta_{12}\cos\theta_{13} \tag{29a}$$
$$\lambda_2^2=-\cos\theta_{31}/\cos\theta_{23}\cos\theta_{21} \tag{29b}$$
$$\lambda_3^2=-\cos\theta_{12}/\cos\theta_{31}\cos\theta_{32} \tag{29c}$$

which are obtained by solving Eqs. (27) for the individual $\lambda_i$ values. All three $\lambda$ values obtained in this way then satisfy the auxiliary conditions (28a, b). This proves the statement given in the introduction that the most general $sp^2$ hybrid AO's contain *two* free parameters.

An explicit expression for the most general hybrid orbital $h_1$ can also be derived from Eq. (29):

$$h_1=\left(s-\frac{\cos\theta_{23}}{N}p_1\right)\cdot(\mathrm{ctg}\,\theta_{12}\,\mathrm{ctg}\,\theta_{31})^{1/2} \tag{30a}$$

with the abbreviation

$$N=(-\cos\theta_{12}\cos\theta_{23}\cos\theta_{31})^{1/2} \tag{30b}$$

The expressions for $h_2$ and $h_3$ follow from Eqs. (30a, b) by a single or double cyclic permutation of the subscripts $1\rightarrow2\rightarrow3\rightarrow1$.

### 2.4. The $sp^2$ Hybrid Orbitals for $L_2ZL'$ Molecules with $C_{2v}$ Symmetry

This special case with *two equivalent* hybrid AO's for the two identical ligands is obtained from the formulas given in Section 2.3 with $\lambda_2=\lambda_3=\lambda$. It then follows from Eqs. (27a–c) that $\theta_{23}=2\alpha$ and $\theta_{12}=\theta_{31}=180°-\alpha$, *i.e.* that the two equivalent hybrid orbitals $h_2$ and $h_3$ form the same angle with the axis of symmetry (see Fig. 3b). In total, for these one-parameter hybrid AO's we have the explicit formulas[5]:

$$h_1=(\cos\alpha\cdot s+(-\cos2\alpha)^{1/2}p_1)/\sin\alpha \tag{31a}$$
$$h_i=((-\cos2\alpha)^{1/2}\cdot s+p_i)/\sqrt{2}\sin\alpha\qquad i=2,3 \tag{31b}$$

### 2.5. The Special Trigonal $sp^2$ Hybrid Orbitals with $D_{3h}$ Symmetry

These are obtained from Eqs. (31a, b) for $\alpha=60°$. They no longer contain free parameters. Their form is[2]:

$$\mathrm{tri}_i=\frac{1}{\sqrt{3}}(s+\sqrt{2}p_i)\qquad i=1,2,3 \tag{31c}$$

### 2.6. The Most General $sp^3$ Hybrid Orbitals of Symmetry $C_1$

Equations (20) to (22) of Section 1.2 apply to these orbitals. It was also shown in Section 1.2 that there are only *three* independent valence angles $\theta_{ij}$ or hybridization parameters $\lambda_i$. It still remains to be shown that when one of these two sets of parameters is given, all the remaining parameters can be determined unambiguously. In some cases, however, there may be more than one solution.

When the four $\lambda$ values, which must satisfy the one auxiliary condition (21a) and the inequalities (23, 24), are given beforehand, all six valence angles can be determined from the OR's of Eq. (20). The identity (22), which is a consequence of the special form of the OR's, is thereby automatically satisfied.

If, conversely, *three* valence angles, such as $\theta_{12}$, $\theta_{23}$, and $\theta_{31}$, are given, the values for $\lambda$ can be determined from the following generalized form of Eqs. (29a—c):

$$\lambda_i^2 = -\cos\theta_{jk}/\cos\theta_{ij}\cos\theta_{ik} \tag{32}$$

Here the triad of subscripts *i, j, k* is any combination of three numbers from the index set 1, 2, 3, 4. The remaining three valence angles $\theta_{i,4}$ with $i = 1, 2, 3$ are then obtained from the OR's according to Eq. (20).

*More special* $sp^3$ hybrids can easily be derived from Eqs. (20) to (22) and (32). This is done in Sections 2.7—2.11.

### 2.7. General $sp^3$ Hybrid Orbitals for "Perpendicular" ZLL′L″L‴ Molecules with $C_1$ Symmetry

This sub-case in which the two planes LZL‴ and L′ZL″ are perpendicular to each other is mentioned only for the sake of completeness. No examples are known to the authors, and therefore no formulas are given here. Formulas can be obtained—if necessary—from those of Section 2.6 when the two "digonal" valence angles $\theta_{14}$ and $\theta_{23}$ of Figure 2 intersect each other at 90°.

A *possible* realization would be given by the $L_2ZL'L''$ molecules of the next section if the two identical ligands L are not—as assumed there—mirror-images, but lie *unsymmetrically* with respect to the plane determined by L′, Z, L″. In spite of only three different types of ligands, such a central atom would then be *chiral*; with a symmetrical position of the two identical ligands it would be *prochiral*.

### 2.8. $sp^3$ Hybrid Orbitals for $L_2ZL'L''$ Molecules with $C_s$ Symmetry

Normally, the two identical ligands L will lie in *mirror-image relationship* with respect to the plane defined by L′, Z, and L″, *i.e.* they will assume *equivalent* positions in the molecule. The spherical quadrilateral of Figure 2 then assumes the special form of Figure 4a, from which it can be seen that $\theta_{12} = \theta_{13} = \theta$ and $\theta_{24} = \theta_{34} = \vartheta$. Of the six OR's of Eq. (20), there are two identical pairs:

$$\cos\theta = -1/\lambda_1\lambda_2 = -1/\lambda_1\lambda_3 \tag{33a}$$
$$\cos\vartheta = -1/\lambda_2\lambda_4 = -1/\lambda_3\lambda_4 \tag{33b}$$

*i.e.* $\lambda_2 = \lambda_3 = \lambda$.

Naturally, equivalent hybrid AO's must be assigned to the two identical ligands. The two free parameters are the two angles $\theta$ and $\vartheta$, from which the value of $\lambda_i$ can be determined according to Eq. (32) with Eq. (21a) satisfied. If, on the other hand, two of the $\lambda$'s are known the two angles are obtained from Eq. (21a) and Eqs. (33a, b).

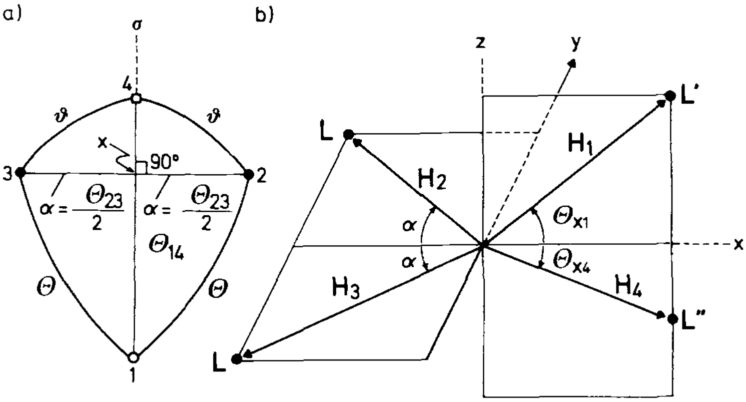


Fig. 4. $sp^3$ hybrids for $L_2ZL'L''$ molecules with $C_s$ symmetry. a) The valence angles in the spherical quadrilateral. The L, L′, and L″ ligands are located at corners 2 and 3, 1, and 4. b) Spatial orientation of valence directions *i* in an xyz coordinate system.

However, this route is unsuitable for a *calculation*, since in each case the two other angles $\theta_{14}$ and $\theta_{23}$ must also be determined by trigonometric transformations. Our aim is achieved faster if one starts from the explicit formulas (31a, b) for $L_2ZL'$ molecules. The $h_1$ hybrid of Eq. (31a) is then mixed unsymmetrically with the $p_z$ AO, which was not used there, *i.e.* the *new* hybrid orbitals

$$H_1 = \cos\beta \cdot h_1 + \sin\beta \cdot p_z$$

and

$$H_4 = \sin\beta \cdot h_1 - \cos\beta \cdot p_z$$

with the mixing parameter $\beta$ (which is *not* a valence or bond angle!) are introduced by analogy to Eqs. (25a, b). They are represented by capital letters to distinguish them from the $h_i$ of Eq. (31a, b).

Substitution of (31a) gives, after a short calculation, the following two *nonequivalent* hybrid orbitals:

$$H_1 = (\cos\beta \cdot s + \sqrt{tg^2\alpha - \cos^2\beta} \cdot p_1) \cdot ctg\,\alpha \tag{34a}$$
$$H_4 = (\sin\beta \cdot s + \sqrt{tg^2\alpha - \sin^2\beta} \cdot p_4) \cdot ctg\,\alpha \tag{34b}$$

The valence directions $\boldsymbol{n}_1$ and $\boldsymbol{n}_4$ of the two orbitals lie in the xz plane (see Fig. 4b), which is the mirror plane of the molecule, but they form *different* angles with the x-axis:

$$tg\,\theta_{x1} = tg\beta \frac{\sin\alpha}{(-\cos 2\alpha)^{1/2}} \tag{35a}$$

$$tg\,\theta_{x4} = -ctg\beta \frac{\sin\alpha}{(-\cos 2\alpha)^{1/2}} \tag{35b}$$

The two *equivalent* hybrid orbitals are taken over unchanged from Eq. (31b) and are now denoted by capital letters in order to have agreement with (34a, b):

$$H_i = ((-\cos 2\alpha)^{1/2} \cdot s + p_i)/\sqrt{2}\sin\alpha \qquad i = 2, 3 \tag{34c, d}$$

Their valence directions $\boldsymbol{n}_2$ and $\boldsymbol{n}_3$ lie in the xy plane in mirror-image relationship to the $\sigma_{xz}$ mirror plane (see Fig. 4b).

In Appendix II of a paper from 1951[6], *Torkington* stated that, "there is no set of four $sp^3$ hybrid orbitals with $C_s$ symmetry". The fact that this statement and the proof given for it are incorrect is shown by Eqs. (34), which explicitly give just such a set. This set also contains—as stated—two parameters, namely the bond angle $LZL=\theta_{23}=2\alpha$ and the mixing parameter $\beta$ (which can be limited to the range 0 to 45°).

For the valence angle $\theta_{14}$ of Figure 4b we obtain from Eqs. (35a, b):

$$\mathrm{tg}\,\theta_{14}=-2\,\mathrm{tg}\,\alpha\sqrt{\mathrm{tg}^2\alpha-1}/\sin 2\beta \tag{36}$$

The following special cases for particular values of the mixing parameter $\beta$ are of interest, and also provide an opportunity to check the correctness of the formulas derived:

1) $\beta=0$, *i.e.* no mixing of $h_1$ and $p_z$, restores the original $sp^2$ hybrid orbitals (31) and the $p_z$ orbital:

$$H_1\rightarrow h_1,\ H_4\rightarrow p_z,\ H_2=h_2 \text{ and } H_3=h_3$$

2) $\beta=45°$; here $H_1$ and $H_4$ are *equivalent* and according to Eqs. (35a, b) make the same angle with the x-axis. One thus obtains the hybrid orbitals of Eq. (39) for $L_2ZL'_2$ molecules.

## 2.9. $sp^3$ Hybrid Orbitals for $L_2ZL'_2$ Molecules with $C_{2v}$ Symmetry

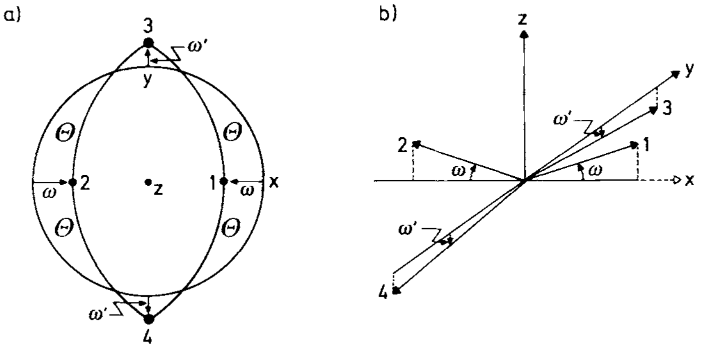


Fig. 5. $sp^3$ Hybrids for $L_2ZL'_2$ molecules with $C_{2v}$ symmetry. a) Representation of the spherical quadrilateral; $\theta_{12}=180°-2\omega$, $\theta_{34}=180°-2\omega'$. b) Spatial representation (*van Vleck*'s $\omega$-model [4]).

Here *two* pairs of two equivalent hybrid AO's each are required. Consequently, we put $\lambda_1=\lambda_2=\lambda$ and $\lambda_3=\lambda_4=\mu$ and obtain from Eq. (21a) the relations:

$$\mu=\left(\frac{\lambda^2+3}{\lambda^2-1}\right)^{1/2} \quad\text{and}\quad \lambda=\left(\frac{\mu^2+3}{\mu^2-1}\right)^{1/2} \tag{37}$$

Of the six OR's only three are left, one for each of the two ZL and ZL′ bonds (see Fig. 5a, b)

$$\cos 2\omega=1/\lambda^2 \tag{38a}$$
$$\cos 2\omega'=1/\mu^2 \tag{38b}$$

and one *between* the two groups, *i.e.* for $\sphericalangle LZL'=\theta$

$$\cos\theta=-1/\lambda\mu \tag{38c}$$

A fairly long calculation gives the final formulas[5]

$$h_i=\begin{cases}((\cos 2\omega)^{1/2}\cdot s+p_i)/\sqrt{2}\cos\omega & i=1,2 \quad (39a)\\ ((\cos 2\omega')^{1/2}\cdot s+p_i)/\sqrt{2}\cos\omega' & i=3,4 \quad (39b)\end{cases}$$

and also the angular relationship derivable from Eqs. (37) and (38)

$$\cos\theta=-\sin\omega\cdot\sin\omega'=-(\cos 2\omega\cos 2\omega')^{1/2} \tag{40}$$

from which it also follows that

$$\mathrm{tg}^2\omega+\mathrm{tg}^2\omega'=1 \tag{41}$$

Again, everything is determined by *one* angle, such as $\omega$. One should note that according to Eq. (41) $|\omega|$ and $|\omega'|$ must be less than 45°, which again shows that valence angles <90° cannot be constructed from hybrids of s and p AO's (see Section 1.2), which is already well known.

The angles $\omega$ and $\omega'$ are defined—differently from *van Vleck*[4]—in such a way that they are *both* positive. In Figure 5b, therefore, *one* hybrid pair must point in the direction of the negative z axis[25].

If the hybrid orbital $h_1$ of Eq. (31a) is mixed *symmetrically* with the $p_z$ AO, the two new orbitals $(h_1+p_z)/\sqrt{2}$ and $(h_1-p_z)/\sqrt{2}$, together with $h_2$ and $h_3$ of Eq. (31b), must give the same result (39a, b) as the above derivation.

If we put $\lambda=\mu$, Eq. (37) gives the common value $\sqrt{3}$, and we obtain the special case described in Section 2.11 of the tetrahedral $sp^3$ hybrid AO's with no free parameters ($\mathrm{tg}\,\omega=\mathrm{tg}\,\omega'=1/\sqrt{2}$).

## 2.10. $sp^3$ Hybrid Orbitals for $L_3ZL'$ Molecules with $C_{3v}$ Symmetry

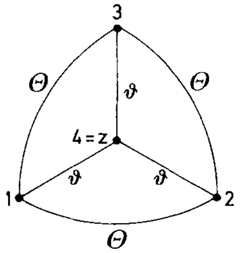


Fig. 6. $sp^3$ Hybrids for $L_3ZL'$ molecules with $C_{3v}$ symmetry. Here $2\cos\theta=3\cos^2\vartheta-1$.

This case requires three equivalent hybrid orbitals. If, therefore, we put $\lambda_1=\lambda_2=\lambda_3=\lambda$ and $\lambda_4=\mu$, Eq. (21a) gives

$$\mu=\left(\frac{3}{\lambda^2-2}\right)^{1/2} \quad\text{and}\quad \lambda=\left(\frac{3+2\mu^2}{\mu^2}\right)^{1/2} \tag{42}$$

Of the OR's [Eq. (20)], two sets of three are identical; with $\theta_{12}=\theta_{23}=\theta_{31}=\theta$ and $\theta_{i4}=\vartheta$ for $i=1, 2, 3$, we obtain

$$\cos\theta=-1/\lambda^2 \tag{43a}$$
$$\cos\vartheta=-1/\lambda\mu \tag{43b}$$

and also from (42) and (43a, b) the relation

$$2\cos\theta=3\cos^2\vartheta-1 \tag{44}$$

which can be read off from the spherical triangle 1, 2, 4 of Figure 6. After a short calculation, we obtain[4]

$$h_i = \left[(1-2\,\mathrm{ctg}^2\vartheta)^{1/2}\cdot s + \frac{\sqrt{2}}{\sin\vartheta}\cdot p_i\right]/\sqrt{3} \qquad i=1,2,3 \tag{45a}$$

$$h_4 = [-\sqrt{2}\,\mathrm{ctg}\,\vartheta\cdot s + (1-2\,\mathrm{ctg}^2\vartheta)^{1/2}\cdot p_4] \tag{45b}$$

Therefore all quantities are expressed in terms of the *one* valence angle $\vartheta$, the other is obtained from Eq. (44). If, conversely, one of the two hybridization parameters $\lambda$ or $\mu$ is given, the other is obtained from Eq. (42) and the two angles from (43a, b)[25]. If now we put $\lambda=\mu=\sqrt{3}$, the above equations specialize to the tetrahedral $sp^3$ hybrid orbitals (see Section 2.11), since according to Eq. (43) we have $\cos\theta=\cos\vartheta=-1/2$.

### 2.11. The Special Tetrahedral $sp^3$ Hybrid Orbitals for $ZL_4$ Molecules of Symmetry $T_d$

These may be obtained by the specialization given at the end of Section 2.10. They have the well-known form:

$$h_i = \frac{1}{2}(1+\sqrt{3}\,p_i) \qquad i=1,2,3,4 \tag{46}$$

where the p orbitals of the central atom point toward the vertices of a tetrahedron.

## 3. Applications: Examples and Possibilities

Since the structural properties of a molecule are determined by its electron distribution, and since the constituent atoms approximately retain their individuality in the molecular association ("atoms in molecules"[26]), each atom Z contributes to the overall structure of the molecule according to the hybridization of its electron arrangement. All structural quantities (particularly geometry, energetics, charge distribution and, consequently, also reactivity) should therefore be capable of being described by the nature of the hybrid orbitals involved in the bonds[10,16,27].

### 3.1. Molecular Geometry

Covalent molecules are characterized by a definite geometric structure which manifests itself in the appearance of directed bonds and definite interatomic distances. The reason for this is that in each case a minimum energy is associated with a certain spatial arrangement of the nuclei and the electrons.

To the extent that the *stereochemistry* of a molecule is given by its *bond angles*, it is described by the relationships between the s or p character of the hybrid orbitals and the valence angles as summarized in Section 1.2. As is well known, according to these relations the angles of the bonds issuing from an atom Z become larger, if the s character of its hybrid orbitals increases. According to recent theoretical investigations[27,28], for sterically unstrained compounds the bond angles are very close to the valence angles or are practically equal to them.

In molecules with ring strain, however, according to both calculation and experiment, the directions of the hybrid orbital axes differ substantially from those of the lines linking the atoms ("bent bonds"[29]); thus in cyclopropane and its derivatives, for example, angular deviations of about 22° have been calculated[27,29-32], or measured in X-ray studies[33-36] of the so-called *deformation densities* of the electrons. It is thus obvious to try to relate the magnitudes of these angular deviations to the ring strain energy.

The occurrence of definite CC and CH *bond lengths* in organic compounds, especially hydrocarbons (but different for different substance classes), was ascribed first by *Coulson*[37] and then with particular emphasis by *Dewar* and *Schmeising*[38] to the fact that the C atom has a so-called *covalent radius* $R_c$ which depends on its status of hybridization: $R_c$ is the smaller, the greater is the s character of the C orbital involved in the bonding. A rule of thumb is that the length decreases by about 0.04 Å in each case on passing from $sp^3$-$sp^3$ to $sp^2$-$sp^2$, and finally, to sp-sp bonding; if the CC $\sigma$-bonds are also accompanied by one or two $\pi$-bonds, an additional contraction takes place, which in conjugated compounds occurs to a weaker degree even in normal single bonds.

According to *Coulson*[37], the following expression describes the dependence of the covalent radius $R_c$ of an atom on the hybridization parameter $\lambda$:

$$R_c\,[\text{Å}] = \mathit{Const.}\cdot\frac{1+(4/3)\sqrt{3}\cdot\lambda+(3/2)\cdot\lambda^2}{1+\sqrt{3}\cdot\lambda+\lambda^2} \tag{47}$$

This relation applies only to the CC bonds of unstrained compounds; it does not give the unusually short bonds of strained compounds with their anomalous hybridization (*e.g.* those of cyclopropane or bicyclobutane); consequently, *Maksić* and *Eckert-Maksić*[39] proposed a different type of equation for the latter case, which approximates the distance along the "bent bonds" by a parabola. Other relations for $R_c=f(\lambda)$ have been given by *Brown*[40], *Somayajulu*[41], *Zeil et al.*[20a,42], *Bak et al.*[20b,43,44], *Mikhailov*[45], *Dewar* and *Schmeising*[38], *Bastiansen* and *Traetteberg*[46], and others. For further information reference may be made to the symposium report "An Epistologue on Carbon Bonds"[47].

### 3.2. Bond Energy

The fact that not only the molecular geometry but also the *energies* of the individual bonds depend on the character of the hybrid orbitals of the atoms involved in the bonding was shown by *Förster*[8] as early as 1939, for strained and unstrained hydrocarbons. *Förster* recognized as the cause of the different bond energies the different electron densities, after hybridization, between the bound atoms: stronger and less stretchable CC and CH bonds should correspond to a higher percentage s character. This can be explained as a consequence of the principle of maximum overlap of hybrid orbitals (cf. [16,48]). What is particularly convincing is *Förster*'s analysis of the observation that the energies of CH bonds, and therefore their CH force constants and vibrational frequencies[49,50], are also determined by the hybrid nature of the orbitals of the C atoms involved in bonding.

### 3.3. Bond Polarity

Another fundamental property of chemical bonds is their *polarity*[16,51,52]. The polarity is substantially determined by the *electronegativities* of the atoms involved. As was shown by *Walsh*[53] in 1948 and has been demonstrated experimentally by *Zeil*[20a], the electronegativity that an atom exhibits in a bond is the higher, the greater is the s character of its hybrid orbital involved in the bond. According to *Hinze* and *Jaffé et al.*[54,55], the electronegativity of a C orbital increases linearly with its s character. To this principle—recently confirmed by quantum-chemical analysis[56]—corresponds the fact that when a polar substituent is added to a carbon atom, the latter's hybrid orbitals become polarized in such a way that the p character of the C orbital directed toward this substituent increases. According to Eq. (21a), the p character of the other hybrid orbitals of this C atom must then decrease correspondingly, *i.e.* their s character must increase. Because of this, not only the polarities but also the corresponding bond angles and lengths undergo a change. Using a large volume of data, *Domenicano, Vaciago,* and *Coulson*[57,58] have confirmed this convincingly for variously substituted benzene derivatives.

### 3.4. NMR Coupling Constants

Hybridization also substantially affects the characteristic quantities of *nuclear magnetic resonance spectra.* Thus, the $^1$H- and $^{13}$C-NMR signals of organic compounds are concentrated on the basis of their chemical shifts in characteristic regions determined by the hybridization of the C atom. This applies analogously to the HH, CH, and CC coupling constants and is due to the fact that the spin-spin coupling is brought about to a substantial extent by the s contribution of the bonding electrons at the position of the nucleus. Correspondingly, according to Eq. (48) $^1J_{CH}$ is proportional to the s character of the hybrid orbital of the C atom involved in the CH bond[59,60], and according to Eq. (49) $^1J_{CC}$ is proportional to the product of the s characters of the hybrid orbitals of the C atoms involved in the CC bond[28,61-63]. A theoretical substantiation of these relationships has been given by *Pople et al.*[18,64-66].

$$^1J_{CH} = \frac{500}{1+\lambda^2} \quad [\mathrm{Hz}] \qquad (48)$$

$$^1J_{C\text{-}1,C\text{-}2} = A\,\frac{1}{1+\lambda_1^2}\cdot\frac{1}{1+\lambda_2^2} - B \quad [\mathrm{Hz}] \qquad (49)$$

Other structural properties connected with hybridization cannot be considered here; reference may be made to reviews[67,68].

Up to this point it has been shown how structural properties can be explained by the particular hybridization involved. Now the inverse aim must be considered, namely a quantitative characterization of the electron distribution with the aid of experimentally determined structural quantities. To this end explicit relationships between chemical structure and $\lambda$'s (or s characters) are necessary, permitting numerical values relating to, for instance, the s character of all the hybrid orbitals of a central atom Z or the discrepancy between bond and valence angles to be obtained from experimental results.

Corresponding quantitative relations such as Eq. (47)—partly of an empirical nature and partly substantiated by theory—have long been known for many important and readily measured structural quantities, although not for all. Information on the corresponding values of $\lambda$ is obtained from bond lengths with the aid of formulas such as (47), and from bond angles by the formulas of Section 2. Here it is best to use the CCH, HCH, or $CH_3$ bond angles, because even in strained compounds, *inter alia,* these differ only slightly from the corresponding valence angles which are related to the hybrid character.

The widest range of variation of the results when the accuracy of measurement is good is found in the NMR coupling constants $^1J_{CH}$[59,60] and $^1J_{CC}$[18,63]; of these, the CH coupling constants are preferred as hybridization indicators, since they are determined almost solely by the *Fermi* contact term, which depends on the C hybridization[59,66], while all three possible coupling mechanisms act on $^1J_{CC}$[69-72].

Thus, $^1$H-NMR measurements on molecules with natural $^{13}$C abundance give coupling constants $^1J_{CH}$ proportional to the s contribution $1/(1+\lambda^2)$ of the sp hybrid orbital of the C atom for the localized CH bond[59,60,66], in astonishingly good agreement with the empirical relation (48). In this way *experimental values of* $\lambda$ are obtained from which by means of the formulas summarized here experimental valence angles $\alpha^{\mathrm{val}}$ are obtained, which can then be compared with the bond angles $\alpha$ obtained from other experiments.

Similarly—within the above-mentioned limitations—conclusions about the product of the s character of the two hybrid AO's involved in the CC bond can be drawn from measured CC coupling constants of directly linked C atoms[61-63,70].

Hybrid-orbital data that are obtained experimentally in such a fashion can be used to test theories of chemical bonding and the associated methods of calculation if they are compared with the corresponding data obtained by quantum-chemical calculations (for example, by the Maximum Overlap process[72], by the INDO method[14], or by an *ab-initio* method with subsequent localization[27]).

In the search for relationships between structure and hybridization, small-ring hydrocarbons and, among them, the bi-, tri-, and tetra-cycles have always evoked the interest of theoreticians[27], spectroscopists, and preparative chemists[73-81], since they provide the opportunity to change hybridization within wide limits, even up to "abnormal" values, by varying the ring size. Substitution by polar groups can serve as another "structure variable"; according to *Walsh*[53,56], their effects on $\sigma$-bonds can also be explained by changes in hybridization.

The requirement that all molecular structural quantities are determined by the electron distribution and thus by the hybrid nature of localized orbitals can finally also help to clarify empirical correlations between experimental quantities and theory, some of which have been known for a long time, and thus make them more applicable.

The empirical rules of *molecular spectroscopy* of diatomic molecules, also applicable to the corresponding groups of polyatomic molecules, have been comprehensively discussed by *Müller* and *Bräuer*[82]. For CH bonds, *McKean*[83] has worked out various correlations valuable for structure determinations between vibrational frequencies, bond lengths, dissociation energies, and coupling constants. The relationship recently found by *Kamienska-Trela*[84] between CC force constants and the CC coupling constants $^1J_{CC}$ deserves particular attention.

### 3.5. Bond Angles and Valence Angles

So far as concerns the *bond angles* and their relationship to the *valence angles*, the cases summarized in Table 1 can be divided into three groups:

1) In the first group there are the special hybrids of cases 2, 5, and 11. As mentioned in the introduction, they no longer contain free parameters. Furthermore, for reasons of symmetry their bond angles $\alpha$ must coincide with their valence angles $\alpha^{val}$ and take the special values 180°, 120°, and 109.5°[85]. Only in these cases can we be sure that the bonds are not strained.

In all other cases there is at first no convincing reason for an exact equality of these two angles. As already mentioned, one must reckon here with greater or smaller deviations $\delta\alpha = \alpha - \alpha^{val}$, which correspond to "bent" bonds[29].

Such deviations *must* naturally always occur when bond angles $\leq 90°$ appear in the equilibrium geometry of a molecule, as for example in the small-ring hydrocarbons $(CH_2)_3$ and $(CH_2)_4$.

Deviations—even if small ones—are to be expected also in molecules with highly *polar* bonds such as $CH_2Cl_2$ and $CH_2Br_2$ (Nos. 3 and 1 in Table 2). Steric hindrance will also lead to deviations of this type. If, however, none of these reasons exists, a substantial equality of the bond and valence angles is to be expected, as in example No. 8 of Table 2, propane.

2) The second group includes cases 3, 4, and 10 with two or one free parameter and the *same* number of independent bond and valence angles. Consequently, the formulas given here at first provide no help in determining whether a certain molecule of this group has "strained" bonds. Rather, to begin with, values for $\alpha^{val}$ must be obtained by a different route. This can be done theoretically by subjecting quantum-chemical MO calculations optimized for the energetically most favorable configuration of the particular molecule to a localization process[12-15] (see Section 1). The hybrid AO's of the atoms concerned can then be read off from the resulting localized bond orbitals and the orbitals of lone electron pairs. However, this procedure is applicable only to a limited extent, since—particularly for molecules with low symmetry—it does not always provide *unambiguous* results[86]. For larger molecules of chemical interest sufficiently accurate MO calculations are still not yet available in many cases.

3) Finally, the third group includes cases 6—9 with one to a maximum of three free parameters, in which the number of *independent* bond angles is *larger* than the number of independent valence angles. Here again, of course, the methods described for the second group can be used. In addition to this, however, it is also possible in this case to deduce the presence of strained bonds from the experimentally determined bond angles *alone*. Consider as an example the $L_2ZL'_2$ molecules given in Table 2.

Table 2. Bond angles and their deviations from the valence angles for some $L_2ZL'_2$ molecules.

| No. | Molecule $L_2ZL'_2$ | No. according to [a] | $\sphericalangle LZL = \alpha$ | $\sphericalangle L'ZL' = \beta$ | $\delta\beta'$ [b] |
|---|---|---|---|---|---|
| 1 | $H_2CBr_2$ | 68 | 113.6 | 112.7 | 6.9 |
| 2 | $(NH)_2S(CH_3)_2$ | 316 | 135.0 | 101.2 | 5.8 |
| 3 | $H_2CCl_2$ | 70 | 113.0 | 111.8 | 5.5 |
| 4 | $H_2C(SiH_3)_2$ | 140 | 108.1 | 114.4 | 3.5 |
| 4 | $(SiH_3)_2CH_2$ | 140 | 114.4 | 108.1 | 2.9 |
| 5 | $H_2CF_2$ | 74 | 113.7 | 108.3 | 2.6 |
| 5 | $F_2CH_2$ | 74 | 108.3 | 113.7 | 3.0 |
| 6 | $O_2S(CH_3)_2$ | 299 | 121.0 | 103.3 | 2.3 |
| 7 | $Cl_2Si(NCO)_2$ | 152 | 107.7 | 113.0 | 1.7 |
| 7 | $(NCO)_2SiCl_2$ | 152 | 113.0 | 107.7 | 1.4 |
| 8 | $H_2C(CH_3)_2$ | 428 | 106.1 | 112.8 | −0.4 |
| 8 | $(CH_3)_2CH_2$ | 428 | 112.8 | 106.1 | −0.7 |
| 9 | $H_2Ge(CH_3)_2$ | 314 | 108.5 | 110.0 | −0.5 |
| 9 | $(CH_3)_2GeH_2$ | 314 | 110.0 | 108.5 | −0.5 |
| 10 | $(CN)_2CH_2$ | 350 | 109.4 | 108.7 | −0.8 |
| 10 | $H_2C(CN)_2$ | 350 | 108.7 | 109.4 | −0.9 |

[a] The experimental bond angles in the fourth and fifth colums have been taken from *K. H. Hellwege, A. M. Hellwege: Landolt-Börnstein,* Neue Serie Vol. 7. Springer-Verlag, Berlin 1976. [b] Calculated deviations of the angles (see text) arranged in order of decreasing values.

In case 9 of Table 1 (cf. Section 2.9) the two *bond angles* $\alpha$ and $\beta$ are independent of each other. On the other hand, there is only one independent *valence angle*, since $\alpha^{val} = 180° - 2\omega$ and $\beta^{val} = 180° - 2\omega'$ (cf. Fig. 5) are linked through the following relation which follows from Eq. (41):

$$\operatorname{ctg}^2\frac{\alpha^{val}}{2} + \operatorname{ctg}^2\frac{\beta^{val}}{2} = 1 \qquad (50)$$

This relationship is shown graphically in Figure 7.

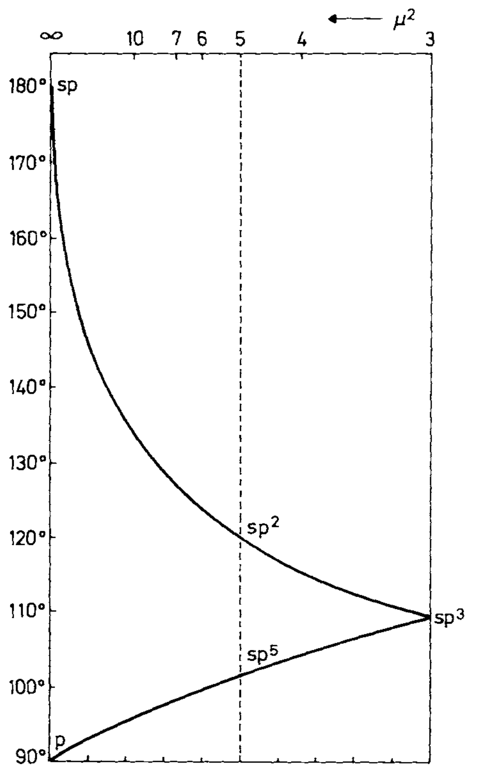


Fig. 7. The two valence angles $\alpha^{val} = \theta_{12}$ and $\beta^{val} = \theta_{34}$ of Figure 5 as functions of $\lambda^2$ ($=\lambda_1^2 = \lambda_2^2$) and $\mu^2$ ($=\lambda_3^2 = \lambda_4^2$).

It can be seen that—starting from the common value $\alpha^{\mathrm{val}}=\beta^{\mathrm{val}}=109.5^\circ$ (right-hand side of Fig. 7)—an increase in one angle automatically results in a decrease in the other. Therefore in examples 1 and 3 of Table 2, in which *both* bond angles are larger than the tetrahedral angle of 109.5°, the existence of "strained" bonds can be deduced directly from the experimental values of the bond angles without any quantum-chemical calculations of the valence angles[87]. In the other examples of the table it is possible to tell whether unstrained bonds are present by using the corresponding bond angles $\alpha$ and $\beta$ collected in Table 2 in connection with Figure 7. The bonds are unstrained only if the two points $\alpha$ and $\beta$ of the two branches of the curve lie vertically one above the other, *i.e.* belong to the *same* value of the lower abscissa $\lambda^2$. This, together with the value of the upper abscissa $\mu^2$, then gives the s contribution for the ZL and ZL′ bonds.

If this construction is impossible, deviations in at least one—and probably both—bond angles $\delta\alpha$ and $\delta\beta$ must occur. The *sum* of the deviations can be obtained in the following manner:

$\alpha^{\mathrm{val}}$ is first put equal to $\alpha$ from the fourth column of Table 2 (*i.e.* one puts $\delta\alpha=0$) and the corresponding value of $\beta^{\mathrm{val}}$ is calculated from Eq. (50). The difference between the latter and the bond angle $\beta$ from column five then gives the value shown in the sixth column $\delta\beta'=\beta-\beta^{\mathrm{val}}$. By splitting this value equally between the two angles one obtains approximate angular deviation values $\delta\alpha=\delta\beta=\delta\beta'/2$. If it is desired to avoid the unsymmetry associated with this procedure, the above simple calculation can be repeated with $\alpha$ and $\beta$ interchanged (which has been done for Nos. 4, 5, and 7—10) and averaging the two results.

The results in Table 2 confirm, in general, the statements made above relating to the reasons for "strained" bonds. As expected, propane (No. 8) and the analogous Ge compound (No. 9) have the smallest $\delta\beta$ values. But even with these compounds, which are usually regarded as certainly unstrained, small deviations lying outside the limits of error of the bond angle can be found.

### 3.6. Conclusion

In conclusion, it may be said that in the interpretation of his results by means of hybrid AO's the experimentalist must take into account the possibility illustrated here of bonds that are strained to at least some extent, even in cases in which he perhaps does not expect them to be so.

On the whole, the use of localized hybrid orbitals has proved useful on the one hand by giving the formalism of quantum chemistry an embodiment corresponding to the way of thinking of experimental chemists and on the other hand by opening up a theoretically based and at the same time descriptive correlation of experimental magnitudes of structural chemistry.

*We thank Dr. B. Klahn (Göttingen) for his most valuable help with the numerical calculations and literature search and Professor M. Klessinger (Münster) for critical perusal of the manuscript. Thanks are also due to the Fonds der Chemischen Industrie for continued support of our work.*

Received: February 27, 1980 [A 387 IE]
revised: March 5, 1981
German version: Angew. Chem. 93, 944 (1981)
Translated by AD-EX Translations Ltd., London

---

[1] As, for example, the elegant Figures 1 to 6 in the stereoscopic three-dimensional picture appendix to *Hollemann-Wiberg*, Lehrbuch der Anorganischen Chemie, 71st-80th edition, Walter de Gruyter, Berlin (1971).

[2] *L. Pauling*, Proc. Natl. Acad. Sci. USA *14*, 359 (1928); J. Am. Chem. Soc. *53*, 1367 (1931).

[3] Thus, we do *not* use valence angle as a synonym for *bond* angle or interatomic angle, in this we follow *Förster* [8].

[4] *J. H. van Vleck*, J. Chem. Phys. *1*, 219 (1933).

[5] *W. G. Penney*, Proc. R. Soc. London *A 144*, 166 (1934); *A 146*, 233 (1934).

[6] *P. Torkington*, J. Chem. Phys. *19*, 528 (1951).

[7] In contrast to this terminology, in the literature the *individual* hybrid AO of Eq. (3) is frequently also described as an sp$^{\lambda^2}$ hybrid in which $\lambda^2$ now no longer needs to be *integral*.

[8] *Th. Förster*, Z. Phys. Chem. *B 43*, 58 (1939).

[9] *L. Pauling*, The Nature of the Chemical Bond, 3rd edition, Cornell University Press 1960.

[10] *R. McWeeny:* Coulson's Valence, 3rd edition, Oxford University Press, Oxford 1979, Chap. 5.

[11] *J. E. Lennard-Jones, J. A. Pople*, Proc. R. Soc. London *A 210*, 190 (1951).

[12] *J. M. Foster, S. F. Boys*, Rev. Mod. Phys. *32*, 296 (1960).

[13] *W. England, L. S. Salmon, K. Ruedenberg*, Fortschr. Chem. Forsch. *23*, 31 (1971).

[14] *J. P. Foster, F. Weinhold*, J. Am. Chem. Soc. *102*, 7211 (1980).

[15] *O. Chalvet, R. Daudel, S. Diner, J. P. Malrieu:* Localisation and Delocalisation in Quantum Chemistry, Vol. I: Atoms and Molecules in the Ground State, Reidel, Boston 1975.

[16] *W. Kutzelnigg:* Einführung in die Theoretische Chemie, Vol. 2: Die chemische Bindung, Verlag Chemie, Weinheim 1978, especially Chap. 10.

[17] *K. Siegbahn, et al.* ESCA Applied to Free Molecules, North Holland, Amsterdam 1971.

[18] For a rewiev of the theory of nuclear spin-spin coupling constants see: *J. Kowalewski*, Progr. in NMR-Spectroscopy *11*, 1 (1977); experimental data of coupling constants cf. [60].

[19] *C. H. Townes, A. L. Schawlow:* Microwave Spectroscopy, McGraw-Hill, New York 1955; *E. A. C. Lucken:* Nuclear Quadrupole Coupling Constants, Academic Press, London 1969.

[20] Of many papers, we may cite only two as examples: a) *W. Zeil*, Angew. Chem. *73*, 751 (1961); b) *B. Bak, J. J. Led*, J. Mol. Structure *3*, 379 (1969).

[21] *See, e.g., W. J. Orville-Thomas:* The Structure of Small Molecules, Elsevier, Amsterdam 1966.

[22] This is no restriction on generality, but can always be achieved by the choice of the sign of $p_i$.

[23] 100 times these quantities is also called the percentage s or p character.

[24] These relations appear to have been given first by *C. A. Coulson*, Victor Henri Memorial Volume, Contribution a l'Etude de la Structure Moleculaire, Maison Desoer, Liège (1947-48).

[25] The *second* solution mentioned by *Torkington* [6] in which all four $h_i$ are arranged like the ribs of an umbrella is incorrect, since it leads to valence angles <90°, which is impossible for real s-p hybrid orbitals.

[26] *W. Moffitt*, Proc. R. Soc. London *A 210*, 245 (1951).

[27] *M. D. Newton:* "Strained Organic Molecules" in *H. F. Schaefer III:* Modern Theoretical Chemistry, Vol. 4, Plenum Press, New York 1977, Chap. 6.

[28] *D. M. Chipman*, J. Am. Chem. Soc. *102*, 3377 (1980).

[29] *C. A. Coulson, W. Moffitt*, Philos. Mag. *40*, 1 (1949).

[30] *C. A. Coulson, T. H. Goodwin*, J. Chem. Soc. *1962*, 2851; *1963*, 3161.

[31] *G. Wipf*, Thèse d'État, Université Strasbourg 1974.

[32] *M. Randić, Z. Maksić*, Theor. Chim. Acta *3*, 59 (1965).

[33] *C. R. Fritchie*, Acta Crystallogr. *20*, 27 (1966).

[34] *A. Hartman, F. L. Hirshfeld*, Acta Crystallogr. *20*, 80 (1966).

[35] *T. Ito, S. Sakurai*, Acta Crystallogr. *B 29*, 1594 (1973).

[36] *T. Ito*, Bull. Chem. Soc. Jpn. *48*, 3035 (1975).

[37] *C. A. Coulson* in [24], p. 16.

[38] *M. J. S. Dewar, H. N. Schmeising*, Tetrahedron *5*, 166 (1959); *11*, 96 (1960).

[39] *Z. B. Maksić, M. Eckert-Maksić*, Croat. Chem. Acta *42*, 433 (1970).

[40] *M. G. Brown*, Trans. Faraday Soc. *55*, 694 (1969).

[41] *G. R. Somayajulu*, J. Chem. Phys. *31*, 919 (1969).

[42] *W. Zeil, J. Haase, M. Dakkouri,* Z. Naturforsch. *A 22,* 1644 (1967).
[43] *B. Bak, L. Hansen-Nygaard,* J. Chem. Phys. *33,* 418 (1966).
[44] *B. Bak, L. Hansen-Nygaard,* J. Mol. Struct. *2,* 209 (1968).
[45] *B. M. Mikhailow,* Tetrahedron *21,* 1227 (1965).
[46] *O. Bastiansen, M. Traetteberg,* Tetrahedron *17,* 147 (1962).
[47] Tetrahedron *17,* 123 (1962).
[48] *A. Maccoll,* Trans. Faraday Soc. *46,* 369 (1950).
[49] *Z. B. Maksić, Z. Meić, K. Kovacević,* Z. Naturforsch. *A 28,* 797 (1973).
[50] *D. C. McKean,* Chem. Soc. Rev. *7,* 398 (1978).
[51] *M. Klessinger,* Angew. Chem. *82,* 534 (1970); Angew. Chem. Int. Ed. Engl. *9,* 500 (1970).
[52] Ref. [10], p. 153ff., p. 171ff.
[53] *A. D. Walsh,* Discuss. Faraday Soc. *2,* 18 (1947).
[54] *J. Hinze, H. H. Jaffé,* J. Am. Chem. Soc. *84,* 540 (1962).
[55] *J. Hinze, M. Whitehead, H. H. Jaffé,* J. Am. Chem. Soc. *85,* 148 (1963).
[56] *E. Shustorovitch, P. A. Dobosh,* J. Am. Chem. Soc. *100,* 7513 (1978); *101,* 4090 (1979); *E. Shustorovich,* Inorg. Chem. *18,* 1030, 1039, 2108 (1979).
[57] *A. Domenicano, A. Vaciago, C. A. Coulson,* Acta Crystallogr. Sect. *B 31,* 221, 1630 (1978); *B 35,* 1382 (1979).
[58] Vgl. auch *Z. V. Zvonkova,* Russ. Chem. Rev. *46,* 479 (1977).
[59] *N. Muller, D. E. Pritchard,* J. Chem. Phys. *31,* 768, 1471 (1959).
[60] Review: *P. E. Hansen,* Prog. NMR Spectrosc. *15,* 65 (1981).
[61] *N. Sheppard, R. M. Lynden-Bell,* Proc. R. Soc. London *A 269,* 385 (1962).
[62] *K. Frei, H. J. Bernstein,* J. Chem. Phys. *38,* 1216 (1963).
[63] Reviews: a) *V. Wray,* Prog. NMR-Spectrosc. *13,* 177 (1979); b) *P. E. Hansen, ibid. 15,* 65 (1981).
[64] *J. A. Pople, D. P. Santry,* Mol. Phys. *8,* 1 (1964).
[65] *J. A. Pople, J. W. McIver, N. S. Ostlund,* J. Chem. Phys. *49,* 2960, 2965 (1968).
[66] *G. E. Maciel, J. W. McIver, N. S. Ostlund, J. A. Pople,* J. Am. Chem. Soc. *92,* 1 (1970).
[67] *H. A. Bent,* Chem. Rev. *61,* 276 (1961).
[68] *H. A. Bent,* J. Chem. Educ. *37,* 616 (1960).
[69] *A. C. Blizzard, D. P. Santry,* J. Chem. Phys. *55,* 950 (1971); *58,* 4714 (1973).
[70] *J. M. Schulman, M. D. Newton,* J. Am. Chem. Soc. *96,* 6295 (1974).
[71] a) *J. M. Schulman, T. Venanzi,* J. Am. Chem. Soc. *98,* 6739 (1976); b) *W. S. Lee, J. M. Schulman, ibid. 101,* 3182 (1979); *102,* 5184 (1980).
[72] *M. Randić, Z. B. Maksić,* Chem. Rev. *72,* 43 (1972).
[73] *E. Vogel,* Angew. Chem. *72,* 4 (1960).
[74] *G. Maier, S. Pfriem, U. Schäfer, R. Matusch,* Angew. Chem. *90,* 552 (1978); Angew. Chem. Int. Ed. Engl. *17,* 520 (1978).
[75] *A. de Meijere,* Angew. Chem. *91,* 867 (1979); Angew. Chem. Int. Ed. Engl. *18,* 809 (1979).
[76] *H. Musso, U. Biethan,* Chem. Ber. *100,* 119 (1967).
[77] *K. B. Wiberg,* Adv. Alicyclic Chem. *2,* 185 (1965).
[78] *K. B. Wiberg,* J. Am. Chem. Soc. *102,* 7467 (1980).
[79] *K. B. Wiberg, G. B. Ellison,* Tetrahedron *30,* 1573 (1974).
[80] *L. N. Ferguson,* J. Chem. Educ. *46,* 404 (1969).
[81] *A. Greenberg, J. F. Liebman:* Strained Organic Molecules, Academic Press, New York 1978.
[82] *H. Müller, P. Bräuer,* Z. Chem. *5,* 241 (1965).
[83] *D. C. McKean,* Chem. Soc. Rev. *7,* 399 (1978).
[84] *K. Kamienska-Trela,* Spectrochim. Acta, Part *A 36,* 239 (1980).
[85] Case 1 also has the special value of $\alpha = \alpha^{\mathrm{val}} = 180°$, but still contains one free paramenter $\lambda$.
[86] An example of this is given in the following paper: *D. Peters,* J. Chem. Soc. (London) *1963,* 4017, in which for each of the molecules $H_2O$, $NH_3$, and $H_2CO$ *one* set of delocalized MO's was localized in two different ways. It should be noted (cf. Figure 1 of that paper) that here under certain conditions valence angles <90° can occur, since only the localized MO's but not the hybrid AO's contained in them need be orthogonal.
[87] This has been pointed out previously by *R. J. Myers* and *W. D. Gwinn* (J. Chem. Phys. *20,* 1420 (1952).
[88] A partial review is also given in *K. Mislow:* Introduction to Stereochemistry, W. A. Benjamin, Inc. (1965).

---

# Anodic and Cathodic CC-Bond Formation

## By Hans J. Schäfer[*]

*Dedicated to Professor Leopold Horner on the occasion of his 70th birthday*

Electrolysis allows the reactivity of a substrate to be changed, or its polarity to be reversed ("*redox umpolung*"). The carbon skeleton and the functional groups of a synthetic building block can thus be utilized more economically, and at the same time the number of reaction steps in multistage syntheses can be reduced. The tools necessary for an electrolytic process are a cell, a power source, electrodes, and an electrolyte, the latter being chosen in accordance with the reduction or oxidation potential of the substrate. A series of electroanalytical methods provides information on the electrode reaction mechanisms. At the *anode,* arenes, phenolic ethers, and electron-rich olefins dimerize *via* intermediate radical cations. In the Kolbe electrolysis, carboxylic acid anions decarboxylate to form radicals which can couple to form *e.g.* long chain alkene derivatives having pheromone activity, or add to olefins. At the *cathode,* activated olefins hydrodimerize *via* radical anions or, in the presence of appropriate reagents, can be acylated, alkylated, and carboxylated. Pinacols, crossed hydrodimers, and cyclic and arylated compounds are accessible *via* the cathodically produced radicals, while the formation of strained small rings or the reductive addition of halides to carbonyl compounds takes place through intermediate carbanions.

## 1. Introduction

In the course of electrolysis a substrate is subjected to the removal *(anodic oxidation)* or addition *(cathodic reduction)* of electrons. The reactive intermediates formed anodically can be radical cations, radicals, and carbenium ions, while those formed cathodically can be radical anions, radicals, and carbanions. The transfer of electrons changes the reactivity, or leads to an *umpolung*[1] of the substrate. The carbon skeleton and the functional groups of a given synthesis unit can thus be utilized in several different ways—as a nucleophile, a radical, or an electrophile. Bond formation between reactants of the same polarity, usually

---

[*] Prof. Dr. H. J. Schäfer
Organisch-chemisches Institut der Universität
Orléansring 23, D-4400 Münster (Germany)

*Angew. Chem. Int. Ed. Engl. 20, 911-934 (1981)* *0570-0833/81/1111-0911 $ 02.50/0*

possible only after several steps, can be brought about electrochemically in a single step by a preceeding *"redox umpolung"*. Thus, in the hydrodimerization of acrylonitrile[2], a one-step coupling of the two electrophiles is achieved by reducing one reactant to a Michael donor[3]. The nucleophilic styrene dimerizes, after the oxidation of one olefin molecule, to the radical cation[4].

An electrode has *advantages* over chemical redox reagents. Compounds with several electroactive groups *(electrophores)*, whose half-wave potentials differ by 200 mV, can be converted selectively due to the continuously adjustable voltage of the working electrode[5], whereas the restricted number of chemical redox reagents permits this only to a limited extent. Solubility and work-up problems, frequently encountered with inorganic redox reagents are diminished, and the appearance of ecologically objectionable end-products can be avoided. Finally, electrolysis is cheaper, since it does not require the often expensive chemical electron-transfer agents (*e.g.* $OsO_4$, Li, or $Pb(OAc)_4$), but transfers the electrons directly.

The *disadvantages* are the often longer reaction times and, because of the required conductivity, the necessity of using polar solvents; both of these factors promote undesirable competing side reactions. The frequent and troublesome problem of electrode coverage *(passivation)* can often be overcome by changing the electrolyte or the electrode material, or by pulsing the voltage[6].

The present review is restricted to preparative CC-bond formation at the anode and cathode. Functional group interconversion will be dealt with in a later review. Electroanalytical methods are described only when they refer to syntheses; studies of electrode mechanisms and the reactivities of electrolytically produced radicals and radical ions have been largely omitted.

Up to the beginning of the seventies there were only a few textbooks[7-10] dealing with organic electrochemistry. The classic representative of them is *Fichter*'s book[8], which even today is a treasure-house for many interesting reactions. Several monographs then appeared within a few years[11-20], of which those by *Baizer*[16], *Beck*[17], and *Weinberg*[18] are the most comprehensive. There are also shorter[21-29] or more exhaustive[30-34] reviews, annual surveys[35,36], and a bibliography of the field[36a]. Besides these, more specialized articles have been published dealing with the electrochemistry of functional groups[37-49], with biologically active compounds[50], with electroorganic syntheses of natural products[51,52], with anodic[53-55] and cathodic[56-63] reactions, and also with electrode mechanisms and the properties of radical ions[64-70].

The present review will be limited essentially to electrosyntheses published since 1973.

## 2. Procedure

### 2.1. The Requirements for Electrolysis

Let us begin with the *electrode*. This must be mechanically stable and chemically inert, and have the least possible tendency toward passivation. Many materials can be used as cathodes[71-73]: the platinum metals (low hydrogen overvoltages), copper, silver, iron, aluminum, and titanium (medium hydrogen overvoltages), and mercury, lead, cadmium, tin, lead- and cadmium-amalgams, and graphite (high hydrogen overvoltages). In contrast, the selection of materials for anodes is much smaller[71,74,75]: platinum is used in sheet form or as a foil on steel, carbon, or titanium; gold is usable only to a limited extent; graphite is employed as synthetic carbon, glassy carbon[76], graphite felt, or carbon paste electrodes[77]. Lead dioxide[78-80] on graphite or titanium, and ruthenium-dioxide-activated titanium anodes[81-84] can also be used, though no organic electrosyntheses with the latter have so far been described.

Electrodes with chemically modified surfaces have so far mainly been investigated electroanalytically[85,86] for their suitability as electrocatalysts, sensitizers in photoelectrochemistry, or as electrosensors. Stable derivatives of platinum are produced by the adsorption of surface-active compounds[87], by coating with electro-active polymers[88], or through the reaction of chemically activated hydroxy-, carboxy-, or oxo-groups at oxidized platinum, graphite, ruthenium dioxide, or stannic oxide electrodes with cyanuryl chloride[86], chlorosilanes[89,90], amino acids[91-94], amines[95], carboxylic acids[95], or cyclodextrins[96]. Their applications in organic electrosyntheses are still minor. 2-Acetylpyridine and phenylglyoxylic acid have been reduced with 10% asymmetric induction at a graphite electrode chirally modified with phenylalanine[91-93], but other authors have been unable to reproduce these results[94]. At a surface-oxidized graphite cathode the carbinol : pinacol ratio in the reduction of acetophenone is reversed[94]. The anodic chlorination of anisole at a cyclodextrin-modified anode leads, like the corresponding chemical chlorination[97], preferentially to *p*-chloroanisole[96]. The advantages of the electrochemical method consist in a small consumption of cyclodextrin and an easier separation of the product.

The *electrolyte*, consisting of a solvent and a conducting salt (supporting electrolyte), should have a high conductivity, be a good solvent for the substrate, should be easily separable, and should moreover exhibit a high anodic or cathodic decomposition potential. Essential data and methods of purifying electrolytes are summarized in [98-102]. The decomposition potentials of some electrolytes are shown in Table 1.

Table 1. Decomposition potentials of selected electrolytes [103].

| Electrolyte (Solvent/conducting salt) | Decomposition potential in Volts [a] cathodic | anode |
|---|---|---|
| Methanol/$Bu_4NClO_4$ | −2.2 (Hg) | +1.3 (Pt),<br>+1.9 (Glass-C) |
| Acetonitrile/$Bu_4NClO_4$ | −2.6 (Pt) | +2.7 (Pt) |
| *N,N*-Dimethylformamide/$Et_4NClO_4$ | −2.8 (Hg) | +1.9 (Pt) [104] |
| Dichloromethane/$Bu_4NClO_4$ | −2.3 (Pt) | +2.45 (Pt) [105] |
| Tetrahydrofuran/$Bu_4NClO_4$ | −3.75 (Pt) | +1.75 (Pt) [106] |
| Pyridine | −2.2 (Hg) | +3.3 (Pt) [104] |
| Nitromethane/$LiClO_4$ | −2.8 (Pt) | +2.7 (Pt) [107] |

[a] Relative to the saturated calomel electrode (SCE). In the chamber working electrode. Glass-C signifies glassy carbon.

An electrolyte consisting of dichloromethane/trifluoroacetic acid/$Bu_4NBF_4$[108], and amounts of trifluoroacetic anhydride and alumina[108, 109], have proved satisfactory for investigations of radical cations; a salt melt of aluminum chloride and *n*-butylpyridinium chloride at +40°C has also been used in the formation of radical cations[110]. For oxidations at high anodic potentials, trifluoromethanesulfonic acid[111], ethylene carbonate[112], sulfolane[113], and sulfur dioxide[114], with high anodic decomposition potentials, are also available in addition to dichloromethane/trifluoroacetic acid. Even the nonpolar solvents chlorobenzene and benzene can be used in cyclic voltammetry, although only at microelectrodes; they are characterized by a wide potential range and stability to radical ions[115]. Liquid ammonia is suitable for the production of radical anions[116]; ethylenediamine can also be used as a solvent for reductions[117]. The electrolyte consisting of dimethylformamide and $Bu_4NBF_4$ can be purified so well by a recycling apparatus with an alumina column that even aromatic dianions remain stable[118].

Optical activity can be induced by using chiral electrolytes. This is best done by the addition of catalytic amounts of surface-active chiral compounds[119-122], an optical yield of almost 50% being achievable in the case of strychnine. With chiral supporting electrolytes[123, 124], in spite of numerous variations in the structure of the supporting electrolyte, the pH, the potential, and the temperature, the inductions are below 15% in protic electrolytes, though somewhat higher in aprotic media[125]. In the case of reduction in chiral solvents, activities of only up to 6% are induced[126].

The potential of the working electrode is kept constant relative to a *reference electrode* with the aid of a potentiostat[127]. Various reference electrodes have been described for protic and aprotic solvents[101, 128-130].

To prevent unwanted reactions of the educt and product at the counterelectrode, particularly in reductions, the cathode and anode compartments are separated by a clay, porous glass, unglazed porcelain, Teflon, or polyethylene *diaphragm*, or by an ion-exchange membrane[131-134].

Cells with and without diaphragms have been developed for a wide variety of applications[135-139]; cells have been described for voltammetry and coulometry, for working under pressure or under high vacuum[140], with rotating[141a], vibrating[141b], continually scraped[141c], or three-dimensional electrodes[142], together with cells for low-temperature voltammetry[143], or for a combination of electrochemical methods with ESR[144] or UV spectroscopy[145]. The capillary gap cell, an undivided cell with a small electrode distance, avoids high cell resistances and permits good space-time yields. It is used in the form of a stacked cell[146] or a concentric version[147-149] for hydrodimerizations, acetoxylations, Kolbe electrolyses, or for the preparation of propylene oxide. An interesting new development is the "Swiss roll" cell consisting of rolled-up metal gauzes and an insulating plastic fabric[150]. Various divided cells have been described by *Horner et al.*[151], *Cauquis et al.*[152], *Bard et al.*[153a], and others[153b].

For a preliminary laboratory experiment the following setup, which can be set up quickly and inexpensively, suffices in most cases: a beaker is fitted with a clay cylindrical diaphragm and with electrodes made of suitable material, and the potential at the working electrode is measured with a pH-meter against an Ag/AgCl electrode (a chlorinated silver wire in saturated KCl solution) and adjusted through a rectifier with a variable transformer.

### 2.2. What are the Requirements for a Successful Electrolysis?

The first information needed is the approximate oxidation or reduction potential of the substrate; some potential ranges are given in Figure 1.

The potentials of many classes of substances have been summarized in the literature[11, 18] and also specifically for

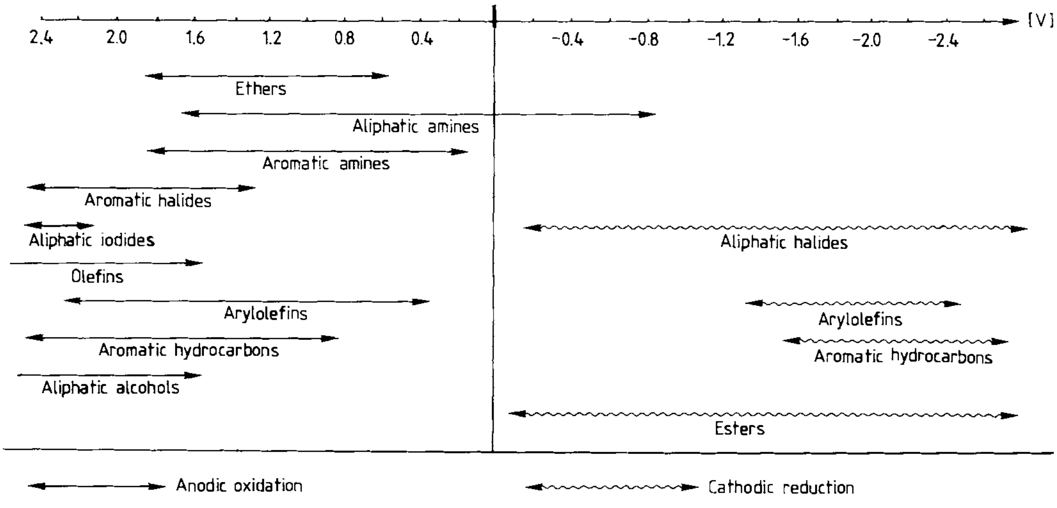


Fig. 1. Potential ranges for the oxidation and reduction of some electrophores (against SCE, after [18]).

alkanes[154], alkenes[155], arenes[156], amines[157], phenolic ethers, and phenols[158]. The anodic oxidation potentials and photoelectronic ionization potentials correlate in a remarkably linear manner in many cases, *e.g.* for dienes[159], arylalkenes[4], cyclopropanes[160], and other substrates[161], since both are determined by the energy of the highest occupied molecular orbital (HOMO).

The *electrolyte* is selected on the basis of the known reduction or oxidation potential. Its decomposition potential should, in oxidations, be *ca.* 200 mV more anodic, and in reductions more cathodic than the half-wave potential of the substrate; in addition, the electrolyte must be a good conductor, must dissolve the substrate well, and be readily separable from the product by distillation.

The *electrode material* must show minimum passivation, resist corrosion, and have a high overvoltage for decomposition of the electrolyte.

### 2.3. What Information can be Obtained about the Reaction Mechanism?

The electroanalytical methods available for elucidating reaction pathways have been summarized in several monographs[162-172] and reviews[173-176]. The first indication of the mechanism is given by the number of electrons transferred. This is determined by comparing the limiting current from cyclic voltammetry ($i_L$) or at a rotating disk electrode with those of standard compounds (*e.g.* ferrocene) or, more accurately but also more laboriously, by coulometry at a controlled potential[177]. Whether the reaction in the limiting current region is diffusion-controlled is shown polarographically from the relation $i_L \approx \sqrt{h}$[178] (where $h$ is the height of the Hg level above the capillary opening), voltammetrically from the relation $i_L \approx \sqrt{v}$[179] (where $v$ is the scan rate in V/s), or at the rotating disk electrode from the relation $i_L \approx \sqrt{\omega}$[180] (where $\omega$ is the angular velocity of the disk). The reactants which are involved in the rate-determining electrochemical step are shown by the electrochemical order of the reaction $\nu$[181].

Information on the lifetime of the electrochemically produced intermediate stages is supplied by cyclic voltammetry[182] from the ratio of the anodic and cathodic peak currents ($i_{p,a}$ and $i_{p,c}$, respectively). Thus, $i_{p,c}/i_{p,a} = 1$ indicates that an oxidatively produced intermediate product is long-lived[183]. A difference of 59 mV between the anodic and cathodic peak potentials ($E_{p,a}$ and $E_{p,c}$, respectively) shows that the electron transfer takes place rapidly[184]. The chemical reaction rate $k$ of the intermediate $B^{+\cdot}$ with a nucleophile $Nu^-$

$$A \xrightarrow{-e} B^{+\cdot} \xrightarrow[k]{Nu^-} \dot{B}\text{—}Nu$$

can be determined from the change in the anodic peak current $i_{p,a}$ at different scan rates[185a]. By analog differentiation of the cyclovoltammetric current/voltage curves, the peak potentials can be determined accurately even for very rapid scan rates[185b]. Conclusions concerning the reaction mechanism can be drawn from their kinetic displacement[185c], so that by this method even very fast follow-up reactions can be analyzed. Cyclic voltammetry can also be performed at low temperatures (−80 °C)[143], and has thus been used for conformational analysis studies[186]. At the rotating disk electrode[174, 187] or the rotating ring-disk electrode[188] the kinetics of the reactive intermediates can be determined from the dependence of the limiting current[189] or the collection efficiency $i_R/i_D$[190] (R = ring, D = disk) on the rate of rotation. Spectro-electrochemical methods afford additional information about the structure of the intermediates. The following spectroscopic methods have been used so far: absorption spectroscopy (UV-VIS-NIR)[191], ESR[192], IR[193], resonance Raman[194], NMR[195], and mass spectroscopy[196].

It has been possible to determine the redox potentials of short-lived free radicals by a combination of pulsed radiolysis with polarography[197]. The adsorption of organic compounds on the electrode can be determined by means of electrocapillary curves[198a], capacity measurements[198b], isotopic labeling[199], the change in the roughness of the electrode (polaromicrotribometry)[200a], and other techniques[200b].

## 3. Preparative Applications: CC-Coupling Reactions at the Anode

It appears advantageous to arrange the methods for CC bond formation, not according to the type of educt or product but rather according to the reactive intermediates. This makes the broad scope of the reaction and new possibilities of application more obvious, though a disadvantage is that this arrangement is not free from some arbitrariness, since the mechanisms of many electrosyntheses are not accurately known.

### 3.1. Radical Cations as Intermediates

Alkylarenes[201] yield biphenyl and/or diphenylmethane derivatives, depending on their substitution pattern (Table 2). The cation radical *(1)* first formed reacts either with the educt to give the biphenyl *(2)* (route *a*) or is deprotonated to the benzyl radical (route *b*), which, after oxidation, reacts with the educt to give a diphenylmethane *(3)*.

A low charge density on an unsubstituted C atom of *(1)* favors route *a*, whereas a low charge density on a substituted C atom favors route *b*. The intermediate radical cations become increasingly more stable when the positive charge density is uniformly distributed (as in perylene) or the reactive sites are blocked, as in *e.g.* 9,10-diphenylanthracene and rubrene[202].

Unsymmetric biphenyl derivatives can be obtained in moderate to good yields by the coelectrolysis of naphthalene with mesitylene (13%) or with tetra- (42%) or pentamethylbenzene (56%)[203]. Correspondingly, unsymmetric diphenylmethanes can be obtained in yields of 5—81% by the electrolysis of hexamethylbenzene in the presence of benzene, toluene, *p*-xylene, or mesitylene[204]. [2.2]-*m*-Cyclophanes can be coupled intramolecularly to give pyrene derivatives[205]. The oxidation of phenols has been compre-

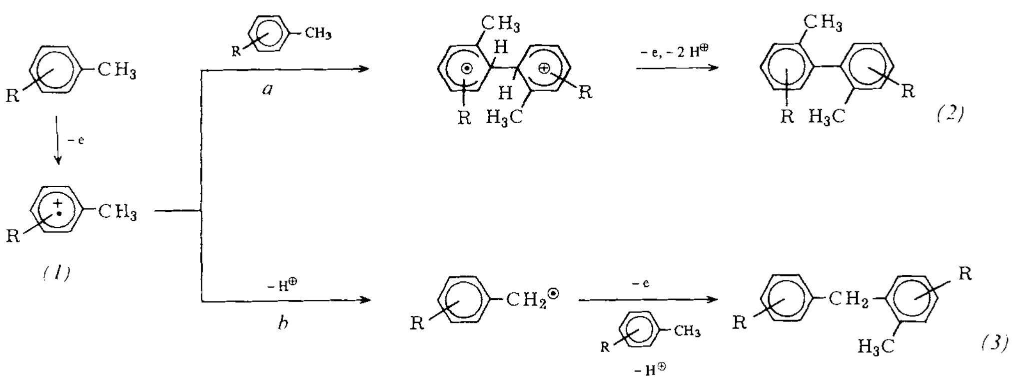
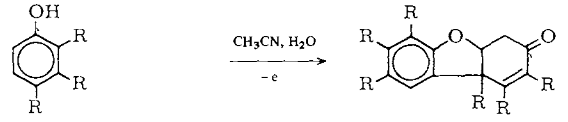


Table 2. Anodic coupling of alkylarenes *via* radical cations *(1)* [201].

| Alkylarene | *(2)* : *(3)* | *(2)*+*(3)*, Yield [%] |
|---|---|---|
| 1,4-Dimethylbenzene | 1 : 99 | 10 |
| 1,2,4-Trimethylbenzene | 46 : 54 | 38 |
| 1,3,5-Trimethylbenzene | 100 : 0 | 63 |
| 1,2,4,5-Tetramethylbenzene | 0 : 100 | 32 |

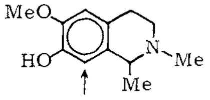
hensively reported[40,206]; they dimerize[*] *via* neutral radicals, cation radicals, and cations. In basic electrolytes, phenoxides give rise to phenoxy radicals; these react to form CC- and CO-dimers, which are easily oxidized further, leading to less useful product mixtures[207]. Blocking the 2-, 6-, or 4-position makes the couplings more selective. Thus, the phenol *(4)* dimerizes in good yield to the enone *(5)*[208].

2,4,6-Tri-*tert*-butyl phenoxide can be oxidized reversibly to the phenoxy radical (aryl-O·) at −0.2 V, while at the higher potential of +1.0 V the phenoxylium ion (aryl-$O^+$) is formed irreversibly[209]. Phenolic benzylisoquinolines couple inter- and intramolecularly with CC and C—O bond formation[207,210], and under these circumstances *(6)* only forms one diastereomer as a coupling product[211]. It has thus been deduced that *(6)* is adsorbed on the anode *via* the benzene ring and the nitrogen, and that the transition state is sterically most favorable when two configurationally identical radical cations couple.



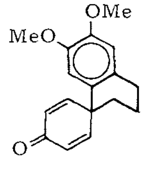
*(4)*, R = H, $CH_3$, $C_2H_5$ *(5)*

In neutral or acidic media, phenoxylium ions are formed from phenols that react intermolecularly *via* CC-coupling with anisole to give anisylcyclohexadienone[212] or intramolecularly in 1,3-diarylpropanes to give the spirodienone *(7)*[213]. The phenoxylium ion *(8)* can be detected cyclovoltammetrically starting from phenol or the phenoxy radical, or be prepared from the quinol by the action of acid[214]. In the oxidation of the phenol *(9)*, the intermediate phenoxylium ion *sym*-proportionates to phenoxyl radicals, which couple in 95% yield to give the quinhydrone *(10)*[215].

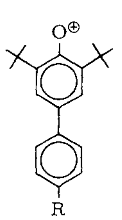


*(6)*

Unblocked phenols give good yields of dimers only after they are etherified[216]. A mixture of dichloromethane/trifluoroacetic acid (2 : 1) has proved to be a satisfactory electrolyte for these oxidations, since it protects the product against oxidative degradation[217]. Moreover, the addition of alumina and of trifluoroacetic anhydride has proved to be advantageous[108,109]. Methoxybiphenyls can be coupled intramolecularly in low yield in acetonitrile but in almost quantitative yield in 4 : 1 dichloromethane/trifluoroacetic acid[218,219]. 1,n-Bis(3,4-dimethoxyphenyl)alkanes *(11)* cyclize almost quantitatively when n = 1—4, but when n = 6—10 only in moderate yields, and then intermolecularly[219,220].

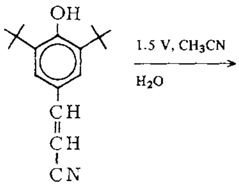


*(7)*, 73%

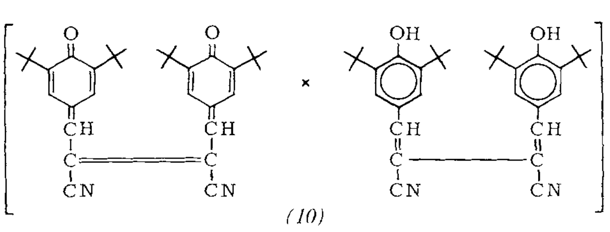


*(8)*, R = $OCH_3$, $N(CH_3)_2$

The cyclic voltammograms of unsymmetrically methoxylated diphenylalkanes exhibit two oxidation potentials, at



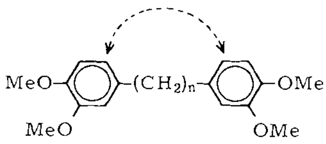
*(9)*



*(10)*

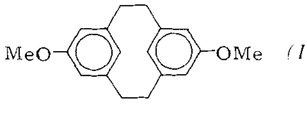
---

[*] The term "dimerize" here only refers to the molecular skeleton.



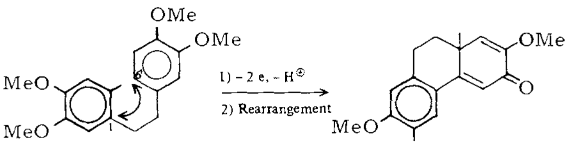
(11)

which either intramolecularly—or intermolecularly—formed products arise, permitting some conclusions to be drawn about the dimerization mechanism[221]. In the case of the [2.2]-*m*-cyclophane *(12)*, two anisyl radical cations couple in 90% yield to give the tetrahydropyrene derivative[222].



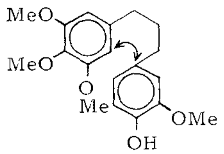
(12)

The tetramethoxybibenzyl derivative *(13)* cyclizes in an anodic 1,6′-coupling reaction, with a subsequent dienone/phenol rearrangement, to give an 88—98% yield of the dihydrophenanthrone *(14)*, which contains the essential structural elements of the B, C, and D rings of steroids[223].

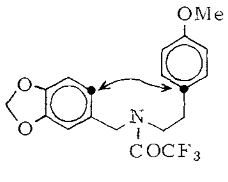


(13) (14)

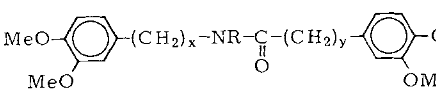
With the corresponding dimethoxybibenzyl derivative, ring closure takes place to form a structure analogous to the A, B, and C rings[224], but the yield is only moderate (22%) because of the lower activation of the arene system. Similar intramolecular aryl couplings as in *(15)*[225] and *(16)*[226] have been used in a synthesis of colchicine and for the preparation of (+)-oxocrinine respectively and of (+)-cryptopleurine[227]. Diarylamides *(17)* can be cyclized when the amide is tertiary and the carbonyl and amino groups are not conjugated with the aromatic system ($x,y \neq 0$)[228].



*(15)*, 80%

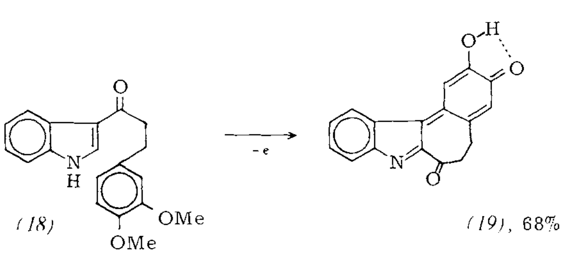


*(16)*, 62%



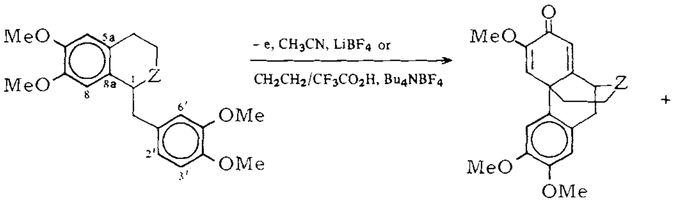
(17)

In a series of indole and dihydroindole derivatives only *(18)* couples intramolecularly to give *(19)*[229], this reaction probably being favored by a six-membered transition state[230]; the other indoles usually dimerize intermolecularly.

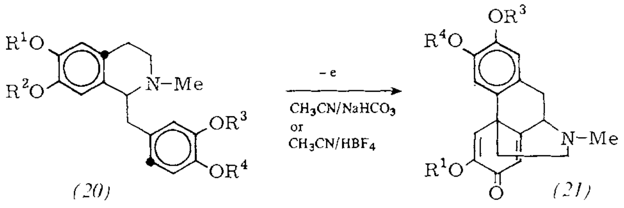


*(18)* *(19)*, 68%

The anodic cyclization of benzyltetrahydroisoquinolines *(20)* to the morphinane skeleton is particularly interesting from the preparative point of view, since it cannot be achieved satisfactorily with chemical oxidants. *(21a)* and *(21b)* can be obtained in good yield in acetonitrile/sodium bicarbonate using a divided cell[224,231-233]; *(21c—e)* can even be obtained under less mild conditions in an undivided cell and in acidic electrolytes[234].



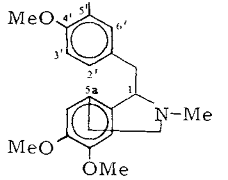
*(24)* *(25)*



*(20)* *(21)*

| | | |
|---|---|---|
| *(21a)*, $R^1 = R^3 = R^4 = CH_3$; *O*-methylflavinantine | | (52-85%) |
| *(21b)*, $R^1 = R^3 = CH_3$, $R^4 = PhCH_2$; *O*-benzylflavinantine | | (43-63%) |
| *(21c)*, $R^1 = R^3 = CH_3$, $R^4 = H$; flavinantine | | (63%) |
| *(21d)*, $R^1 = R^4 = CH_3$, $R^3 = H$; pallidine | | (50%) |
| *(21e)*, $R^1 = CH_3$, $—R^3—R^4— = —OCH_2O—$; amurine | | (80%) |

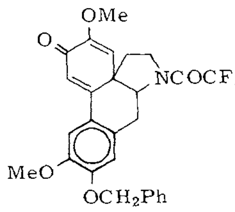
However, it is disadvantageous that in *(22)*, because of the −I-effect and the steric hindrance of the 5′-methoxy group, a C2′—C5a coupling to the flavinanthine type of compound takes place, and not a C6′—C5a coupling to the desired morphine type.



(22)

Attempts to enforce the "morphine type" of coupling have so far been unsuccessful[235,236]. 2′-Bromo *(22)* cyclizes at C2′ with debromination[224]; 2′-chloro[224,235], 2′-nitro- and 2′-N-acetylamino[236] substituents lead to cleavage at Cl; 3′-bromo or 3′-iodo substituents hardly hinder the C2′

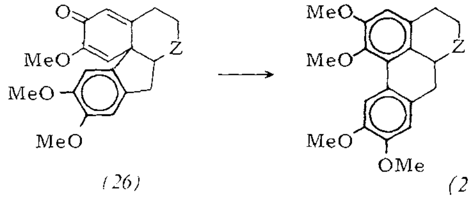
ring closure (3'-Br: 89%; 3'-I: 29%)[224,235]. 3'-Methoxy *(22)*, in which the C2'- and C6'-couplings are identical, forms



*(23)*

35—55% of the cyclization product[232,235]. *N*-Acyl substituents considerably affect the formation of products; while *N*-formyl *(22)* is cleaved at C1, *N*-trifluoroacetyl *(22)* gives the dienone *(23)* in good yield[236].

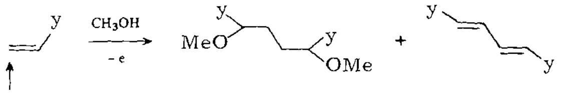
Carbon analogs (*(24)*, Z=$CH_2$) of benzyltetrahydroisoquinolines[237] couple at C2' and C5a in good yield to give



*(26)* *(27)*

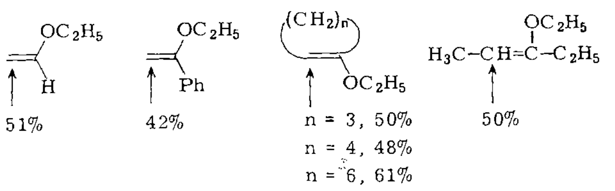
*(25)* or at C8a to give *(26)*; in acidic electrolytes ($CF_3CO_2H/CH_2Cl_2$), the intermediate product first formed by cyclization at C2'—C8a rearranges to give *(27)*.

Olefins *(28)* with electron donating substituents Y (alkoxy, acylamino, phenyl, or vinyl) can be dimerized in methanol to give 1,4-dimethoxy compounds *(29)* and/or dienes *(30)*.



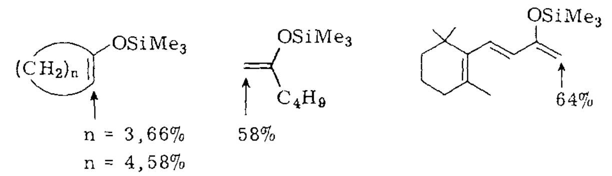
*(28)* *(29)* *(30)*

Enol ethers (*(28)*, Y=OR) with half-wave potentials between $E_{1/2}=+1.2$ and $+1.8$ V (Ag/AgCl) couple in methanol/2,6-lutidine at a graphite anode to give the acetals of 1,4-dicarbonyl compounds[238,239].

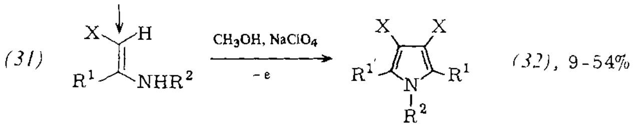


The tail-to-tail coupling of the dimers and the electrochemical reaction orders $\nu_{\text{enolether}} \approx 1$, $\nu_{\text{methanol}}=0$, suggest coupling *via* the radical cation. Silyl enol ethers (*(28)*, Y=$OSi(CH_3)_3$) can also be dimerized to 1,4-dicarbonyl compounds in good yields[240]:

Unsymmetric ketones can be linked uniformly in this way in the α- or α'-position, since the corresponding silyl enol ethers can be prepared regioselectively[241]. Enamino ketones or enamino esters *(31)* yield *via* the radical cations



by subsequent ring closure, and pyrrole derivatives *(32)*[242].

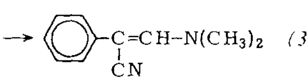


*(31)* *(32)*, 9-54%

X = $CO_2CH_3$, $COCH_3$, CN;

$R^1$ = $CH_3$, H, 4-$CH_3O$–$C_6H_4$; $R^2$ = H, $CH_3$, $CH_2$–$C_6H_5$, $C_6H_5$

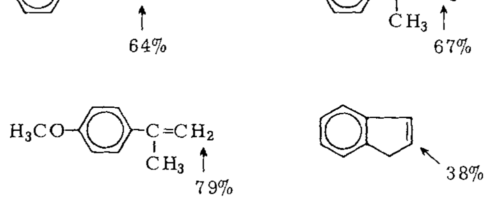
In the case of the enamino nitrile *(33)* coupling through the phenyl ring is observed[243].



$$\rightarrow C_6H_5\text{–}\underset{\displaystyle CN}{C}\text{=CH–N}(CH_3)_2$$

*(33)*

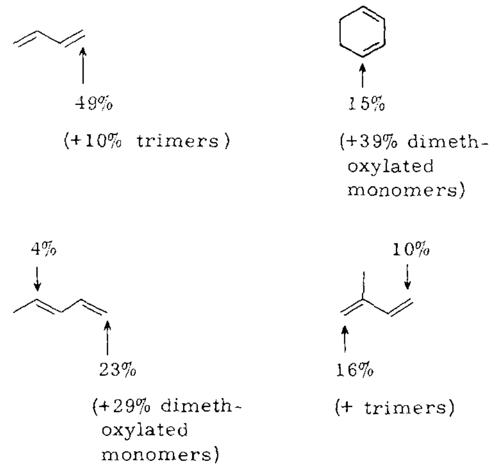
Styrene- and indene-derivatives (*(28)*, Y=aryl) are dimerized to 1,4-dimethoxy-1,4-diphenylbutane derivatives or 1,4-diphenylbutadiene derivatives[238,244]:



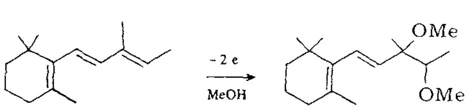
The product distribution is in some cases decisively affected by the anode potential and the supporting electrolyte. β-Alkyl substituents decrease the yield of dimers drastically and favor the formation of dimethoxylated monomers. For the dimerization of 4,4'-dimethoxystilbene it has been possible to prove spectro-electrochemically[245] and at the rotating ring-disk electrode[246] that the product is formed by the radical dimerization of the intermediate radical cations. When methanol is replaced by aqueous dichloromethane or by aqueous acetonitrile as solvent, styrene[247a] and α-methylstyrene[247b] yield 2,5-diphenyltetrahydrofurans. On anodic acetoxylation, presumably in a chain reaction *via* the radical cation[248a], 5,6-dimethoxyindene yields a [2+2]-cycloadduct as by-product[248b].

Dienes *(28)* (Y=vinyl) are dimerized to dimethoxyoctadienes or are dimethoxylated to dimethoxybutenes at graphite, platinum, or glassy carbon anodes in a methanol/sodium perchlorate electrolyte[238,249]:

Dimerization is favored by graphite- or carbon-cloth anodes, by high olefin concentrations, and by terminally unsubstituted dienes[249,250]. Butadienyl acetate and the β-ionone derivative *(34)* could not be dimerized but yielded dimethoxylated monomers, whereby *(34)* regioselectively forms 73% of the α,β-dimethoxy product[249].

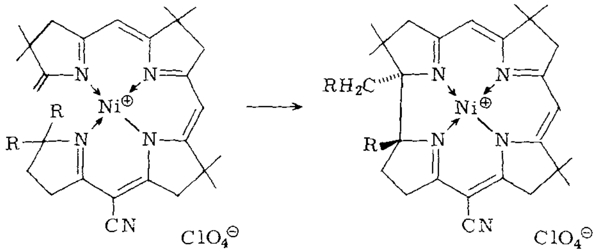


The polyene derivative *(35)* can be cyclized to form the nickelcorrin complex *(36)* if it is first oxidized to the radical cation, which undergoes a 1,16-hydrogen shift and then



*(34)*

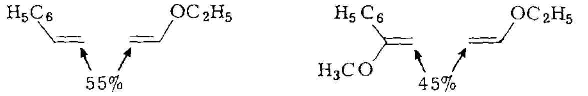
couples intramolecularly through cathodic reduction[251] (Conditions: +1.22 V, −0.3 V; Pt/LiClO$_4$, CH$_3$CN, Ac$_2$O, HOAc; yield 18% with R = H).



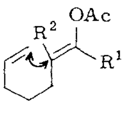
*(35)* *(36)*

Alkenes without +M-substituents can be coupled only if they are dialkylated at one carbon atom of the double bond and are unsubstituted at the other—a further indication that the dimerization of radical cations responds sensitively to steric hindrance[252]:

Unsymmetric dimers are accessible through the coelectrolysis of different olefins[253].



Unsaturated enol acetates *(37)* can be cyclized to cyclohexenyl ketones in yields of 18—40%[254].



*(37)*

### 3.2. Radicals as Intermediates

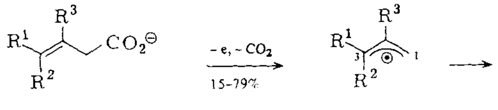
#### 3.2.1. Coupling of Radicals

Radicals can be generated in preparative amounts by an experimentally simple procedure using the Kolbe electrolysis; for reviews see [16-18,20,37,53,255]. Here, carboxylic acid anions are decarboxylated to radicals *via* 1e-oxidation or to carbenium ions *via* 2e-oxidation. The radicals couple or react with olefins to give "additive" dimers and/or monomers (see Section 3.2.2); alcohols, amides, esters, alkenes, and rearranged products are formed from the carbenium ions. The radical route is favored by platinum anodes and sometimes also by those of glassy carbon or sintered graphite[256], *i.e.* electrode materials with smooth surfaces, and also by a high current density, by an acidic electrolyte in which only 5—10% of the acid is neutralized, by methanol as solvent, and finally, by hydrogen or electron-attracting substituents on the α-carbon atom of the carboxylic acid[257]. Some selected Kolbe dimerizations are listed in Table 3.

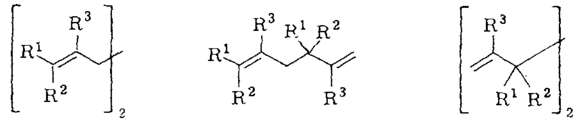
Table 3. Some examples of the Kolbe electrolysis of carboxylic acids.

| Carboxylic acid | Yield of dimers [%] | Ref. |
|---|---|---|
| H$_3$C(CH$_2$)$_n$CO$_2$H, n = 5-15 | 60-90 | [53b] |
| RO$_2$C(CH$_2$)$_n$CO$_2$H, n = 4-16 | 45-95 | [53b] |
| (CH$_3$)$_2$CH—CH(CO$_2$Et)CO$_2$H | 67 | [258] |
| AcO(CH$_2$)$_n$CO$_2$H, n = 3-5 | 73-83 | [259] |
| F(CH$_2$)$_n$CO$_2$H, n = 4-10 | 45-70 | [260] |
| EtCO(CH$_2$)$_4$CO$_2$H | 75 | [261] |
| Oleic acid | 75 | [262] |
| R$^1$CO—CR$^2$R$^3$CO$_2$H | ≈35 | [263a] |
| F$_2$CCl—CO$_2$H | 45 | [263b] |

Anions *(38)* of β,γ-unsaturated carboxylic acids can be coupled in methanol *via* allyl radicals *(39)* to the isomeric 1,5-dienes *(40)*—*(42)* in satisfactory yields[264,265].



*(38)* *(39)*

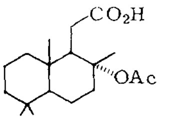


*(40)* *(41)* *(42)*

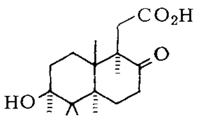
R$^1$ = H$_3$C(CH$_2$)$_7$, (CH$_3$)$_2$CHCH$_2$, MeO$_2$CCH$_2$, (CH$_3$)$_2$CH, (CH$_3$)$_3$C
R$^2$ = H, CH$_3$
R$^3$ = H
—R$^1$—R$^2$—, —R$^1$—R$^3$— = —(CH$_2$)$_4$—

In this process, the configurations of the double bonds are almost totally (≈90%) retained; terminal double bonds sometimes migrate if the electrolyte becomes alkaline[264]. The diene *(40)* is formed more and more selectively with increasing size of $R^1$, $R^2$, and $R^3$, presumably due to the steric shielding of C3 in the allyl radical *(39)*. The passivation that is frequently observed can be diminished and the yield increased reproducibly if the carboxylic acids are neutralized with tributylamine or triethylamine[266]. In the case of 4-alkene-6-ynoic acids[267] or 6-heptenoic acid[264] a more or less pronounced cyclization to cyclopropylmethyl or cyclopentylmethyl radicals is observed.

If a target compound can be divided into two symmetrical fragments, Kolbe electrolysis is a favorable method for its synthesis. For example, in the dimerization of *(43)* or *(44)* it is the key step in syntheses of pentacyclosqualene[268] and of α-onocerin[269], respectively.



*(43)*, 34%

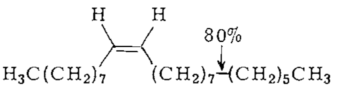


*(44)*, 40%

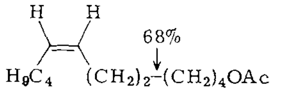
Unsymmetric compounds can also be prepared *via* mixed Kolbe electrolyses of different carboxylates. The disadvantageous but unavoidable formation of symmetric dimers can be reduced to one by-product if the cheaper carboxylic acid is used in 5- to 10-fold excess. Hydrogenated carotenoids, saturated and unsaturated fatty acids, optically active ω-hydroxy carboxylic acids, and intermediates for the preparation of muscone and humulene have been obtained in this way[53b]. The method has recently been applied to the synthesis of pheromones[255]. For example, muscalure *(45)* has been synthesized in yields of 40%[270] or even 80%[271], and its antagonist (*Z*)-11-heneicosene[271], looplure *(46)*[272], (*E*)-7-dodecenyl acetate *(47)*[273], brevicomin *(48)*[274], disparlure *(49)*[275], the attractant *(50)* of the German cockroach[276], and optically active *(51)*, a *Trogoderma* pheromone[277a], have also been synthesized (the arrows indicate the positions where coupling occurs). In addition, alkynecarboxylic esters having different chain lengths, which can be hydrogenated at will to (*E*)- or (*Z*)-pheromones, can be obtained[271]. C-Analogs of cystine peptides have been prepared from glutamic acids protected in various ways[277b]. A further selection of mixed Kolbe electrolyses is summarized in Table 4.

It is quite certain that the intermediate "Kolbe radicals" react as free radicals and are not bound to the anode. This follows from the formation of completely racemic products in electrolyses with carboxylic acids whose α-carbon is a center of chirality *e.g.* 2-methyloctadecanoic acid[285] or ethyl ethylmethylmalonate[286]. Moreover, the *cis*- and *trans*-4-*tert*-butylcyclohexanecarboxylic acids yield the three stereoisomeric 4,4'-di-*tert*-butylcyclohexanes *(aa, ae, ee)* in the statistical ratio 1 : 2 : 1)[287]. Furthermore, addition of methoxycarbonylmethyl radicals from malonic acid hemiesters to β-methylstyrene produces additive dimers and monomers in the same ratio as in their reductive preparation in homogeneous solution from the $H_2O_2$ adduct of dimethyl acetonedicarboxylate[288].

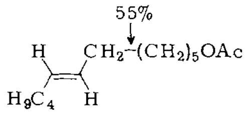
In addition to the carboxylates, other anions can also be dimerized at anodes, presumably *via* radicals. Anionized 1,3-dicarbonyl compounds and heteroanalogs of CH acids couple in satisfactory yields[289]. With some substrates, the yield is substantially improved with iodide as supporting electrolyte; probably an indirect electrolysis takes place here, with iodine as an electrocatalyst. In one of the rare examples in which a useful product is obtained simultaneously at the working electrode and the counter electrode



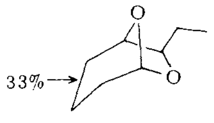
*(45)*



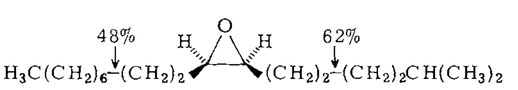
*(46)*



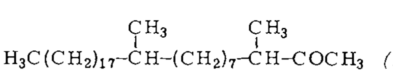
*(47)*



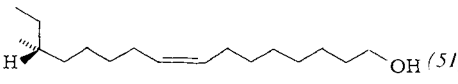
*(48)*



*(49)*



$H_3C(CH_2)_{17}\overset{CH_3}{C}H-(CH_2)_7-\overset{CH_3}{C}H-COCH_3$ *(50)*



*(51)*

Table 4. Selected examples of mixed Kolbe electrolyses of carboxylic acids.

| Carboxylic acid A | B | Product A—B [%] | Ref. |
|---|---|---|---|
| $MeO_2C(CH_2)_4CO_2H$ | $H_3C(CH_2)_8CO_2H$ | 38 | [278] |
| $MeO_2C(CH_2)_7CO_2H$ | $H_3C(CH_2)_7CH(CH_3)CH_2CO_2H$ | 35 | [279] |
| $CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$ | $HO_2C(CH_2)_6CO_2Me$ | 35 | [280] |
| $EtO_2C(CH_2)_6CO_2H$ | $Br(CH_2)_{10}CO_2H$ | 54 | [281] |
| $(CH_3)_2CHCH{=}CHCH_2CO_2H$ | $MeO_2C(CH_2)_nCO_2H$ (n = 1, 2, 4) | | [282] |
| $CF_3CO_2H$ | $EtO_2CCH_2CO_2H$ | 46 | [283] |
| $CF_3CO_2H$ | $CD_3CO_2H$ | 68 | [284] |

*(coupled electrosynthesis)*, diethyl malonate dimerizes at the anode to give tetraethyl ethanetetracarboxylate and ethyl acrylate dimerizes at the cathode to give diethyl adipate in yields of over 90% in each case[290,291]. Furthermore, anions of nitroaliphatic compounds are coupled to give vicinal dinitroalkanes[292], Grignard compounds[293] and borates[294] couple to give alkanes, acetylides give diacetylenes[295], and amides give azoalkanes[296].

### 3.2.2. Addition of Radicals to Double Bonds

If anions $R^{\ominus}$ are oxidized in the presence of olefins, additive dimers *(53)* and substituted monomers *(54)*, *(56)*, and *(57)* are obtained (Table 5):

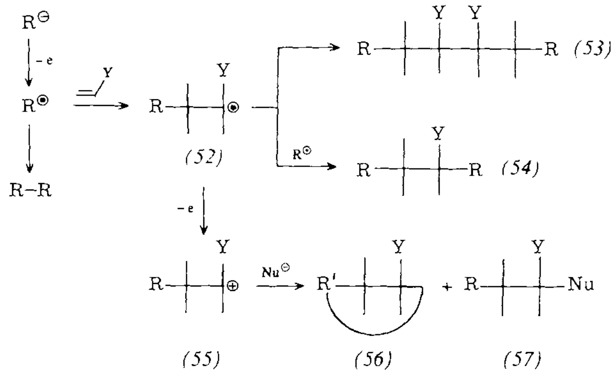


Table 5. Addition of anodically generated radicals to alkenes to give adducts of the type *(53)*, *(54)*, *(56)* and *(57)*. Y = Vinyl, Alkyl, Phenyl, Alkoxy; $Nu^{\ominus} = CH_3O^{\ominus}$.

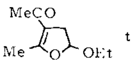
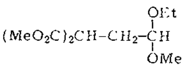
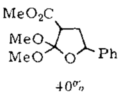
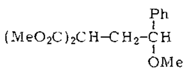
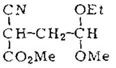
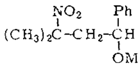
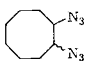
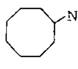
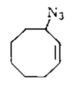
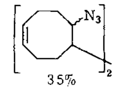
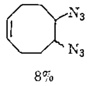
| No. | Anion $R^{\ominus}$ | Alkene —CH=CY— | Type *(53)* | Type *(54)*, *(56)*, *(57)* | Ref. |
|---|---|---|---|---|---|
| 1 | $MeO_2C—\overset{\ominus}{C}H—COMe$ | $H_2C{=}CHOEt$ | |  type *(56)*<br>36% | [297] |
| 2 | $(MeO_2C)_2\overset{\ominus}{C}H$ | $H_2C{=}CHOEt$ | |  $(MeO_2C)_2CH{-}CH_2{-}\overset{OEt}{\underset{OMe}{C}}H$ type *(57)*<br>37% | [297] |
| 3 | $(MeO_2C)_2\overset{\ominus}{C}H$ | $H_2C{=}CHPh$ | $[(MeO_2C)_2CH—CH_2—CHPh]_2$<br>10% |  40% type *(56)*<br> $(MeO_2C)_2CH{-}CH_2{-}\overset{Ph}{\underset{OMe}{C}}H$<br>17% type *(57)* | [297] |
| 4 | $(MeCO)_2\overset{\ominus}{C}H$ | $H_2C{=}CH—CH{=}CH_2$ | $[(MeCO)_2CH—CH_2—CH{=}CH—CH_2]_2$<br>+ isomers, 46% | | [297] |
| 5 | $MeO_2C—\overset{\ominus}{C}H—CN$ | $H_2C{=}CHOEt$ | |  $\overset{CN}{\underset{CO_2Me}{C}}H{-}CH_2{-}\overset{OEt}{\underset{OMe}{C}}H$ type *(56)*<br>19% | [298] |
| 6 | $(CH_3)_2\overset{\ominus}{C}NO_2$ | $H_2C{=}CHPh$ | |  $(CH_3)_2\overset{NO_2}{C}{-}CH_2{-}\overset{Ph}{\underset{OMe}{C}}H$ type *(56)*<br>43% | [299] |
| 7 | *n*Bu—MgBr | $H_2C{=}CHPh$ | $[nBu—CH_2—CHPh]_2$<br>29% | | [300] |
| 8 | $(C_6H_{13})_3B^{\ominus}OMe$ | $H_2C{=}CH—CH{=}CH_2$ | $[H_{13}C_6—CH_2—CH{=}CH—CH_2]_2$<br>+ isomers, 5% | $H_{13}C_6—CH_2—CH{=}CH—CH_2—C_6H_{13}$<br>type *(54)*<br>$H_{13}C_6—CH_2—CH{=}CH—CH_2OMe$<br>+ isomers, 14%, type *(56)* | [301] |
| 9 | $EtO_2CCO_2^{\ominus}$ | $H_2C{=}CH—CH{=}CH_2$ | $[EtO_2C—CH_2—CH{=}CH—CH_2]_2$<br>+ isomers, 66% | $EtO_2C—CH_2—CH{=}CH—CH_2—CO_2Et$<br>4% | [302] |
| 10 | $MeO_2C(CH_2)_4CO_2^{\ominus}$ | $H_2C{=}CH_2$ | $[MeO_2C(CH_2)_6]_2$<br>4—14% | $MeO_2C(CH_2)_{10}CO_2Me$<br>4—14%, type *(54)* | [304] |
| 11 | $MeO_2CCH_2CO_2^{\ominus}$ | $H_2C{=}CHOEt$ | $[MeO_2C—CH_2—CH_2—CH(OEt)]_2$<br>35% | | [303] |
| 12 | $MeO_2CCH_2CO_2^{\ominus}$ | $H_2C{=}CHPh$ | $[MeO_2C—CH_2—CH_2—CHPh]_2$<br>38% | | [302] |

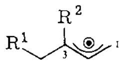
Table 5. Cont.

| No. | Anion $R^{\ominus}$ | Alkene —CH=CY— | Type *(53)* | Type *(54)*, *(56)*, *(57)* | Ref. |
|---|---|---|---|---|---|
| 13 | $MeO_2C(CH_2)_4CO_2^{\ominus}$ | $H_2C{=}CH{-}CH{=}CH_2$ | $[MeO_2C(CH_2)_4CH_2{-}CH{=}CH{-}CH_2{+}_2$ 47% | $MeO_2C(CH_2)_4{-}CH_2{-}CH{=}CH{-}CH_2{-}CH_2)_4CO_2Me$ 47%, type *(54)* | [305] |
| 14 | $F_3CCO_2^{\ominus}$ | $HC{\equiv}C{-}(CH_2)_3CH_3$ [a] | | $F_3CCH{=}C(CF_3){-}(CH_2)_3CH_3$ type *(54)* | [306] |
| 15 | $H_3CCO_2^{\ominus}$ | $H_2C{=}C(CH_3){-}CHO$ | $[H_3C{-}CH_2{-}C(CH_3)(CHO){+}_2$ 80% | | [307] |
| 16 | $N_3^{\ominus}$ | $H_2C{=}CHPh$ | $[N_3{-}CH_2{-}CHPh{+}_2$ 57% | | [308] |
| 17 | $N_3^{\ominus}$ | *cis*-Cyclooctene | |  24% type *(54)*<br> 15%<br> 17%<br>both type *(57)* | [309] |
| 18 | $N_3^{\ominus}$ | *cis,cis*-1,5-Cyclooctadiene |  35% |  8% type *(54)* | [309] |

[a] For purposes of comparison an alkyne was taken.

The following pathway appears to be plausible: the radical $R^{\bullet}$ obtained by a 1e-oxidation from the anion $R^{\ominus}$ adds to the alkene to give the primary adduct *(52)* which dimerizes to give the additive dimer *(53)* with regiospecific head-to-head linkage of the two olefins, or couples with $R^{\bullet}$ to give the additive monomer *(54)*. If the substituent Y in the olefin can stabilize a carbenium ion, *(52)* is oxidized to the cation which reacts intra- or intermolecularly with nucleophiles to give *(56)* or *(57)*.

Satisfactory to good yields of adducts have been found for styrenes (Y = phenyl), conjugated dienes (Y = vinyl), and enol ethers (Y = alkoxy) particularly if they are unsubstituted at the β-carbon atom. Nonactivated alkenes react less satisfactorily. In vicinal disubstituted styrenes, upon addition of the Kolbe radical $MeO_2CCH_2^{\bullet}$, the yields of adducts decrease with increasing size of the β-substituent: H = 42%, Me = 27%, Et = 11%, *i*Pr = 5%, *t*Bu = 2%[288]. The yields also depend on the radical's reactivity: thus, cyclohexene gives 18% of adducts with the $N_3^{\bullet}$ radical[309] but only 9% with $EtO_2C^{\bullet}$[302], while the stable $NO_2(CH_3)_2C^{\bullet}$ radical no longer adds[299b]. The additive dimer *(53)* : monomer *(54)* ratio can be affected to some extent by the current density ($\bar{i}$). With butadiene and ethyl oxalate (Table 5, No. 9), *(53)* : *(54)* = 15.6 for $\bar{i}$ = 0.025 mA/cm², but only 0.67 for $\bar{i}$ = 0.66 mA/cm². Obviously, at low current densities the radicals $R^{\bullet}$ are mainly trapped by the olefin to give *(52)* [→ 1/2 *(53)*], a process which no longer occurs at higher current densities, *i.e.* higher radical concentrations, so that now the mixed coupling to give *(54)* is favored. In the oxidation of anionized 1,3-dicarbonyl compounds (Table 5, Nos. 1—4) between 0.6 and 1.4 V (SCE) in the presence of butadiene only the additive dimer *(53)* is obtained, while with ethyl vinyl ether only the disubstituted monomer *(56)* or *(57)* arises, and with styrene both types of products *(53)* and *(56)* are formed. This result makes it probable that the primary adduct *(52)* is oxidized to the carbenium ion as a ethoxymethyl radical (Y = OEt) below 0.6 V, as an allyl radical (Y = vinyl) above 1.4 V, and as a benzyl radical (Y = phenyl) within this potential range[297]. Addition to butadiene forms an allyl radical *(58)*, which couples at C1 and C3 to give isomeric 1,5-dienes [cf. *(40)*—*(42)*]. It follows from the higher proportion of 1,1′-linked dimers that C1 reacts about 2.7 times faster as C3, probably due to the greater steric shielding of C3[297].


*(58)*

Taking the different reactivities of the allyl radicals into account indicates that they couple almost statistically to form the 1,1′-, 1,3′-, and 3,3′-dimers[297]. With more bulky substituents, *e.g.* $R^1 = NO_2(CH_3)_2C$ and $R^2 = CH_3$, the C1 : C3 reactivity ratio may rise to greater than 15[299b]. In the addition of the Kolbe radicals $MeO_2C(CH_2)_{n-1}CH_2^{\bullet}$ to butadiene (Table 5, Nos. 9 and 13), the distribution of the isomers is independent of the chain length (n = 0 to 4, respectively). Reports that adipic acid hemiesters only give unbranched additive dimers[305] have not been confirmed[310].

The preparative advantages of anodic addition comprise simpler reaction conditions and short routes to complex compounds. The disadvantages are the formation of isomers by parallel reactions and the non-regioselective coupling of the intermediate allyl radicals. The one-step preparation of dihydrofurans (Table 5, No. 1), of the diene diesters (Nos. 9 and 13), of the 1,4-dicarbonyl compounds (No. 15), and of the diazides (Nos. 16 and 18) could be of preparative interest.

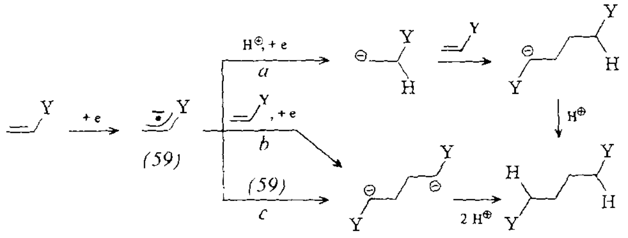
## 4. Preparative Applications: CC-Bond Formation at the Cathode

At the cathode it is possible to obtain radical anions, carbanions, and neutral radicals, whose reactions with electrophiles or whose coupling leads to the formation of new CC-bonds.

### 4.1. Radical Anions as Intermediates

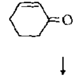
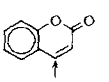
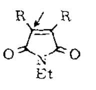
Olefins that are activated by electron-attracting substituents form tail-to-tail linked hydrodimers at the cathode, presumably *via* radical anions. This hydrodimerization[12,16-18,61,62] has been developed, particularly by *Baizer*, into a large technical-scale synthesis of adipodinitrile[311,312], has been extended to numerous olefins[313], and has been applied in mixed couplings and intramolecular cyclizations[57,59,61]. Some examples of these reactions are summarized in Table 6.

The intermediate radical anion *(59)* can dimerize in three ways:



$Y = -\underset{|}{C}=O,\ -CO_2R,\ -C\equiv N$

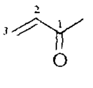
Tabelle 6. Hydrodimerization of activated olefins at the positions shown by the arrows.

| Olefin | Yield [%] [a] | Ref. |
|---|---|---|
| *Nitriles* | | |
| $\overset{\downarrow}{C}H_2{=}CHCN$ | 90 (95) | [313] |
| $(CH_3)_2\overset{\downarrow}{C}{=}CHCN$ | 90 | [313] |
| $\overset{\downarrow}{C}H_2{=}C(CH_3)CN$ | 75 | [313] |
| $\overset{\downarrow}{C}H_2{=}CH{-}CH{=}CHCN$ | | [314] |
| $PhCO{-}CH{=}\overset{\downarrow}{C}H{-}CN$ | (55) | [315] |
| *α,β-Unsaturated Carbonyl Compounds* | | |
| $\overset{\downarrow}{C}H_2{=}CHCOCH_3$ | (80) | [316] |
|  | (80) | [317] |
| $(CH_3)_2\overset{\downarrow}{C}{=}CHCOCH_3$ | (90) | [318] |
| $ArylCO{-}CH{=}\overset{\downarrow}{C}HCl$ | (30-50) | [319] |
| $\overset{\downarrow}{C}H_2{=}CHCO_2Et$ | (87) | [313] |
| $Ph\overset{\downarrow}{C}H{=}CHCO_2H$ | (70) | [320] |
|  | (93) | [321] |
|  R = H, CH₃ | | [322] |

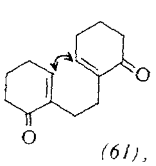
[a] Current yield; the material yields are given in parentheses.

Route *a*, protonation and reduction to a β-substituted carbanion, is assumed for the hydrodimerization of acrylonitrile[62]; route *b*, the Michael addition of the radical anion to the educt, has been suggested for the cathodic hydrocyclization[323]; finally, route *c* has been shown to be probable for the radical dimerization of the dimethyl maleate radical anion[324].

α,β-Unsaturated ketones and aldehydes *(60)* usually yield 3,3′-coupled dimers in neutral media (Table 6), while in acidic media larger amounts, up to 100%, of the 1,1′- and 1,3′-dimers are formed[325]. The dienedione *(61)*, which

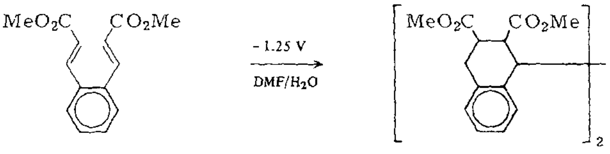


*(60)*



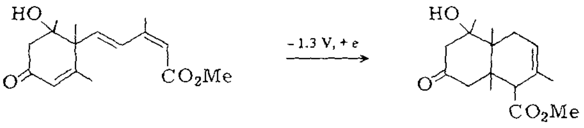
*(61)*, 80%

can be obtained by the Kolbe dimerization of Hagemann's ester, yields, in a regio- and stereospecific reaction, the potential steroid-building block *trans,trans*-perhydrophenanthrene[326]. An intramolecular ring closure followed by dimerization is observed for the dienic diester *(62)* in dimethylformamide/water[327].



*(62)* 29%

Methyl abscisate *(63)* likewise cyclizes intramolecularly in a 6-*exo-trig* reaction[328] to give the decalin derivative *(64)*[329]:



*(63)* *(64)*, 51%

In cyclopropyl ketones only the carbonyl group is hydrogenated or coupled to form the pinacol; only if the three-membered ring is additionally phenyl-substituted can it also undergo hydrogenative cleavage[330].

Acylations, carboxylations, and alkylations of activated alkenes are possible by reaction of the intermediate radical anions with the corresponding electrophiles E (Table 7).

The radical anion *(59)* reacts in a CEC step[*] to give an acylated or dicarboxylated monomer[332,333,341] (route *a*); didecarboxylated dimers arise in route *b* from diactivated double bonds, or by reduction of olefins which can be reduced in two steps at the potential of the first step[342]. If the reduction potential of the olefin is more cathodic than the reduction potential of $CO_2$ ($E_{1/2} = -2.3$ V), the latter can be reduced to the anion radical and react with the olefin as an electrophile. While with $CO_2$ dicarboxylations are the rule, diacylations *e.g.* diformylation are the exception[336]. Acylations can be classified as *umpolung* reactions of type d³[1].

---

[*] C = chemical, E = electrochemical.

Table 7. Acylation, carboxylation, and alkylation of cathodically produced radical anions.

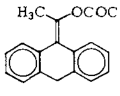
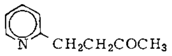
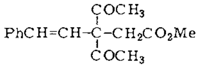
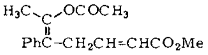
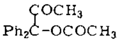
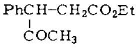
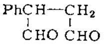
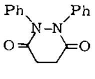
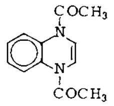
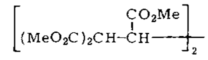
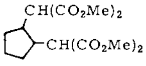
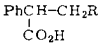
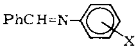
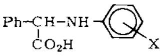
| Substrate | Electrophile | Product | Ref. |
|---|---|---|---|
| *Acylation* | | | |
| Anthracene | $(CH_3CO)_2O$ | <br>66-75% | [331] |
| $H_2C{=}CHCO_2Me$ | $(CH_3CO)_2O$ [a] | $H_3CCOCH_2{-}CH_2CO_2Me$<br>62% | [332] |
| $(CH_3)_2C{=}CHCO_2Me$ | $(CH_3CO)_2O$ [a] | $H_3CCOC(CH_3)_2{-}CH_2CO_2Me$<br>64% | |
| 2-Styrylpyridine | $(CH_3CO)_2O$ | <br>45% | [333] |
| $PhCH{=}CH{-}CH{=}CHCO_2Me$ | $(CH_3CO)_2O$ | <br>$PhCH{=}CH{-}\underset{COCH_3}{\underset{\mid}{\overset{COCH_3}{\overset{\mid}{C}}}}{-}CH_2CO_2Me$<br>30%<br><br>$\overset{\overset{H_3C\diagdown_{C}\diagup OCOCH_3}{\Vert}}{PhC}{-}CH_2CH{=}CHCO_2Me$<br>15% | [333] |
| PhCOPh | $(CH_3CO)_2O$ | <br>$Ph_2\overset{COCH_3}{\overset{\mid}{C}}{-}OCOCH_3$ [b]<br>66% | [334] |
| $PhCH{=}CHCO_2Et$ | $(CH_3CO)_2O$ | <br>$Ph\underset{COCH_3}{\underset{\mid}{CH}}{-}CH_2CO_2Et$<br>75% | [335] |
| α-Methylstyrene | $CH_3C{\equiv}N$ | $PhCH(CH_3){-}CH_2{-}COCH_3$<br>68% [c] | [336] |
| Styrene | $Me_2N{-}CHO$ | <br>$Ph\underset{CHO}{\underset{\mid}{CH}}{-}\underset{CHO}{\underset{\mid}{CH_2}}$<br>82% [d] | [336] |
| Azobenzene | $ClCO(CH_2)_2COCl$ | <br>49% | [337] |
| Quinoxaline | $(CH_3CO)_2O$ | <br>92% | [338] |
| *Carboxylations* | | | |
| Dimethyl maleate | $CO_2$, −1.84 V<br>(2nd half-wave), $CH_3I$ | $[(MeO_2C)_2CH_2{-}]{-}$<br>31% | [339] |
| Dimethyl maleate | $CO_2$, −1.65 V<br>(1st half wave), $CH_3I$ | <br>$\left[(MeO_2C)_2CH{-}\overset{CO_2Me}{\overset{\mid}{CH}}{-}\right]_2$<br>46% | [340] |
| $[MeO_2CCH{=}CHCH_2]_2CH_2$ | $CO_2$, $CH_3I$ | <br>50% | [340] |
| $PhCH{=}CHR$<br>R = CN, COMe, $CO_2Et$ | $CO_2$ | <br>$Ph\underset{CO_2H}{\underset{\mid}{CH}}{-}CH_2R$<br>38-70% | [341] |
| $H_2C{=}CH_2$ | $CO_2$ | $HO_2C(CH_2)_2CO_2H$ | [342] |
|  | |  | [343] |

Table 7. (Cont.)

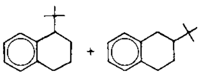
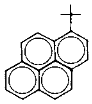
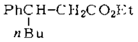
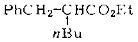
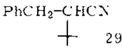
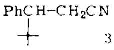
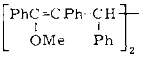
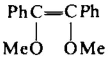
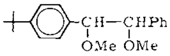
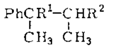
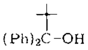
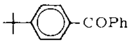
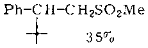
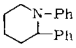
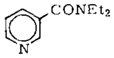
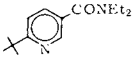
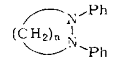
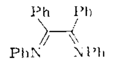
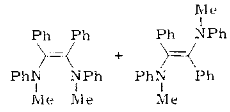
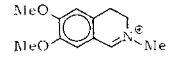
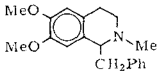
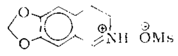
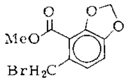
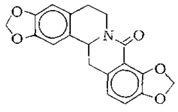
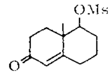
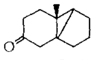
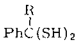
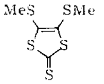
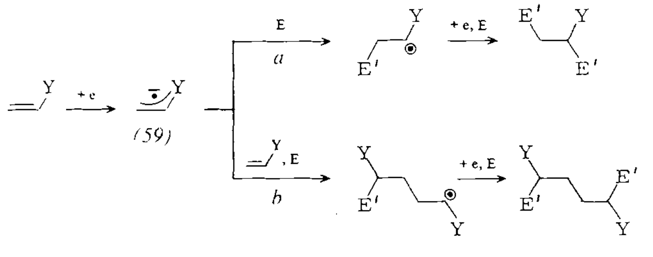
| Substrate | Electrophile | Product | Ref. |
|---|---|---|---|
| *Alkylation* | | | |
| Naphthalene | $tBuCl$<br>$tBuN^{\oplus}Me_3$ | <br>and tert-butyldihydro isomers<br>70% | [344, 349] |
| Pyrene | $tBuCl$<br>$tBuN^{\oplus}Me_3$ | <br>52% | [345] |
| $EtO_2CCH{=}CHCO_2Et$ | RBr, R = nBu, sBu, tBu, $cC_6H_{11}$, $nC_8H_{17}$ | $EtO_2CCHR{-}CH_2CO_2Et$<br>22-45% | [346, 348] |
| $PhCH{=}CHCO_2Et$ | nBuBr |  $Ph\underset{nBu}{C}H{-}CH_2CO_2Et$<br>17%<br> $PhCH_2{-}\underset{nBu}{C}HCO_2Et$<br>28% | [346] |
| *trans*-$PhCH{=}CHCN$ | tBuBr | <br>29%<br><br>38% | [347a] |
| $PhCO{-}CPh{=}CHPh$ | $Me_2SO_4$ |  $\left[Ph\underset{OMe}{C}{=}CPh{-}\underset{Ph}{C}H\right]_2$ | [347b] |
|  $\underset{MeO}{PhC}{=}\underset{OMe}{CPh}$ | tBuCl | <br>47% | [347a] |
| $PhCR^1{=}CHR^2$<br>$R^1, R^2 = H, Me$ | $CH_3I$ |  $Ph\underset{CH_3}{C}R^1{-}\underset{CH_3}{C}HR^2$<br>33-45% | [348] |
| PhCOPh | $tBu\overset{\oplus}{S}Me_2$ | <br>34%<br><br>24% | [349] |
| $PhCH{=}CHSO_2Me$ | tBuBr | <br>35%<br>and tert-butylated cleavage products<br>31% | [351] |
| Cyclopropyl methyl ketone | $Et_4N^{\oplus}Br$ | 2-pentanone, 2-pentanol, 3-methyl-3-hexanol<br>70-75% | [350] |
| $PhCH_2{-}N{=}C(CH_3){-}CO_2CH_2Ph$ | RBr<br>$R = CH_2Ph$, $CH_2CO_2Et$, $CH_3$, $C_2H_5$ | $H_2N{-}CR(CH_3){-}CO_2H$<br>15-86% | [352] |
| $PhCH{=}NPh$ | $Br(CH_2)_4Br$ | <br>59% | [353] |
| Quinoline | EtBr, nBuBr | 1,2-Dihydro-1,2-dialkyl- and 1,4-dihydro-1,4-dialkyl derivatives | [354] |
|  | tBuCl | <br>22% | [355] |

Table 7. (Cont.)

| Substrate | Electrophile | Product | Ref. |
|---|---|---|---|
| PhN=NPh | $Br(CH_2)_nBr$ | <br>n = 3: 62%; n = 4: 81%<br>n = 5: 58%; n = 6: 14% | [356a] |
|  | $CH_3Cl$ | <br>12% 88% | [356b] |
|  | $PhCH_2Br$ |  65% | [356c] |
| *Alkylations* | | | |
|  |  | <br>85% | [356c] |
|  | | <br>74% | [356d] |
| $PhCS_2R$ | RX |  $Ph\overset{R}{\underset{}{C}}(SH)_2$ | [357b] |
| $CS_2$ | $CH_3I$ |  | [357c] |
| $SO_2$ | $H_2C{=}CH{-}CH_2Br + CH_3Br$ | $CH_2{=}CH{-}CH_2{-}SO_2Me$<br>42% | [357a] |
| S | $PhCH_2Cl$ | $(PhCH_2)_2S$ | [357b] |

[a] Similarly with $(nPrCO)_2O$ and $(iPrCO)_2O$. [b] No analogous reactions take place with benzaldehyde or acetophenone. [c] Similar reduction also possible with lithium. [d] Isolated as the bismethoxime.


(59)

E = RCOX, $CO_2$; Y = $-\underset{|}{C}{=}O$, $-CO_2R$, –Aryl

The reductive alkylation of double bonds with alkyl halides or 'onium salts takes place largely *via* a transfer of electrons to the solution (SET = solution electron transfer)[347a, 358]:

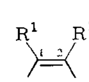
$$Su \xrightarrow{+e} Su^{\cdot-}$$

$$RX + Su^{\cdot-} \longrightarrow Su^{\cdot-} + RX^{\cdot-}$$

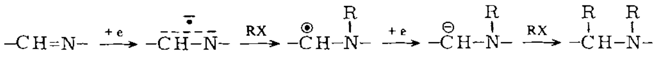
$$RX^{\cdot-} \longrightarrow R^{\cdot} + X^{\ominus}$$

$$R^{\cdot} + Su^{\cdot-} \longrightarrow R{-}Su^{\ominus} \xrightarrow{H^{\oplus}} R{-}Sn{-}H$$

The substrate radical anion $Su^{\cdot-}$ reduces the alkyl halide to $RX^{\cdot-}$ which dissociates to the alkyl radical, and this couples with $Su^{\cdot-}$ to give the alkylation product. An $S_N2$ substitution with $Su^{\cdot-}$ as the nucleophile can be excluded, since the best yields are obtained with *tert*-butyl halides[344], and in the case of mixed 'onium salts containing the *tert*-butyl residue only this is transferred[349]. Activated double bonds *(65)* with $R^1$ = alkyl, $R^2 = CO_2Et$, or $R^1$ = phenyl, $R^2 = SO_2Me$ are alkylated selectively at C1, while with $R^1$ = phenyl, $R^2 = CO_2Et$, alkylation takes place only nonspecifically[346, 347a, 351].


(65)

Schiff's bases[353] and quinoline[354] react with primary halides by an ECEC mechanism:



$$-CH{=}N- \xrightarrow{+e} \overline{-\overset{\cdot}{C}H{-}\overset{-}{N}-} \xrightarrow{RX} -\overset{\cdot}{C}H{-}\overset{R}{\underset{}{N}}- \xrightarrow{+e} -\overset{\ominus}{C}H{-}\overset{R}{N}- \xrightarrow{RX} -\overset{R}{C}H{-}\overset{R}{N}-$$

Reductive alkylations merit preparative interest particularly for the tertiary alkylation of aromatics and double bonds and for the preparation of α-alkylated amino acids and nitrogen heterocycles.

The reductive oligomerization of $CO_2$ is also industrially of potential interest for the synthesis of large carbon units, and has therefore been treated fairly frequently. Reduction in aqueous electrolytes leads to formic acid[359]. The preparation of longer-chain hydroxy carboxylic acids[360] is not always reproducible[359], but other workers[361] have managed to obtain 70% of malic acid at pH 10 with a mercury cathode. In partly aprotic media, formic and oxalic acids or, by subsequent reduction, glycolic, glyoxylic, tartaric, and malic acids are formed[359,362]. Up to 90% yield of oxalic acid is formed in aprotic media[359,363].

### 4.2. Radicals as Intermediates

Aldehydes and ketones can be hydrodimerized cathodically to form pinacols; in acidic media hydroxyalkyl radicals are probable intermediates in this process[364]. While with aromatic carbonyl compounds good yields of pinacols are generally obtained, yields are only moderate with aliphatic compounds, because of the competing reduction to alcohols and hydrocarbons. Formation of pinacols is favored by a high concentration of the carbonyl compound, an acidic medium, and cathodes with a low hydrogen overvoltage[365]. Older investigations have been described in [366], while more recent results are summarized in Table 8.

Table 8. Cathodic formation of pinacols from carbonyl and analogous reactions of Schiff's bases at the positions marked wich arrows, as well as crossed hydrodimerization and cyclization reactions.

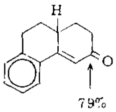
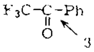
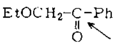
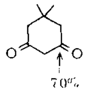
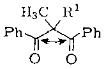
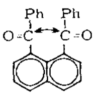
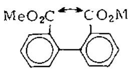
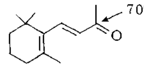
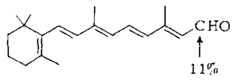
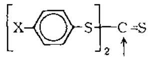
| No. | Substrate (yield of dimers) | Ref. |
|---|---|---|
| *Pinacol formation* | | |
| 1 |  79% | [367] |
| 2 |  $F_3C-\underset{\underset{O}{\Vert}}{C}-Ph$ 35% | [368] |
| 3 |  $EtOCH_2-\underset{\underset{O}{\Vert}}{C}-Ph$ 50% | [369] |
| 4 |  70% | [370] |
| 5 |  [a]<br>$R^1$ = $CH_3$: 80%; $R^1$ = H: 80% | [371] |
| 6 |  [a] 87% | [373] |
| 7 |  [b] 35% | [374] |

Table 8. (Cont.)

| No. | Substrate (yield of dimers) | Ref. |
|---|---|---|
| 8a |  | [375] |
| 8b |  11%<br>50% | [375, 377a] |
| 8c |  7-62%<br>X = $OCH_3$, $CH_3$, H, Cl, $CH_3CO$ | [377b] |

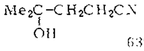
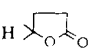
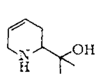
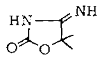
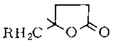
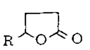
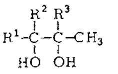
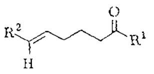
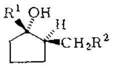
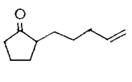
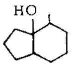
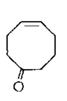
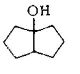
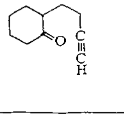
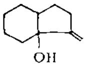
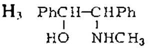
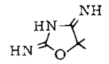
| No. | Substrate | Product | Ref. |
|---|---|---|---|
| *Crossed hydrodimerization* | | | |
| 9 | $(CH_3)_2C{=}O$, $H_2C{=}CHCN$ |  $Me_2\underset{\underset{OH}{\vert}}{C}-CH_2CH_2CN$ 63% | [378] |
| 10 | $(CH_3)_2C{=}O$, $H_2C{=}CHCO_2H$ |  51% | [378a] |
| 11 | $(CH_3)_2C{=}O$, Pyridine |  78% | [378a] |
| 12 | $(CH_3)_2C{=}O$,<br>$H_2N-CO-NHCN$ |  70-90% | [378a] |
| 13a | $H_3CCO-CH_2R$,<br>$H_2C{=}CHCO_2Et$ |  47-80%<br>R = $CH_3$, $C_2H_5$, $C_4H_9$, $C_5H_{11}$ | [381a, 378b] |
| 13b | RCHO, $H_2C{=}CHCO_2Me$ |  91-92%<br>R = $CH_3$, $C_2H_5$ | [381b] |
| 14 | $R^1R^2C{=}O$,<br>$CH_2{=}CR^3OCOCH_3$<br>$R^1$ = Ph, $R^2$ = $R^3$ = H, $CH_3$,<br>Ph, Furyl, Pyridyl |  $R^1-\underset{\underset{HO}{\vert}}{\overset{\overset{R^2}{\vert}}{C}}-\underset{\underset{OH}{\vert}}{\overset{\overset{R^3}{\vert}}{C}}-CH_3$ 34-62% | [382a] |
| *Cyclization* | | | |
| 15a |  |  23-98%<br>$R^1$ = $CH_3$ - $nC_6H_{11}$<br>$R^2$ = H - $(CH_3)_2CH$ | [382b] |
| 15b |  |  65% | [382b] |
| 15c |  |  69% | [382b] |
| 16 |  |  | [382c] |

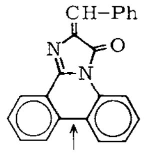
Table 8. (Cont.)

| No. | Substrate | Product | Ref. |
|---|---|---|---|
| *Schiff's bases* | | | |
| 17 | $PhCH{=}N{-}cC_6H_{11}$<br>↑<br>45% | | [383] |
| 18 | $PhCHO$<br>$PhCH{=}NCH_3$ |  $PhCH(OH){-}CH(NHCH_3)Ph$ 22% | [383] |
| 19 | $(CH_3)_2C{=}O$ $-CN$<br>$(H_2N)_2C{=}N$ |  | [384] |

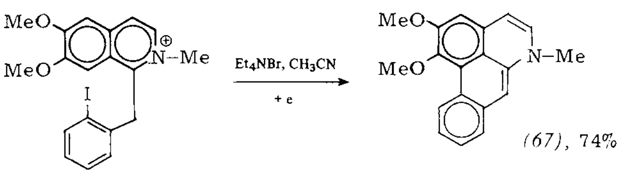
[a] Intramolecular reaction. [b] Reaction product 9,10-dihydrophenanthrene-9,10-diol.

Tetrahydrophenanthrones (Table 8, No. 1) couple more or less preferentially to give *R,R*- or *S,S*-diols, due to adsorption of the intermediate radicals (see also [211]). While ketones with heterosubstituents in the α-position do not form pinacols in aqueous acidic media but eliminate the hetero substituents, pinacols are formed in aprotic (acetonitrile), neutral, or weakly basic media (Table 8, Nos. 2 and 3). 1,3-Diketones react intramolecularly in aprotic media[372], and in weakly acidic and protic solutions to cyclopropanediols; two alkyl substituents in position 2 are favorable, but not essential, conditions to this end (Table 8, No. 5). An α-hydroxy carbanion which adds nucleophilically to the carbonyl group, has been discussed as an intermediate here. In acidic media 1,8-dibenzoylnaphthalene (Table 8, No. 6) forms a *cis*-acenaphthenediol stereoselectively, which can be explained by the formation of a hydrogen bond; the formation of the *trans*-diol in basic media is explained by electrostatic repulsion of the intermediate ketyls. α,β-Unsaturated carbonyl compounds generally hydrodimerize to 1,6-diketones (Table 7), but if the double bond is sterically shielded, as in β-ionone or in retinal, they couple to form 1,2-diols (Table 8, No. 8a, 8b). The yields can be increased by the addition of chromium(III) salts[376], which probably act as complexing agents, but still better by the replacement of the coelectrolyte acetic acid by the weak CH-acid diethyl malonate[377a]. The crossed hydrodimerization between a carbonyl compound and a second electrophile discovered by *Baizer*[379] (Table 8, Nos. 9—13b) takes place particularly well in strongly acidic media, while the yields fall in weakly acidic or neutral electrolytes. Radical[380] and nucleophilic[378a] additions of $R_2(HO)C^{\ominus}$ or $R_2(HO)C^{\ominus}$ to the electrophile have been proposed for the reaction mechanism. As an alternative to the mixed electrolysis of ketones[382c], unsymmetric pinacols can be obtained by the coelectrolysis of aromatic ketones and enolic esters (Table 8, No. 14). The cyclization of δ- or ε-unsaturated ketones to cyclopentanols or cyclohexanols with alkyl groups in the *cis*-position takes place remarkably stereoselectively and is of preparative interest (Table 8, No. 15). The reaction mechanism is assumed to be a radical attack of the ketyl on the double bond. Correspondingly, *exo*-cycloalkenols are formed with ketoalkynes (Table 8, No. 16). Schiff's bases hydrodimerize to form diamines or undergo a crossed reaction with carbonyl compounds to give α-amino alcohols (Table 8, Nos. 17–19).

Benzyl, allyl, and even alkyl bromides are dimerized *via* indirect electrolysis with chromium(II) chloride[385] or by using iron 2,4-pentadionate[386] as electron carrier, presumably *via* radical intermediates. Suitable aryl halides can be cleaved to σ-radicals, which cyclize by intramolecular aryl addition to azaphenanthrenes *(66)*[387a] or aporphines *(67)*[387]. The latter synthesis is claimed at present to be the shortest route to this biologically active class of compounds.

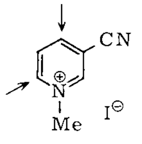


*(66)*

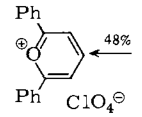


*(67)*, 74%

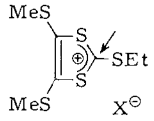
Cations are reduced cathodically to give radicals, which then dimerize. The nicotinamide model *(68)* thus gives four stereoisomeric hydrodimers[388], and 2,6-diphenylpyrylium perchlorate *(69)* gives the corresponding substituted bipyranyl[389].



*(68)*



*(69)*



*(70)*

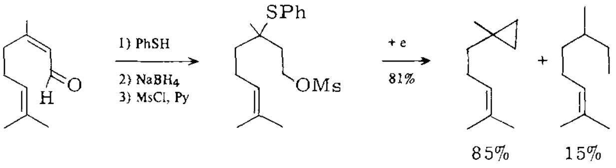
Tropylium tetrafluoroborate gives a quantitative yield of 7,7-bitropyl[390], and the sulfonium salts *(70)* can be coupled to tetrathiafulvalene precursors[391]. Diazonium salts of 2-aminophenylcinnamic acids are reduced, with the elimination of nitrogen, to phenyl radicals which cyclize to phenanthrene derivatives with a better yield (>90%) than in the alternative Pschorr reaction[392a]. Benzyl-, cinnamyl-, and polyenyl-substituents in phosphonium salts can be dimerized in yields of 6—56%[392b].

### 4.3. Carbanions as Intermediates

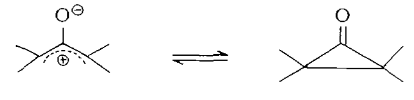
Carbanions are usually obtained by the cathodic cleavage of carbon-halogen bonds and are used for the preparation of small rings by intramolecular substitution, for additions to carbonyl compounds and activated double bonds, or as bases for deprotonations.

Cathodic 1,3-eliminations have repeatedly proved their value for the preparation of cyclopropanes[393]. α,β-Unsaturated carbonyl compounds can also be converted into cyclopropanes by this principle, if they are previously modified by the addition of thiophenol, reduction of the carbonyl group, and mesylation[394].

The tetramethyl cyclopropanone *(72)* should be accessible from 2,4-dibromo-2,4-dimethyl-3-pentanone by a 1,3-

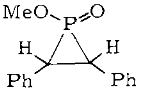


elimination, but in spite of numerous variations of the reaction conditions and trapping reagents, a complex mixture of products was formed in acetonitrile/ethanol, which was ascribed to the intermediate zwitterion *(71)*[395]. In contrast to this, the methyl hemiacetal of *(72)* was obtained in almost quantitative yield starting from the same dibromide in methanol[396]. This difference in results has been explained by a solvent-dependent position of the equilibrium: *(71)*⇄*(72)*.



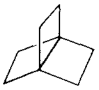
*(71)* *(72)*

A cyclic phosphinate *(73)* has been assumed to be an intermediate in the reduction of the corresponding α,α′-dihalophosphinate to *cis*- and *trans*-stilbenes[397].



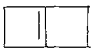
*(73)*

The results on the mechanism of the 1,3-elimination are controversial. While the fact that the reduction potentials of the 1,3-dihalides are more anodic than those of the monohalides indicates a synchronous mechanism[398a], the stereochemistry of the cyclopropane formation supports the idea of a two-step pathway *via* a carbanion and an $S_N2$ substitution reaction[398b]. For the cyclization of *endo,endo*-2,6-dibromonorbonane to tricyclene, where an $S_N2$ substitution is sterically impossible, a diradical has been proposed as intermediate[399]. Some strained, reactive hydrocarbons have been prepared by 1,n-eliminations. While the synthesis of [2.2.1]propellane *(75)* was unsuccessful[400], [2.2.2]-propellane *(74)* was obtained from 1,4-dibromobicyclo[2.2.2]octane, although only in 12% yield[401]. [2.2.0]Bicyclohexene *(76)*, prepared by the electrolysis of 1-bromo-4-chlorobicyclo[2.2.0]hexane, has been trapped as the cyclopentadiene adduct[402].



*(74)*

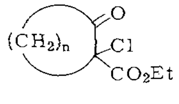
*(75)*



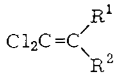
*(76)*

A 1,4- and a subsequent 1,2-elimination in xylylidene tetrabromide led to benzocyclobutadiene, which was isolated as the Diels-Alder dimer[403]. Cyclic dicarboxylic acid diesters are obtainable in satisfactory to good yields from 2,(n−1)dibromo alkanedioates, n=3 (74%), 4 (32%), 5 (52%), 6 (60%), 7 (20%)[404]. Hexamethyldisilane can be obtained from trimethylsilyl chloride, probably *via* a 2e-reduction to the silyl anion[405]. By reductive 1,1-elimination and α-elimination with cathodically produced bases, it is possible to obtain dichlorocyclopropanes[406] and bromofluorocyclopropanes[407] from carbon tetrachloride, chloroform, and tribromofluoromethane with alkenes in current yields of up to 80%; a considerable improvement over the original adduct yields of only 8%[408a]. A Fritsch-Buttenberg-Wiechell rearrangement of 1,1-diaryl-2,2-dihaloethylenes can be initiated cathodically, giving 1,2-diarylacetylenes in yields of 85—92%[408b]. Tosyl-[409] and alkoxycarbonyl-nitrenes[410] are accessible cathodically from the corresponding dichloro precursors and can be trapped as insertion products with dioxane in yields of 2—32%.

Carbanions obtained cathodically from halides have been treated with carbonyl compounds, activated double bonds, or other electrophiles. With acetone, allyl halides form isomeric homoallyl alcohols, the product distribution depending slightly on the electrode material[411]. With aldehydes and ketones, carbon tetrachloride and 1,1,1-trichloroethane yield 2,2,2-trichloroethyl alcohol[412a,418b] and 2,2-dichloropropyl alcohols[412b]; the yields are considerably increased in some cases by additions of magnesium perchlorate[413]. With ethyl trichloroacetate and cyclic ketones, the β-keto esters *(77)* are formed *via* ring expansion[412a]. The dichloroolefins *(78)* or α-chloroacrylic esters can be prepared in a Wittig-Horner reaction, without the use of bases, by the reduction of trichloromethyl phosphonates or dichloro(ethoxycarbonyl)methyl phosphonates in the presence of carbonyl compounds[414].



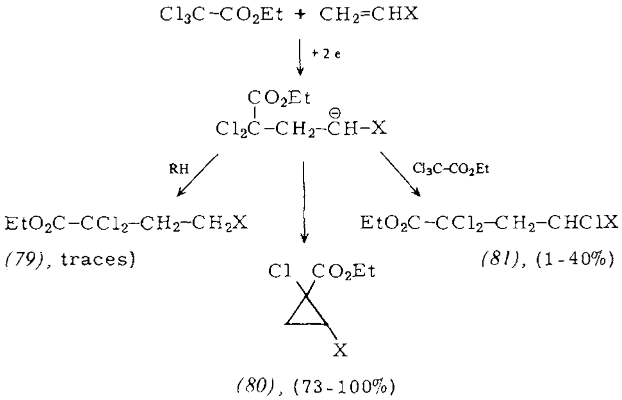
*(77)*, n = 3 (43%)
n = 4 (27%)



$Cl_2C{=}C(R^1)(R^2)$

*(78)*, $R^1$ = 4-$CH_3OC_6H_4$, $R^2$ = H (40%)
$R^1$ = $CH_2{=}\underset{CH_3}{\underset{|}{C}}{-}$, $R^2$ = H (45%)
$R^1$, $R^2$ = $-(CH_2)_5-$ (52%)

β-Halogeno esters[415] and α,β-unsaturated esters[416] can be added cathodically in the presence of trimethylsilyl chloride to aldehydes and ketones to give γ-lactones in satisfactory to good yields. Benzyl chlorides are acylated by acid chlorides to form benzyl ketones[417]. Ethyl trichloroacetate adds cathodically to activated double bonds forming, in addition to the adduct *(79)*, the cyclopropane esters *(80)* by intramolecular substitution and the trichlorinated ester *(81)* by nucleophilic attack on the educt[418a].



*(79)*, traces)
*(81)*, (1-40%)
*(80)*, (73-100%)

With ethyl dichloroacetate, electrolysis initiates a chain addition[418a], a principle which was later applied to the addition of chloroform to carbonyl compounds[418b]. Acrylic esters are alkylated by alkylboranes in undivided cells with very good yields[419a]. Here it is assumed that the boranes react with iodine, produced anodically from the sodium iodide supporting electrolyte, to give alkyl iodides which add cathodically to the activated esters. Under catalysis by vitamin $B_{12}$, bromomethylenecyclohexenones can be cyclized cathodically in good yield[419b].

While the reaction of dichloromethane with dialkylboranes forms dialkylmethanols reductively in good yield[420], the corresponding reaction of benzylidene chloride and $CO_2$ gives mandelic acid in low yield[421].

A series of nucleophilic substitutions, eliminations, and additions of preparative interest can be achieved with cathodically produced bases. For example, nitro aliphatic compounds[422], nitriles[423], and terminal alkynes[424a] are alkylated by trialkylboranes in undivided cells. As discussed above, it is considered that the alkylboranes form alkyl iodides with anodically produced iodine and alkylate the cathodically anionized CH acids. Reduction in the presence of alkyl halides yield the corresponding products[424b]. The cyanomethyl anion reacts with benzaldehyde and phenyl ketones to give phenylated-propionitriles and -glutaronitriles[425]. Esters and amides react analogously[426]. While allylphosphonium salts are mainly cleaved by direct reduction with a cathodically produced base such as the radical anion of 9-(dicyanovinylidene)fluorene, they can be deprotonated to ylides and react with carbonyl compounds to form polyenes[367a]. 2,2′-Di-*tert*-butylazobenzene and tetrabutyl ethylenetetracarboxylate are favorable probases which, when reduced cathodically to dianions, deprotonate weak CH acids. Thus, it has been possible to carboxylate ethyl phenylacetate and 9-phenylfluorene with $CO_2$ in high yields. The dianions are substantially protected against the attack of the electrophile by steric hindrance (*tert*-butyl and *n*-butyl groups), and the protonated bases can be regenerated to the probase by aerial oxidation or anodically[427]. With the above probases, for example, diglycolic acid N-methylimide has been carboxylated in 85—88% yield to *O*-carboxymethyltartronic acid, a potential detergent[428].

## 5. Final Remarks

Distinct *advantages* can be seen if electrochemical methods of forming CC bonds are compared with the chemical methods. The reactivity of a building block for synthesis can be changed without altering its functionality only by the transfer of electrons, which decreases the number of reaction steps. Polyfunctional compounds can be transformed potential-selectively. Scaling-up the reaction is usually no problem. On the other hand, there are *disadvantages* that must be taken into account and for which long-term solutions must be found. In electrolysis, the substrate frequently reacts with the product formed by its *umpolung*, which makes selective couplings to unsymmetric compounds difficult. The required conductivity demands polar solvents whose proton activity, electrophilicity, and nucleophilicity can lead to difficulties in the case of reactive anionic or cationic intermediates. Transformations at low temperatures, which, particularly with organometallic reactions can lead to remarkable selectivity, are usually possible in preparative electrolyses only at temperatures down to −50 °C. Short reaction times and therefore reduced non-electrochemical competing reactions are in principle possible in new types of cells; likewise, passivation can be effectively suppressed. Here too, however, the practical solution may raise problems in individual cases.

*The author's own work described here was made possible by the assistance of committed co-workers and the effective support of the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Arbeitsgemeinschaft Industrieller Forschungsvereinigungen, to all of whom thanks are gratefully extended.*

Received: July 29, 1981 [A 388 IE]
German version: Angew. Chem. *93*, 978 (1981)

---

[1] For chemical umpolung: *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979); for electrochemical umpolung: *H. Schäfer:* 25 Jahre Fonds der chemischen Industrie 1950–1975, Verband der chemischen Industrie, Frankfurt 1975, p. 73; Habilitationsarbeit, Göttingen 1970.
[2] *M. M. Baizer*, J. Electrochem. Soc. *111*, 215 (1964).
[3] *F. Beck*, Angew. Chem. *84*, 798 (1972); Angew. Chem. Int. Ed. Engl. *11*, 760 (1972).
[4] *R. Engels, H. J. Schäfer, E. Steckhan*, Justus Liebigs Ann. Chem. *1977*, 204.
[5] *A. J. Fry, M. Mitnick, R. A. Reed*, J. Org. Chem. *35*, 1232 (1970).
[6] *H. Schäfer, A. Al Azrak*, Chem. Ber. *105*, 2398 (1972).
[7] *C. J. Brockmann:* Electro-organic Chemistry, Wiley, New York 1926.
[8] *F. Fichter*, Organische Elektrochemie in *K. F. Bonhoeffer:* Die Chemische Reaktion, Vol. 4, Theodor Steinkopff, Leipzig 1942.
[9] *S. Swann, Jr.* in *A. Weissberger:* Technique of Organic Chemistry, Vol. 2, 2nd ed., Wiley-Interscience, New York 1956, p. 385.
[10] *M. J. Allen:* Organic Electrode Processes, Reinhold, New York 1958.
[11] *C. K. Mann, K. K. Barnes:* Electrochemical Reactions in Nonaqueous Systems, Dekker, New York 1970.
[12] *L. Eberson, H. Schäfer*, Fortschr. Chem. Forsch. (Top. Curr. Chem.) *21*, 1 (1971).
[13] *E. Yeager, A. J. Salkind:* Techniques in Electrochemistry, Wiley, New York 1972.
[14] *A. P. Tomilov, S. G. Mairanovskii, M. Y. Fioshin, V. A. Sirnov:* The Electrochemistry of Organic Compounds, Halsted Press, New York 1972.
[15] *A. J. Fry:* Synthetic Organic Electrochemistry, Harper and Row, New York 1972.
[16] *M. M. Baizer:* Organic Electrochemistry, Dekker, New York 1973.
[17] *F. Beck:* Elektroorganische Chemie, Verlag Chemie, Weinheim 1974.
[18] *N. L. Weinberg:* Technique of Electroorganic Synthesis, Part I, II in Techniques of Chemistry, Vol. 5, Wiley-Interscience, New York 1974.
[19] *M. Rifi, F. H. Covitz:* Introduction to Organic Electrochemistry, Dekker, New York 1974.
[20] *S. D. Ross, M. Finkelstein, E. J. Rudd:* Anodic Oxidation, Academic Press, New York 1975.
[21] *S. Wawzonek*, Science *155*, 39 (1967).
[22] *M. M. Baizer*, Naturwissenschaften *56*, 405 (1969).
[23] *P. E. Iversen*, Chem. Unserer Zeit *5*, 178 (1971).
[24] *F. Beck*, Chem. Ing. Tech. *42*, 153 (1970).
[25] *L. Eberson, N. L. Weinberg*, Chem. Eng. News *49*, Jan. 25, 1971, p. 40 (1971).
[26] *F. Beck*, Metalloberfläche Angew. Elektrochem. *26*, 214 (1972).
[27] *J. H. P. Utley*, Chem. Ind. (London) *1972*, 230.
[28] *G. Popp*, Eastman Org. Chem. Bull. *45*, (3), 1 (1973).
[29] *K. A. Korinek*, Chem. Ind. (London) *1976*, 931.
[30] *F. Müller* in Houben-Weyl: Methoden der Organischen Chemie, Vol. 4, Part 2, Thieme, Stuttgart 1955.
[31] *N. L. Weinberg, H. R. Weinberg*, Chem. Rev. *68*, 449 (1968).
[32] *S. Wawzonek*, Synthesis *1971*, 285.
[33] *J. Chang, R. F. Large, G. Popp* in *A. Weissberger, B. Rossiter:* Physical Methods of Chemistry, Vol. I, Part IIB, Wiley, New York 1971.
[34] a) *L. Eberson, K. Nyberg*, Tetrahedron *32*, 2185 (1976); b) *L. Eberson* in *R. Scheffold:* Modern Synthetic Methods 1980, Salle und Sauerländer, Frankfurt/M. 1980; c) *M. Y. Fioshin*, Sov. Electrochem. *13*, 1 (1977).

[35] Electrochemistry, A Specialist Periodical Report, The Chemical Society, London.

[36] a) Annu. Rep. Prog. Chem., Sect. *B*, The Chemical Society, London; b) *S. Swann, Jr., R. Alkire:* Bibliography of Electroorganic Syntheses 1801-1975, The Electrochemical Society, Princeton 1980.

[37] *L. Eberson* in *S. Patai:* The Chemistry of Carboxylic Acids and Esters, Wiley-Interscience, New York 1969, Chap. 2.

[38] *H. Lund* in *S. Patai:* The Chemistry of the Carbon-Nitrogen Double Bond, Wiley-Interscience, New York 1970, Chap. 11.

[39] *H. Lund*, Adv. Heterocycl. Chem. *12*, 213 (1970).

[40] *H. Lund* in *S. Patai:* The Chemistry of the Hydroxyl Group, Vol. 1, Wiley, London 1971, Chap. 5.

[41] *J. H. P. Utley, R. Lines* in *S. Patai:* The Chemistry of the Carbon-Carbon-Triple Bond, Vol. 2, Wiley-Interscience, New York 1978, Chap. 17.

[42] *A. J. Fry* in *S. Patai:* The Chemistry of the Diazo- and Diazonium group, Vol. 1, Wiley-Interscience, New York 1978, Chap. 10.

[43] *J. Casanova, L. Eberson* in *S. Patai:* The Chemistry of the Carbon-Halogen Bond, Vol. 2, Wiley, New York 1973, Chap. 15.

[44] *J. Q. Chambers* in *S. Patai:* The Chemistry of Quinonoid Compounds, Part 2, Wiley, New York 1974, Chap. 14.

[45] *F. G. Thomas, K. G. Boto* in *S. Patai:* The Chemistry of the Hydrazo, Azo and Azoxy Groups, Vol. 1, Wiley, New York 1975, Chap. 12.

[46] *H. Lund* in *S. Patai:* The Chemistry of Amidines and Imidates, Wiley, New York 1975, Chap. 5.

[47] *A. J. Fry, R. G. Reed* in *S. Patai:* The Chemistry of Double-Bonded Functional Groups, Vol. 1, Wiley, New York 1977, Chap. 5.

[48] *O. Hammerich, V. D. Parker* in *S. Patai:* The Chemistry of Cyanates and Their Thioderivatives, Vol. 1, Wiley, New York 1977, Chap. 9.

[49] *A. J. Bard, H. Lund:* Encyclopedia of Electrochemistry of the Elements, Vol. 11-13, Dekker, New York 1978, 1979.

[50] *L. Underwood, R. W. Burnett*, Electroanal. Chem. *6*, 1 (1973).

[51] *J. M. Bobbitt*, Heterocycles *1*, 181 (1973).

[52] *H. J. Schäfer*, Chem. Weekbl. *1977*, 536.

[53] a) *G. E. Svadkovskaya, S. A. Voitkevich*, Russ. Chem. Rev. *29*, 161 (1960); b) *B. C. L. Weedon*, Adv. Org. Chem. *1*, 1 (1963).

[54] *A. P. Tomilov*, Russ. Chem. Rev. *30*, 639 (1961).

[55] *K. Sasaki, W. J. Newby*, J. Electroanal. Chem. *20*, 137 (1969).

[56] *F. D. Popp, H. P. Schultz*, Chem. Rev. *62*, 19 (1962).

[57] *M. M. Baizer, J. D. Anderson, J. H. Wagenknecht, M. R. Ort, J. P. Petrovich*, Electrochim. Acta *12*, 1377 (1967).

[58] *O. R. Brown, J. A. Harrison*, J. Electroanal. Chem. *21*, 387 (1969).

[59] *J. D. Anderson, J. P. Petrovich, M. M. Baizer*, Adv. Org. Chem. *6*, 257 (1969).

[60] *G. J. Hoytink:* Adv. Electrochem. Electrochem. Eng. *7*, 221 (1970).

[61] *M. M. Baizer, J. P. Petrovich*, Prog. Phys. Org. Chem. *7*, 189 (1970).

[62] *F. Beck*, Angew. Chem. *84*, 798 (1972); Angew. Chem. Int. Ed. Engl. *11*, 760 (1972).

[63] *Ph. J. Elving*, Can. J. Chem. *55*, 3392 (1977).

[64] *A. P. Tomilov, M. Y. Fioshin*, Russ. Chem. Rev. *32*, 30 (1962).

[65] *R. N. Adams*, Acc. Chem. Res. *2*, 175 (1969).

[66] *L. L. Miller*, J. Chem. Educ. *48*, 168 (1971).

[67] *N. L. Holy, J. D. Marcum*, Angew. Chem. *83*, 132 (1971); Angew. Chem. Int. Ed. Engl. *10*, 115 (1971).

[68] *M. Fleischmann, D. Pletcher*, Adv. Phys. Org. Chem. *10*, 155 (1973).

[69] *L. Eberson, K. Nyberg*, Adv. Phys. Org. Chem. *12*, 2 (1975).

[70] *A. J. Bard, A. Ledwith, H. J. Shine*, Adv. Phys. Org. Chem. *13*, 156 (1976).

[71] *D. T. Sawyer, J. L. Roberts, Jr.:* Experimental Electrochemistry for Chemists, Wiley, New York 1974.

[72] See [18], Part I, p. 21.

[73] See [17], p. 94.

[74] See [18], Part I, p. 14.

[75] See [17], p. 97.

[76] *O. Vohler, P. L. Reiser, R. Martina, D. Overhoff*, Angew. Chem. *82*, 401 (1970); Angew. Chem. Int. Ed. Engl. *9*, 414 (1970); *L. Dunsch*, Z. Chem. *14*, 463 (1974).

[77] *R. N. Adams*, Anal. Chem. *30*, 1576 (1958).

[78] *R. Huß, D. W. Wabner*, Metalloberfläche Angew. Elektrochem. *28*, 305 (1974).

[79] *D. W. Wabner, H. P. Fritz, D. Missol, R. Huß, F. Hindelang*, Z. Naturforsch. *B31*, 39 (1976).

[80] *J. P. Carr, N. A. Hampson*, Chem. Rev. *72*, 679 (1972).

[81] *D. Bergner, H. Hund, H. Schaefer*, Chem. Ing. Tech. *47*, 136 (1975).

[82] *O. De Nora*, Chem. Ing. Tech. *42*, 222 (1970).

[83] *K. R. Koziol, K. H. Sieberer, H. C. Rathjen, J. B. Zenk, E. F. Wenk*, Chem. Ing. Tech. *49*, 288 (1977).

[84] *L. D. Burke, O. J. Murphy*, J. Electroanal. Chem. *101*, 351 (1979).

[85] *R. W. Murray*, Acc. Chem. Res. *13*, 135 (1980).

[86] a) *D. C. S. Tse, Th. Kuwana, G. P. Roger*, J. Electroanal. Chem. 98, 345 (1979); b) *N. Oyama, K. B. Jap, F. Anson, ibid.* 100, 233 (1979).

[87] *Y. Umezawa, T. Yamamura*, J. Electroanal. Chem. *95*, 113 (1979).

[88] *A. Merz, A. J. Bard*, J. Am. Chem. Soc. *100*, 3222 (1978); *A. F. Diaz, W. Y. Lee, A. Logan, D. C. Green*, J. Electroanal. Chem. *108*, 377 (1980); *N. Oyama, F. C. Anson*, J. Am. Chem. Soc. *101*, 740 (1979).

[89] *K. Itaya, A. J. Bard*, Anal. Chem. *50*, 1487 (1978); *M. S. Wrighton, R. G. Austin, A. B. Bocarsly, J. M. Bolts, O. Haas, K. D. Legg, L. Nadjo, M. C. Palazotto*, J. Electroanal. Chem. *87*, 429 (1978).

[90] *D. F. Smith, K. Willman, K. Kuo, R. W. Murray*, J. Electroanal. Chem. *95*, 217 (1979).

[91] *B. F. Watkins, J. R. Behling, E. Kariv, L. L. Miller*, J. Am. Chem. Soc. *97*, 3549 (1975).

[92] *B. E. Firth, L. L. Miller, M. Mitani, T. Rogers, J. Lennox, R. W. Murray*, J. Am. Chem. Soc. *98*, 8271 (1976).

[93] *B. E. Firth, L. L. Miller*, J. Am. Chem. Soc. *98*, 8272 (1976).

[94] *L. Horner, W. Brich*, Justus Liebigs Ann. Chem. *1977*, 1354.

[95] *N. Oyama, A. P. Brown, F. C. Anson*, J. Electroanal. Chem. *87*, 435 (1978).

[96] *T. Matsue, M. Fujihira, T. Osa*, J. Electrochem. Soc. *126*, 500 (1979); Bull. Chem. Soc. Jpn. *52*, 3692 (1979).

[97] *R. Breslow, P. Campbell*, J. Am. Chem. Soc. *91*, 3085 (1969); *R. Breslow, H. Kohn, B. Siegel*, Tetrahedron Lett. *1976*, 1645.

[98] See [17], p. 104.

[99] See [18], Part I, p. 25.

[100] See [71], p. 167.

[101] *Ch. K. Mann*, Electroanal. Chem. *3*, 57 (1969).

[102] *H. O. House, E. Feng, N. P. Peet*, J. Org. Chem. *36*, 2371 (1971).

[103] For a detailed summary see [69], p. 42.

[104] *S. Andreades, W. E. Zahnow*, J. Am. Chem. Soc. *91*, 4181 (1969).

[105] *D. Coutagne*, Bull. Soc. Chim. Fr. *1971*, 1940.

[106] *J. Perichon, R. Buvet*, Bull. Soc. Chim. Fr. *1968*, 1279.

[107] *G. Cauquis, D. Serve*, Bull. Soc. Chim. Fr. *1966*, 302.

[108] *O. Hammerich, V. D. Parker*, Electrochim. Acta *18*, 537 (1973).

[109] *A. Ronlan, K. Beechgard, V. D. Parker*, Acta Chem. Scand. *27*, 2375 (1973).

[110] *J. Robinson, R. A. Osteryoung*, J. Am. Chem. Soc. *101*, 323 (1979); *D. Bauer, J. Beck*, Collect. Czech. Chem. Commun. *36*, 323, 940 (1971).

[111] *J. Verastegui, G. Durand, B. Trémillon*, J. Electroanal. Chem. *54*, 269 (1974).

[112] *J. J. Cabon, M. LHer, M. LeDémezet*, Bull. Soc. Chim. Fr. *1975*, 1020.

[113] *J. F. Cotzee*, Pure Appl. Chem. *49*, 219 (1977).

[114] *L. A. Tinker, A. J. Bard*, J. Am. Chem. Soc. *101*, 2316 (1979); *P. C. Lacaze, J. E. Dubois, M. Delamar*, J. Electroanal. Chem. *102*, 135 (1979).

[115] *R. Lines, V. D. Parker*, Acta Chem. Scand. *B31*, 369 (1977).

[116] *I. Vartires, W. H. Smith, A. J. Bard*, J. Electrochem. Soc. *1975*, 894; *W. H. Smith, A. J. Bard*, J. Am. Chem. Soc. *97*, 5203, 6491 (1975); *W. H. Smith, A. J. Bard*, J. Electroanal. Chem. *76*, 19 (1977); *E. M. Abbot, A. J. Bellamy*, J. Chem. Soc. Perkin Trans. II *1978*, 254.

[117] *O. Sock, P. Lemoine, M. Gross*, Electrochim. Acta *25*, 1025 (1980).

[118] *R. Lines, B. S. Jensen, V. D. Parker*, Acta Chem. Scand. *B 32*, 510 (1978), *H. J. Hunze*, Universität Freiburg, personal communication; *H. Kiesele*, IX Scandinavian Meeting.

[119] *R. N. Gourley, J. Grimshaw, P. G. Millar*, J. Chem. Soc. *C1970*, 2318.

[120] *M. Jubault, E. Raoult, D. Peltier*, Electrochim. Acta *19*, 865 (1974).

[121] *J. Kopilov, E. Kariv, L. L. Miller*, J. Am. Chem. Soc. *99*, 3450 (1977).

[122] *J. Hermolin, J. Kopilov, E. Gileadi*, J. Electroanal. Chem. *71*, 245 (1976).

[123] *L. Horner, D. Degner*, Electrochim. Acta *19*, 611 (1974); *L. Horner, W. Brich*, Chem. Ber. *111*, 574 (1978); Justus Liebigs Ann. Chem. *1978*, 710.

[124] *L. Horner, D. Skaletz*, Justus Liebigs Ann. Chem. *1977*, 1365.

[125] *W. J. M. van Tilborg, C. J. Smit*, Recl. Trav. Chim. Pays-Bas *97*, 89 (1978).

[126] *D. Seebach, H. A. Oei, H. Daum*, Chem. Ber. *110*, 2316 (1977).

[127] Some manufacturers and suppliers of potentiostats: AMEL, Via Bolzano, 30, I-20127 Milano (Italy); G. Bank Elektronik (Wenking), Werner-v.-Siemens-Strasse 3, D-3400 Göttingen; Ergotron AG, Enzianstraße 483, CH-5212 Hausen b. Brugg (Switzerland); Heinzinger, Regel- und Meßtechnik, Happinger Strasse 71, D-8200 Rosenheim; A. Jaissle, Elektronik-Labor, Spitalhaldenweg 4, D-7051 Neustadt; EG & G Instruments GmbH, Hohenlindener Strasse 12, D-8000 München 80; Tacussel Electronique Solea, 72 rue d'Alsace, F-69100 Villeurbanne (France).

[128] See [17], p. 103.

[129] See [71], p. 34.

[130] See [16], p. 202.

[131] See [17], p. 110.

[132] See [16], p. 195.

[133] See [18], Part I, p. 38.

[134] *C. Jackson, B. A. Cooke, B. J. Woodhall* in *A. T. Kuhn:* Industrial Electrochemical Processes, Elsevier, Amsterdam 1971, Chap. 15.

[135] See [16], p. 169.

[136] See [17], p. 116.

[137] See [18], Part I, p. 58.

[138] See [71], p. 117.

[139] *M. Fleischmann, R. E. W. Jansson,* Chem. Weekbl. *1977,* 539.

[140] *C. D. Schmulbach, T. V. Oommen,* Anal. Chem. *45,* 820 (1973).

[141] a) *R. E. W. Jansson, R. J. Marshall, J. E. Rizzo,* J. Appl. Electrochem. *8,* 281, 287 (1978); *R. E. W. Jansson,* Electrochim. Acta *23,* 1345 (1978); *A. B. Ferreira, R. E. W. Jansson,* Trans Inst. Chem. Eng. *57,* 262 (1979); *R. E. W. Jansson, N. R. Tomov,* Electrochim. Acta *25,* 497 (1980); b) *J. Haufe, F. Beck,* Chem. Ing. Tech. *42,* 170 (1970); c) *W. Eisenbach, ibid. 46,* 965 (1974); *M. Farvoque, T. Z. Fahidy,* Electrochim. Acta *24,* 547 (1979).

[142] *F. Goodridge, C. J. H. King, A. R. Wright,* Electrochim. Acta *22,* 347, 1087 (1977).

[143] *R. P. Van Duyne, C. N. Reilley,* Anal. Chem. *44,* 142, 153, 158 (1972).

[144] *I. B. Goldberg, A. J. Bard,* J. Phys. Chem. *75,* 3281 (1971); *R. I. Deming, A. L. Allred, A. R. Dahl, A. W. Herlinger, M. O. Kestner,* J. Am. Chem. Soc. *98,* 4132 (1976).

[145] *N. Winograd, Th. Kuwana,* Electroanal. Chem. *7,* 1 (1974).

[146] *F. Beck,* Pure Appl. Chem. Spec. Suppl. XXIV IUPAC Congr. *5,* 111 (1974).

[147] *H. G. Thomas,* Chem. Ber. *108,* 967 (1975).

[148] *L. Eberson, K. Nyberg, H. Sternerup,* Chem. Scr. *1973,* 12; *L. Cedheim, L. Eberson, B. Helgée, K. Nyberg, R. Servin, H. Sternerup,* Acta Chem. Scand. *B 29,* 617 (1975).

[149] *L. Eberson, J. Hlavaty, L. Jönsson, K. Nyberg, R. Servin, H. Sternerup, L. G. Wistrand,* Acta Chem. Scand. *B 33,* 113 (1979).

[150] *P. M. Robertson, F. Schwager, N. Ibl,* J. Electroanal. Chem. *65,* 883 (1975); *P. M. Robertson, Ph. Cettou, D. Matic, F. Schwager, A. Storck, N. Ibl,* AICh Symp. Ser. No. 185, Vol. *75,* 115 (1979).

[151] a) *L. Horner, H. Hönl,* Justus Liebigs Ann. Chem. *1977,* 2058; b) *L. Horner, J. Röder, ibid. 1977,* 2067; c) *L. Horner, W. Brich, ibid. 1977,* 1354.

[152] *G. Cauquis, B. Haemmerlé,* Bull. Soc. Chim. Fr. *1970,* 2000.

[153] a) *W. H. Smith, A. J. Bard,* J. Am. Chem. Soc. *97,* 5203 (1975); b) *O. Manoušek, J. Volke, J. Hlavaty,* Electrochim. Acta *25,* 515 (1980). – Commerzially: Ergotron AG, Enzianstrasse 483, CH-5212 Hausen b. Brugg (Switzerland); Swedish National Development Co., Dept. of Energy and Environmental Technology, Box 34, S-18400 Åkersberga (Sweden).

[154] See [49], Vol. 11, p. 6.

[155] See [49], Vol. 11, p. 18.

[156] See [49], Vol. 11, p. 105.

[157] See [49], Vol. 14, Chap. 1.

[158] See [49], Vol. 11, Chap. 2.

[159] *H. Baltes, E. Steckhan, H. J. Schäfer,* Chem. Ber. *111,* 1294 (1978).

[160] *M. Klehr,* Dissertation, Universität Münster 1976.

[161] *L. L. Miller, G. D. Nordblom, E. A. Mayeda,* J. Org. Chem. *37,* 916 (1972).

[162] *A. Weissberger, B. Rossiter:* Physical Methods of Chemistry, Electrochemical Methods, IIa, b, Wiley, New York 1971.

[163] *R. N. Adams:* Electrochemistry at Solid Electrodes, Dekker, New York 1969.

[164] See [16], Chap. 1, 2.

[165] See [18], Part I, Chap. 3.

[166] See [15], Chap. 3.

[167] See [17], Chap. 2.

[168] See [71], Chap. 6-8.

[169] *H. H. Bauer:* Electrodics, Thieme, Stuttgart 1972.

[170] *L. Meites:* Polarographic Techniques, Wiley-Interscience, New York 1965.

[171] *K. J. Vetter:* Elektrochemische Kinetik, Springer, Berlin 1961.

[172] *D. B. MacDonald:* Transient Techniques in Electrochemistry, Plenum Press, New York 1977.

[173] *Ch. L. Perrin,* Prog. Phys. Org. Chem. *3,* 165 (1965).

[174] *J. Heitbaum, W. Vielstich,* Angew. Chem. *86,* 756 (1974); Angew. Chem. Int. Ed. Engl. *13,* 683 (1974).

[175] *D. Pletcher,* Chem. Soc. Rev. *4,* 471 (1975).

[176] *D. H. Evans,* Acc. Chem. Res. *10,* 313 (1977).

[177] *A. J. Bard, K. S. V. Santhanam,* Electroanal. Chem. *4,* 215 (1970); *V. D. Parker,* Acta Chem. Scand. *24,* 2768 (1970).

[178] *P. Zuman:* The Elucidation of Organic Electrode Processes, Academic Press, New York 1969.

[179] See [163], p. 124; *J. E. B. Randles,* Trans. Faraday Soc. *44,* 327 (1948); *A. Sevčik,* Collect. Czech. Chem. Commun. *13,* 349 (1948).

[180] See [163], p. 80; *B. Levich,* Acta Physicochim. URSS *17,* 257 (1942).

[181] See [17], p. 77.

[182] *E. R. Brown, R. F. Large* in [162], IIa, p. 465; *B. Speiser,* Chem. Unserer Zeit *15,* 62 (1981).

[183] See [163], p. 152.

[184] See [182a], p. 435.

[185] a) *R. S. Nicholson, I. Shain,* Anal. Chem. *36,* 706 (1964); b) *E. Ahlberg, B. Svensmark, V. D. Parker,* Acta Chem. Scand. *B 34,* 53, 85, 97 (1980); c) *J. M. Saveant, L. Nadjo,* J. Electroanal. Chem. *48,* 113 (1973); *V. D. Parker,* Acta Chem. Scand. *B 34,* 359 (1980).

[186] *S. F. Nelsen, L. Echegoyen, E. L. Clennan, D. H. Evans, D. A. Corrigan,* J. Am. Chem. Soc. *99,* 1130 (1977); *S. F. Nelsen, E. L. Clennan, D. H. Evans, ibid. 100,* 4012 (1978); *A. J. Klein, D. H. Evans, ibid. 101,* 757 (1979).

[187] See [163], p. 80; see [162], p. 566; *G. Ritzler, M. Gross,* J. Electroanal. Chem. *94,* 209 (1978).

[188] *W. J. Albery, M. L. Hitchman:* Ring-disc Electrodes, Clarendon Press, Oxford 1971.

[189] *S. Feldberg,* Electroanal. Chem. *3,* 199 (1969); *L. Müller,* Z. Chem. *12,* 209 (1972).

[190] *K. B. Prater, A. J. Bard,* J. Electrochem. Soc. *117,* 207, 335 (1970).

[191] *N. Winograd, T. Kuwana,* Electroanal. Chem. *7,* 1 (1974); *T. Kuwana,* Ber. Bunsenges. Phys. Chem. *77,* 858 (1973); *T. P. De Angelis, W. R. Heinemann,* J. Chem. Educ. *53,* 594 (1976); *W. R. Heinemann,* Anal. Chem. *50,* 390 A (1978); *H. Debrodt, K. E. Heusler,* Ber. Bunsenges. Phys. Chem. *81,* 1172 (1977); *83,* 1019 (1979); *E. Steckhan,* J. Am. Chem. Soc. *100,* 3526 (1978); *A. Bewick, D. J. Brown,* Electrochim. Acta *21,* 979 (1976).

[192] *I. B. Goldberg, A. J. Bard,* J. Phys. Chem. *75,* 3281 (1971); *78,* 290, 295 (1974); *R. D. Allendoerfer, G. A. Martincheck, S. Bruckenstein,* Anal. Chem. *47,* 890 (1975); *H. P. Fritz, R. O. Artes,* Electrochim. Acta *26,* 417 (1981). – For use of spin cases: *G. L. McIntire, H. N. Blount, H. J. Stronks, R. V. Shetty, E. G. Janzen,* J. Phys. Chem. *84,* 916 (1980); *A. J. Bard, J. C. Gilbert, R. D. Goodin,* J. Am. Chem. Soc. *96,* 621 (1974); *B. Kräutler, C. D. Jäger, A. J. Bard, ibid. 100,* 4903 (1978).

[193] *D. Laser, M. Ariel,* J. Electroanal. Chem. *41,* 381 (1973).

[194] *D. L. Jeanmaire, M. R. Suchanski, R. P. Van Duyne,* J. Am. Chem. Soc. *97,* 1699 (1975); *D. L. Jeanmaire, R. P. Van Duyne,* J. Electroanal. Chem. *66,* 235 (1975).

[195] *J. A. Richards, D. H. Evans,* Anal. Chem. *47,* 964 (1975).

[196] *M. Petek, S. Bruckenstein,* J. Electroanal. Chem. *47,* 329 (1973); *M. Petek, S. Bruckenstein, B. Feinberg, R. N. Adams, ibid. 42,* 397 (1973).

[197] *J. Lilie, G. Beck, A. Henglein,* Ber. Bunsenges. Phys. Chem. *75,* 458 (1971); *K. M. Bansal, A. Henglein, R. M. Sellers, ibid. 78,* 569 (1974).

[198] a) *B. B. Damaskin, A. N. Frumkin* in *N. S. Hush:* Reactions of Molecules at Electrodes, Wiley-Interscience, London 1971; see [171], p. 76; b) see [169], p. 72.

[199] *G. Horanyi, G. Vertes,* J. Electroanal. Chem. *51,* 417 (1974); *G. Horanyi,* Electrochim. Acta *25,* 43 (1980).

[200] a) *J. E. Dubois, A. Desbene-Monvernay, P. C. Lacaze,* J. Electroanal. Chem. *72,* 353 (1976); b) *D. M. Drazic, N. R. Tomov,* Electrochim. Acta *19,* 307 (1974); *J. O'M. Bockris, A. Damjanovic, W. E. O'Grady,* J. Colloid Interface Sci. *34,* 387 (1970); *M. Fujihira, T. Kuwana,* Electrochim. Acta *20,* 565 (1975); *N. Winograd,* Acc. Chem. Res. *13,* 406 (1980).

[201] *K. Nyberg,* Acta Chem. Scand. *24,* 1609 (1970); *25,* 2499 (1971).

[202] *R. N. Adams,* Acc. Chem. Res. *2,* 175 (1969).

[203] *K. Nyberg,* Acta Chem. Scand. *27,* 503 (1973).

[204] *K. Nyberg, A. Trojánek,* Collect. Czech. Chem. Commun. *40,* 526 (1975).

[205] *T. Sato, M. Kamada,* J. Chem. Soc. Perkin Trans. II *1977,* 384.

[206] See [49], Vol. 11, p. 242.

[207] *J. M. Bobbitt, H. Jagy, S. Shibuya, J. T. Stock,* J. Org. Chem. *36,* 3006 (1971); *J. M. Bobbitt, K. H. Weisgraber, A. S. Steinfeld, S. G. Weiss,* ibid. *35,* 2884 (1970); *J. M. Bobbitt, R. C. Halcher,* Chem. Commun. *1971,* 543.

[208] *L. L. Miller, R. F. Stewart, J. P. Gillespie, V. Ramachandran, J. H. So, F. R. Stermitz,* J. Org. Chem. *43,* 1580 (1978).

[209] *J. A. Richards, P. E. Whitson, D. H. Evans,* J. Electroanal. Chem. *63,* 311 (1975).

[210] *J. M. Bobbitt,* Heterocycles *2,* 181 (1974).

[211] *J. M. Bobbitt, I. Noguchi, H. Jagy, K. H. Weisgraber,* J. Org. Chem. *41,* 845 (1976).

[212] *A. Ronlan,* Chem. Commun. *1971,* 1643.

[213] *U. Palmquist, A. Ronlan, V. D. Parker,* Acta Chem. Scand. *B 28,* 267 (1974).

[214] *B. Speiser, A. Rieker,* J. Chem. Res. *S 1977,* 314.

[215] *A. Rieker,* DFG-(Dtsch. Forschungsgem.-)Report „Angewandte Elektrochemie“ 1979, p. 154.

[216] *V. D. Parker* in [49], Vol. 11, p. 276.

[217] *A. Ronlan, K. Beechgard, V. D. Parker,* Acta Chem. Scand. *27,* 2375 (1973).

[218] *A. Ronlan, V. D. Parker,* Chem. Commun. *1970,* 1567.

[219] *A. Ronlan, O. Hammerich, V. D. Parker,* J. Am. Chem. Soc. *95,* 7132 (1973).

[220] *A. Ronlan, V. D. Parker,* J. Org. Chem. *39,* 1014 (1974).

[221] *V. D. Parker, A. Ronlan,* J. Am. Chem. Soc. *97,* 4714 (1975).

[222] *J. Y. Becker, L. L. Miller, V. Boekelheide, T. Morgan,* Tetrahedron Lett. *1976,* 2939.

[223] *J. R. Falck, L. L. Miller, F. R. Stermitz,* J. Am. Chem. Soc. *96,* 2981 (1974).

[224] *L. L. Miller, R. T. Stewart, J. P. Gillespie, V. Ramachandran,* J. Org. Chem. *43,* 1580 (1978).

[225] *E. Kotani, F. Miyazaki, S. Tobinaga*, J. Chem. Soc. Chem. Commun. *1974*, 300.
[226] *E. Kotani, N. Takeuchi, S. Tobinaga*, J. Chem. Soc. Chem. Commun. *1973*, 550.
[227] *E. Kotani, M. Kitazawa, S. Tobinaga*, Tetrahedron *30*, 3027 (1974).
[228] *M. Sainsbury, J. Wyatt*, J. Chem. Soc. Perkin Trans. I *1976*, 661.
[229] *M. Sainsbury, J. Wyatt*, J. Chem. Soc. Perkin Trans. I *1979*, 108.
[230] *M. Sainsbury*, Heterocycles *9*, 1349 (1978).
[231] *L. L. Miller, F. R. Stermitz, J. R. Falck*, J. Am. Chem. Soc. *93*, 5941 (1971); *95*, 2651 (1973).
[232] *J. Y. Becker, L. L. Miller, F. R. Stermitz*, J. Electroanal. Chem. *68*, 181 (1976).
[233] *L. L. Miller, F. R. Stermitz, J. Y. Becker, V. Ramachandran*, J. Am. Chem. Soc. *97*, 2922 (1975); *J. B. Kerr, T. C. Jempty, L. L. Miller, ibid. 101*, 7338 (1979).
[234] *E. Kotani, S. Tobinaga*, Tetrahedron Lett. *1973*, 4759.
[235] *J. R. Falck, L. L. Miller, F. R. Stermitz*, Tetrahedron *30*, 931 (1974).
[236] *H. Klünenberg*, Dissertation, Universität Münster 1981.
[237] *U. Palmquist, A. Nilsson, T. Pettersson, A. Ronlan, V. D. Parker*, J. Org. Chem. *44*, 196 (1979).
[238] *H. Schäfer, E. Steckhan*, Angew. Chem. *81*, 532 (1969); Angew. Chem. Int. Ed. Engl. *8*, 518 (1969); *B. Belleau, Y. K. Au-Young*, Can. J. Chem. *47*, 2117 (1969).
[239] a) *D. Koch, H. Schäfer, E. Steckhan*, Chem. Ber. *107*, 3640 (1974); b) *M. A. Le Moing, G. Le Guillanton, J. Simonet*, Electrochim. Acta *26*, 139 (1981).
[240] *R. Engels*, Dissertation, Universität Münster 1978.
[241] *H. O. House, L. J. Czuba, M. Gall, H. D. Olmsted*, J. Org. Chem. *34*, 2324 (1969); *R. D. Miller, D. R. McKean*, Synthesis *1979*, 730; *G. Olah, B. G. B. Gupta, S. C. Narang, R. Malhotra*, J. Org. Chem. *44*, 4272 (1979).
[242] a) *D. Koch, H. Schäfer*, Angew. Chem. *85*, 264 (1973); Angew. Chem. Int. Ed. Engl. *12*, 245 (1973); b) *H. W. Handiak*, Dissertation, Universität Göttingen 1976; c) *N. Dahrenmöller*, Diplomarbeit, Universität Münster 1976.
[243] *M. Masui, T. Michida, C. Ueda, H. Ohmori*, Chem. Ind. (London) *1978*, 922.
[244] *R. Engels, H. J. Schäfer, E. Steckhan*, Justus Liebigs Ann. Chem. *1977*, 204.
[245] *E. Steckhan*, J. Am. Chem. Soc. *100*, 3526 (1978).
[246] *G. Burgbacher, H. J. Schäfer*, J. Am. Chem. Soc. *101*, 7590 (1979).
[247] a) *E. Steckhan, H. J. Schäfer*, Angew. Chem. *86*, 480 (1974); Angew. Chem. Int. Ed. Engl. *13*, 472 (1974); b) *H. Sternerup*, Acta Chem. Scand, *B 28*, 579 (1974).
[248] a) *A. Ledwith*, Acc. Chem. Res. *5*, 133 (1972); b) *L. Cedheim, L. Eberson*, Acta Chem. Scand. *B 30*, 527 (1976).
[249] *H. Baltes, E. Steckhan, H. J. Schäfer*, Chem. Ber. *111*, 1294 (1978); *M. Y. Fioshin, Z. N. Zhurinov, L. A. Mirkind*, Elektrokhimiya *1969*, 1257.
[250] *M. Katz, O. Saygin, H. Wendt*, Electrochim. Acta *19*, 193 (1974).
[251] *B. Kräutler, A. Pfaltz, R. Nordmann, K. O. Hodgson, J. D. Dunitz, A. Eschenmoser*, Helv. Chim. Acta *59*, 924 (1976).
[252] *H. Nehring, H. J. Schäfer*, unpublished results.
[253] *H. Schäfer, E. Steckhan*, Tetrahedron Lett. *1970*, 3835.
[254] *T. Shono, I. Nishiguchi, S. Kashimura, M. Okawa*, Bull. Chem. Soc. Jpn. *51*, 2181 (1978).
[255] *H. J. Schäfer*, Chem. Phys. Lipids *24*, 321 (1979).
[256] *M. P. J. Brennan, R. Brettle*, J. Chem. Soc. Perkin Trans. I *1973*, 257.
[257] *J. P. Coleman, R. Lines, J. H. P. Utley, B. C. L. Weedon*, J. Chem. Soc. Perkin Trans. II *1974*, 1064.
[258] *L. Eberson*, Acta Chem. Scand. *13*, 40 (1959).
[259] *J. Haufe, F. Beck*, Chem. Ing. Tech. *42*, 170 (1970).
[260] *F. L. M. Pattison, J. B. Stothers, R. G. Woolford*, J. Am. Chem. Soc. *78*, 2255 (1956).
[261] *F. Fichter, S. Lurie*, Helv. Chim. Acta *16*, 885 (1933).
[262] *J. Peterson*, Z. Elektrochem. *18*, 710 (1912).
[263] a) *D. Lelandais, M. Chkir*, Tetrahedron Lett. *1974*, 3113; b) *J. P. Waefler, P. Tissot*, Electrochim. Acta *23*, 899 (1978).
[264] *R. F. Garwood, N. Ud Din, C. J. Scott, B. C. L. Weedon*, J. Chem. Soc. Perkin Trans. I *1973*, 2714.
[265] *J. Knolle*, Dissertation, Universität Münster 1976.
[266] *J. Knolle, H. J. Schäfer*, Electrochim. Acta *23*, 5 (1978).
[267] *W. Seidel, H. J. Schäfer*, unpublished results
[268] *E. J. Corey, R. R. Sauers*, J. Am. Chem. Soc. *81*, 1739 (1959).
[269] *G. Stork, A. Meisels, J. E. Davies*, J. Am. Chem. Soc. *85*, 3419 (1963).
[270] *G. W. Gribble, J. K. Sanstead*, J. Chem. Soc. Chem. Commun. *1973*, 735; *I. I. Krasavtsev*, Ukr. Khim. Zh. *46*, 776 (1980).
[271] *W. Seidel*, Dissertation, Universität Münster 1980.
[272] *W. Seidel, J. Knolle, H. J. Schäfer*, Chem. Ber. *110*, 3544 (1977).
[273] *C. Wittenbrink*, Staatsexamensarbeit, Universität Münster 1977.
[274] *J. Knolle, H. J. Schäfer*, Angew. Chem. *87*, 777 (1975); Angew. Chem. Int. Ed. Engl. *14*, 758 (1975).
[275] *H. Klünenberg, H. J. Schäfer*, Angew. Chem. *90*, 48 (1978); Angew. Chem. Int. Ed. Engl. *17*, 47 (1978).
[276] *W. Seidel, H. J. Schäfer*, Chem. Ber. *113*, 451 (1980).
[277] a) *U. Jensen, H. J. Schäfer*, Chem. Ber. *114*, 292 (1981); b) *R. F. Nutt, R. G. Strachan, D. F. Veber, W. F. Holly*, J. Org. Chem. *45*, 3078 (1980).
[278] *W. S. Greaves, R. P. Linstead, B. R. Shephard, S. L. S. Thomas, B. C. L. Weedon*, J. Chem. Soc. *1950*, 3326.
[279] *R. P. Linstead, J. C. Lunt, B. C. L. Weedon*, J. Chem. Soc. *1950*, 3331.
[280] *D. G. Bounds, R. P. Linstead, B. C. L. Weedon*, J. Chem. Soc. *1954*, 448.
[281] *Y. Suhura, S. Miyazaki*, Bull. Chem. Soc. Jpn. *42*, 3022 (1969).
[282] *M. Takahashi, K. Osawa, J. Ueda, K. Okada*, Yakugaku Zasshi *96*, 1000 (1976).
[283] *R. N. Renaud, Ph. J. Champagne*, Can. J. Chem. *53*, 529 (1975).
[284] *R. N. Renaud, D. E. Sullivan*, Can. J. Chem. *50*, 3084 (1972).
[285] *L. Eberson, K. Nyberg, R. Servin*, Acta Chem. Scand. *B 30*, 906 (1976).
[286] *L. Eberson, G. Ryde-Petterson*, Acta Chem. Scand. *27*, 1159 (1973).
[287] *G. E. Hawkes, J. H. P. Utley, G. B. Yates*, J. Chem. Soc. Chem. Commun. *1973*, 305; J. Chem. Soc. Perkin Trans. II *1976*, 1709; *J. H. P. Utley, G. B. Yates, ibid. 1978*, 395.
[288] *H. J. Schäfer, R. Pistorius*, unpublished results; *R. Pistorius*, Dissertation, Universität Göttingen 1974.
[289] *R. Brettle, J. C. Parkin*, J. Chem. Soc. *C 1967*, 1352; *T. Okubo, S. Tsutsumi*, Bull. Chem. Soc. Jpn. *37*, 1794 (1964); *R. Hertwig, G. Schlegel, H. J. Schäfer*, unpublished results; *M. Laćan, I. Tabaković, M. Vukićević*, Croat. Chem. Acta *45*, 465 (1973).
[290] *H. G. Thomas, E. Lux*, Tetrahedron Lett. *1972*, 965.
[291] *M. M. Baizer, R. C. Hallcher*, J. Electrochem. Soc. *123*, 809 (1976).
[292] *H. J. Schäfer*, Chem. Ing. Tech. *41*, 179 (1969).
[293] *J. L. Morgat, R. Pallaud*, C. R. Acad. Sci. *260*, 574, 5579 (1965).
[294] a) *T. Taguchi, M. Itoh, A. Suzuki*, Chem. Lett. *1973*, 719; b) *T. Taguchi, Y. Takahashi, M. Itoh, A. Suzuki, ibid. 1974*, 1021.
[295] *R. Bauer, H. Wendt*, J. Electroanal. Chem. *80*, 395 (1977).
[296] *H. Wendt, R. Bauer*, Angew. Chem. *90*, 214 (1978); Angew. Chem. Int. Ed. Engl. *17*, 202 (1978); *R. Bauer, H. Wendt, ibid. 90*, 390 (1978) bzw. *17*, 370 (1978).
[297] *H. Schäfer, A. Al Azrak*, Chem. Ber. *105*, 2398 (1972).
[298] *H. Schäfer, E. Steckhan*, unpublished results; *E. Steckhan*, Diplomarbeit, Universität Göttingen 1969.
[299] a) *H. Schäfer*, unpublished results; Habilitationsschrift, Universität Göttingen 1970; b) *H. Schäfer, H. W. Handiak*, unpublished results; *H. W. Handiak*, Diplomarbeit, Universität Göttingen 1971.
[300] *H. Schäfer, H. Küntzel*, Tetrahedron Lett. *1970*, 3333.
[301] *H. Schäfer, D. Koch*, Angew. Chem. *84*, 32 (1972); Angew. Chem. Int. Ed. Engl. *11*, 48 (1972).
[302] *H. Schäfer, R. Pistorius*, Angew. Chem. *84*, 893 (1972); Angew. Chem. Int. Ed. Engl. *11*, 841 (1972).
[303] *H. Schäfer, L. Stork*, unpublished results.
[304] *Y. B. Vasilev, L. S. Kanewskii, K. G. Karapetyan, E. P. Kovsman, A. M. Skundin, G. A. Tarkhanov, G. N. Freidlin*, Elektrokhimiya *14*, 770 (1978).
[305] *M. Y. Fioshin, L. A. Salmin, L. A. Mirkind, A. G. Kornienko*, Zh. Obshch. Khim. *10*, 594 (1965).
[306] *C. J. Brookes, P. L. Coe, A. E. Pedler, J. C. Tatlow*, J. Chem. Soc. Perkin Trans. I *1978*, 202.
[307] *M. Chkir, D. Lelandais*, Chem. Commun. *1971*, 1369; additive monomers: *R. N. Renaud, P. J. Champagne*, Can. J. Chem. *57*, 990 (1979); *58*, 1101 (1980).
[308] *H. Schäfer*, Angew. Chem. *82*, 134 (1970); Angew. Chem. Int. Ed. Engl. *9*, 158 (1970).
[309] *R. Buhmann, H. Schäfer*, unpublished results; *R. Buhmann*, Diplomarbeit, Universität Göttingen 1972.
[310] *H. J. Schäfer, H. Pastors*, unpublished results; *H. Pastors*, Staatsexamensarbeit, Universität Münster 1979.
[311] *M. M. Baizer*, J. Electrochem. Soc. *111*, 215 (1964).
[312] Chem. Eng. *72*, 238 (1965).
[313] *M. M. Baizer, J. D. Anderson*, J. Electrochem. Soc. *111*, 223 (1964).
[314] *M. M. Baizer, J. D. Anderson*, J. Electrochem. Soc. *111*, 226 (1964).
[315] *J. P. Petrovich, M. M. Baizer, M. R. Ort*, J. Electrochem. Soc. *116*, 743, 749 (1969).
[316] *J. Wiemann, M. L. Bouguerra*, Ann. Chim. (Paris) *3*, 215 (1968).
[317] *E. Touboul, F. Weisbuch, J. Wiemann*, Bull. Soc. Chim. Fr. *1967*, 4291; C. R. Acad. Sci. Ser. *C 268*, 1170 (1969); Stereochemistry of hydrodimer: *J. Grimshaw, R. J. Haslett*, J. Chem. Soc. Perkin Trans. I *1979*, 395.
[318] *J. Wiemann, M. L. Bouguerra*, Ann. Chim. (Paris) *2*, 35 (1967).
[319] *H. Matschiner, R. Voigtländer, R. Liesenberg, G. W. Fischer*, Electrochim. Acta *24*, 331 (1978).
[320] *C. L. Wilson, K. B. Wilson*, Trans. Electrochem. Soc. *84*, 153 (1947).
[321] *R. N. Gourley, J. Grimshaw, P. G. Millar*, J. Chem. Soc. *C 1970*, 2318.
[322] *P. H. Zoutendam, P. T. Kissinger*, J. Org. Chem. *44*, 758 (1979).

[323] *J. P. Petrovich, J. D. Anderson, M. M. Baizer,* J. Org. Chem. *31,* 3897 (1966).

[324] *L. S. R. Yeh, A. J. Bard,* J. Electrochem. Soc. *124,* 189 (1977).

[325] *J. Simonet,* C. R. Acad. Sci. Ser. *C267,* 1548 (1968); *J. Wiemann, M. L. Bouguerra,* Ann. Chim. (Paris) *2,* 35 (1967); *J. C. Johnston, J. D. Faulkner, L. Mandell, R. A. Day,* J. Org. Chem. *41,* 2611 (1976).

[326] *L. Mandell, R. F. Daley, R. A. Day,* J. Org. Chem. *41,* 4087 (1976).

[327] *J. Andersson, L. Eberson,* J. Chem. Soc. Chem. Commun. *1976,* 565; *J. Andersson, L. Eberson, C. Svensson,* Acta Chem. Scand. *B32,* 234 (1978).

[328] *J. E. Baldwin,* J. Chem. Soc. Chem. Commun. *1976,* 734.

[329] *B. Terem, J. H. P. Utley,* Electrochim. Acta *24,* 1081 (1979).

[330] *L. Mandell, J. C. Johnston, R. A. Day, Jr.,* J. Org. Chem. *43,* 1616 (1978).

[331] *H. Lund,* Acta Chem. Scand. *B31,* 424 (1977).

[332] *T. Shono, I. Nishiguchi, H. Ohmizu,* J. Am. Chem. Soc. *99,* 7396 (1977).

[333] *H. Lund, C. Degrand,* Acta Chem. Scand. *B33,* 57 (1979).

[334] *T. J. Curphy, L. D. Trivedi, T. Layloff,* J. Org. Chem. *39,* 3831 (1974).

[335] *H. Lund, C. Degrand,* Tetrahedron Lett. *1977,* 3593.

[336] *R. Engels, H. J. Schäfer,* Angew. Chem. *90,* 483 (1978); Angew. Chem. Int. Ed. Engl. *17,* 460 (1978).

[337] *C. Degrand, D. Jacquin,* Tetrahedron Lett. *1978,* 4955.

[338] *H. Lund, J. Simonet,* C. R. Acad. Sci. Ser. *C277,* 1387 (1973).

[339] *D. A. Tyssee, M. M. Baizer,* J. Org. Chem. *39,* 2819 (1974).

[340] *D. A. Tyssee, M. M. Baizer,* J. Org. Chem. *39,* 2823 (1974).

[341] *E. Lamy, L. Nadjo, J. M. Saveant,* Nouv. J. Chim. *3,* 21 (1979).

[342] *S. Gambino, G. Silvestri,* Tetrahedron Lett. *1973,* 3025.

[343] *N. L. Weinberg, A. K. Hoffmann, T. B. Reddy,* Tetrahedron Lett. *1971,* 2274; *S. Kato, Y. Mizutani,* 1. Meeting Electroorg. Chem., 21. Apr. 1980, Kyoto, S. 9; *U. Hess, P. Fuchs, E. Jacob, H. Lund,* Z. Chem. *20,* 64 (1980).

[344] *J. Simonet, M. A. Michel, H. Lund,* Acta Chem. Scand. *B29,* 489 (1975).

[345] *P. E. Hansen, A. Berg, H. Lund,* Acta Chem. Scand. *B30,* 267 (1976).

[346] *T. Shono, M. Mitani,* Nippon Kagaku Kaishi *1972,* 2370.

[347] a) *C. Degrand, H. Lund,* Nouv. J. Chim. *1,* 35 (1977); b) *T. Troll,* DFG-(Dtsch. Forschungsgem.-)Report „Angewandte Elektrochemie“ 1977, p. 228.

[348] *S. Satoh, T. Taguchi, M. Itoh, M. Tokuda,* Bull. Chem. Soc. Jpn. *52,* 951 (1979).

[349] *P. Martigny, J. Simonet,* J. Electroanal. Chem. *101,* 275 (1979); *L. H. Kristensen, H. Lund,* Acta Chem. Scand. *B33,* 735 (1979).

[350] *E. M. Abbot, A. J. Bellamy,* J. Chem. Soc. Perkin Trans. II *1978,* 254.

[351] *H. Lund, C. Degrand,* C. R. Acad. Sci. Ser. *C287,* 535 (1978).

[352] *T. Iwasaki, K. Harada,* J. Chem. Soc. Perkin Trans. I *1977,* 1730.

[353] *C. Degrand, C. Grosgemouge, P. L. Compagnon,* Tetrahedron Lett. *1978,* 3023; *C. Degrand, P. L. Compagnon, G. Belot, D. Jacquin,* J. Org. Chem. *45,* 1189 (1980).

[354] *W. H. Smith, A. J. Bard,* J. Am. Chem. Soc. *97,* 6491 (1975); *C. Degrand, H. Lund,* Acta Chem. Scand. *B31,* 593 (1977); adamantylation: *U. Hess, D. Huhn, H. Lund, ibid. B34,* 413 (1980).

[355] *C. Degrand, D. Jacquin, P. L. Compagnon,* J. Chem. Res. *1978,* 246.

[356] a) *T. Troll, W. Elbe,* Electrochim. Acta *22,* 615 (1977); *T. Troll, M. M. Baizer, ibid. 19,* 951 (1974); *20,* 33 (1975); b) *J. Simonet, H. Lund,* Bull. Soc. Chim. Fr. *1975,* 2547; c) *T. Shono, Y. Usui, T. Mizutani, H. Hamaguchi,* Tetrahedron Lett. *1980,* 1351, 3073; *T. Shono, K. Yoshida, K. Ando, Y. Usui, H. Hamaguchi, ibid. 1978,* 4819; Heterocycles *9,* 114 (1978); d) *R. A. J. Smith, D. J. Hannah,* Tetrahedron Lett. *1980,* 1081.

[357] a) *D. Knittel, B. Kastening,* Ber. Bunsenges. Phys. Chem. *77,* 833 (1973); b) *H. Lund,* 14. Research Conference, Foundation of Res. Conferences in Chemistry, Osaka, Apr. 1980, p. 60; c) *S. Wawzonek, S. M. Heilmann,* J. Org. Chem. *39,* 511 (1974).

[358] *H. Lund, J. Simonet,* J. Electroanal. Chem. *65,* 205 (1975).

[359] *U. Kaiser, E. Heitz,* Ber. Bunsenges. Phys. Chem. *77,* 818 (1973).

[360] *A. Bewick, G. P. Greener,* Tetrahedron Lett. *1969,* 4623; *1970,* 391.

[361] *F. Wolf, J. Rollin,* Z. Chem. *17,* 337 (1977).

[362] *J. C. Gressin, D. Michelet, L. Nadjo, J. M. Saveant,* Nouv. J. Chim. *3,* 545 (1979).

[363] *D. A. Tyssee, J. H. Wagenknecht, M. M. Baizer, J. L. Chruma,* Tetrahedron Lett. *1972,* 4809.

[364] *P. Zuman, D. Barnes, A. Rivolowa-Kijarowa,* Discuss. Faraday Soc. *45,* 87 (1968); *J. H. Stocker, R. M. Jenevein,* J. Org. Chem. *33,* 294, 2145 (1968).

[365] See [18], Part II, p. 95.

[366] See [12], p. 113; see [17], p. 217.

[367] *E. Touboul, G. Dana,* J. Org. Chem. *44,* 1397 (1979); analogical: Wieland-Miescher-Ketone: *L. Mandell, H. Hamilton, R. A. Day, ibid. 45,* 1710 (1980).

[368] *C. P. Andrieux, J. M. Savéant,* Bull. Soc. Chim. Fr. *1973,* 2090.

[369] *C. P. Andrieux, J. M. Savéant,* Bull. Soc. Chim. Fr. *1972,* 3281.

[370] *E. Kariv, E. Gileadi,* Collect. Czech. Chem. Commun. *36,* 476 (1971).

[371] *J. Armand, L. Boulares,* Can. J. Chem. *54,* 1197 (1976).

[372] *T. J. Curphy, C. W. Amelotti, T. P. Layloff, R. L. McCartney, J. H. Williams,* J. Am. Chem. Soc. *91,* 2817 (1969).

[373] *T. Nonaka, M. Asai,* Bull. Chem. Soc. Jpn. *51,* 2976 (1978).

[374] *L. Horner, H. Hönl,* Justus Liebigs Ann. Chem. *1977,* 2036.

[375] *R. E. Sioda, B. Terem, J. H. P. Utley, B. C. L. Weedon,* J. Chem. Soc. Perkin Trans. I *1976,* 561.

[376] a) *J. H. P. Utley, V. L. Pardini, J. H. Riley, D. W. Sopher, A. Webber,* Electrochem. Soc. Meeting, St. Louis, Mai 1980, Ext. Abstr. 422; b) *D. W. Sopher, J. H. P. Utley,* J. Chem. Soc. Chem. Commun. *1979,* 1087.

[377] a) *L. A. Powell, R. M. Wightman,* J. Am. Chem. Soc. *101,* 4412 (1979); J. Electroanal. Chem. *117,* 321 (1981); b) *M. Falsig, H. Lund, L. Nadjo, J. M. Savéant,* Acta Chem. Scand. *B34,* 685 (1980).

[378] a) *T. Nonaka, T. Sekine, K. Odo, K. Sugino,* Electrochim. Acta *22,* 271 (1977); b) *S. M. Makarochkina, P. P. Tomilov,* Zh. Obshch. Khim. *44,* 2566 (1974).

[379] *M. M. Baizer,* Tetrahedron Lett. *1963,* 973; J. Org. Chem. *29,* 1670 (1964).

[380] *O. R. Brown, K. Lister,* Discuss. Faraday Soc. *45,* 106 (1968).

[381] a) *A. Fröling,* Recl. Trav. Chim. Pays-Bas *93,* 47 (1974); b) *A. P. Tomilov, B. L. Klyuev, V. D. Nechepurnoi,* Zh. Org. Khim. *11,* 1984 (1975).

[382] a) *T. Shono, H. Ohmizu, S. Kawakami,* A. C. S. Meeting, Hawaii 1979, Ext. Abstract. 186, Org. Chem.; b) *T. Shono, I. Nishiguchi, H. Ohmizu, M. Mitani,* J. Am. Chem. Soc. *100,* 545 (1978); Chem. Lett. *1976,* 1233; c) *R. Pallaud, M. Nicolaus,* C. R. Acad. Sci. Ser. *C267,* 1834 (1968); *M. J. Allen, J. A. Siragusa, W. Pierson,* J. Chem. Soc. *1960,* 1045.

[383] *L. Horner, D. H. Skaletz,* Justus Liebigs Ann. Chem. *1975,* 1210.

[384] *T. Nonaka, H. Omura, T. Fuchigami, K. Odo,* Denki Kagaku *45,* 111 (1977).

[385] *J. Wellmann, E. Steckhan,* Synthesis *1978,* 901.

[386] *J. L. Hall, R. D. Geer, P. W. Jennings,* J. Org. Chem. *43,* 4364 (1978).

[387] a) *J. Grimshaw, S. A. Hewitt,* Electrochem. Soc. Meeting, St. Louis, Mai 1980, Ext. Abstr. 423; *J. Grimshaw, R. J. Haslett,* J. Chem. Soc. Perkin Trans. I *1980,* 657; b) *R. Gottlieb, J. L. Neumeyer,* J. Am. Chem. Soc. *98,* 7108 (1976).

[388] *I. Carelli, M. E. Cardinali, A. Casini, A. Arnone,* J. Org. Chem. *41,* 3967 (1976).

[389] *F. Pragst, U. Seydewitz,* J. Prakt. Chem. *319,* 952 (1977); *F. Pragst, M. Janda, I. Stibor,* Electrochim. Acta *25,* 779 (1980).

[390] *R. Breslow, R. F. Drury,* J. Am. Chem. Soc. *96,* 4702 (1974).

[391] *P. R. Moses, J. Q. Chambers,* J. Am. Chem. Soc. *96,* 945 (1974).

[392] a) *R. M. Elofson, F. F. Gadallah,* J. Org. Chem. *36,* 1769 (1971); b) *J. H. P. Utley, A. Webber,* J. Chem. Soc. Perkin Trans. I *1980,* 1154.

[393] See [18], Part II, p. 175.

[394] *T. Shono, Y. Matsumura, S. Kashimura, H. Kyutoku,* Tetrahedron Lett. *1978,* 1205.

[395] *J. P. Dirlam, L. Eberson, J. Casanova,* J. Am. Chem. Soc. *94,* 240 (1972).

[396] *A. J. Fry, R. Scoggins,* Tetrahedron Lett. *1972,* 4079; see also: *W. J. M. v. Tilborg, R. Plomp, R. D. Ruiter, C. J. Smit,* Recl. Trav. Chim. Pays-Bas *99,* 206 (1980).

[397] *A. J. Fry, L. L. Chung,* Tetrahedron Lett. *1976,* 645.

[398] a) *M. R. Rifi,* Tetrahedron Lett. *1969,* 1043; b) *A. J. Fry, W. E. Britton,* J. Org. Chem. *38,* 4016 (1973).

[399] *Azizullah, J. Grimshaw,* J. Chem. Soc. Perkin Trans. I *1973,* 425.

[400] *K. B. Wiberg, W. F. Bailey, M. E. Jason,* J. Org. Chem. *41,* 2711 (1976); *W. F. Carroll, D. G. Peters,* J. Am. Chem. Soc. *102,* 4127 (1980).

[401] *K. B. Wiberg, G. A. Epling, M. Jason,* J. Am. Chem. Soc. *96,* 912 (1974).

[402] *J. Casanova, H. R. Rogers,* J. Org. Chem. *39,* 3803 (1974).

[403] *L. Rampazzo, A. Inesi, R. M. Bettolo,* J. Electroanal. Chem. *83,* 341 (1977).

[404] *S. Satoh, M. Itoh, M. Tokuda,* J. Chem. Soc. Chem. Commun. *1978,* 481.

[405] *E. Hengge, G. Litscher,* Angew. Chem. *88,* 414 (1976); Angew. Chem. Int. Ed. Engl. *15,* 370 (1976); *R. J. P. Corriu, G. Dabosi, M. Martineau,* J. Organomet. Chem. *188,* 63 (1980).

[406] *H. P. Fritz, W. Kornrumpf,* Justus Liebigs Ann. Chem. *1978,* 1416.

[407] *H. P. Fritz, W. Kornrumpf,* Electrochem. Soc. Meeting, St. Louis, May 1980, Ext. Abstr. 453.

[408] a) *S. Wawzonek, R. C. Duty,* J. Electrochem. Soc. *108,* 1135 (1961); b) *A. Merz, G. Thumm,* Justus Liebigs Ann. Chem. *1978,* 1526.

[409] *T. Fuchigami, T. Nonaka, K. Iwata,* J. Chem. Soc. Chem. Commun. *1976,* 951.

[410] *T. Fuchigami, T. Nonaka,* Chem. Lett. *1977,* 1087.

[411] *S. Satoh, M. Tokuda,* 1. Meeting Electroorg. Chem., Kyoto, 21. Apr. 1980, Abstr. No. 3.

[412] a) *F. Karrenbrock, H. J. Schäfer,* Tetrahedron Lett. *1978,* 1521; b) *M. Steiniger,* Diplomarbeit, Universität Münster 1980.

[413] *M. Wilken,* Staatsexamensarbeit, Universität Münster 1980.

[414] *F. Karrenbrock, H. J. Schäfer, I. Langer*, Tetrahedron Lett. *1979*, 2915; *J. M. v. Tilborg, C. J. Smit*, Recl. Trav. Chim. Pays-Bas *99*, 202 (1980).

[415] *Y. Matsumara*, 14. Research Conference, Foundation for Res. Conferences in Chemistry, Osaka, April 1980, Abstr. p. 57.

[416] *T. Shono, H. Ohmizu, S. Kawakami*, 41. Meet. Chem. Soc. Japan, Osaka 1980.

[417] *T. Shono, I. Nishiguchi, H. Ohmizu*, Chem. Lett. *1977*, 1021.

[418] a) *M. M. Baizer, J. L. Chruma*, J. Org. Chem. *37*, 1951 (1972); b) *T. Shono, H. Ohmizu, S. Kawakami, S. Nakano, N. Kise*, Tetrahedron Lett. *1981*, 871.

[419] a) *Y. Takahashi, K. Yuasa, M. Tokuda, M. Itoh, A. Suzuki*, Bull. Chem. Soc. Jpn. *51*, 339 (1978); b) *R. Scheffold, M. Dike, S. Dike, T. Herold, L. Walder*, J. Am. Chem. Soc. *102*, 3642 (1980).

[420] *M. Tokuda, Y. Takahashi, M. Itoh, A. Suzuki*, 1. Meeting Electroorg. Chem., Kyoto, 21. Apr. 1980, Abstr. No. 9.

[421] *S. Wawzonek, J. M. Shradel*, J. Electrochem. Soc. *126*, 401 (1979).

[422] *Y. Takahashi, M. Tokuda, M. Itoh, A. Suzuki*, Synthesis *1976*, 617.

[423] *Y. Takahashi, M. Tokuda, M. Itoh, A. Suzuki*, Chem. Lett. *1975*, 523.

[424] a) *Y. Takahashi, M. Tokuda, M. Itoh, A. Suzuki*, Chem. Lett. *1977*, 999; *1980*, 461; Bull. Chem. Soc. Jpn. *51*, 339 (1978); b) *M. Tokuda, T. Taguchi, O. Nishio, M. Itoh*, J. Chem. Soc. Chem. Commun. *1979*, 606; *M. Tokuda, O. Nishio, ibid. 1980*, 188.

[425] *E. M. Abbot, A. J. Bellamy, J. Kerr*, Chem. Ind. (London) *1974*, 828.

[426] *L. Kistenbrügger, P. Mischke, J. Voß, G. Wiegand*, Liebigs Ann. Chem. *1980*, 461.

[427] *R. C. Hallcher, M. M. Baizer*, Justus Liebigs Ann. Chem. *1977*, 737.

[428] *R. C. Hallcher, D. A. White, M. M. Baizer*, J. Electrochem. Soc. *126*, 404 (1979).

# Transition Metal Thiometalates: Properties and Significance in Complex and Bioinorganic Chemistry

**By Achim Müller, Ekkehard Diemann, Rainer Jostes, and Hartmut Bögge**[*]

*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

In their highest oxidation states the early transition metals V, Nb, Ta, Mo, W, and Re form tetrahedral, strongly colored thioanions endowed with some remarkable properties. Thiometalates can be formed by solid-state reactions or in solution from the oxometalates. Polythiometalates with mixed valences can be produced by new types of intramolecular condensation-redox reactions from thioanions. The metal-sulfur bonds can react either nucleophilically or electrophilically, and in the case of the Mo—S bonds this is of biochemical interest. It is important to mention the applications of thiometalates as ligands in complex chemistry (generation of multi-metal complexes, versatile coordination behavior, unique electronic properties of the ligands), in which thiometalato complexes with a variety of electron populations can exist because of the marked electron delocalization. Apart from this, $MoS_4^{2-}$ has a significance in bioinorganic problems, *e.g.* the nitrogenase problem and Cu—Mo antagonism.

## 1. Introduction

On account of their range of colors, the thioanions of the early transition metals have long been of interest to the chemist. For example, at the beginning of nineteenth century *Berzelius*[1] investigated their formation by passing $H_2S$ into aqueous solutions of $MoO_4^{2-}$ or $WO_4^{2-}$. However, their true composition was not established until the turn of the century. Both the thiometalate and the selenometalate ions formed from V, Nb, Ta, Mo, W, and Re in their highest oxidation states exhibit interesting properties. Anions of nearly any color can be produced by varying the chalcogen. The reactivities of the thiometalates and their application in complex chemistry are especially interesting, since they display unique ligand properties. For example, these anions can be used to produce multimetal complexes (heterothioanions), which are either interesting from a structural point of view, or have unusual electronic properties. Some of the complexes comprise four-membered metal-sulfur ring systems $M'S_2M$ with very different formal valences of the M and M′ atoms and metal-metal interactions. Moreover, poly(thiometalates) with mixed valences can be produced from the thiometalates by new types of condensation-redox reactions. In addition, the thiomolybdate and thiotungstate anions are currently of interest since they play a part in certain problems in the domains of bioinorganic chemistry (cf. the existence of polymetallic centers), nutrition physiology, and veterinary medicine. (Several years ago we had already indicated the possible relevance of the Fe thiometalato complexes to the nitrogenase problem.) In the present article we shall review the chemistry and bioinorganic chemistry of certain thiometalates which we have investigated systematically (preparation, reactions, and electronic structure) and introduced as ligands in complex chemistry.

---

[*] Prof. Dr. A. Müller, Dr. E. Diemann, Dipl.-Chem. R. Jostes,
Dr. H. Bögge
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld 1 (Germany)

## 2. Discrete Thiometalate Ions

### 2.1. Formation of Thiometalate Ions in Solution and Preparation of the Salts

Table 1 shows the known transition metal thioanions with a $d^0$ configuration of the central atom, and the salts that can be prepared easily from them, together with some characteristic data. The corresponding selenoanions are also shown, since they are important for understanding the electronic properties.

The chalcogenometalates are prepared either by reactions in the solid state from the constituent elements themselves (*e.g.* $K_3VS_4$[45] or $Tl_3MX_4$ [M = V, Nb, Ta; X = S, Se[10]]), or by the reaction of $H_2S$ (or $H_2Se$) with an aqueous solution of the corresponding oxometalate. Only the solid-state reaction is effective when the oxometalate in question cannot exist in solution, or only in a very strongly alkaline medium (except in the isolation of $NbO_2S_2^{3-}$ with organic cations[46]). Most of the known chalcogenometalates have only been isolated in pure form within the last fifteen years (*e.g.* the salts of the anions $MoOS_3^{2-}$ [21], $WOS_3^{2-}$ [21], $MoO_3S^{2-}$ [14a], and $ReS_4^-$ [42] and nearly all the Se compounds) or detected in solution (Table 1). The pre-

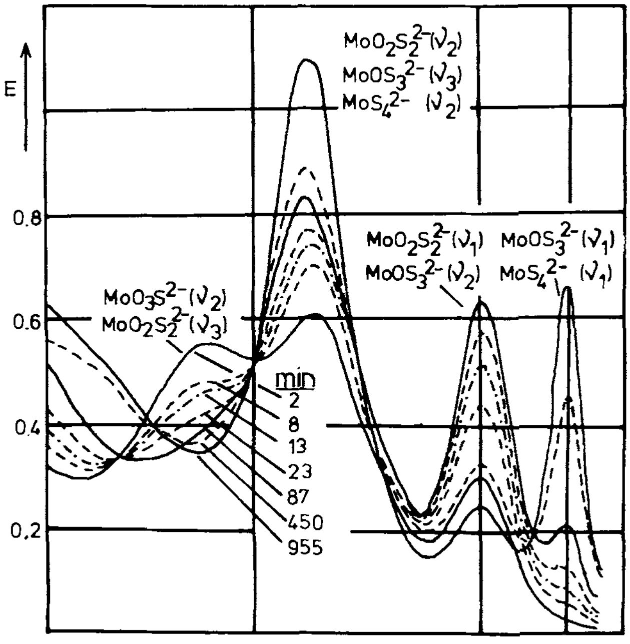


Fig. 1. Electronic absorption spectra of the reaction products from $MoO_4^{2-}$ and $H_2S$ in aqueous solution, as a function of time.

Table 1: Discrete thio- and seleno-anions of V, Nb, Ta, Mo, W, and Re.

| Anion or comp. | Color in solution | VIS/UV [$10^3$ cm$^{-1}$] [c] | Preparation of M'salt from solution M' | IR/Ra [cm$^{-1}$] [b] | Typical M—S(Se) bond length (average) [Å] |
|---|---|---|---|---|---|
| $VO_2S_2^{3-}$ | yellow- orange | 21.8, 27.8, 32.8 [2] | — | — | — |
| $VOS_3^{3-}$ | red | 19.2, 21.8, 30.8, 33.9 [2, 3] | (Na) [4] | — | — |
| $VS_4^{3-}$ | red-violet | 18.6 (3.76), 25.4, 28.5, 37.5 [5, 88] | $NH_4$ [6] | 404.5, 193.5, 470, 193.5 [7] | 2.15 ($NH_4$ salt) [8] |
| $Tl_3NbS_4$ | red brown [a] | 24.0 [a] [9] | [10] | 408, 163, 421, 163 [7] | — |
| $Tl_3TaS_4$ | brown [a] | 25.5 [a] [9] | [10] | 424, 170, 399, 170 [7] | — |
| $VO_2Se_2^{3-}$ | red | 19.2 (?) [11] | — | — | — |
| $VOSe_3^{3-}$ | red-violet | 15.6, 19.2 [11] | — | — | — |
| $VSe_4^{3-}$ | violet | 15.6, 21.45 [12] | Tl [10] | (232), 121, 365, 121 [d] [7] | — |
| $Tl_3NbSe_4$ | deep violet [a] | 19.3 [a] [9] | [10] | 239, 100, 316, 100 [7] | — |
| $Tl_3TaSe_4$ | yellow-green [a] | 21.2 [a] [9] | [10] | 249, 103, 277, 103 [7] | — |
| $MoO_3S^{2-}$ | yellow | 25.4, 34.7, 44.7, 52.0 [13] | K [14a] | [14a] | — |
| $MoO_2S_2^{2-}$ | orange | 25.4, 31.4, 34.7 [13, 15] | $NH_4$ [16] | [17–19] | — |
| $MoOS_3^{2-}$ | orange-red | 21.5, 25.5, 32.0, ≈38.5, 44.1 [3, 20] | Cs [21] | [18, 22] | 2.178 (Cs salt) [23] |
| $MoS_4^{2-}$ | red | 21.4 (4.11), 31.5, 41.3, 48.3 [5] | $NH_4$ [16] | 458, 184, 472, 184 [18, 22] | 2.178 ($NH_4$ salt) [e, f] |
| $MoO_3Se^{2-}$ | orange | 22.2, 31.75 [25] | — | — | |
| $MoO_2Se_2^{2-}$ | red | 22.0, 28.5, 32.0, 40.8 [26] | $NH_4$ [27] | [18] | — |
| $MoOSe_3^{2-}$ | red-violet | 17.9, 22.0, 28.45, 35.5, 40 [20, 28] | Cs [28] | [18] | — |
| $MoSe_4^{2-}$ | blue-violet | 18.0, 27.8, 37.2 [5] | $NH_4$ [12, 29] | 255, 120, 340, 120 [7] | — |
| $MoSSe_3^{2-}$ | red-violet | 18.5, 28.4, 38.0 [20] | [24] | — | — |
| $MoS_2Se_2^{2-}$ | red-violet | 19.65, 29.5, 39.45 [20] | | | |
| $MoS_3Se^{2-}$ | red | 20.6, 30.6, 40.35 [20] | Cs [30, 74] | [30] | — |
| $WO_3S^{2-}$ | pale yellow | 30.6, 41.0 [13, 20] | [31a] | [31b] | — |
| $WO_2S_2^{2-}$ | yellow | 30.6, 36.6, 41.0 [13, 15] | $NH_4$ [31a] | [17, 18] | 2.193 ($NH_4$ salt) [32] |
| $WOS_3^{2-}$ | yellow | 26.7, 29.9, 37.0, 41.1 [3, 20] | Cs [21] | [18, 22] | 2.20 ($K_3(WOS_3)Cl$) [33] |
| $WS_4^{2-}$ | yellow | 25.5 (4.27), 36.1, 46.2 [5] | $NH_4$ [31a] | 479, 182, 455, 182 [18, 22] | 2.177 ($NH_4$ salt) [24] [e, f] |
| $WO_3Se^{2-}$ | yellow | 27.0, 38.0 [20, 25] | — | — | — |
| $WO_2Se_2^{2-}$ | orange | 27.0, 34.0, 38.0 [12, 26] | $NH_4$ [34] | [18] | — |
| $WSSe_3^{2-}$ | red | 21.9, 32.5, 42.6 [20] | Cs [30, 74a] | [30] | — |
| $WOSe_3^{2-}$ | orange | 22.1, 26.0, 34.1, 38.2 [20] | Cs [35a] | [18] | — |
| $WSe_4^{2-}$ | red | 21.6 (4.20), 31.6, 41.3 [5] | $NH_4$ [34] | 281, 107, 309, 107 [7] | 2.344 (Cs salt) [24]<br>2.317 ($NH_4$ salt) [35b] |
| $MoOS_2Se^{2-}$ | red | 24.3, 31.0, 42.5 [20] | Cs [36] | [36] | — |
| $WOS_2Se^{2-}$ | yellow | 29.1, 36.0, 41, 48.4 [20] | Cs [36] | [36] | — |
| $MoOSSe_2^{2-}$ | red | 18.5, 23.15, 30.75 [20] | Cs [37] | [37] | — |
| $WOSSe_2^{2-}$ | orange | 23.25, 26.75, 33.5 [20] | Cs [37] | [37] | — |
| $ReO_3S^-$ | yellow | 28.6, 33.6, 46.5 [15, 20] | Tl [38] | [39, 40] | 2.14 (Rb salt) [41] |
| $ReO_2S_2^-$ | orange | 25 (?), 32 (?) [2] | — | — | — |
| $ReOS_3^-$ | red | 19.8, 25.5, 32.3 [2, 20] | — | — | — |
| $ReS_4^-$ | red-violet | 19.8 (3.98), 32.0, 44.0 [5] | $PPh_4$ [42] | 501, 200, 488, 200 [42] | 2.155 ($PPh_4$ salt) [43] |

[a] Reflectance, in $MgSO_4$. [b] Band maxima sequence: $\nu_1(A_1)$, $\nu_2(E)$, $\nu_3(F_2)$, $\nu_4(F_2)$ (in some solid state spectra $\nu_2$ and $\nu_4$ do not coincide [76]). [c] In brackets values of log $\varepsilon$ for $\nu_1$ [44]. [d] Tl salt. [e] *J. Lapasset, N. Chezeau, P. Belougne,* Acta Crystallogr. *B 32,* 3087 (1976). [f] The deviations of the mean bond lengths in salts with other cations such as $Cs^+$, $PPh_4^+$, and guanidinium cannot be significantly interpreted (structure investigations see [24]).

paration of the selenometalates, and particularly of the mixed thioselenometalates, is difficult (*inter alia* because of their high sensitivity to $O_2$).

The salts with organic cations are important, since they can be used for the synthesis of multimetal complexes in organic solvents. Most of them can be obtained simply from aqueous solutions of their alkali metal salts. While compounds with $Tl^+$ ions can still be regarded as salts[47], in copper compounds such as $NH_4Cu(MoS_4)$ the Cu—S interaction is so strong that the thiometalate ions are no longer isolated (cf. Section 4).

Since all the chalcogenometalates have strong and characteristic absorption bands in the UV/VIS region, the reactions in which they are formed and decomposed can be readily followed by spectrophotometric methods (Fig. 1)[48-51] (see also in Table 1 the literature cited concerning anions that could only be detected in solution). When hydrogen sulfide is passed into an aqueous solution of an oxometalate the electronic spectrum changes, the bands of all the species $MO_{4-n}S_n^{m-}$ (n = 1—4; M = V, Mo, W, Re) appearing in succession. From the existence of isobestic points it follows that almost only two species can coexist in the solution at any one time[50]. Thus, to isolate a chalcogenometalate a cation that will form a sparingly soluble salt with only one of the two anionic species must be added.

The rate of formation of thiometalates depends markedly on the nature of the central atom; the greater the electron density on the oxygen the higher the rate (see Section 2.4). Thus, thiomolybdates form more rapidly than thiotungstates[51]. The rate falls markedly as the sulfur content of the anion (with the same central atom) is increased[51]. It is therefore difficult to isolate the monothiomolybdate and the monothiotungstate. (For example, various workers have attempted in vain to produce a monothiomolybdate[14a]. The contamination of $MoO_3S^{2-}$ by other molybdates can, for instance, clearly be detected by determining the $^{95}$Mo-NMR spectra in water[14b]).

The kinetics of thiomolybdate formation were recently investigated quantitatively by *Sykes*[52,53], using the assumption that $SH^-$ was the reacting agent. We had already concluded on the basis of qualitative observations that this could not be the doubly negative ion $S^{2-}$ but that $H_2S$ is probably also involved[51]. Equilibrium investigations of the systems $MO_4^{2-}/H_2X$ (M = Mo, W; X = S, Se) have also been carried out[54]. The formation of the $MoS_4^{2-}$ ion in solution can also be utilized for the qualitative and quantitative determination of Mo[55] (for analytical applications cf. also [81]).

Besides $MoS_4^{2-}$ there are two other interesting sulfur-rich thiomolybdates (Fig. 2): $Mo_2S_{12}^{2-}$[56] (the only known complex with exclusively $(S_2)^{2-}$ ligands) and $Mo_3S_{13}^{2-}$[57] (the first discrete metal-sulfur cluster). Both complexes can be obtained in almost quantitative yields[58] by reducing $MoO_4^{2-}$ with ammonium polysulfide (which should contain a high proportion of $(S_2)^{2-}$), and have been characterized comprehensively by physical measurements and structural analyses[59,60]. The formation of these thiomolybdates, as well as of the complexes $[Mo_4(NO)_4S_{13}]^{4-}$ and $[Mo_4(NO)_4S_{12}O]^{2-}$ in $H_2O$ (see Section 2.5) bears witness to the high affinity of Mo (in various valence states) for S, and particularly for $(S_2)^{2-}$ (see [58,59]). $(NH_4)_2Mo_2S_{12}\cdot 2H_2O$ contains enantiomeric complex anions[61] (ideal symmetry $D_2$, crystallographic $C_2$). Thermal decomposition of $(NH_4)_2Mo_3S_{13}\cdot nH_2O$ (n = 0—2) yields $MoS_2$[62a], and when $Cs_2Mo_2S_{12}$ is thermally decomposed $S_2$ is formed even at relatively low temperatures in a reductive elimination step[62b].

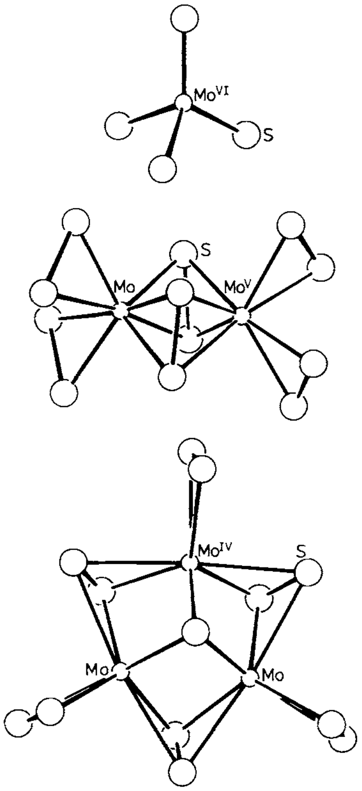


Fig. 2. Thioanions of molybdenum: $MoS_4^{2-}$, $Mo_2S_{12}^{2-}$, and $Mo_3S_{13}^{2-}$.

## 2.2. Behavior in Solution

Thiometalates are not very stable in aqueous solution, especially at low pH. Their decomposition may either be caused by hydrolysis to oxometalates, by intramolecular redox processes (Section 3), or by their marked tendency to form sulfides. With molybdates and tungstates the stability decreases with increasing oxygen content and increasing electron density on the ligands. When they decompose in acid media, binary sulfides (or with selenometalates, selenides) such as $MoS_3$[63] are formed. The decomposition kinetics of the $MoS_4^{2-}$ ion at low pH have been investigated semiquantitatively[64,65], as has its hydrolysis in neutral and weakly alkaline solutions[66]; in this range, the hydrolysis is found to be independent of the pH. No intermediate hydrolysis products, for example mixed oxothiometalates, are detected in dilute solutions[66]. $^{95}$Mo-NMR spectra[67,68] of concentrated solutions of $MoO_2S_2^{2-}$, however, also show signals due to $MoO_3S^{2-}$ and $MoOS_3^{2-}$[14b] (in ref.[67] the signal of $MoO_3S^{2-}$ had erroneously been assigned to that of $MoS_4^{2-}$[14b]).

A protonated species, $(PPh_4)[WS_3(SH)]$ (the only known hydrothio salt), can be isolated from an aqueous solution of $WS_4^{2-}$[69]. $[WS_3(SH)]^-$ reacts in solution with bases such as $N(CH_3)_3$ to give $WS_4^{2-}$. In nonaqueous systems, for example dimethyl ether/HCl, the acids corresponding to the ions are probably present[70,71]. This can be utilized, for example, for the extraction of tungsten[72].

### 2.3. Properties of Solids with Discrete Thiometalate Ions

Most of the alkali metal and ammonium thiomolybdates and thiotungstates crystallize in the $\beta$-$K_2SO_4$ type[73,74a] (cf. Table 1) (except for the monothio salts, salts of the type $A_3(MOS_3)Cl$[74b] (A = K, Rb) and $(NH_4)_2MO_2S_2$ (M = Mo, W), in which strong hydrogen bonds are present[75]). Little is known about the structures of salts with other cations, *e.g.* $Tl^+$[10]. In the structures of solids containing both sulfur and selenium in the anion the respective positions of the two elements are occupied statistically[74a]. A review has been published[76] on the vibrational spectra of solids, which yield information about the cation-anion interactions.

On heating, the ammonium salts of the tetrachalcogenomolybdates and -tungstates decompose to give $NH_3$, $H_2S$ (or $H_2Se$), and the corresponding X-ray amorphous trisulfide (or triselenide) (see [12,77-79a] and the literature cited therein), which *via* release of one mole of the chalcogen forms the dichalcogenide at higher temperatures[78,79a]. From $(NH_4)_3VS_4$ one can obtain the amorphous $V_2S_5$, whose structure we recently investigated[79b]. The decomposition reactions of $(NH_4)_2MoO_2S_2$ and $(NH_4)_2WO_2S_2$ are complex, and the original assumption that $MoOS_2$ is formed as an independent compound[80] has not yet been clearly confirmed[77].

The alkali metal and ammonium salts are soluble in water (the solubility decreasing from $Na^+$ to $Cs^+$), and the $XR_4^+$ salts (X = N, P, As; R = aryl or alkyl) are soluble in various organic solvents. The ammonium salts are relatively unstable even at room temperature *(vide supra).*

### 2.4. Spectroscopic Investigations and Chemical Bonding

Chalcogenometalate ions are distinguished by characteristic high-intensity absorption bands in the UV/VIS region (see Table 1); they can also be traced by IR and Raman spectroscopy (characteristic stretching vibrations: $\nu$(MO): $\approx 800-1000$, $\nu$(MS): $\approx 400-500$, $\nu$(MSe): $\approx 250-350$ $cm^{-1}$; for reasons of space, Table 1 shows only the frequencies for the high-symmetry ions with $T_d$ symmetry). Total assignments and normal coordinate analyses are available for many of the species[81] (also with recourse of isotope shifts[81], as in the case of $^{92/100}MoO_2S_2^{2-}$[19], $^{92/100}MoOS_3^{2-}$[82], or $^{92/100}MoS_4^{2-}$[83]). The vibrational spectra of transition metal-chalcogen compounds have been reported in a review[81].

The first indication of the type of bonding is given by the metal-sulfur bond lengths (Table 1), which are significantly shorter than the sum of the ionic or covalent radii, and thus suggest a bond order $>1$ *i.e.* the involvement of $\pi$ bonds. The MoS bond length in $MoS_4^{2-}$ or $MoOS_3^{2-}$ lies between those for a double and single bonds. (Both bond types are present in the $Mo_2S_4$ moiety; cf. Fig. 13).

The involvement of $\pi$-bonding MO's is also demonstrated by various physical measurements and by MO-calculations [for the $MS_4^{m-}$ ions with $T_d$ symmetry from the stretching-force constants[81] (some of which have been determined fairly reliably[83] from the vibrational spectra of isotopically substituted compounds), from the Raman intensities of $\nu_1(A_1)$[85], from MO-calculations[86,87], and from the oscillator strengths of the $\nu_1(t_1 \rightarrow 2e)$ electronic transitions[88]]. Both calculations and empirical findings, *e.g.* the linear relationship between the energy of the longest-wavelength electronic transition $\nu_1$ and the stretching force constants[89], demonstrate that there is a stabilization of the strongly $\pi$-bonding MO 1e (see Fig. 3). The MO-coefficients for 1e and 2e MO's can be determined from the measured oscillator strengths (2e has mainly metal AO character)[88]. The proportion of $\pi$-contributions in the respective metal-sulfur bonds of analogous species increases in the sequence V < Mo < W < Re. It is also appreciably higher than in the thioanions of the main group elements such as $PS_4^{3-}$, $AsS_4^{3-}$, and $SbS_4^{3-}$[84].

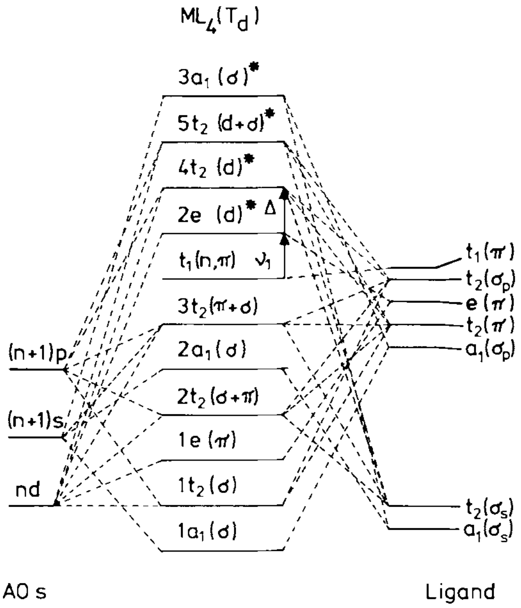


Fig. 3. Simplified MO scheme for $MS_4^{m-}$ ions with $T_d$ symmetry.

The band maxima of the allowed electronic transitions are shown in Table 1. Unambiguous assignments are only possible for the longest-wavelength bands of ions with $T_d$ and $C_{3v}$ symmetry[44]. However, from our own investigations on a large number of anions (Table 1)[44] all bands can be assigned qualitatively to metal reduction transitions (from MO's with predominantly ligand character to ones essentially localized on the central atom). Empirically, this follows *e.g.* from the practically linear relationship between the transition energy and the optical electronegativity of the central atom (for a given ligand) or of the ligand (for a given central atom) (Fig. 4). For ions with $T_d$ symmetry the assignment $t_1 \rightarrow 2e$ (Fig. 3) for the longest-wavelength transition is, furthermore, clearly demonstrable by means of MCD measurements[90]. (In the case of the tetrathiometalates well-defined MCD spectra whose interpretation is beyond question can be obtained: see Fig. 5;

MCD = magnetic circular dichroism). On the basis of empirical considerations[90] and of our investigations of the influence of various coordination centers on the UV/VIS bands of $MoS_4^{2-}$, the assignments $\nu_2 \triangleq 3t_2 \rightarrow 2e$ and $\nu_3 \triangleq t_1 \rightarrow 4t_2$ are probable (see Section 5.2). The positions of the metal reduction bands can also be related to the redox behavior (see Sections 2.5 and 3).

Photoelectron spectra[47,91] have also been used to characterize the electronic structure of these compounds. (For

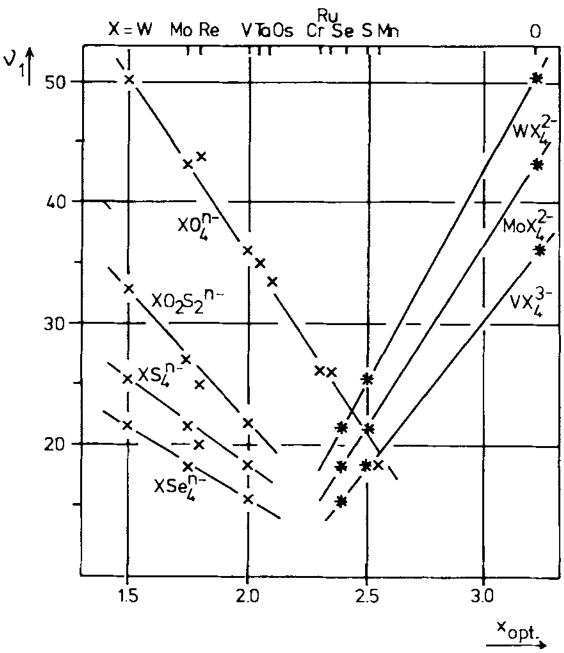


Fig. 4. $\nu_1(t_1 \rightarrow 2e)$ transition energies of species with $T_d$ symmetry, (together with corresponding data for the dithiometalates) as a function of the optical electronegativity of the central atom or the ligands O, S, and Se ($\nu_1$ in $10^3$ $cm^{-1}$).

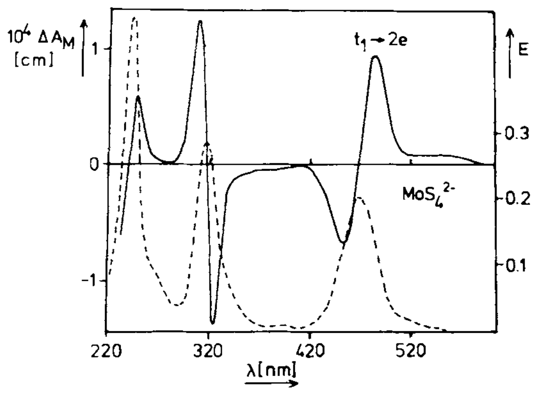


Fig. 5. MCD spectrum (broken line: electronic absorption spectrum) of the $MoS_4^{2-}$ ion.

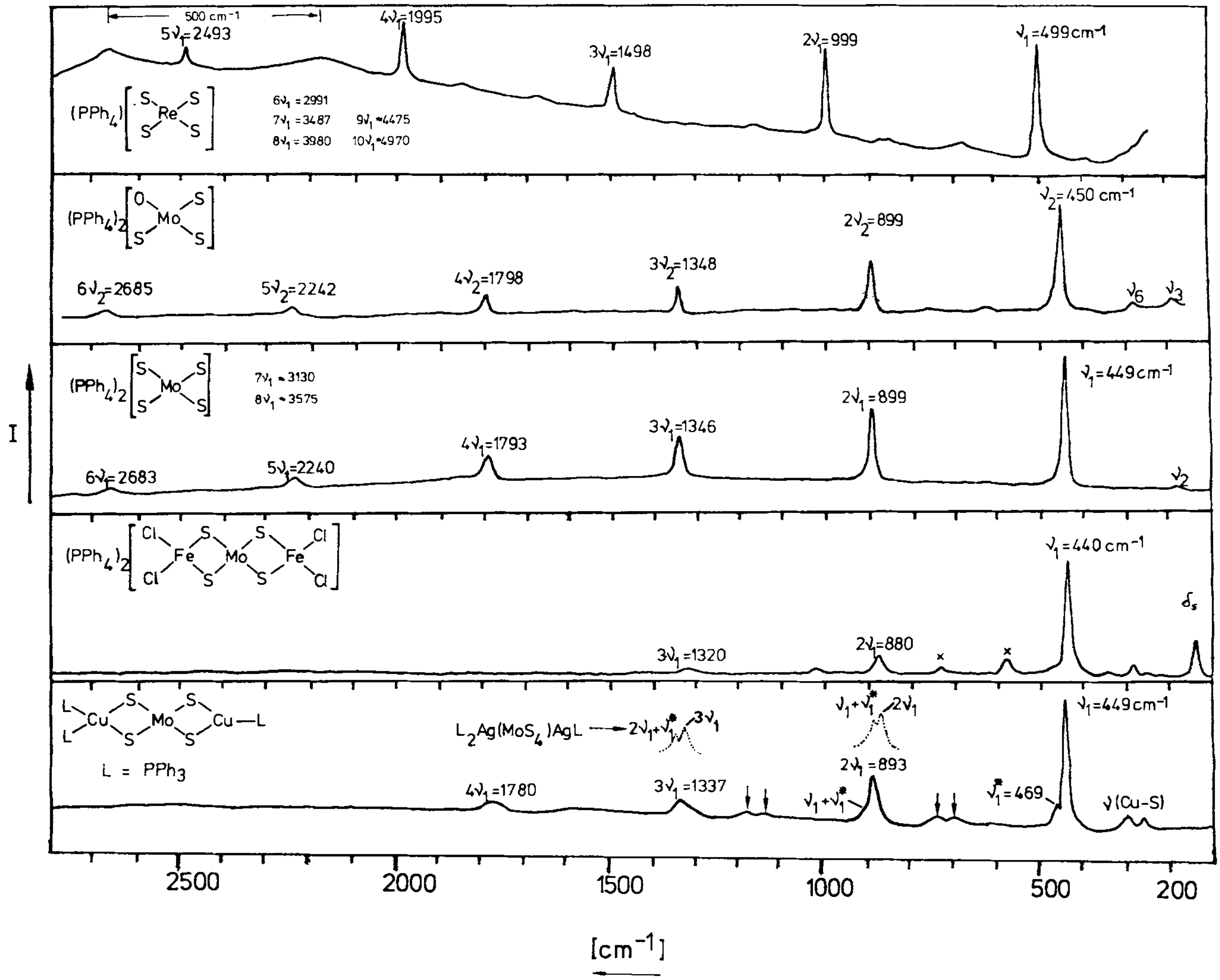


Fig. 6. Resonance Raman spectra of $MoS_4^{2-}$, $MoOS_3^{2-}$, and $ReS_4^-$ and of some thiomolybdato complexes with doubly-bridging $MoS_4^{2-}$ ligands ↓: combination bands of $n\nu_s(MoS)$ with $\nu(CuS)$; × : further combination bands of stretching and bending vibrations [94, 155].

a more complete discussion of the spectra, the electronic structures, and the higher-energy absorption bands, see [44].)

The longest-wavelength bands of the $MOX_3^{2-}$ species $MoOS_3^{2-}$ and $WOSe_3^{2-}$ can be unambiguously assigned to $\pi(X)\rightarrow d(M)$ (or $a_2\rightarrow e$) transitions, since in the resonance Raman spectra (excitation line within the band in question) only the intensities of the lines corresponding to vibrations in corresponding $MX_3$ chromophores are enhanced[92,93,94] (Fig. 6, showing a much better spectrum than the earlier reported one). Resonance Raman spectra could also be obtained for $MoS_4^{2-}$[81,94] (Fig. 6; a particularly fine example, also of biochemical interest) and for $VS_4^{3-}$[94,95], $MoSe_4^{2-}$, $WSe_4^{2-}$[94,96], and $ReS_4^-$[94] (Fig. 6). Particularly informative spectra are obtained from $PPh_4^+$ salts (or those with other bulky organic cations with small anion-anion interaction), since the number of observed overtones and combination tones is particularly large[94] *e.g.* in the spectra of the corresponding compounds with $ReS_4^-$ and $MoS_4^{2-}$, where the series of combination tones $\nu_2+n\nu_1$ could be observed up to $n=7$ and 4, respectively. In the spectrum of $ReS_4^-$ the fluorescence band of the $t_1\rightarrow 2e$ transition is clearly perceptible (*ca.* 18000 $cm^{-1}$ with $\nu_1(A_1)\approx 500$ $cm^{-1}$), together with a non-uniform intensity pattern of the bands of the higher harmonics (to some extent comparable with a resonance fluorescence spectrum). The anharmonicity of the $\nu_1(A_1)$ vibration of the thioanions is clearly smaller than in the case of the oxometalates such as $MnO_4^-$ (see [81]). (Anharmonicity constants: $x_{11}(MoS_4^{2-})=-0.4\pm0.3$;
$x_{11}(ReS_4^-)=-0.3\pm0.2$ $cm^{-1}$[94]).

### 2.5. Reactions

M$\overset{\cdots}{=}$S groups with $\pi$-bond contributions (*e.g.* in the thiometalates) can react either with nucleophiles *(Nu)* or electrophiles *(E)*:

$$\mathrm{Mo}^{r}\overset{\cdots}{=}\mathrm{S} + Nu \rightarrow \mathrm{Mo}^{r-2} + Nu\mathrm{S} \qquad \text{(a)}$$

(abstraction of S/two-electron reduction)

$$\mathrm{Mo}^{r}\overset{\cdots}{=}\mathrm{S} + E \rightarrow \mathrm{Mo}^{r} + E\mathrm{S}^{2-} \qquad \text{(b)}$$

(abstraction of $S^{2-}$).

A further important type of reaction corresponds to an intramolecular redox process:

$$\mathrm{Mo}^{r}(\mathrm{S}^{2-}) \rightarrow \mathrm{Mo}^{r-2}(\mathrm{S}^{0}) \qquad \text{(c)}$$

or

$$\mathrm{Mo}^{r}(\mathrm{S}^{2-})_2 \rightarrow \mathrm{Mo}^{r-2}(\mathrm{S}_2^{2-}) \qquad \text{(d)}$$

The formation of $(S_2)^{2-}$ can formally occur *via* the intramolecular reaction of $(S^0)$ (produced according to eq. (c)) with $S^{2-}$ (Section 3). Until recently, the fact that this type of reaction is of decisive importance for molybdenum-sulfur chemistry (and probably in various catalytic and biochemical problems as well) had been overlooked. (For the formation of polysulfide ligands *vide infra.*) Electron-transfer reactions in $Mo(SR)_2$ groups with partial disulfide formation are probably significant in biochemistry[97a]. For type (a) a number of reactions with $Nu=CN^-$ are known and these are significant for problems in the bioinorganic[97a] and prebiotic[98] fields (*i.e.* in connection with the evolution of primitive Mo enzymes). For example, the following type of reaction has a relevance for the deactivation of xanthine oxidase by $CN^-$[99]:

$$\mathrm{Mo}^{r}{=}\mathrm{S} + \mathrm{CN}^- \rightarrow \mathrm{Mo}^{r-2} + \mathrm{NCS}^- \qquad \text{(e)}$$

*i.e.* a sulfur-atom-transfer reaction with a two-electron reduction of the central atom.

$MoO_3S^{2-}$ and $MoO_2S_2^{2-}$ react with $CN^-$ by two- or four-electron reductions to form cyano-complexes, which no longer contain any sulfur, and $SCN^-$[100,101]. In general, a briding sulfide ligand ($\mu_2$ or $\mu_3$) is better protected against attack by $CN^-$. This can be demonstrated with the $Mo_3S_{13}^{2-}$ "thiomolybdate", which reacts with $CN^-$ to form $[Mo_3S_4(CN)_9]^{5-}$, where the triangular $Mo_3S_4$ system with sulfur bridges between the Mo atoms and the apical sulfur atom are not attacked[102], and also by the reaction of $Mo_2S_{12}^{2-}$ to $[Mo_2S_2(CN)_8]^{6-}$[103]. In this last process a central $Mo_2S_4^{2+}$ unit of an intermediate product may react according to reaction type (a)[103].

The reactions of oxoanions with $H_2S$ in the presence of cyanide may also proceed according to type (a) (though up to now, thiometalate ions as intermediate products have not been detected). These reactions are interesting because they lead either to new types of $\mu_n$-thio(cyano) complexes or to cyano complexes whose preparation is otherwise difficult.

The reaction of $VO_4^{3-}$ with $H_2S$[104] in the presence of cyanide leads to $[V(CN)_7]^{4-}$[105-107]; if the system also contains hydroxylamine, then $[V(NO)(CN)_6]^{4-}$ will be produced[105,108,109]. $MoO_4^{2-}$ reacts with $H_2S$ and $CN^-$ to give $[Mo_2S_2(CN)_8]^{6-}$[100,110], $[(CN)_6MoSMo(CN)_6]^{6-}$[111] (Fig.

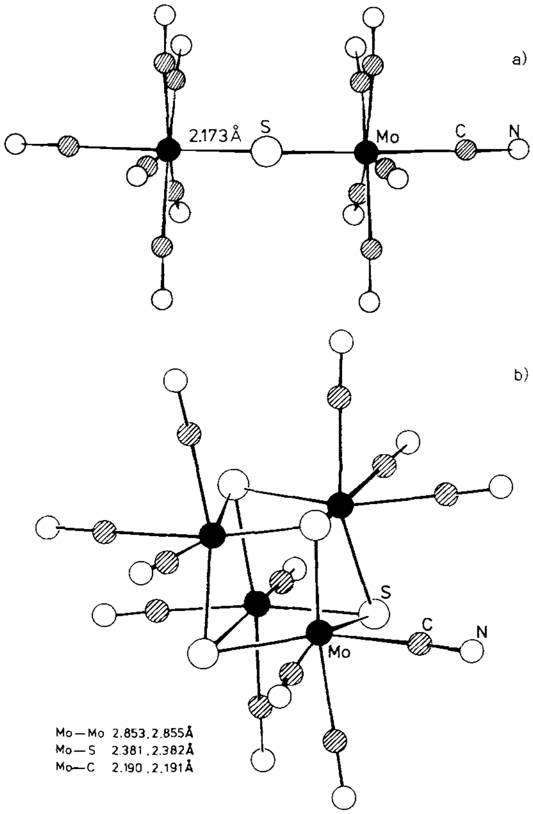


Fig. 7. Structure of a) $[(CN)_6MoSMo(CN)_6]^{6-}$ [111, 114] and of b) $[Mo_4S_4(CN)_{12}]^{8-}$ [223] with cubane-like structure.

7a), $[Mo_4S_4(CN)_{12}]^{8-}$[223] (Fig. 7b), but also to $[Mo(CN)_7]^{5-}$[100]. Under suitable conditions $ReO_4^-$ or $WO_4^{2-}$ form $[Re_2S_2(CN)_8]^{4-}$[112] and probably a cyano(thiocyanato)tungstate, respectively[113].

It is interesting that in $[(CN)_6MoSMo(CN)_6]^{6-}$ there is a nearly linear MoSMo bridge with very short bond lengths (Fig. 7a)[114]. Our own MO-calculations on this complex show that there are π-MO's delocalized over the three centers. The remarkable π(S)→d(Mo) donation induces a decrease of electron density on the sulfur and are thus responsible for an unusual CT transition Mo→S (band at 27 100 $cm^{-1}$).

The thio(cyano)metalates are regarded as a key species in the evolution of metal enzymes[98]. For example, the last of the above mentioned complexes, first reported by us, is also formed when freshly precipitated $MoS_2$ is treated with $CN^-$[98,101]. It is important in this connection that in cyanomolybdates the $CN^-$ can be easily substituted by sulfur-containing ligands[210].

Thus, while with vanadium the preferred process is abstraction of sulfur, in the case of Mo the high sulfur affinity leads mainly to the formation of complexes that still include bridging $S^{2-}$ ligands. In this connection we should also mention the remarkable species $[Mo_4(NO)_4S_{13}]^{4-}$[59,115a] and $[Mo_4(NO)_4S_{12}O]^{2-}$[116] (Fig. 8), produced using similar conditions as $[V(NO)(CN)_6]^{4-}$.

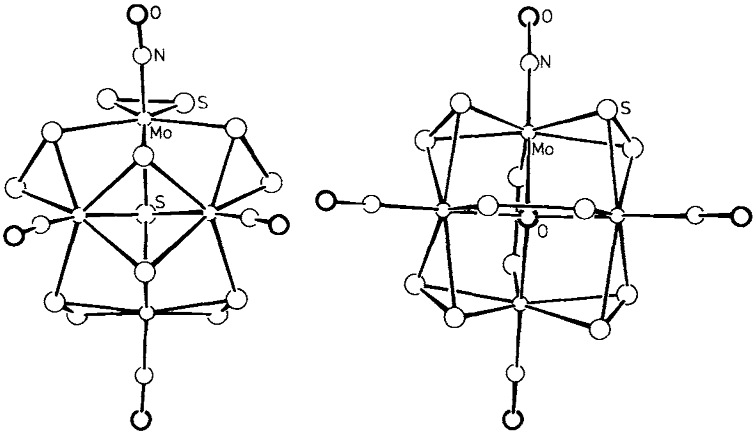


Fig. 8. Structure of $[Mo_4(NO)_4S_{13}]^{4-}$ and $[Mo_4(NO)_4S_{12}O]^{2-}$, two unusual polynuclear complexes with four different types of coordinated $S_2^{2-}$ ligands [59, 115a, 116].

The complexity of the mode of formation of these compounds mentioned is well known, and certain proposals have been suggested for the system $MoO_4^{2-}/H_2S/CN^-$[114].

The reaction of $MoS_4^{2-}$ with $H^+$ to give $MoS_3$ formally takes place according to type (b). This reaction type (*i.e.* $E{=}S_x$) also seems relevant to the reaction of $MoS_4^{2-}$[115b] or $MoOS_3^{2-}$[115c] with sulfur to form $S_4^{2-}$ ligands. In the formation of $[Mo^{IV}O(S_4)_2]^{2-}$ (see Fig. 12) from $MoOS_3^{2-}$ and $S_8$, the reduction probably takes place according to eq. (c) or (d) with r = 6+. The possible intermediate product $\{OMo^{IV}(S_2^{2-})S^{2-}\}^{2-}$ (or $\{OMo^{IV}S^0(S^{2-})_2\}^{2-}$) may react with the sulfur *via* ring expansion (or ring formation). $[Mo_2O_2S_2(S_4)_2]^{2-}$[115c] is also formed as a by-product (or from $[MoO(S_4)_2]^{2-}$) (cf. Fig. 12). In the interpretation of this it is important in this context that in solution $MoOS_3^{2-}$ "decomposes" rapidly already at room temperature, even without the addition of sulfur, in a process involving intramolecular condensation-redox process[115c]. In this case binuclear complexes of the type $[Mo_2X_2S_2(S_2)_2]^{2-}$ (with $X_{term}$) are formed (probably *via* the intermediates mentioned) (see Fig. 12) with the X-positions occupied randomly by O and S ($PPh_4^+$ salts characterized by crystal structure analysis[115c]), as well as trinuclear complexes of the type $M_3OX_8^{2-}$ (see Fig. 9)[115c].

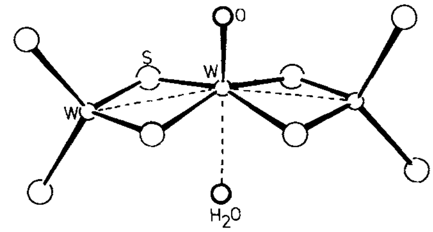


Fig. 9. Structure of $[W_3OS_8(H_2O)]^{2-}$) ($Cs^+$ salt [120]).

## 3. Formation of Poly(thiometalates); Chalcogenometalates with Mixed Valences

While a great deal of research has been done on condensations of oxometalates in aqueous solutions, there has been little such work on thiometalates (cf. [117]). In the interpretation of the results, those authors who have approached the subject have not considered the fact that intramolecular redox processes may take place in addition to the condensation reactions[118,119]. The condensation reactions subsequent to protonation of thiometalate ions take place at a lower pH than that of the oxoanions, since the proton affinity of S is appreciably lower than that of O. Investigations of the condensation behavior of thiometalate ions are made more difficult, since various complex decomposition processes are also involved. For example, no definite condensation products has yet been isolated from an aqueous solution containing $MoS_4^{2-}$.

The behavior of $WS_4^{2-}$ is again different from that of $MoS_4^{2-}$ and of the oxothiometalates, since protonation only takes place at relatively low pH values (the proton affinity of $WS_4^{2-}$ is lower than that of $MoS_4^{2-}$, since the electron density on the sulfur atoms in $MoS_4^{2-}$ is larger; see Section 2.4). When an aqueous $WS_4^{2-}$ solution is acidified, condensed species are formed besides $[(HS)WS_3]^-$ (Section 2.2). $[W_3OS_8(H_2O)]^{2-}$ or $W_3OS_8^{2-}$ ions (Fig. 9) (a species with mixed valences) can be precipitated from the solution by various cations, such as $Cs^+$[120], $PPh_4^+$[121], and $NMe_4^+$[118,122,225].

$[W_3OS_8(H_2O)]^{2-}$, which can also be formulated as $W_3OS_8^{2-}$[212] since the very weakly bound $H_2O$ can also be regarded as water of crystallization, formally contains $2\,W^{VI}$ and $1\,W^{IV}$, in common with $W_3S_9^{2-}$[123], and is possibly formed as follows:

$$WS_4^{2-} + 2H_2O \rightarrow WO_2S_2^{2-} + 2H_2S$$

$$WO_2S_2^{2-} + H^+ \xrightarrow{aq} OW(OH)S_2(aq)^-$$

$$OW^{VI}(OH)S_2(aq)^- \rightarrow OW^{IV}(OH)(S_2)(aq)^- \qquad \text{(f)}$$

$$OW^{IV}(OH)(S_2)(aq)^- + 2WS_4^{2-} \rightarrow [OW(WS_4)_2(H_2O)]^{2-} + OH^- + (S_2)^{2-}$$

The condensation takes place after partial hydrolysis. The pure sulfur compound $W_3S_9^{2-}$ (Fig. 10) probably cannot be obtained directly from aqueous solution but, *e.g.* quite simply by heating a solution of $(NH_4)_2WS_4$ in an organic solvent[124]. The homologous species $W_4S_{12}^{2-}$ (Fig. 11) was also recently isolated[125]; this formally contains the central unit $W_2^{V}S_4^{2+}$ and two $W^{VI}S_4^{2-}$ ligands. The "$WS_4^{2-}$ ligands" can be abstracted from $W_3S_9^{2-}$ and $W_4S_{12}^{2-}$ with $FeCl_2$ to give $[Cl_2Fe(WS_4)]^{2-}$[211]. While the $Mo_2^{V}X_2S_2^{2+}$ units (X = O, S) are characteristic species for the chemistry of $Mo^{V}$ (Figs. 12 and 13), little is known as yet about the corresponding W units. $W_3OS_8^{2-}$ can be obtained easily from $W_3S_9^{2-}$ in organic solvents containing a little water[211], and this must be borne in mind in the latter's preparation (by heating $WS_4^{2-}$ in organic solvents). There is a marked tendency for the formation of these trinuclear poly(thiometalate).

EH-SCCC-MO calculations on the new types of polythiometalates $W_3XS_8^{2-}$ (X = O, S) also show that these can be described approximately as coordination compounds of $W^{IV}X^{2+}$ with $WS_4^{2-}$ ligands. An occupied MO is about 50% localized on the central W atom, but owing to the appreciable participation of orbitals of the outer W atom there is a clear metal-metal interaction[126]. After diamagnetic correction for the W centers a weak paramagnetism is found. Correspondingly, there is a metal-metal bond in the central $W_2^{V}S_4^{2+}$ unit of $W_4S_{12}^{2-}$[126].

Mixed oxothiometalates should show a particularly characteristic and marked tendency toward polymerization, because of the appreciably higher proton affinity of oxygen compared to sulfur. For example, $MoO_2S_2^{2-}$ ions are only stable at high pH. In near-neutral aqueous solutions, "decomposition" or condensation takes place quite rapidly with the probable involvement of the following intramolecular redox processes (see Section 2.4):

$$2\,S^{2-} \xrightarrow{\text{ox}} (S_2)^{2-} \qquad \text{(g)}$$

$$Mo^{VI} \xrightarrow{\text{red}} Mo^{IV} \qquad \text{(h)}$$

$$(Mo^{VI} + Mo^{IV} \rightarrow 2\,Mo^{V})$$

Here too, the first step of the reaction should be a protonation of the oxygen atom. This protonation favors both condensation and an intramolecular redox process, since it reduces the effective electron density on the Mo center by decreasing the Mo—O-π bond order, and thus enhances the oxidizing action of the Mo atom. Similar redox-condensation reactions of $MoOS_3^{2-}$ in methanol, which also lead to the formation of polythioanions, are mentioned in Section 2.5.

The $[Mo_2O_2S_2(S_2)_2]^{2-}$ anion (see Fig. 12) has already been isolated from a solution of $MoO_2S_2^{2-}$[127], and in this reaction an $(S_2)^{2-}$ ligand is thus formally generated by oxidation of two $S^{2-}$ ligands (with reduction of Mo). In the presence of other sulfur-containing ligands complexes with the central $Mo_2O_2S_2^{2+}$ unit, such as $Mo_2O_2S_2(dtc)_2$[119], are formed.

In recent years there have been many investigations of $Mo^{V}$ complexes with the central unit $Mo_2X_2S_2^{2+}$ (X = O, S), principally with bio-relevant ligands such as cys-

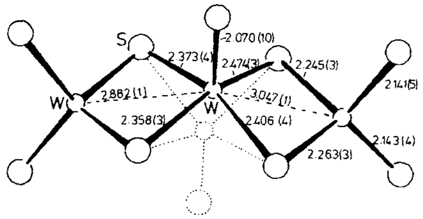


Fig. 10. Structure of $W_3S_9^{2-}$ ($PPh_4^+$ salt) [124] (the central $WS_5$ unit is disordered, the midpoint of the W—W vector lies at the center of symmetry (see [120, 123, 124]).

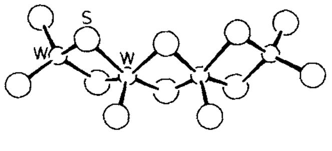


Fig. 11. Structure of $W_4S_{12}^{2-}$ [125].

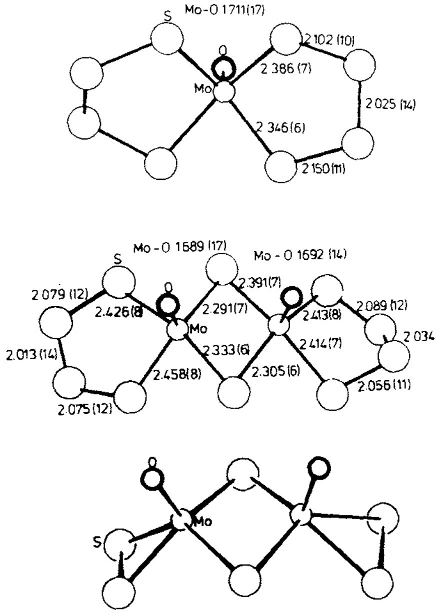


Fig. 12. Species with $S_n^{2-}$ ligands in whose formation from thiomolybdates intramolecular redox processes are involved: $[MoO(S_4)_2]^{2-}$ [115c], $[Mo_2O_2S_2(S_4)_2]^{2-}$ [115c] ($PPh_4^+$ salts), and $[Mo_2O_2S_2(S_2)_2]^{2-}$ [127].

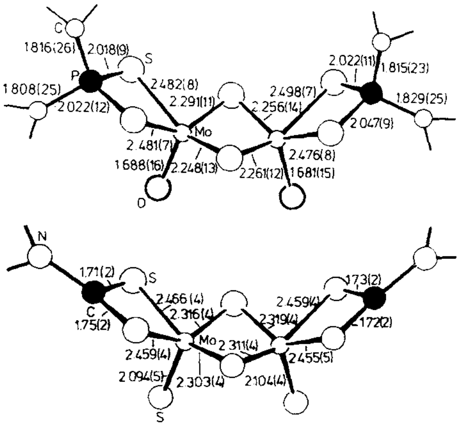


Fig. 13. Structure of $[Mo_2O_2S_2(S_2PPh_2)_2]$ [129b] and $[Mo_2S_4(dtc)_2]$ [129a]; dtc = diethyldithiocarbamate.

teine[128]. The unit, in which X = O, is significant for the chemistry of $Mo^V$ because of its high tendency to be formed. The unit with X = S appears, for example, in the reactions of thiomolybdate $Mo_2S_{12}^{2-}$ with S-bearing ligands such as $dtc^-$[129a] in organic solvents. Figure 13 shows the structure of $Mo_2O_2S_2(S_2PPh_2)_2$[129b] and $Mo_2S_4(dtc)_2$[129a] with the corresponding bond lengths. In the second of these, there are bond lengths characteristic of Mo—S single and Mo—S double bonds, longer and shorter than the bond length in $MoS_4^{2-}$ respectively (Section 2.4).

## 4. Multimetal Complexes with Thiometalate Ligands

Thioanions have remarkable ligand properties, *e.g.* versatile coordination behavior and very low-lying unoccupied orbitals. Thus, the complexes show strong metal-ligand interactions (see [144]). We first described complexes with such ligands about ten years ago[117, 130]. It is worth noting that there are multimetal complexes of this type with a variety of electron populations (see Section 5.2) and with coordinatively unsaturated metal centers *e.g.* $[Fe(WS_4)_2]^{2-}$ (possible catalytic significance). Some of the complexes catalyze the photoreduction of water[213].

The reaction of various divalent transition metal cations with thiometalates in solution (*e.g.* in $H_2O$) takes place as follows:

$$2XR_4^+ + 2MO_{4-n}S_n^{2-} + M' \rightarrow (XR_4)_2[M'(MO_{4-n}S_n)_2] \qquad \text{(i)}$$

M' = Fe, Co, Ni, Pd, Pt, Zn, Cd, Hg; M = Mo, W; n = 2, 3, 4;
X = P, As

leading to the formation of bis(thiometalato) complexes (multi-metal complexes with bidentate ligands), which can be isolated *e.g.* as quaternary phosphonium salts (cf. Table 2, exception: the combination M' = Fe, M = Mo). Spectroscopic investigations show that in solution other species may be present before the precipitation: for example, solutions of $Co^{2+}$ and $WO_{4-n}S_n^{2-}$ (n = 4, 3) in water do not show the characteristic electron absorption spectra of $[Co(WO_{4-n}S_n)_2]^{2-}$ complexes[131] (although they do in organic solvents); from an orange solution of $Fe^{2+}$ and $WS_4^{2-}$ in $H_2O$ a green precipitate of $(PPh_4)_2[Fe(WS_4)_2]$ is obtained.

Table 2: Complexes of the types $[M'(MO_{4-n}S_n)_2]^{m-}$ and $[LM'(MS_4)_n]^{2-}$, and their properties [a], term = terminal, br = bridged.

| Anion | Color | NIR/VIS/UV [$10^3$ cm$^{-1}$] [b, m] | | IR [cm$^{-1}$] [p] | | | | $-E^{I}_{1/2}$ [o] [V] | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| | | L→d(M') | L→L* | d→d | $\nu(MO_{term})$ | $\nu(MS_{term})$ | $\nu(MS_{br})$ | | |
| $[Fe(MoS_4)_2]^{3-}$ | violet | 15.9 (17.3 [c]) | 19.7, 24.4 | | — | 495/472 | 438 | | [148, 149] |
| $[Fe(WS_4)_2]^{3-}$ | orange | 18 (20 [c]) | 23, 27 | | — | 470 | 430 | | [d] |
| $[Fe(WS_4)_2]^{2-}$ | green | 16.2 | 23.4, 26.7 | 8.7 | — | 493/484 | 438 | 0.25 | [144, 180, 188] |
| $[Co(MoO_2S_2)_2]^{2-}$ | green | 14.7 (22.6 [c]) | 29.1, 33.1 | ≈ 8.3 | 903/884 | | 453/447 | 0.64 | [135, 139] |
| $[Co(WS_4)_2]^{2-}$ | olive green | 12.2 | 25.8 | ≈ 8.6 | — | 500/491 | 450/442 | 0.48 | [136, 142, 187] |
| $[Co(WOS_3)_2]^{2-}$ | olive green | 13.8 | 27.2, 30.3 | ≈ 8.3 | 917/907 | 490/485 | 445 | 0.52 | [137, 180] |
| $[Co(WO_2S_2)_2]^{2-}$ | blue-green | 16.4 (27.9 [c]) | 31.7 | ≈ 7.5 | 927/892 | — | 440 | 0.68 | [135, 138] |
| $[^{58}Ni(^{92}MoS_4)_2]^{2-}$ | dark brown | | 19.5, 25.3, 30.0 | | — | 513/494.0 | 455.5/442.5 | 0.52 | [134, 180, 182] [g, l] |
| $[Ni(MoOS_3)_2]^{2-}$ | brown | | 21.8, 27.6, 31.0 | | 896/884 | 500/492 | 458/446 | 0.58 | [139, 180] |
| $[Ni(MoO_2S_2)_2]^{2-}$ | brown | | 27.0, (31.0), 34.7 | 14.3 | 896/880 | — | 463/453 | 0.62 | [135, 139] |
| $[^{58}Ni(WS_4)_2]^{2-}$ | red-brown | | 23.8, 26.3 | ≈ 14.3 | — | 496/490 | 449 | 0.54 | [136, 183] [l] |
| $[Ni(WOS_3)_2]^{2-}$ | brown | | 26.3, 30.1 | 14.5 | 921/908 | 496/486 | 450 | 0.58 | [137, 180] |
| $[^{58}Ni(WO_2S_2)_2]^{2-}$ | brown-yellow | | 31.5, 34.7 | 15.0 | 916.1/882.4 | — | 451.1 | 0.68 | [135, 138, 184] [l, q] |
| $[Pd(MoS_4)_2]^{2-}$ | red | | 21.2, 26.1, 28.6, 31.6 | | — | 513/497 | 450/435 | 1.09 | [191, 192a, 180] |
| $[Pd(WS_4)_2]^{2-}$ | brown-red | | 25.2, 27.2, 31.9 | | — | 499/491 | 440 | 1.05 | [191, 192a, 180] |
| $[Pt(MoS_4)_2]^{2-}$ | red | | 19.5, 24.3, ≈ 27.5, 32.5 | | — | 510/496 | 454/433 | | [191, 192a, 180] |
| $[Pt(WS_4)_2]^{2-}$ | brown-orange | | 24, 32.0 | | — | 498/489 | 446/438 | | [180] [f] |
| $[^{64}Zn(^{92}MoS_4)_2]^{2-}$ | brown | — | 17.5, 21.4, 31.9, 40.5, 42.9 [j] | — | — | 516/499 | 456/434.5 | | [134, 185, 186b] [l] |
| $[Zn(MoOS_3)_2]^{2-}$ | orange | — | ≈ 21.7, 25.1, 33.0 | — | 898 | 502 | 456/437 | | [139, 186b] |
| $[^{68}Zn(WS_4)_2]^{2-}$ | orange | — | 21.7, 25.3 | — | — | 492.4/487.2 | 445.5/435 | | [136, 141, 186b] [l] |
| $[Zn(WOS_3)_2]^{2-}$ | yellow | — | ≈ 25.3, 29.5 | — | 918/904 | 495/485 | 440 | | [137, 186b] |
| $[Cd(WS_4)_2]^{2-}$ | orange | — | 21.6, 25.3 [e] | — | — | 493/486 | 435 | | [178, 186b] |
| $[Hg(WS_4)_2]^{2-}$ | orange | — | ≈ 22.3, 25.3 [e] | — | — | 493/486 | 431 | | [178, 186b] |
| $[Cl_2Fe(^{92}MoS_4)]^{2-}$ [h, i] | dark red | 17.1, 19.2 | 21.2, 23.0, 31.9, 35.2 | 9.5 | — | 503/488 | 452/(427) | | [188] [k] |
| $[Cl_2Fe(^{100}MoS_4)]^{2-}$ [h, i] | v. sup. | v. sup. | v. sup. | v. sup. | — | 496/483.5 | 447.5/(427) | | [188] [k, l] |
| $[Cl_2Fe(WS_4)]^{2-}$ [h] | red | 19.4, 22.6 | 24.1, 26.8 | 8.7 | — | 492/482 | 443/438 | | [188] |
| $[(NO)Fe(WS_4)_2]^{2-}$ | dark red | 22.5 | 25.6 | (15.6) | — | 487 | 450/443 | | [144, 180] [n] |
| $[(dmf)_2Fe(WS_4)_2]^{2-}$ | red | | | | — | 484/472 | 462/446 | | [178, 180] |
| $[NCCu(^{92}MoS_4)]^{2-}$ | red | — | 21.2, ≈ 22.2, 31.5, 40.5, 44.6 [j] | — | — | 500/486 | 447/416 | | [186b] [k, l] |
| $[NCCu(^{100}MoS_4)]^{2-}$ | v. sup. | — | v. sup. | — | — | 493/481 | 443/415 | | [186b] [k, l] |

[a] M = Mo, W; M' = Fe, Co, Ni, Pd, Pt, Cu, Zn, Cd, Hg; n = 2, 3, 4. [b] The assignment of the electronic spectra is only approximate when the M'—L interactions are strong (see text). [c] Possibly a band of type d(M')→L*. [d] *W. E. Newton*, personal communication; *W. E. Newton, A. Müller*, unpublished results. [e] Solid-state reflectance spectra. [f] *A. Müller, M. C. Chakravorti, H. Dornfeld*, Z. Naturforsch. *B 30*, 162 (1975). [g] The spectra given in [192a] for the complexes $[M'(MS_4)_2]^{2-}$ (M' = Ni, Pd, Pt) are not all correct, since some $NEt_4^+$ salts decompose rapidly in solution (*e.g.* $(NEt_4)_2[Ni(MoS_4)_2]$, for which, therefore, the weak longest-wavelength band maxima not given in [192a] are difficult to measure). The band maxima given by us for the spectra in solution agree with those of the solid-state reflectance spectra. [h] Representative for complexes of the type $[X_2Fe(MS_4)]^{2-}$ (see Table 3). [i] $PPh_4^+$ salt. [j] Measured on $NMe_4^+$ salts (see Fig. 23 and text). [k] See also Table 1 (isotope data and normal coordinate analysis: *A. Müller, E. Krickemeyer, W. Jaegermann, Sun Che*, unpublished results). [l] The isotope data relate to the IR frequences; see the corresponding literature. [m] Unless otherwise indicated, the unpublished spectra were measured on $PPh_4^+$ salts in $CH_2Cl_2$ or $CH_3CN$ (often only the main absorption maxima are given). [n] The $PPh_4^+$ salt is isostructural with the corresponding Co complex [144]. [o] Cyclovoltammetric values of the Ni- (see also [192a], $Co^-$, and Fe-complexes: $PPh_4^+$ salts in dimethyl formamide ($10^{-3}$ M); supporting electrolyte $NEt_4I$ or $NPr_4(PF_6)$; Pt electrode; versus Ag/AgCl/LiCl(sat.)EtOH ($E_N = +0.143$ V); 200 [mV/s]; Pd complexes versus SCE [191, 192a]; $E^{I}_{1/2}$values correspond to eq. (I). [p] $\nu(M'S)$: ≈ 270–330 cm$^{-1}$. [q] $PPh_4^+$ salt/Nujol; $\nu(WS)$ with $\Delta\nu = \nu(^{58}Ni) - \nu(^{62}Ni) \approx 0$; $\nu(NiS) = 315.0$ ($\Delta\nu = 6.1$) and 322.5 (1.3) cm$^{-1}$.

Particularly with tetrathiometalate ions—due to the high electron density on the S atoms—species in which the ligand acts as a doubly bridging entity can form[227a]. (This property of the ligand is demonstrated by the existence of the well characterized species $[Cl_2Fe(MoS_4)FeCl_2]^{2-}$[132] (see also[150]) and $NH_4Cu(MoS_4)$[133], which will be discussed later). In some cases inhomogeneous and X-ray-amorphous products with polymeric ions can also be formed. For example, in the case of $Ni^{2+}$, the reaction in $H_2O$ produces not only the species $(XR_4)_2[Ni(MS_4)_2]$ (M = Mo, W), but also amorphous products which, in contrast to the complex, are insoluble in nitromethane and so can be separated off[134, 136]. However, only the complex is produced in $CH_3CN/H_2O$[192a]. If dioxodithiometalates are used, then as expected, no by-products are produced in water. However, it is necessary to work very quickly in this case, because of the high decomposition rate of the dithioanions (see Section 3)[135].

In all complexes of Table 2, $MO_{4-n}S_n^{2-}$ ions coordinate as bidentate ligands to the metal atom[137-139]. Figure 14 shows the types of structures we found earlier with the aid of spectroscopic methods in bis(thiometalato) complexes

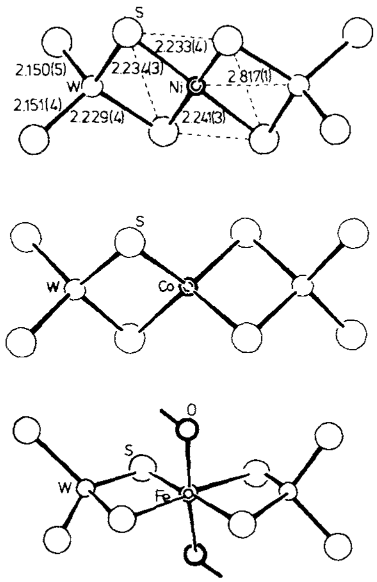


Fig. 14. Bis(tetrathiometalato) complexes: $[Ni(WS_4)_2]^{2-}$ ($AsPh_4^+$ salt), $[Co(WS_4)_2]^{2-}$, and $[Fe(dmf)_2(WS_4)_2]^{2-}$ ($PPh_4^+$ salt) with square planar, tetrahedrally or octahedrally coordinated central atom resp. (cf. Tables 2 and 3) [121, 142, 178, 180].

Table 3. Multimetal complexes with thiometalate ligands (averaged M—S and M...M' distances in Å) [a].

| Compound | Color | M—S$_{br}$ | M—S$_{term}$ | M...M' | Ref. |
|---|---|---|---|---|---|
| $((PPh_3)_2N)_2(NEt_4)[Fe(MoS_4)_2]$ | violet | 2.256 | 2.171 | 2.740 | [148] |
| $(NEt_4)_2[(PhS)_2Fe(MoS_4)]$ | dark red | 2.246 | 2.154 | 2.750 | [151] |
| $(NEt_4)_2[(PhS)_2Fe(MoS_4)]$ | dark red | 2.255 | 2.153 | 2.756 | [152] |
| $(NEt_4)_2[Cl_2Fe(MoS_4)]$ | dark brown | [e] | [e] | 2.786 | [152] |
| $[Fe(dmso)_6]\,[Cl_2Fe(MoS_4)]$ | dark red | [e] | [e] | 2.775 | [155] |
| $(PPh_4)(N(C_7H_7)Me_3)[Cl_2Fe(MoS_4)]$ | dark red | [e] | [e] | 2.775 | [154, 157] |
| $[Fe(dmso)_6]\,[Cl_2Fe(WS_4)]$ | brown | [e] | [e] | ≈2.77 | [158] |
| $(PPh_4)(N(C_7H_7)Me_3)[Cl_2Fe(WS_4)]$ | red | [e] | [e] | 2.808 | [157] |
| $[Fe(dmso)_6]\,[Cl_2Fe(MoOS_3)]$ | dark brown | [e] | [e] | ≈2.78 | [156] |
| $(PPh_4)_2[(S_5)Fe(MoS_4)]$ | dark brown | 2.253 | 2.145 | 2.731 | [153] |
| $(PPh_4)_2[(S_5)Fe(WS_4)]$ | dark red | 2.255 | 2.157 | 2.753 | [153] |
| $(PPh_4)_2[(FeCl_2)_2(MoS_4)]$ | brown | 2.204 | — | 2.775 | [132] |
| $(PPh_4)_2[Co(WS_4)_2]$ | olive green | 2.219 | 2.139 | 2.798 | [142] |
| $(PPh_4)_2[Ni(MoS_4)_2]$ | dark brown | 2.227 | 2.151 | 2.798 | [140] |
| $(AsPh_4)_2[Ni(WS_4)_2]$ | red brown | 2.232 | 2.151 | 2.817 | [121] |
| $(PPh_4)_2[Zn(WS_4)_2]$ | orange | 2.233 | 2.156 | 2.927 | [141] |
| $(PPh_4)_2[Hg(WS_4)_2]$ | orange | 2.246 | 2.173 | 3.088 | [143] |
| $NH_4Cu(MoS_4)$ | red | 2.19 | — | 2.70 | [133] |
| $NH_4Cu(WS_4)$ | bright red | [d] | — | 2.72 [b] | [160] |
| $\{Cu_3MoS_3Cl\}(PPh_3)_3S$ | red | 2.254 | 2.118 | 2.700 | [165] [o] |
| $\{Cu_3MoS_3Cl\}(PPh_3)_3O$ | dark red | 2.259 | 1.769 [c] | 2.718 | [154] [o] |
| $\{Cu_3WS_3Cl\}(PPh_3)_3S$ | yellow | 2.251 | 2.131 | 2.717 | [166] [o] |
| $\{Cu_3WS_3Cl\}(PPh_3)_3O$ | yellow | 2.241 | 1.754 [c] | 2.738 | [164] [o] |
| $\{Cu_4W_2S_6\}(PPh_3)_4O_2$ | orange-red | 2.251 | 1.696 [c] | 2.780 | [172] |
| $\{Cu_4W_2S_6\}(P(C_7H_7)_3)_4O_2$ | orange | 2.248 | 1.70 [c] | 2.784 | [i] |
| $\{Ag_4Mo_2S_6\}(PPh_3)_4S_2$ | violet | 2.227 | 2.108 | 2.975 | [167] [j, n] |
| $\{Ag_4W_2S_6\}(PPh_3)_4S_2$ | orange-red | 2.234 | 2.121 | 2.997 | [167] [k, n] |
| $\{Ag_4W_2S_6\}(PMePh_2)_4S_2$ | orange | 2.225 | 2.131 | 3.002 | [170] |
| $(PMePh_2)_2Au_2(WS_4)$ | [d] | 2.219 | — | 2.840 | [l] |
| $(PPh_3)_3Ag_2(MoS_4)\cdot 0.8\,CH_2Cl_2$ | red | 2.205 | — | 2.945 | [169] [o] |
| $(PPh_3)_3Ag_2(WS_4)\cdot 0.8\,CH_2Cl_2$ | yellow | 2.207 | — | 2.971 | [168] |
| $(PPh_3)_3Cu_2(MoS_4)\cdot 0.8\,CH_2Cl_2$ | red | 2.208 | — | 2.709 | [154] [m] |
| $(PPh_3)_3Cu_2(WS_4)\cdot 0.8\,CH_2Cl_2$ | yellow | 2.214 | — | 2.740 | [169] [o] |
| $(PPh_4)_2[NCCu(MoS_4)]$ | red | 2.245 | 2.163 | 2.630 | [155] |
| $(NMe_4)_2NCCu(MoS_4)\{CuCN\}$ | dark brown | 2.218 | — |  | [174] |
| $(PPh_4)_2[Au_2(WS_4)_2]$ | dark red | [e, h] | 2.136 [h] | 3.169 | [175] |
| $(PPh_4)_2[Au_2(WOS_3)_2]$ | orange | [e, h] | 1.745 [c] | 3.221 | [176] |
| $(PPh_4)_4[Sn_2(WS_4)_4]$ | orange | 2.231 [f]<br>2.199 [g] | 2.154 [f]<br>2.168 [g] |  | [177] |

[a] M = Mo, W; M' = Fe, Co, Ni, Zn, Hg, Cu, Ag, Au, Sn. [b] Corresponding to half the length of the c-axis. [c] M—O distance. [d] Not given. [e] Not determined because of statistical disorder. [f] Values for the bidentate ligands. [g] Values for the tridentate ligands. [h] See Fig. 20. [i] *R. Doherty, C. R. Hubbard, A. D. Mighell, A. R. Siedle, J. Stewart*, Inorg. Chem. *18*, 2991 (1979). [j] *A. Müller, H. Bögge, E. Königer-Ahlborn, W. Hellmann*, ibid. *18*, 2301 (1979). [k] *A. Müller, H. Bögge, E. Königer-Ahlborn*, J. Chem. Soc. Chem. Commun. *1978*, 739. [l] *J. C. Huffmann, R. S. Roth, A. R. Siedle*, J. Am. Chem. Soc. *98*, 4340 (1976). [m] *A. Müller, H. Bögge, U. Schimanski*, Inorg. Chim. Acta *45*, L249 (1980). [n] The structures of the Ag complexes, having the same stoichiometry [167] with the ligands $MOS_3^{2-}$ (M = Mo, W) and $WO_2S_2^{2-}$ have not yet been determined, due to lack of suitable single crystals. [o] *A. Müller, H. Bögge, U. Schimanski, T. K. Hwang*, Inorg. Chim. Acta, in press.

with various coordinations of the central M′ atom. (These have been confirmed by single-crystal structure analyses in the cases of $[Ni(MoS_4)_2]^{2-}$[140], $[Co(WS_4)_2]^{2-}$[142], $[Ni(WS_4)_2]^{2-}$[121], $[Zn(WS_4)_2]^{2-}$[141], and $[Hg(WS_4)_2]^{2-}$[143] (cf. Table 3)).

There are some bis(thiometalato) complexes with different electron populations, for example $[Co(WS_4)_2]^{n-}$ (n = 2, 3, 4) and $[Fe(WS_4)_2]^{n-}$ (n = 2, 3). The Fe complexes can be isolated in crystalline form. That $[Fe(WS_4)_2]^{3-}$ should exist was to be expected, since in a cyclic voltammogram the doubly-negative anion shows a reversible one-electron reduction with only a relatively small negative $E^{I}_{1/2}$ value (Section 5.2)[227b].

The reactions in the system $Fe^{2+}/MS_4^{2-}/H_2O$ (M = Mo, W), which is of bioinorganic interest, are complicated. Whereas $[Fe(WS_4)_2]^{2-}$ (as also *e.g.* $[Co(WS_4)_2]^{2-}$ and other complexes with a double negative charge (Table 2)) can be isolated from aqueous media[144], the corresponding reaction between $Fe^{2+}$ and $MoS_4^{2-}$ according to eq. (i) generally gives variable products whose composition depend on the nature of the precipitation conditions[144, 145] (approximate composition $(PPh_4)_2\{Fe(MoS_4)_2\}$); according to our data[144] these samples do not contain the discrete $[Fe(MoS_4)_2]^{2-}$ ion, however they could not be clearly characterized because of their amorphous state. The Mössbauer spectrum (Section 5.2, Fig. 26[149]) of the frozen solution shows that in the $Fe^{2+}/MoS_4^{2-}/H_2O$ system, the anion $[Fe(MoS_4)_2]^{3-}$ with a triply negative charge is formed[147], which until now could only be obtained from Fe complexes with S-containing ligands and $MoS_4^{2-}$[148] (the UV/VIS spectrum of the solution proves the existence of $MoS_4^{2-}$ in equilibrium). This indicates the high stability of $[Fe(MoS_4)_2]^{3-}$, and demonstrates that sulfur-containing organic ligands are not necessary for the reduction, as was previously assumed[148, 221]. It was also, therefore, possible to isolate the $[Fe(MoS_4)_2]^{3-}$ ion in high yield as the $NMe_4^+$ salt from a solution of $(NH_4)_2MoS_4$ and $FeSO_4 \cdot 7H_2O$ in $CH_3CN/H_2O$ (1:1) (precipiation after filtration and addition of isopropanol)[149]. (The reduced species is also formed by the reaction of a suspension of $Fe(C_2O_4)$ in dimethyl formamide with $MoS_4^{2-}$[149].) While the greater stability of the triply negatively charged compared to the doubly negatively charged complex can be understood on the basis of the MO scheme (Section 5.2), the mechanism of reduction has not been clarified. (In the reaction of $Cu^{II}$ with $MoS_4^{2-}$ or with $WS_4^{2-}$, $Cu^{I}$ complexes are also formed.) This result is also of interest in relation to attempts to prepare FeSMo clusters with low-valence Mo (Section 6), since the one-electron reduction in the above system takes place in the absence of any additional reducing agent.

The tendency of the $MoS_4^{2-}$ ligands to form bridges ("further" coordination occurs easily as a result of the high $Fe \rightarrow MoS_4$ electron delocalization, see Section 5) is illustrated by the reaction[150]:

$$[Cl_2Fe(MoS_4)]^{2-} + \{FeCl_2\} \rightarrow [Cl_2Fe(MoS_4)FeCl_2]^{2-} \qquad (j)^{[150]}$$

In the trinuclear complex, $MoS_4^{2-}$ acts as a doubly bridging ligand (Fig. 15) (and also in the first two complexes of Fig. 18).

Whereas the discrete bis(tetrathiomolybdato) complex of $Fe^{II}$ (formally) is unstable, the following corresponding mixed ligand complexes of the type $[X_2Fe(MS_4)]^{2-}$ (M = Mo, W) have been isolated. They also contain $Fe^{II}$ and a thiometalate ligand (because the lower energy group of orbitals with predominantly d-character is destabilized relative to the corresponding orbitals in pure thiometalato complexes; see Fig. 25 and Section 5.2): $(NEt_4)_2[(PhS)_2Fe(MoS_4)]$[151, 152], $(PPh_4)_2[(S_5)Fe(MoS_4)]$[153], $(PPh_4)_2[(S_5)Fe(WS_4)]$[153], $(PPh_4)(N(C_7H_7)Me_3)[Cl_2Fe(MoS_4)]$[154, 157] (see Fig. 16); $(NEt_4)_2[Cl_2Fe(MoS_4)]$[152], $[Fe(dmso)_6][Cl_2Fe(MoS_4)]$[155], $[Fe(dmso)_6][Cl_2Fe(MoOS_3)]$[156], $(PPh_4)(N(C_7H_7)Me_3)[Cl_2Fe(WS_4)]$[157], and $[Fe(dmso)_6][Cl_2Fe(WS_4)]$[158]. (For the preparation of $(NEt_4)_3[(PhS)_2FeS_2Fe(MoS_4)]$ see [159]). All these compounds (except for the last) have been characterized by single-crystal structure analysis (see Table 3). $MS_4^{2-}$ (M = Mo, W) acts as a bidentate ligand in all these complexes (see Fig. 16). Owing to their high Fe content, the compounds containing $[Fe(dmso)_6]^{2+}$ may be of interest as starting substances for the preparation of MoFeS clusters.

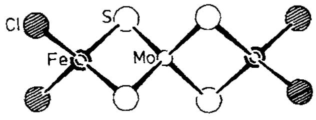


Fig. 15. Structure of $[(Cl_2Fe)_2(MoS_4)]^{2-}$: a complex with a doubly bridging $MoS_4^{2-}$ ligand (see also Fig. 18) [132].

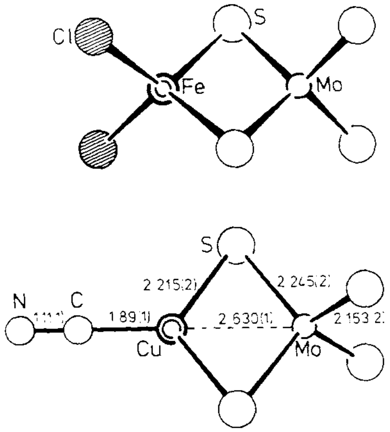


Fig. 16. Structure of $[Cl_2Fe(MoS_4)]^{2-}$ and $[NCCu(MoS_4)]^{2-}$: simple dinuclear complexes with one bidentate $MoS_4^{2-}$ ligand [152, 155, 157].

The reaction of $Cu^{2+}$ with $MS_4^{2-}$ ions (M = Mo, W) leads to the formation of reaction products with polymeric anions, for example $NH_4Cu(MoS_4)$[133] and $NH_4Cu(WS_4)$[160]. In the solid-state structures of these compounds there are chains of $CuS_4$- and $MS_4$-tetrahedra connected *via* the edges. Here, the thiometalate ion acts formally as a doubly bridging ligand (cf. also a further chain-forming complex with $Cu^+$ and $MoS_4^{2-}$ ions in Fig. 17).

$CuX_4$ and $MX_4$ tetrahedra connected *via* the edges are also present in $Cu_3MX_4$[161-163] (M = V, Nb, Ta; X = S, Se) with sulvanite structure.

The "polymerization" of a copper thiometalate system can be inhibited by additional ligands at the Cu atom, such as $PPh_3$ or $CN^-$. In the reaction system $M'^+/MO_{4-n}S_n^{2-}/PR_3$ (M' = Cu, Ag, Au; M = Mo, W; n = 4, 3; $R_3 = Ph_3$, $(C_7H_7)_3$, $MePh_2$) the following types of compounds are formed, which are interesting from the standpoint of structural chemistry, containing doubly, triply, and quasi-quadruply bridging thiometalate ligands:

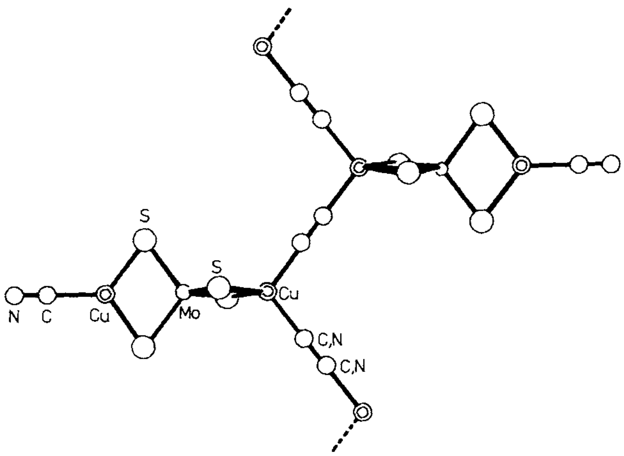


Fig. 17. Structure of the polymeric anion in the compound $(NMe_4)_2NCCu(MoS_4)\{CuCN\}$[174].

a) *Compounds with a central cubic unit* $\{Cu_3MS_3Cl\}(PPh_3)_3X$ *(M = Mo, W; X = S, O):* These have a strongly distorted cube as their central unit (see Figs. 18 and 19). The $MXS_3^{2-}$ ligand here is triply bridging. The coordination polyhedra of the three Cu atoms are not equivalent: while one Cu atom is enclosed in a distorted tetrahedron, in the case of the other two atoms there is a transition to trigonal planar coordination (cf. Table 3).

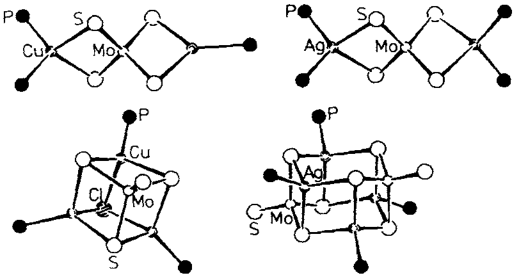


Fig. 18. Examples of multimetal complexes in the system $M'^+/MO_{4-n}S_n^{2-}/PPh_3$ (n = 3, 4; M' = Cu, Ag; M = Mo, W): $(PPh_3)_3Cu_2(MoS_4)$,
$(PPh_3)_4Ag_2(MoS_4)$, $\{Cu_3MoS_3Cl\}(PPh_3)_3S$, and $\{Ag_4Mo_2S_6\}(PPh_3)_4S_2$ (cf. references in Table 3).

b) *Compounds with a novel type of cage structure of composition* $\{M'_4M_2S_6\}(PR_3)_4X_2$ *(M' = Cu, Ag; M = Mo, W; X = S, O; $R_3 = Ph_3$, $(C_7H_7)_3$, $MePh_2$):* The central unit is a new type of cage, formally arising from a fusion of two $MS_2M'_2S$ rings (see Figs. 18 and 19). Here, the $MXS_3^{2-}$ ligand acts as a quasi-quadruple bridge (bonds to all four M' atoms) (see Table 3).

c) *Trinuclear complexes of composition* $(PR_3)_nM'_2(MS_4)$ *(M' = Cu, Ag, Au; M = Mo, W; $R_3 = Ph_3$, $MePh_2$; n = 2, 3, 4):* In these compounds each pair of M' atoms is connected *via* a doubly bridging $MS_4^{2-}$ ligand. The M' atoms each carry one or two $PR_3$ ligands, and hence for n = 4 both atoms are surrounded by distorted tetrahedra, for n = 2 both have almost trigonal planar configurations, and for n = 3 one atom is coordinated tetrahedrally while the other has a trigonal planar environment (see Fig. 18 and Table 3). The structures of the compounds with n = 4 ($(PPh_3)_4Ag_2(WS_4)$[168], $(PPh_3)_4Ag_2(MoS_4)$[155, 169], and $(PMePh_2)_4Ag_2(WS_4)$[170]) have not yet been confirmed by single-crystal structure analyses, but the structure type shown in Figure 18 has been established from spectroscopic investigations ($^{31}P$-NMR[170], IR, Raman, and in particular resonance-Raman spectroscopy[155, 171]).

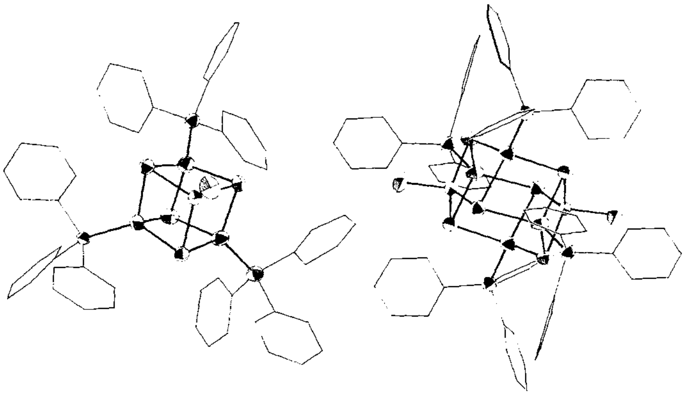


Fig. 19. ORTEP plot of the total molecular structure of $\{Cu_3WS_3Cl\}(PPh_3)_3S$ and $\{Ag_4W_2S_6\}(PPh_3)_4S_2$ with $PPh_3$ ligands (cf. Fig. 18).

In the compounds with cage structures it is worth noting that one thiometalate ligand provides six bonds to Cu or Ag atoms (see Fig. 18 and 19).

Since the compound types a) to c) above have roughly the same tendencies to form, in a given reaction different compounds can easily appear side by side[167, 172, 173]: slight variations of the concentration ratios of the reactants can shift the equilibrium strongly in favor of one of the compounds. For example, if the Cu concentration is reduced, the formation of $\{Cu_4W_2S_6\}(PPh_3)_4O_2$ becomes preferred over that of $\{Cu_3WS_3Cl\}(PPh_3)_3O$[172], as would be expected on the grounds of the different compositions.

In the $Cu^+/MoS_4^{2-}/CN^-/XR_4^+$ system there are also at least two different compounds:
$(PPh_4)_2[NCCu(MoS_4)]$[214] (Fig. 16) and
$(NMe_4)_2NCCu(MoS_4)\{CuCN\}$ (Fig. 17). The latter is worth noting, since here the complex $[NCCuMoS_4]^{2-}$ is coordinated to the Cu atoms of an infinite zigzag CuCN chain[174] (Fig. 17). (It is also interesting that $MoS_4^{2-}$ can be coordinated to a CuCN molecule as well as to a CuCN chain).

Thiometalate ligands are usually coordinated *via* sulfur to *soft cations* such as $Cu^+$, $Ag^+$, and $Au^+$. Thus, it has not yet been possible to prepare any compound of the structural type c) with $MOS_3^{2-}$ ligands. Following this principle, using oxotrithiometalates, we have deliberately prepared certain compounds with a cubane-like structure[164].

Up to now the only non-polymeric thiotungstates with elements of group Ib *without* additional ligands that have been isolated are $[Au_2(WS_4)_2]^{2-}$[175] and $[Au_2(WOS_3)_2]^{2-}$[176], *i.e.* pure metal-sulfur ring systems without organic ligands. In each case the anions consist of two Au atoms bridged by two thiotungstate ligands (see Fig. 20).

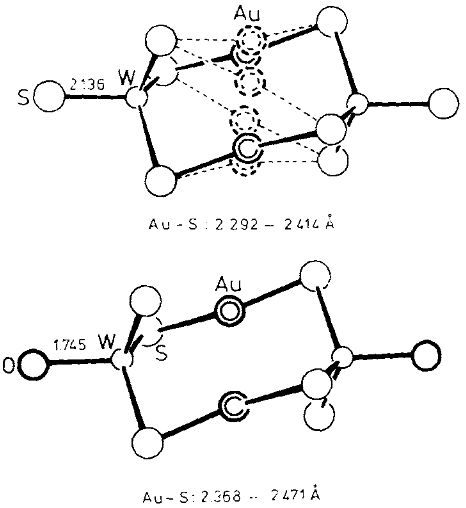


Fig. 20. Structure of $[Au_2(WS_4)_2]^{2-}$ and $[Au_2(WOS_3)_2]^{2-}$. In both ions there is a statistical disorder with the Au atoms distributed over three positions [175, 176].

Compounds with thiometalate ligands involving elements of the 4th main group are also known. In the novel polynuclear complexes of the type $[M'_2(MS_4)_4]^{4-}$ ($M' = Sn$, Pb; $M = Mo$, W) there are nonequivalent, bridging, and terminal bidentate ligands (Fig. 21). Corresponding anions are very probably present in the compounds $(PPh_4)_4[Pb_2(MOS_3)_4]$[177, 178].

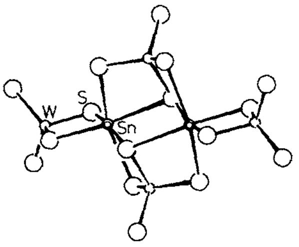


Fig. 21. Structure of $[Sn_2(WS_4)_4]^{4-}$ [177].

Only one[226] *selenometalato complex*, namely $[Zn(WSe_4)_2]^{2-}$, has so far been reported[134, 179].

The bis(thiometalato) complexes of Co and particularly of Fe show a high affinity for the coordination of ligands[144, 178, 180]. ($[Fe(WS_4)_2]^{2-}$ *e.g.* to $N_3^-$ or $NCS^-$, with dmf it forms $[Fe(dmf)_2(WS_4)_2]^{2-}$[178, 180], whose structure, established from vibrational and Mössbauer spectra, is shown in Figure 14). The weak splitting of the bands due to the $\nu(WS)$ stretching modes is a proof that the Fe—$WS_4$ interaction is weaker than in the other complexes in Fig. 14 (no characteristic $\nu(WS_{term})$ and $\nu(WS_{br})$ vibrations; Table 2). The orange $[Fe(H_2O)_x(WS_4)_2]^{2-}$ may be present in aqueous solution. $[Fe(WS_4)_2]^{2-}$ and $[Co(WS_4)_2]^{2-}$ react unusually rapidly with NO to give the mononitrosyl complexes $[M'(NO)(WS_4)_2]^{2-}$[144, 181]. Their $PPh_4^+$ salts are isostructural[181].

## 5. Spectroscopic Investigations and Chemical Bonding in Thiometalato Complexes

Spectroscopic studies were carried out, both to determine the molecular structure, and to investigate the interesting electronic properties (see Table 2).

### 5.1. Vibrational Spectra and Molecular Structure

The structures of complexes of the type $[M'(MO_{4-n}S_n)_2]^{2-}$ have been determined by IR spectroscopic investigations[117, 134–139]. The isotope-substitution technique ($^{54}Fe/^{56}Fe$, $^{58}Ni/^{62}Ni$, $^{63}Cu/^{65}Cu$, $^{64}Zn/^{68}Zn$, $^{92}Mo/^{100}Mo$) has made it possible to produce detailed information of the spectra of the complexes $[Ni(MoS_4)_2]^{2-}$[182], $[Ni(WS_4)_2]^{2-}$[81, 183], $[Ni(WO_2S_2)_2]^{2-}$[180, 184], $[Zn(MoS_4)_2]^{2-}$[81, 185], $[Zn(WS_4)_2]^{2-}$[141], $[NCCu(MoS_4)]^{2-}$[186a], and $[Cl_2Fe(MoS_4)]^{2-}$[186a], and to show that the $\nu(MS_{br})$ and especially the $\nu(MS_{term})$ vibrations are relatively characteristic[182, 183, 185, 186] ($\nu_{as,term}$ is the most, and $\nu_{s,br}$ the least characteristic vibration). Thus, the presence of corresponding bonds can easily be detected from the vibrational spectra (see Fig. 22).

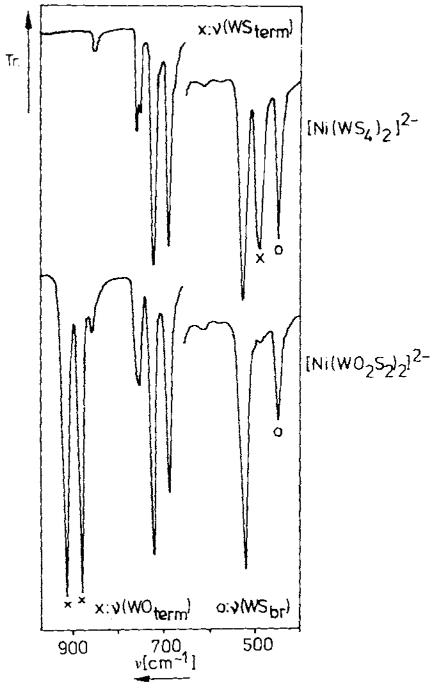


Fig. 22. IR spectra of $(PPh_4)_2[Ni(WS_4)_2]$ and $(PPh_4)_2[Ni(WO_2S_2)_2]$ in the region of the WO and WS stretching vibrations (demonstrating the bidentate nature of the ligands and the S-coordination).

Since the ligand internal transitions in thiomolybdato complexes correspond roughly to those of free $MoS_4^{2-}$, one can obtain resonance Raman spectra[150, 155] also from nearly all the complexes in Tables 2 and 3 (see also [193a]). In these spectra the lines due to the totally symmetric vibrations of the $MoS_4$ chromophore (usually $\nu(MoS)$ stretching vibrations) are significantly intensified. The resonance Raman effect is a sensitive probe for the detection of $MoS_4^{2-}$ ligands, for example at Cu or Fe centers in biological systems (see Section 6). Among other things, significant distinctions can be made between bridging and bidentate ligands[155]. This method offers a unique and sensitive probe for doubly bridging ligands (Fig. 6).

### 5.2. Electronic Structure and Stability

Various physical measurements have demonstrated that in thiometalato complexes with central atoms possessing open d-shells, there are strong metal-ligand interactions, *i.e. delocalized molecular orbitals*. Thus, the assignment of the electronic-transition bands (Table 2) for such systems can only be approximate. The electronic interactions in $M'S_2M$, systems is interesting due to its relevance in the bioinorganic field (Section 6).

The known complexes of the type $[M'(MO_{4-n}S_n)_2]^{2-}$ ($M'$ = Fe, Co, Ni, Pd, Pt) show characteristic absorption bands whose positions are only roughly comparable to those in free thiometalates (*i.e.* $L \rightarrow L^*$ assignment). The reduction of the symmetry due to complex formation often leads to splitting of the bands, whereas the total intensity remains virtually unchanged. However, because of the strong M—L interactions, the spectra in the region of the ligand internal transitions depend markedly on the nature of the central atom (*i.e.* the influence is quite noticeable). For example, there is a characteristic splitting of the $\nu_1$ band of $WS_4^{2-}$ (Table 2) in the Ni complex. In contrast, the longest-wavelength band in $[Ni(MoS_4)_2]^{2-}$ is strongly shifted in the direction of longer wavelengths. This demonstrates different interactions, which should be particularly large in the $MoS_4^{2-}$ complex.

According to EH-SCCC-MO calculations, strong $3d_{xz}$(Ni)- and $3d_{yz}$(Ni)-$\pi$ interactions with the ligand orbitals occur in the $[Ni(MS_4)_2]^{2-}$ complexes (M = Mo, W)[126]. In the trimetallic complexes with square-planar coordination of the central atom, the coordination geometry gives rise to a considerable perturbation of the electronic structure of the ligands. Since the opposite S bridge atoms of the two thiometalate ligands are separated by only *ca.* 2.8 Å, the energies of the occupied nonbonding 3p(S) ligand orbitals are in part markedly increased. Particularly in the $MoS_4^{2-}$ complex, the Ni-ligand interaction is so strong that it can no longer be accurately formulated as a $Ni^{II}$—$Mo^{VI}$ complex, and one must think in terms of a formal reduction of the Ni center and a partial disulfide bond between the bridging S atoms.

The spectra of complexes with $d^{10}$ central atoms[222] show essentially ligand internal transitions corresponding to those of the free thiometalate ions. It is worth noting that, for example in $[NCCu(MoS_4)]^{2-}$ and $[Zn(MoS_4)_2]^{2-}$, of the three longest wavelength bands the first ($\nu_1$) and the third ($\nu_3$) are clearly changed in their structure by complex formation, while the second ($\nu_2$) is practically unaltered in its position, intensity, and half-width (see Fig. 23)[186b]. (The fact that this is not true for $MoS_4^{2-}$ complexes with open d shells, for example those of Fe and Ni, can be explained in terms of MO theory[126]). MO calculations show that on complex formation the $t_1$ orbitals of the $MS_4^{2-}$ ligands, as expected, are much more strongly disturbed than the $3t_2$, 2e, and $4t_2$ MO's[126]. It follows that in the transition corresponding to the $\nu_2$ band in $MoS_4^{2-}$, the $t_1$ orbital is not involved; this lends support to the assignments[90] $\nu_2 \triangleq 3t_2 \rightarrow 2e$ and $\nu_3 \triangleq t_1 \rightarrow 4t_2$[186b]. This probably constitutes an essential contribution to the old assignment problem of the electron transfer transitions of tetrahedral transition-metal chalcogenometalates[44]. It is also interesting to note that the type of perturbation of the $\nu_2$ band of complexes with open-shell metal ions reflects the type of $\pi$-M′-L interaction.

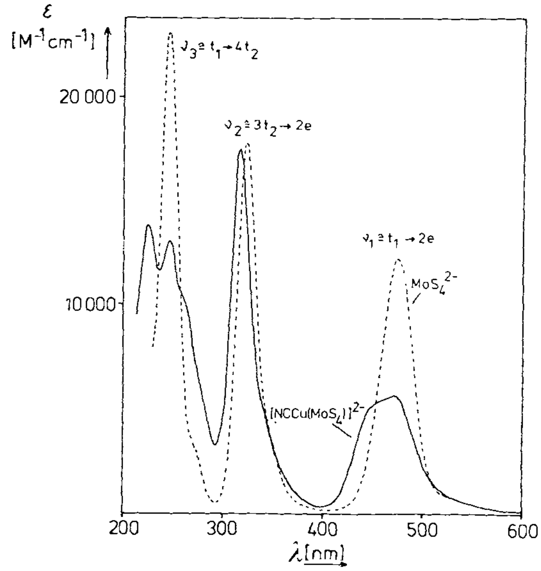


Fig. 23. Influence of a coordination center on the longest-wavelength bands of $MoS_4^{2-}$; electronic spectra of $(NMe_4)_2[NCCu(MoS_4)]$ and $(NMe_4)_2MoS_4$ (in acetonitrile).

The Fe and Co complexes of the above type show a remarkable band of high intensity ($\varepsilon \approx 10^3 - 10^4$ [$M^{-1}$ $cm^{-1}$]) in the NIR/VIS region (Table 2, Fig. 24), which is not present in classical complexes without strong metal-ligand interactions. An assignment can be achieved on the grounds of empirical relations and from MO calculations. For analogous complexes, the transition energy decreases as follows[187]:

Fe > Co complex ($X_{opt}$(Fe) < $X_{opt}$(Co))
Tungstato > molybdato complexes (k)
Dithiometalato > trithiometalato > tetrathiometalato complexes.

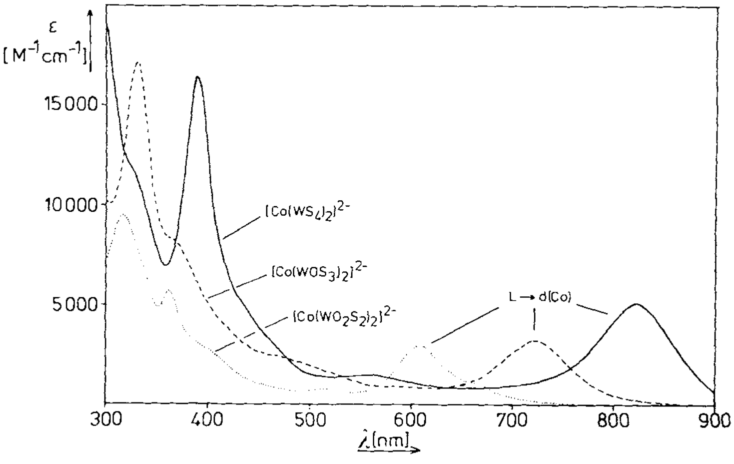


Fig. 24. Electronic absorption spectra of the complexes $[Co(WO_{4-n}S_n)_2]^{2-}$ in $CH_2Cl_2$ ($PPh_4^+$ salts).

Furthermore, there is a linear relationship between the transition energies of the $[Co(MoO_{4-n}S_n)_2]^{2-}$ complexes and those of the corresponding $[Co(WO_{4-n}S_n)_2]^{2-}$ complexes. These findings indicate that the intense bands should be assigned to charge-transfer transitions of the type L→d(M').

This assignment is supported by EH-SCCC-MO calculations on corresponding Co and Fe complexes[126], which lead to the qualitative MO scheme shown in Figure 25[126, 154, 180, 187]. (The problem of the sequence of the MO's in these complicated systems is evident: however, the MO scheme given here can provide answers to certain interesting questions of stability (Section 4 and below)). In this scheme the following classes of MO's with approximately similar energies are included: 1. Nonbonding L—MO's with a predominantly 3p(S) character, 2. Closed or open shell MO's of predominantly 3d(M) character (corresponding to the e and $t_2$ orbitals in a crystal field theory description). 3. Unoccupied L*-MO's of predominantly 4d(Mo) or 5d(W) character (corresponding to the 2e-MO's of the free thiometalate ions[44, 117]). Charge-transfer transitions of the type d(M')→L* should probably be expected at higher energies, possibly in the region of the first ligand internal transitions. (However, as indicated in Table 2, the band assignment is only approximate, because of the strong central-atom ligand interaction; this also applies to the assignments to d→d transitions given in Table 2).

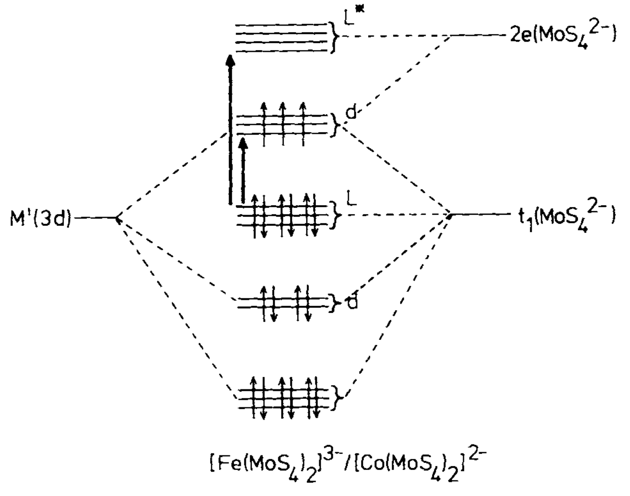


Fig. 25. Qualitative MO scheme of the isoelectronic complexes $[Fe(MoS_4)_2]^{3-}$ and $[Co(MoS_4)_2]^{2-}$, and analogous bis(thiometalato) complexes of Fe and Co with half-occupied and completely occupied "d levels", resp. The braces link together MO's of approximately the same energy; for the probable sequence of the MO's in other Fe and Co complexes, see text.

The remarkable properties of thiometalate ligands can also be demonstrated by calculations: the MO coefficients of the 3d(M')-type MO's show a high electron delocalization (which increases with increasing sulfur content of the ligand), and hence a strong π-acceptor ability (which can be explained by the low-lying unoccupied L* orbitals). Since the 3d(M') level is at an energy comparable to that of the nonbonding MO's of the ligands ($t_1$ of the free $MS_4^{2-}$ ions[44, 117]), it also follows that there is a remarkable M'—L-σ interaction. The overlap integrals between the 3d(M') and 4d(M), or 5d(M) functions show that at an M'—M separation of *ca.* 2.8 Å direct metal-metal interactions should also be taken into consideration.

The calculations also show that due to complex formation the electron density on the M' (M' = Fe, Co) center is diminished, while that on the M center is increased, relative to the free $MS_4^{2-}$. The electron density on the terminal S atoms is hardly altered by electron delocalization compared to that of the free $MoS_4^{2-}$, especially in Fe—Mo complexes. This explains the ability of this anion to function as a bridging ligand (*e.g.* in $[Cl_2Fe(MoS_4)FeCl_2]^{2-}$).

Delocalized (occupied) MO's over the metal centers M' and M occur particularly clearly in complexes with $M'S_2MS_2M'$ units (*e.g.* M' = Fe, and notably also when M' = Cu with a closed d shell[126]; *cf.* the resonance Raman spectrum results mentioned below).

As expected, the electronic spectra of complexes of the type $[X_2Fe(MoS_4)]^{2-}$ (X = Cl[152, 154, 188], PhS[151, 152], *p*-$CH_3C_6H_4S$[152], $1/2\,S_5$[153], where the M'-L interaction is smaller than in the trimetallic species, are very similar. The same is true of the $[X_2Fe(WS_4)]^{2-}$ complexes. For example, the Fe→$WS_4^{2-}$ electron delocalization is greater in $[Fe(WS_4)_2]^{2-}$ than in $[Cl_2Fe(WS_4)]^{2-}$. In the first of these complexes, this is responsible for a lower energy both for the longest-wavelength ligand internal transition and for the L→d(Fe) charge-transfer transition (Table 2).

The stability of the complexes[180] $[Fe(MS_4)_2]^{n-}$ and $[Co(MS_4)_2]^{2-}$ (M = Mo, W), and the special behavior of the Fe species can be explained as follows: the low-energy MO's of the 3d(M') type in the Co complexes (these are occupied here, in contrast to those of the Fe complexes with n = 2) and in $[Fe(MoS_4)_2]^{2-}$ are situated at a lower energy, and in the case of $[Fe(WS_4)_2]^{2-}$ at about the same energy, as the nonbonding L orbital (Fig. 25). Thus, the unstable, discrete $[Fe(MoS_4)_2]^{2-}$ is stabilized by taking up one electron to form $[Fe(MoS_4)_2]^{3-}$, and $[Fe(WS_4)_2]^{n-}$ exists with n = 2 and 3.

The $^{57}$Fe Mössbauer spectra of complexes of the type $[X_2Fe(MS_4)]^{2-}$ show unusually low values for the isomer shift (IS) of the order of 0.5 mm·s$^{-1}$[152-154, 188] (all values relative to α-Fe at room temperature). This also demonstrates the strong electron delocalization Fe→$MS_4^{2-}$. As expected, this delocalization is greater in the Mo complexes than in the analogous W complexes[188]. The effect of a thiometalate ligand is clearly illustrated by the fall of the IS values in the series $[Cl_2FeCl_2]^{2-}$ (IS = 0.76 mm·s$^{-1}$[189a]), $[Cl_2Fe(WS_4)]^{2-}$ (IS = 0.52 mm·s$^{-1}$[188]), $[(WS_4)Fe(WS_4)]^{2-}$ (IS = 0.43 mm·s$^{-1}$[189b]). The Mössbauer spectrum of $[Fe(MoS_4)_2]^{3-}$, with an isomer shift of 0.38 mm·s$^{-1}$, shows that the electron density on the Fe center is much lower than would be expected for a formal oxidation state of +1[148], and is almost identical to that of a frozen solution of $Fe^{2+}$ and $MoS_4^{2-}$ in $H_2O$ (Fig. 26, explanation in Section 4).

The $^{197}$Au Mössbauer spectrum of $[Au_2(WS_4)_2]^{2-}$[175] can be interpreted as indicating that for Au$^{I}$, with a closed d shell, the π-acceptor ability of the $WS_4^{2-}$ ligand does not carry much weight.

The ESR spectrum of $[Fe(MoS_4)_2]^{3-}$ is similar to that of the MoFe cofactor of nitrogenase[148], and that of

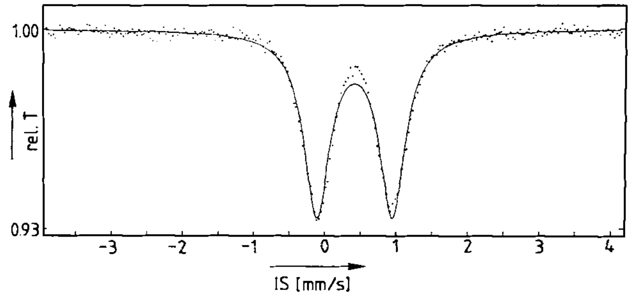


Fig. 26. $^{57}$Fe Mössbauer spectrum of a frozen solution of $Fe^{2+}$ and $MoS_4^{2-}$ in water [146] (1.2 mmol $(NH_4)_2MoS_4$, 0.5 mmol $FeSO_4\cdot 7H_2O$, 10 mL $H_2O$, 77 K. IS = 0.423 ± 0.035 mm/s; QS = 1.060 ± 0.070 mm/s).

$[Co(WS_4)_2]^{2-}$ in $(PPh_4)_2[Zn(WS_4)_2]$ gives a $g_\perp$ value of *ca.* 4.1[190].

Various complexes of the type $[M'(MO_{4-n}S_n)_2]^{2-}$ (M' = Fe, Co, Ni, Pd) and also $[(FeCl_2)_2MoS_4]^{2-}$[180] show a reversible redox behavior[135, 180, 187, 191, 192a]. According to cyclic voltammetric investigations, these complexes can be reduced reversibly in a one-electron process (I), and some also in a second one-electron process (II) (see Fig. 27):

$$[M'(MO_{4-n}S_n)_2]^{2-} \overset{\text{I}}{\underset{-e}{\overset{+e}{\rightleftharpoons}}} [M'(MO_{4-n}S_n)_2]^{3-} \overset{\text{II}}{\underset{-e}{\overset{+e}{\rightleftharpoons}}} [M'(MO_{4-n}S_n)_2]^{4-} \qquad (I)$$

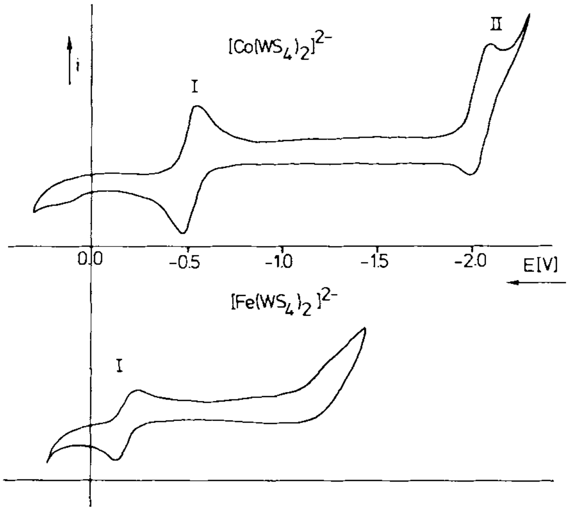


Fig. 27. Cyclic voltammograms of $[Co(WS_4)_2]^{2-}$ [187] ($NEt_4^+$ salt in dimethyl formamide/$NEt_4I$) and $[Fe(WS_4)_2]^{2-}$ [180] ($PPh_4^+$ salts in $CH_3CN/NPr_4(PF_6)$) versus Ag/AgCl/LiCl(sat)EtOH electrode.

(The second process is often only quasi-reversible or irreversible.) Since in the Fe and Co complexes the half-step potential $E^I_{1/2}$ is significantly ligand-dependent, it is likely that the additional electrons are taken up by levels that besides a 3d(M') character also exhibit a ligand component. In the oxothiomolybdato and oxothiotungstato Co complexes, the energy of the L→d charge-transfer transition (see (k)) increases approximately linearly with increasing $|E^I_{1/2}|$. (Due to S→O substitution, the highest energy occupied ligand orbitals are stabilized, and the incompletely occupied orbitals with 3d(Co) character are destabilized because of decreasing delocalization). In the Ni complexes, the corresponding half-wave potentials are somewhat less L-dependent (however, the second reduction step is more markedly ligand-dependent than the first). In this case the first reduction occurs predominantly in the chromophore $NiS_4$, the charge density on the S atoms also being increased (leading to a reduction of the partial disulfide character; see MO calculation results, above).

Correspondingly, $[Fe(MoS_4)_2]^{3-}$ shows a single, reversible reduction[148] which only formally corresponds to the $Fe^I \rightarrow Fe^0$ transition.

These experimental findings also illustrate the marked electron delocalization $M' \rightarrow MO_{4-n}S_n^{2-}$ (M' = Fe, Co), since the stabilization of the formal 0 and +1 oxidation states of the metals M' can only be explained by pronounced π-acceptor properties of the thiometalato ligands.

Resonance Raman spectroscopy allows, for example, an investigation of the kind of bonding in complexes. Whereas in the Raman spectra of tetrathiometalato complexes ($[M'(WS_4)_2]^{2-}$ with M' = Pt, Zn in Fig. 28), the intensities $I_R$ of the $\nu$(MS) bands are basically given by

$$I_R[\nu(MS_{term})] > I_R[\nu(MS_{br})]$$

(reason: higher π-bond-order in $MS_{term}$), the preresonance and resonance Raman spectra can exhibit clear deviations from this rule. (In the interpretation of the spectra it should be borne in mind that $\nu(MS_{term})$ vibrations are more characteristic than $\nu(MS_{br})$, *e.g.* $\nu_s(MS_{br})$ contains a clear $\nu_s(MS_{term})$ component[186a]). The preliminary results will be briefly summarized here[192b].

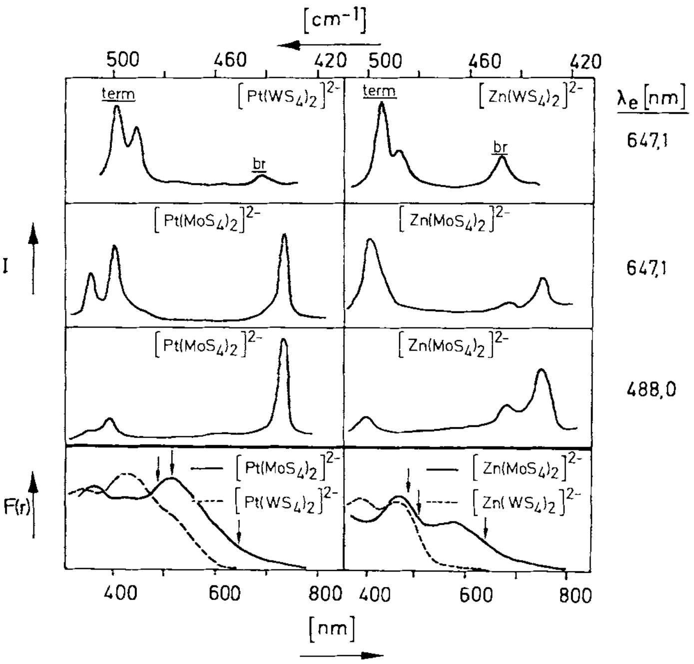


Fig. 28. Raman-, pre-resonance, and resonance Raman spectra (the latter without the overtone region) and reflectance electronic spectra of the $PPh_4^+$ salts of $[M'(MS_4)_2]^{2-}$ complexes (term = $\nu(MS_{term})$, br = $\nu(MS_{br})$).

If an excitation line within the shorter-wavelength band of the $\nu_1$ doublet in the case of $[Zn(MoS_4)_2]^{2-}$ is used, or in the case of $[Ni(MoS_4)_2]^{2-}$ and $[Pt(MoS_4)_2]^{2-}$ within the longest-wavelength bands or their tails (or with the 514.5 nm line; not shown in Fig. 28) an altered intensity relationship will be observed. In contrast, if a line is used within the tail region of the low-energy band of the $\nu_1$ doublet of $[Zn(MS_4)_2]^{2-}$ (M = Mo, W), the intensity relationship given above will be found. This indicates that in the Zn complexes the bands of the doublet can be roughly assigned to transitions in the two chromophores $MS_2$(term) and $MS_2$(br), respectively. Measurements of an excitation profile may contribute toward a final clarification. In $[Ni(MoS_4)_2]^{2-}$ and $[Pt(MoS_4)_2]^{2-}$ it is not possible to distinguish between the corresponding chromophores. The electronic transitions responsible for the resonance Raman effect observed here should, however, be localized mainly in the central $MoS_2M'S_2Mo$ portion[192b]. The resonance Raman spectrum of $[Pt(MoS_4)_2]^{2-}$ (488.0 nm) also contains intensified bands of the following symmetric vibrations: $n\nu(MoS_{br})$, $\nu(PtS)$, $\nu(MoS_{br})+\nu(MoS_{term})$, and $\nu(MoS_{br})+\nu(PtS)$[192b], again indicating the presence of a strongly delocalized bonding system.

The occurrence of intercombination bands of $\nu$(CuS) with $n\nu_s$(MoS) in Cu complexes with bridging $MoS_4^{2-}$ ligands demonstrates that delocalized MO's are present in the $Cu^IS_2MoS_2Cu^I$ fragment itself, as confirmed by the MO calculation (see above) (Fig. 6)[155, 192b].

Magnetic measurements have mainly been used to clarify the structures of the Ni and Co complexes. The isolated Ni complexes are diamagnetic, as would be expected for pseudo-square-planar coordinated $Ni^{II}$. The magnetic moments of the Co complex are essentially closer to spin-only values than to values of "typical" compounds with a tetrahedral $CoS_4$ chromophore[135, 180, 187], because of the strong electron delocalization $M'\rightarrow MO_{4-n}S_n^{2-}$. This behavior is still more clearly expressed in $[Fe(MoS_4)_2]^{3-}$[148].

## 6. The Significance of Thiometalates, and Especially of $MoS_4^{2-}$ for Bioinorganic Problems

### 6.1. Relevance to the Nitrogenase Problem

Sulfur-containing ligands play a dominant part in all Mo enzymes[97a, 97b, 193a], and this is particularly true for the nitrogenases, in which the Mo atom is probably surrounded only by S ligands[97a]. This enzyme is responsible for the fixation of atmospheric nitrogen, which apart from photosynthesis is the most important elementary process for life on Earth. With the help of this enzyme various microorganisms reduce nitrogen to ammonia, more or less in accordance with the following scheme:

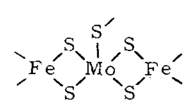
$$\{\text{Fe-protein[MgATP]MoFe-protein}\} \rightarrow \{\text{Fe-protein}_{ox}[\text{MgADP} + P_i]\text{MoFe-protein}_{red}\}$$
$$N_2 + 8e^- + 8H^+ \rightarrow 2NH_3 + H_2$$

As early as 1930 *Bortels*[97c] recognized that *Azotobacter* could not fix $N_2$ in the absence of Mo. However, the exact biochemical significance of the molybdenum is not known, though in recent years important information has been accumulated which is relevant to the subject of this review[216, 217].

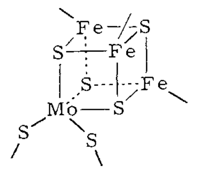
Nitrogenase consists of two separate proteins, an MoFe protein (the reaction carrier) and an Fe protein (the electron carrier)[97d, 193b]. The latter is a dimer with identical subunits and a molecular weight of about 60000. Each subunit comprises a 4Fe—4S cluster[97d, 193b]. The MoFe protein, with a molecular weight of *ca.* 220000, is a tetramer with two pairs of different subunits (with 2 Mo, *ca.* 32—33 Fe, and 27—32 acid-labile S atoms per tetramer)[97d] and was obtained in crystalline form from *A. vinelandii*[194]. The following additional facts seem to be of key importance for the elucidation of the active center. *Shah* and *Brill*[195] were able to isolate a low-molecular, *N*-methyl formamide-soluble MoFe cofactor (MoFe-co) with Fe : Mo : S ≈ 8 : 1 : 6, from MoFe protein (obtained from various microorganism) (or, according to more recent work, about 7 : 1 : 4[216, 217], which on the basis of ESR[198] and EXAFS studies[196, 197] can be regarded as the active center of the protein[198]. This is confirmed by the fact that the MoFe-co is able to reactivate the denaturated MoFe protein, and catalyzes the reduction of acetylene to ethylene[199]. About 50% of the iron content of the nitrogenase (and all of the Mo) is contained in MoFe-co, and probably most of the rest in the 4Fe—4S clusters.

On the basis of EXAFS data, *Cramer et al.*[196, 197] proposed the following models for the surroundings of the Mo atoms (3—4 shorter Mo—S distances of about 2.36 Å, 2—3 Fe atoms at 2.72 Å); however, the nature of the short range order of the Mo surroundings has not yet been clarified[216, 217]:

(1)



(2)

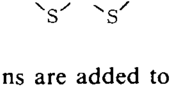


Furthermore, *Zumft*[200] was able to show that $MoS_4^{2-}$ is obtained, among other products, when the protein undergoes acid-base hydrolysis.

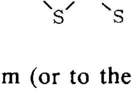
Some groups are now attempting to synthesize MoFeS clusters (and, because of the Mo—W antagonism, WFeS clusters as well) with structures similar to that of MoFe-co, and if possible to use them for the reactivation of the denaturated protein. In all the methods of synthesis published so far, the $MoS_4^{2-}$ ion has been used as the starting material. However, in principle it is also possible to use other Mo—S compounds, such as $[Mo(SR)_4]$[220].

Fe complexes in which the $MS_4^{2-}$ ligand (M = Mo, W) is intact (*e.g.* $[Fe(WS_4)_2]^{2-}$) were prepared for the first time by *Müller et al.*, and later by *Averill et al.*, *Coucouvanis et al.*, and *Newton et al.* (see Section 4 and [144]). These compounds were regarded as ***precursors*** for MoFe-co[97a]. Particular attention should be paid to the unit *(3)*, since it can be obtained from complexes with the moiety *(4)* (see Section 4).

(3)



(4)



When electrons are added to the system (or to the Mo atom) the coordination number of Mo can increase. Thus, in the reaction system $MoS_4^{2-}/3$—3.5 $FeCl_3/9$—12 NaSR in methanol the double-cubane-cluster anions, are formed[201] $[(MoFe_3S_4)_2S(SR)_8]^{3-}$ (type 1), $[(MoFe_3S_4)_2(SR)_9]^{3-}$ (type 2), $[(MoFe_3S_4)_2Fe(SR)_{12}]^{3-}$ (type 3), and $[(MoFe_3S_4)_2Fe(SR)_{12}]^{4-}$ (type 4), which can be isolated in the form of the quaternary ammonium salts (see Fig. 29). (The W analogs of various compounds have also been obtained[201l]). The EXAFS spectrum of (1) agrees quite well with that of the MoFe protein obtained from *C. pasteurianum*[201a]. The clusters can be reversibly reduced in several one-electron steps. In all the species, $MoFe_3S_4$ clusters are connected in various ways. On the basis of $^{57}Fe$ isomer shifts, the following formal electronic descriptions of the central clusters have been given: $[Mo^{4+}Fe_2^{3+}Fe^{2+}S_4]^{4+}$ + $[Mo^{3+}Fe_2^{3+}Fe^{2+}S_4]^{3+}$ (for type 1), and $2[Mo^{3+}Fe_2^{3+}Fe^{2+}S_4]^{3+}$ for types 2, 3, and 4[201].

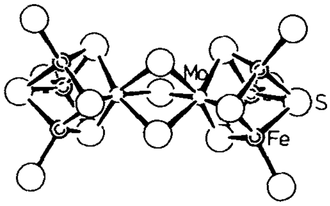


Fig. 29. The skeleton of $[(RS)_3Fe_3MoS_4(\mu\text{-}SR_3)Fe_3MoS_4(SR)_3]^{3-}$.

The reduction of the $Mo^{VI}$ in $MoS_4^{2-}$ probably takes place both by reaction with the nucleophile $SR^-$ and by an intramolecular reaction [according to Section 2.5; reaction type (a), (c), or (d)]. In this connection it is worth noting that S-containing ligands can reduce $Mo^{VI}$ (*e.g.* $(S_2)^{2-}$ reduces $Mo^{VI}$ to $Mo^V$ and $Mo^{IV}$ (Section 2.1)).

In future, an attempt must be made to obtain compounds in which the valence state of the Mo lies between that in the cluster with double-cubane structure and that in the thiomolybdato complexes, and which contain coordinatively unsaturated Mo centers, if it is assumed that $N_2$ is coordinated to Mo in the enzyme.)[218,219]

A recent report deals with non-nitrogenase-like MoFeS proteins[202], isolated from *Desulphovibrio* bacteria. Interestingly enough, the electronic spectrum of such a protein resembles that of complexes of the type $[X_2Fe(MoS_4)]^{2-}$[97a].

### 6.2. Cu—Mo Antagonism

Ruminants pastured on soils rich in Mo show symptoms of disorders (anemia, diarrhea, and retarded growth) that can be traced to a deficiency of Cu[203-209,224] (*"secondary trace-element deficiency"*[207]). In many parts of the world, this deficiency causes a substantial loss of livestock[207], which can only be remedied by a greater intake of Cu. The following facts are known about this Cu—Mo antagonism:

Table 4: Tissue residues of Cu and Mo in rats after various doses of $CuCl_2$ and $(NH_4)_2MoS_4$ [205] [a].

| *Influence of various doses of Cu in food on the residual dietary Mo (6 mg Mo/kg feed)* | | | |
|---|---|---|---|
| Dietary Cu [mg/kg] | 3 | 8 | 16 |
| Carcass retention of $^{99}Mo$ [fraction of oral uptake] | 0.40±0.02 | 0.22±0.01 | 0.15±0.02 |
| Total liver Mo [mg/kg dry weight] | 1.2 | 0.8 | 0.4 |
| *Influence of various doses of Mo (as $MoS_4^{2-}$) in food on the residual dietary Cu (3 mg Cu/kg feed)* | | | |
| Dietary Mo [mg/kg] | 0 | 12 | |
| Carcass retention of $^{64}Cu$ [fraction of oral uptake] | 0.34±0.02 | 0.04±0.01 | |
| Total liver Cu [mg/kg dry weight] | 23 | 12 | |

[a] The rats were given either $^{99}Mo$ (as $(NH_4)_2{}^{99}MoS_4$) or $^{64}Cu$ (as $^{64}CuCl_2$), after having been fed for at least a week on a Cu- or Mo-enriched semisynthetic diet.

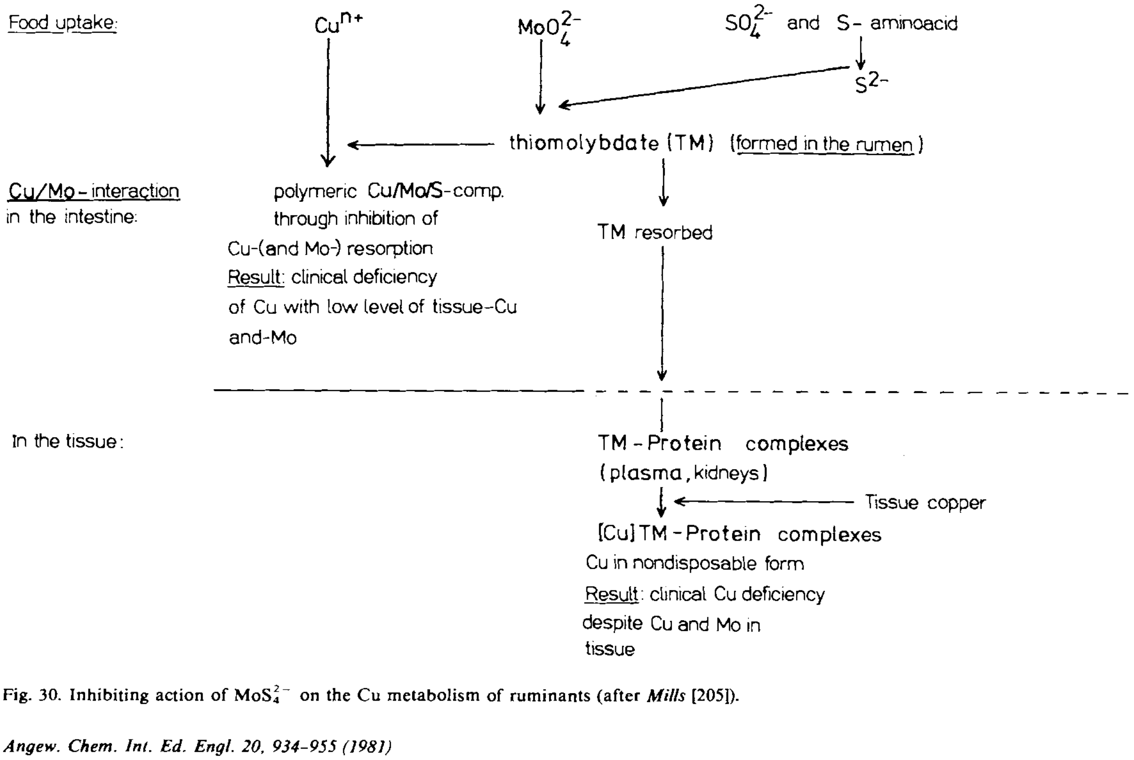


Fig. 30. Inhibiting action of $MoS_4^{2-}$ on the Cu metabolism of ruminants (after *Mills* [205]).

$MoS_4^{2-}$, which is believed to be the strongest Cu antagonist[207], is formed in tests *in vitro*, under physiological conditions, in a medium consisting of rumen contents (18 h at 39 °C) from ammonium molybdate and ammonium sulfate, or organic sulfur compounds[208]. The antagonistic interaction between $Cu^{n+}$ and $MoS_4^{2-}$ has been impressively demonstrated by determining the tissue levels of Cu and Mo in rats given various amounts of radioactive $^{64}CuCl_2$ or $(NH_4)_2{}^{99}MoS_4$ in their food[205] (see Table 4). Since these investigations show that Mo interferes with the Cu metabolism both before and after the resorption (Fig. 30), it is difficult to explain the interaction. According to *Mills*, the latter is due to the formation of a "[Cu]TM-protein complex" (TM = thiomolybdate)[205], which makes the Cu unavailable for metabolic purposes. This is supported by the observation that clinical signs of a Cu deficiency are observed in animals after resorption of $MoS_4^{2-}$, in spite of a high plasma Cu level. Thiomolybdato complexes of Cu are therefore, of interest (Section 4).

*We wish to thank the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie for their financial support.*

Received: Mai 4, 1981 [A 389 IE]
German version: Angew. Chem. 93, 957, 1981

---

[1] *J. J. Berzelius*, Poggendorffs Ann. Phys. Chem. *7*, 262 (1826); *8*, 269 (1826).

[2] *A. C. Ranade, A. Müller, E. Diemann*, Z. Anorg. Allg. Chem. *373*, 258 (1970).

[3] *E. Diemann, A. Müller*, Spectrochim. Acta *A 26*, 215 (1970).

[4] *J. Locke*, Am. Chem. J. *20*, 373 (1898).

[5] *A. Müller, E. Diemann*, Chem. Phys. Lett. *9*, 369 (1971).

[6] *G. Krüss, K. Ohnmais*, Ber. Dtsch. Chem. Ges. *23*, 2547 (1890); Justus Liebigs Ann. Chem. *263*, 39 (1891).

[7] *A. Müller, K. H. Schmidt, K. H. Tytko, J. Bouwma, F. Jellinek*, Spectrochim. Acta *A 28*, 381 (1972).

[8] *H. Schäfer, P. Moritz, A. Weiss*, Z. Naturforsch. *B 20*, 603 (1965).

[9] *W. P. F. A. M. Omloo, F. Jellinek, A. Müller, E. Diemann*, Z. Naturforsch. *B 25*, 1302 (1970).

[10] *C. Crevecoeur*, Acta Crystallogr. *17*, 757 (1964).

[11] *A. Müller, A. C. Ranade, V. V. K. Rao*, Spectrochim. Acta *A 27*, 1973 (1971).

[12] *A. Müller, E. Diemann*, Chem. Ber. *102*, 945 (1969).

[13] *A. Müller, E. Diemann, A. C. Ranade, P. J. Aymonino*, Z. Naturforsch. *B 24*, 1247 (1969).

[14] a) *A. Müller, H. Dornfeld, H. Schulze, R. C. Sharma*, Z. Anorg. Allg. Chem. *468*, 193 (1980); b) *O. Lutz, A. Nolle, P. Kroneck*, Z. Naturforsch. *A 32*, 505 (1977).

[15] *A. Müller, B. Krebs, W. Rittner, M. Stockburger*, Ber. Bunsenges. Phys. Chem. *71*, 182 (1967).

[16] *G. Krüss*, Justus Liebigs Ann. Chem. *225*, 1 (1884).

[17] *A. Müller, B. Krebs, R. Kebabcioglu, M. Stockburger, O. Glemser*, Spectrochim. Acta *A 24*, 1831 (1968).

[18] *K. H. Schmidt, A. Müller*, Spectrochim. Acta *A 28*, 1829 (1972).

[19] *A. Müller, N. Weinstock, K. H. Schmidt, K. Nakamoto, C. W. Schläpfer*, Spectrochim. Acta *A 28*, 2289 (1972).

[20] *A. Müller, E. Diemann, F. Neumann, R. Menge*, Chem. Phys. Lett. *16*, 521 (1972); cf. [70].

[21] *A. Müller, E. Diemann, U. Heidborn*, Z. Anorg. Allg. Chem. *371*, 136 (1969).

[22] *A. Müller, N. Weinstock, H. Schulze*, Spectrochim. Acta *A 28*, 1075 (1972).

[23] *B. Krebs, A. Müller, E. Kindler*, Z. Naturforsch. *B 25*, 222 (1970).

[24] *A. Müller, M. Dartmann, N. Mohan*, unpublished results.

[25] *A. Müller, A. C. Ranade, W. Rittner*, Z. Anorg. Allg. Chem. *380*, 76 (1971).

[26] *A. Müller, E. Diemann*, Z. Naturforsch. *B 23*, 1605 (1968).

[27] *A. Müller, B. Krebs, E. Diemann*, Angew. Chem. *79*, 1065 (1967); Angew. Chem. Int. Ed. Engl. *6*, 1081 (1967).

[28] *A. Müller, E. Diemann*, Chem. Ber. *102*, 3277 (1969).

[29] *A. Müller, B. Krebs, E. Diemann*, Angew. Chem. *79*, 245 (1967); Angew. Chem. Int. Ed. Engl. *6*, 257 (1967).

[30] *A. Müller, K. H. Schmidt, U. Zint*, Spectrochim. Acta *A 32*, 901 (1976).

[31] a) *E. Corleis, Justus Liebigs*, Ann. Chem. *232*, 244 (1886); b) *M. J. F. Leroy, M. Burgard, A. Müller*, Bull. Soc. Chim. Fr. Mineral. *1971*, 1183.

[32] *W. Gonschorek, Th. Hahn, A. Müller*, Z. Kristallogr. *138*, 380 (1973).

[33] *A. Müller, N. Weinstock, B. Krebs, B. Buss, A. Ferwanah*, Z. Naturforsch. *B 26*, 268 (1971).

[34] *V. Lenher, A. G. Fruehan*, J. Am. Chem. Soc. *49*, 3077 (1927).

[35] a) *A. Müller, E. Diemann*, Chem. Ber. *102*, 2044 (1969); b) *A. Müller, B. Krebs, H. Beyer*, Z. Naturforsch. *B 23*, 1537 (1968).

[36] *A. Müller, E. Diemann*, Chem. Ber. *102*, 2603 (1969); cf. also *A. Müller, E. Diemann, H. Schulze*, Z. Anorg. Allg. Chem. *376*, 120 (1970) as well as *J. R. Guenter, H. R. Oswald*, Z. Naturforsch. *B 24*, 1481 (1969).

[37] *A. Müller, E. Diemann*, Z. Anorg. Allg. Chem. *373*, 57 (1970).

[38] *W. Feit*, Z. Anorg. Allg. Chem. *199*, 262 (1931).

[39] *A. Müller, K. H. Schmidt, E. Ahlborn, C. J. L. Lock*, Spectrochim. Acta *A 29*, 1773 (1973).

[40] *B. Krebs, A. Müller, H. Beyer*, Z. Anorg. Allg. Chem. *362*, 44 (1968).

[41] *B. Krebs, E. Kindler*, Z. Anorg. Allg. Chem. *368*, 293 (1969).

[42] *A. Müller, E. Diemann, V. V. K. Rao*, Chem. Ber. *103*, 2961 (1970).

[43] *E. Diemann, A. Müller*, Z. Naturforsch. *B 31*, 1287 (1976).

[44] *A. Müller, E. Diemann, C. K. Jørgensen*, Struct. Bonding (Berlin) *14*, 23 (1973), and literature cited therein.

[45] *J. M. van den Berg, R. de Vries*, Proc. K. Ned. Akad. Wet. Ser. *B 67*, 178 (1964).

[46] *M. Muller, M. J. F. Leroy, R. Rohmer*, C. R. Acad. Sci. Ser. *C 270*, 1458 (1970).

[47] *A. Müller, C. K. Jørgensen, E. Diemann*, Z. Anorg. Allg. Chem. *391*, 38 (1972).

[48] *J. C. Bernard, G. Tridot*, C. R. Acad. Sci. *249*, 1520 (1959); Bull. Soc. Chim. Fr. *1961*, 810, 813.

[49] *G. Tridot, J. C. Bernard*, Acta Chim. Acad. Sci. Hung. *34*, 179 (1962).

[50] *P. J. Aymonino, A. C. Ranade, A. Müller*, Z. Anorg. Allg. Chem. *371*, 295 (1969).

[51] *P. J. Aymonino, A. C. Ranade, E. Diemann, A. Müller*, Z. Anorg. Allg. Chem. *371*, 300 (1969).

[52] *M. Harmer, A. G. Sykes* in *W. E. Newton, S. Otsuka*: Molybdenum Chemistry of Biological Significance, Plenum Press, New York 1980, p. 401.

[53] *M. A. Harmer, A. G. Sykes*, Inorg. Chem. *19*, 2881 (1980).

[54] *A. Neumann*, Dissertation, Universität Göttingen 1979; *W. Rittner, A. Neumann, A. Müller*, unpublished results.

[55] *E. Diemann, A. Müller*, Z. Anal. Chem. *257*, 116 (1971).

[56] *A. Müller, W. O. Nolte, B. Krebs*, Angew. Chem. *90*, 286 (1978); Angew. Chem. Int. Ed. Engl. *17*, 279 (1978); Inorg. Chem. *19*, 2835 (1980).

[57] *A. Müller, S. Sarkar, R. G. Bhattacharyya, S. Pohl, M. Dartmann*, Angew. Chem. *90*, 564 (1978); Angew. Chem. Int. Ed. Engl. *17*, 535 (1978); *A. Müller, S. Pohl, M. Dartmann, J. P. Cohen, J. M. Bennett, R. M. Kirchner*, Z. Naturforsch. *B 34*, 434 (1979).

[58] *A. Müller, R. G. Bhattacharyya, B. Pfefferkorn*, Chem. Ber. *112*, 778 (1979).

[59] *A. Müller, R. G. Bhattacharyya, W. Eltzner, N. Mohan, A. Neumann* and *S. Sarkar* in *H. F. Barry, P. C. H. Mitchell*: Proc. 3rd Int. Conf. Molybdenum, *Ann Arbor* 1979, p. 59. This work contains full experimental details of the preparation of $Mo_2S_{12}^{2-}$, $Mo_3S_{13}^{2-}$, $[Mo_4(NO)_4S_{13}]^{4-}$ (Section 2.5) and $[Mo_2O_2S_2(S_2)_2]^{2-}$ (Section 3); *A. Müller, W. Jaegermann*, Inorg. Chem. *18*, 2631 (1979).

[60] *A. Müller, R. Jostes, W. Jaegermann, R. G. Bhattacharyya*, Inorg. Chim. Acta *41*, 259 (1980).

[61] *A. Müller et al.*, unpublished results.

[62] a) *E. Diemann, A. Müller, P. J. Aymonino*, Z. Anorg. Allg. Chem., *479*, 191 (1981); b) *A. Müller, W. Jaegermann, R. R. Filgueira, A. Loewenschuss, D. Kuck, F. Königer*, unpublished results.

[63] *F. Jellinek*, Ark. Kemi *20*, 447 (1963).

[64] *H. K. Hofmeister, O. Glemser*, Angew. Chem. *72*, 584 (1960).

[65] *H. K. Hofmeister*, Dissertation, Universität Göttingen 1960.

[66] *A. Müller, O. Glemser, E. Diemann, H. Hofmeister*, Z. Anorg. Allg. Chem. *371*, 74 (1969).

[67] *O. Lutz, A. Nolle, P. Kroneck*, Z. Naturforsch. *A 31*, 454 (1976).

[68] *O. Lutz, A. Nolle, P. Kroneck*, Z. Phys. *A 282*, 157 (1977).

[69] *E. Königer-Ahlborn, H. Schulze, A. Müller*, Z. Anorg. Allg. Chem. *428*, 5 (1977).

[70] *G. Gattow, A. Franke*, Z. Anorg. Allg. Chem. *352*, 11, 246 (1967).

[71] *A. Müller et al.*, unpublished results; data cf. [117].

[72] *R. Bock, P. Langrock*, Naturwissenschaften *49*, 279 (1962); Z. Anal. Chem. *219*, 23 (1966).

[73] *A. Müller, W. Sievert*, Z. Anorg. Allg. Chem. *403*, 251 (1974).

[74] a) *A. Müller, W. Sievert*, Z. Anorg. Allg. Chem. *403*, 267 (1974); b) *A. Müller, H. Schulze, W. Sievert, N. Weinstock*, *ibid. 403*, 310 (1974).

[75] *A. Müller, E. Diemann, E. J. Baran*, Z. Anorg. Allg. Chem. *375*, 87 (1970).

[76] *A. Müller, E. J. Baran, R. O. Carter*, Struct. Bonding (Berlin) *26*, 81 (1976).

[77] *T. P. Prasad, E. Diemann, A. Müller*, J. Inorg. Nucl. Chem. *35*, 1895 (1973).

[78] *R. J. H. Voorhoeve, H. B. M. Wolters*, Z. Anorg. Allg. Chem. *376*, 165 (1970).

[79] a) *J. C. Wildervanck, F. Jellinek*, Z. Anorg. Allg. Chem. *328*, 309 (1964); b) *E. Diemann, A. Müller, ibid. 444*, 181 (1978).

[80] *G. Spengler, A. Weber*, Chem. Ber. *92*, 2163 (1959).

[81] Review: *K. H. Schmidt, A. Müller*, Coord. Chem. Rev. *14*, 115 (1974); cf. also *N. Mohan, A. Müller, K. Nakamoto* in *R. J. H. Clark, R. E. Hester:* Advances in Infrared and Raman Spectroscopy, Vol. 1, Heyden, London 1975.

[82] *K. H. Schmidt, A. Müller*, J. Mol. Struct. *18*, 135 (1973).

[83] *A. Müller, N. Weinstock, N. Mohan, C. W. Schläpfer, K. Nakamoto*, Appl. Spectrosc. *27*, 257 (1973).

[84] *A. Müller, E. Diemann, M. J. F. Leroy*, Z. Anorg. Allg. Chem. *372*, 113 (1970).

[85] *H. Schulze, A. Müller*, Adv. Raman Spectrosc. *1*, 546 (1972).

[86] *R. Kebabcioglu, A. Müller*, Chem. Phys. Lett. *8*, 59 (1971).

[87] *R. Kebabcioglu, A. Müller, W. Rittner*, J. Mol. Struct. *9*, 207 (1971).

[88] *S. S. L. Surana, S. P. Tandon, W. O. Nolte, A. Müller*, Can. J. Spectrosc. *24*, 18 (1979).

[89] *A. Müller, B. Krebs*, Spectrochim. Acta *A 23*, 1591 (1967).

[90] *R. H. Petit, B. Briat, A. Müller, E. Diemann*, Mol. Phys. *27*, 1373 (1974).

[91] *E. Diemann, A. Müller*, Chem. Phys. Lett. *27*, 351 (1974).

[92] *A. Müller, E. Diemann*, J. Chem. Phys. *61*, 5469 (1974).

[93] *A. Müller, E. Ahlborn*, Spectrochim. Acta *A 31*, 75 (1975).

[94] *A. Müller, W. Jaegermann*, unpublished results.

[95] *A. C. Ranade, W. Krasser, A. Müller, E. Ahlborn*, Spectrochim. Acta *A 30*, 1341 (1974).

[96] *E. Königer-Ahlborn, A. Müller*, Spectrochim. Acta *A 33*, 273 (1977).

[97] *M. P. Coughlan:* Molybdenum and Molybdenum Containing Enzymes, Pergamon Press, Oxford 1980; Reviews by a) *E. I. Stiefel*, p. 41; b) *M. P. Coughlan*, p. 119; c) *P. T. Pienkos, V. K. Shah, W. J. Brill*, p. 385; d) *W. H. Orme-Johnson, E. Münck*, p. 427; e) *C. F. Mills, I. Bremner*, p. 517.

[98] *M. T. Beck, J. Ling*, Naturwissenschaften *64*, 91 (1977); *M. T. Beck:* Prebiotic Coordination Chemistry; The Possible Role of Transition Metal Complexes in the Chemical Evolution in *H. Sigel:* Metal Ions in Biological Systems, Vol. 7, Dekker, New York 1978.

[99] *S. Gutteridge, S. J. Tannet, R. C. Bray*, Biochem. J. *175*, 887 (1978); see also *V. Massey, D. Edmondson*, J. Biol. Chem. *245*, 6595 (1970).

[100] *M. G. B. Drew, P. C. H. Mitchell, C. F. Pygall*, Angew. Chem. *88*, 855 (1976); Angew. Chem. Int. Ed. Engl. *15*, 784 (1976); cf. also [114].

[101] *P. C. H. Mitchell, C. F. Pygall*, J. Inorg. Biochem. *11*, 25 (1979).

[102] *A. Müller, U. Reinsch*, Angew. Chem. *92*, 69 (1980); Angew. Chem. Int. Ed. Engl. *19*, 72 (1980).

[103] *A. Müller, E. Krickemeyer, U. Reinsch*, Z. Anorg. Allg. Chem. *470*, 35 (1980).

[104] In the reaction of vanadate (V) in $H_2O$ with $H_2S$ in the presence of $SCN^-$ a polyvanadate with low-valence vanadium is obtained, *i.e.* the $H_2S$ acts only as a reducing agent: *P. Werle*, Diplomarbeit, Göttingen 1970.

[105] *A. Müller, P. Werle, E. Diemann, P. J. Aymonino*, Chem. Ber. *105*, 2419 (1972).

[106] Cf. also *R. A. Levenson, R. L. R. Towns*, Inorg. Chem. *13*, 105 (1974).

[107] Cf. also *R. A. Levenson, R. J. G. Dominguez, M. A. Willis, F. R. Young III*, Inorg. Chem. *13*, 2761 (1974).

[108] *M. G. B. Drew, C. F. Pygall*, Acta Crystallogr. *B 33*, 2838 (1977).

[109] *S. Jagner, E. Ljungström*, Acta Crystallogr. *B 34*, 653 (1978).

[110] *A. Müller, P. Christophliemk*, unpublished results; *P. Christophliemk*, Diplomarbeit, Universität Göttingen 1969.

[111] *A. Müller, P. Christophliemk*, Angew. Chem. *81*, 752 (1969); Angew. Chem. Int. Ed. Engl. *8*, 753 (1969).

[112] *M. Laing, J. M. Bregeault, W. P. Griffith*, Inorg. Chim. Acta *26*, L 27 (1978).

[113] *K.-H. Stück*, Dissertation, Universität Dortmund 1978.

[114] *M. G. B. Drew, P. C. H. Mitchell, C. F. Pygall*, J. Chem. Soc. Dalton Trans. *1979*, 1213.

[115] a) *A. Müller, W. Eltzner, N. Mohan*, Angew. Chem. *91*, 158 (1979); Angew. Chem. Int. Ed. Engl. *18*, 168 (1979); b) *D. Coucouvanis*, personal communication; c) *A. Müller, U. Reinsch-Vogell, H. Bögge*, unpublished results.

[116] *A. Müller, W. Eltzner, H. Bögge, S. Sarkar*, Angew. Chem. (in press).

[117] *E. Diemann, A. Müller*, Coord. Chem. Rev. *10*, 79 (1973).

[118] *A. Müller, W. Rittner, A. Neumann, E. Königer-Ahlborn, R. G. Bhattacharyya*, Z. Anorg. Allg. Chem. *461*, 91 (1980).

[119] *A. Müller, W. Rittner, A. Neumann, R. C. Sharma*, Z. Anorg. Allg. Chem. *472*, 69 (1981).

[120] *A. Müller, R. G. Bhattacharyya, E. Königer-Ahlborn, R. C. Sharma, W. Rittner, A. Neumann, G. Henkel, B. Krebs*, Inorg. Chim. Acta *37*, L493 (1979); *A. Müller, G. Henkel, B. Krebs*, unpublished results.

[121] *A. Müller, N. Mohan, H. Bögge, M. Dartmann, E. Krickemeyer*, unpublished results.

[122] In the $N(CH_3)_4^+$-salt (as in the $Cs^+$ and $PPh_4^+$ compounds) the $H_2O$ is also very weakly coordinated to the central W atom *(A. Müller, M. Dartmann*, unpublished results).

[123] *E. Königer-Ahlborn, A. Müller*, Angew. Chem. *87*, 598 (1975); Angew. Chem. Int. Ed. Engl. *14*, 573 (1975).

[124] Complete structure: *A. Müller, E. Krickemeyer, H. Bögge*, Z. Naturforsch, in press.; $P\bar{1}$; $a=9.130(1)$, $b=10.601(2)$, $c=13.339(2)$ Å; $\alpha=87.11(1)$, $\beta=85.18(1)$, $\gamma=83.67(1)°$; $R=0.76$; preparation by the solid state reaction given in [123] and heating in $CH_3NO_2$; this avoids contamination by partial formation of $W_3OS_8^{2-}$.

[125] *F. Sécheresse, J. Lefebre, J. C. Daran, Y. Jeannin*, Inorg. Chim. Acta *45*, L 45 (1980); *A. Müller, H. Tölle*, unpublished work; the bond lengths given by *F. Sécheresse* show that in the crystal S has been partly replaced by O.

[126] *A. Müller, R. Jostes*, unpublished results.

[127] *W. Rittner, A. Müller, A. Neumann, W. Bäther, R. C. Sharma*, Angew. Chem. *91*, 565 (1979); Angew. Chem. Int. Ed. Engl. *18*, 530 (1979); *W. Clegg, N. Mohan, A. Müller, A. Neumann, W. Rittner, G. M. Sheldrick*, Inorg. Chem. *19*, 2066 (1980).

[128] *E. I. Stiefel*, Prog. Inorg. Chem. *22*, 1 (1977).

[129] a) *A. Müller, R. G. Bhattacharyya, N. Mohan, B. Pfefferkorn*, Z. Anorg. Allg. Chem. *454*, 118 (1979); b) *A. Müller, N. Mohan, E. Krickemeyer*, unpublished results.

[130] The first published complex was $[Ni(WS_4)_2]^{2-}$ [136].

[131] Complexes of the type $[Co(MO_{4-n}S_n)_2]^{2-}$ ($n=3, 4$) are formed from $CoCl_2$ and $(PPh_4)_2MO_{4-n}S_n$ in dimethyl formamide or dimethyl sulfoxides. The complex formation (unambiguously proved with $WO_{4-n}S_n^{2-}$) can be detected by recording the NIR/UV/VIS-spectra and the cyclic voltammogram; *A. Müller, R. Jostes*, unpublished results.

[132] *D. Coucouvanis, N. C. Baenziger, E. D. Simhon, P. Stremple, D. Swenson, A. Simopoulos, A. Kostikas, V. Petrouleas, V. Papaefthymiou*, J. Am. Chem. Soc. *102*, 1732 (1980).

[133] *W. P. Binnie, M. J. Redman, W. J. Mallio*, Inorg. Chem. *9*, 1449 (1970).

[134] *A. Müller, E. Ahlborn, H. H. Heinsen*, Z. Anorg. Allg. Chem. *386*, 102 (1971).

[135] *A. Müller, E. Königer-Ahlborn, E. Krickemeyer, R. Jostes*, Z. Anorg. Allg. Chem., in press.

[136] *A. Müller, E. Diemann*, Chem. Commun. *1971*, 65; *A. Müller, E. Diemann, H. H. Heinsen*, Chem. Ber. *104*, 975 (1971).

[137] *A. Müller, H. H. Heinsen*, Chem. Ber. *105*, 1730 (1972).

[138] *A. Müller, H. H. Heinsen, G. Vandrish*, Inorg. Chem. *13*, 1001 (1974).

[139] *E. Königer-Ahlborn, A. Müller*, Angew. Chem. *86*, 709 (1974); Angew. Chem. Int. Ed. Engl. *13*, 672 (1974).

[140] *I. Søtofte*, Acta Chem. Scand. *A 30*, 157 (1976).

[141] *I. Paulat-Böschen, B. Krebs, A. Müller, E. Königer-Ahlborn, H. Dornfeld, H. Schulz*, Inorg. Chem. *17*, 1440 (1978).

[142] *A. Müller, N. Mohan, H. Bögge*, Z. Naturforsch. *B 33*, 978 (1978).

[143] *A. Müller, U. Schimanski*, unpublished results.

[144] *A. Müller, S. Sarkar*, Angew. Chem. *89*, 748 (1977). Angew. Chem. Int. Ed. Engl. *16*, 705 (1977). The first thiometalato complexes of iron were described in this work (*e.g.* $(PPh_4)_2[Fe(WS_4)_2]$), and were isolated in pure form with discrete complex anions; the possible relevance to the nitrogenase problem was pointed out for the first time. Moreover, the strong $M' \rightarrow MS_4^{2-}$ electron delocalization was pointed out, which explains for example the tendency of the Fe and Co complexes to accept more ligands.

[145] *E. Ahlborn*, Diploma thesis, Göttingen 1971. (The UV/VIS spectrum of $[Fe(MoS_4)_2]^{3-}$ is pictured, but no assignments could be made).

[146] *A. Müller, A. Trautwein, U. Bender*, unpublished results.

[147] The $[Fe(MoS_4)_2]^{3-}$ present in equilibrium does not precipitate as a $PPh_4^+$ salt.

[148] *D. Coucouvanis, E. D. Simhon, N. C. Baenziger*, J. Am. Chem. Soc. *102*, 6644 (1980); *J. W. McDonald, G. D. Friesen, W. E. Newton*, Inorg. Chim. Acta *46*, L 79 (1980).

[149] *A. Müller, A. Trautwein, W. Hellmann, S. Sarkar*, unpublished results.

[150] *A. Müller, S. Sarkar, A. M. Dommröse, R. Filgueira*, Z. Naturforsch. *B35*, 1592 (1980).

[151] *D. Coucouvanis, E. D. Simhon, D. Swenson, N. C. Baenziger*, J. Chem. Soc. Chem. Commun. *1979*, 361.

[152] *R. H. Tieckelmann, H. C. Silvis, T. A. Kent, B. H. Huynh, J. V. Waszczak, B. K. Teo, B. A. Averill*, J. Am. Chem. Soc. *102*, 5550 (1980).

[153] *D. Coucouvanis, N. C. Baenziger, E. D. Simhon, P. Stremple, D. Swenson, A. Kostikas, A. Simopoulos, V. Petrouleas, V. Papaefthymiou*, J. Am. Chem. Soc. *102*, 1730 (1980).

[154] *A. Müller, H. Bögge, H. G. Tölle, R. Jostes, U. Schimanski, M. Dartmann*, Angew. Chem. *92*, 665 (1980); Angew. Chem. Int. Ed. Engl. *19*, 654 (1980).

[155] *A. Müller, A. M. Dommröse, C. Römer, E. Krickemeyer, S. Sarkar*, Angew. Chem. (in press).

[156] *A. Müller et al.*, unpublished results.

[157] *A. Müller, H. G. Tölle, H. Bögge*, Z. Anorg. Allg. Chem. *471*, 115 (1980).

[158] *A. Müller et al.*, unpublished results.

[159] *R. H. Tieckelmann, B. A. Averill*, Inorg. Chim. Acta *46*, L35 (1980).

[160] *A. Müller, R. Menge*, Z. Anorg. Allg. Chem. *393*, 259 (1972).

[161] *K. H. Schmidt, A. Müller, J. Bouwma, F. Jellinek*, J. Mol. Struct. *11*, 275 (1972).

[162] *A. Müller, W. Sievert*, Z. Naturforsch. *B 27*, 722 (1972).

[163] *A. Müller, W. Sievert*, Z. Anorg. Allg. Chem. *406*, 80 (1974).

[164] *A. Müller, T. K. Hwang, H. Bögge*, Angew. Chem. *91*, 656 (1979); Angew. Chem. Int. Ed. Engl. *18*, 628 (1979).

[165] *A. Müller, H. Bögge, U. Schimanski*, J. Chem. Soc. Chem. Commun. *1980*, 91.

[166] *A. Müller, H. Bögge, U. Schimanski*, unpublished results.

[167] *E. Königer-Ahlborn, A. Müller*, Angew. Chem. *88*, 725 (1976); Angew. Chem. Int. Ed. Engl. *15*, 680 (1976).

[168] *A. Müller, H. Bögge, E. Königer-Ahlborn*, Z. Naturforsch. *B 34*, 1698 (1979).

[169] *A. Müller, U. Schimanski, H. Bögge, E. Krickemeyer*, unpublished results.

[170] *J. K. Stalick, A. R. Siedle, A. D. Mighell, C. R. Hubbard*, J. Am. Chem. Soc. *101*, 2903 (1979).

[171] In contrast to the case of binuclear and trinuclear complexes (see Section 5.1 and [155]), the complicated structures of type a) and b) compounds cannot be predicted spectroscopically.

[172] *A. Müller, H. Bögge, T. K. Hwang*, Inorg. Chim. Acta *39*, 71 (1980).

[173] In the preparation of the cubane-type compounds with $MS_4^{2-}$ (footnote [o] in Table 3) and the cage-type compound with $WS_4^{2-}$ (see [167] and footnote [k] in Table 3), the unsymmetrically substituted complexes classified unter c) are also produced. $\{Cu_4W_2S_6\}(PPh_3)_4O_2$ also precipitates together with $\{Cu_3WS_3Cl\}(PPh_3)_3O$ [172]. However, a separation is possible in all cases.

[174] *A. Müller, M. Dartmann, C. Römer, W. Clegg, G. M. Sheldrick*, Angew. Chem. (in press).

[175] *A. Müller, H. Dornfeld, G. Henkel, B. Krebs, M. P. A. Viegers*, Angew. Chem. *90*, 57 (1978); Angew. Chem. Int. Ed. Engl. *17*, 52 (1978).

[176] *A. Müller, H. Dornfeld, M. Dartmann, H. Bögge*, unpublished results.

[177] *A. Müller, I. Paulat-Böschen, B. Krebs, H. Dornfeld*, Angew. Chem. *88*, 691 (1976); Angew. Chem. Int. Ed. Engl. *15*, 633 (1976).

[178] *H. Dornfeld*, Dissertation, Universität Dortmund 1978.

[179] The manipulation of Se compounds is more difficult than their S analogs, owing to the sensitivity of the former to oxygen.

[180] *A. Müller, S. Sarkar, E. Königer-Ahlborn, W. Hellmann, R. Jostes, J. Schneider, P. J. Aymonino, R. Potthast*, unpublished results.

[181] The mononitrosyl compound of Fe with $MoS_4^{2-}$ ligands has not yet been obtained in pure crystalline form [144].

[182] The additivity of the isotope shifts of $[^{58}Ni(^{92}MoS_4)_2]^{2-}$, $[^{62}Ni(^{92}MoS_4)_2]^{2-}$, $[^{58}Ni(^{100}MoS_4)_2]^{2-}$ und $[^{62}Ni(^{100}MoS_4)_2]^{2-}$ (*E. Königer-Ahlborn, A. Müller, A. D. Cormier, J. D. Brown, K. Nakamoto*, Inorg. Chem. *14*, 2009 (1975)) has led to the derivation of a new isotope rule: *A. Müller* in *A. J. Barnes, W. J. Orville-Thomas:* Vibrational Spectroscopy – Modern Trends, (Eds.), Elsevier, New York 1977, pp. 139 and 335; Moscow.

[183] *A. Cormier, K. Nakamoto, E. Ahlborn, A. Müller*, J. Mol. Struct. *25*, 43 (1975).

[184] *E. Königer-Ahlborn*, Dissertation, Universität Dortmund 1975.

[185] *A. Müller, H. H. Heinsen, K. Nakamoto, A. D. Cormier, N. Weinstock*, Spectrochim. Acta *A 30*, 1661 (1974).

[186] a) *A. Müller, S. Che, W. Jaegermann, E. Krickemeyer*, unpublished results; b) *A. Müller, R. Jostes*, unpublished results.

[187] *A. Müller, R. Jostes, V. Flemming, R. Potthast*, Inorg. Chim. Acta *44*, L33 (1980).

[188] *A. Müller, R. Jostes, H. G. Tölle, A. Trautwein, E. Bill*, Inorg. Chim. Acta *46*, L121 (1980).

[189] a) *P. R. Edwards, C. E. Johnson, R. J. P. Williams*, J. Chem. Phys. *47*, 2074 (1967); b) *A. Müller, A. Trautwein*, unpublished results.

[190] *A. Müller, G. Gatteschi et al.*, unpublished results. However, no clearly interpretable spectrum with Co hyperfine structure has yet been obtained.

[191] *K. P. Callahan, P. A. Piliero*, J. Chem. Soc. Chem. Commun. *1979*, 13.

[192] a) *K. P. Callahan, P. A. Piliero*, Inorg. Chem. *19*, 2619 (1980); b) *A. Müller, W. Jaegermann*, unpublished results.

[193] a) *A. Müller, E. Diemann* in *A. Müller, E. Diemann:* Transition Metal Chemistry - Current Problems of General, Biological and Catalytical Relevance, Verlag Chemie, Weinheim 1981, p. 221; b) *R. R. Eady, J. R. Postgate*, Nature *249*, 805 (1974).

[194] *V. K. Shah, W. J. Brill*, Biochim. Biophys. Acta *305*, 445 (1973).

[195] *V. K. Shah, W. J. Brill*, Proc. Natl. Acad. Sci. USA *74*, 3249 (1977).

[196] *S. P. Cramer, W. O. Gillum, K. O. Hodgson, L. E. Mortenson, E. I. Stiefel, J. R. Chisnell, W. J. Brill, V. K. Shah*, J. Am. Chem. Soc. *100*, 3814 (1978).

[197] *S. P. Cramer, K. O. Hodgson, W. O. Gillum, L. E. Mortenson*, J. Am. Chem. Soc. *100*, 3398 (1978).

[198] On the basis of the combined ESR and Mössbauer investigations (*E. Münck, H. Rhodes, W. H. Orme-Johnson, L. C. Davis, W. J. Brill, V. K. Shah*, Biochim. Biophys. Acta *400*, 32 (1975); *R. Zimmermann, E. Münck, W. J. Brill, V. K. Shah, M. T. Henzl, J. Rawlings, W. H. Orme-Johnson*, ibid. *537*, 185 (1978); *B. E. Smith, G. Lang*, Biochem. J. *137*, 169 (1974), there are four categories of Fe surroundings in the MoFe protein. One of them, the $M_{ESR}$, is the ESR-active center that, according to *Orme-Johnson* et al. (*W. H. Orme-Johnson, W. D. Hamilton, T. L. Jones, M.-Y. W. Tso, R. H. Burris, V. K. Shah, W. J. Brill*, Proc. Natl. Acad. Sci. USA *69*, 3142 (1972)), gives reversible redox reactions during the "turnover" of the enzyme system. According to *Rawlings* et al. (*J. Rawlings, V. K. Shah, J. R. Chisnell, W. J. Brill, R. Zimmermann, E. Münck, W. H. Orme-Johnson*, J. Biol. Chem. *253*, 1001 (1978)), $M_{ESR}$ is present in MoFe-co, and this is of fundamental significance to the solution of the nitrogenase problem (detailed summary in [97c] and [216]).

[199] *V. K. Shah, J. R. Chisnell, W. J. Brill*, Biochem. Biophys. Res. Commun. *81*, 232 (1978).

[200] *W. G. Zumft*, Eur. J. Biochem. *91*, 345 (1978); the mode of formation of the $MoS_4^{2-}$ is not yet definitely understood. The possibility that the thioanion is formed from $S^{2-}$ and $MoO_4^{2-}$ on decomposition of the protein (via $MoS_3$, which can, in principle, be produced by acid hydrolysis) is not supported by the fact that only mixed oxothiometalates are produced when $MoS_3$ is treated with alkali.

[201] a) *T. E. Wolff, J. M. Berg, C. Warrick, K. O. Hodgson, R. H. Holm, R. B. Frankel*, J. Am. Chem. Soc. *100*, 4630 (1978); b) *T. E. Wolff, J. M. Berg, K. O. Hodgson, R. B. Frankel, R. H. Holm, ibid. 101*, 4140 (1979); c) *T. E. Wolff, J. M. Berg, P. P. Power, K. O. Hodgson, R. H. Holm, R. B. Frankel, ibid. 101*, 5454 (1979); d) *G. Christou, C. D. Garner, F. E. Mabbs, T. J. King*, J. Chem. Soc. Chem. Commun. *1978*, 740; e) *G. Christou, C. D. Garner, F. E. Mabbs, M. G. B. Drew, ibid. 1979*, 91; f) *S. R. Acott, G. Christou, C. D. Garner, T. J. King, F. E. Mabbs, R. M. Miller*, Inorg. Chim. Acta *35*, L337 (1979); g) *G. Christou, C. D. Garner, R. M. Miller, T. J. King*, J. Inorg. Biochem. *11*, 349 (1979); h) *T. E. Wolff, P. P. Power, R. B. Frankel, R. H. Holm*, J. Am. Chem. Soc. *102*, 4694 (1980); i) *G. Christou, C. D. Garner*, J. Chem. Soc. Dalton Trans. *1980*, 2354; j) *G. Christou, C. D. Garner, R. M. Miller, C. E. Johnsen, J. D. Rush, ibid. 1980*, 2363.

[202] a) *J. J. G. Moura, A. V. Xavier, M. Bruschi, J. Le Gall, D. O. Hall, R. Cammack*, Biochem. Biophys. Res. Commun. *72*, 782 (1976); b) *J. J. G. Moura, A. V. Xavier, M. Bruschi, J. Le Gall, J. M. P. Cabral*, J. Less-Common Metals *54*, 555 (1977); c) *J. J. G. Moura, A. V. Xavier, R. Cammack, D. O. Hall, M. Bruschi, J. Le Gall*, Biochem. J. *173*, 419 (1978).

[203] *E. J. Underwood:* Trace Elements in Human and Animal Nutrition, Academic Press, New York 1977.

[204] *W. R. Chappell, K. Kellogg Petersen:* Molybdenum in the Environment, Vol. 1, Dekker, New York 1976.

[205] *C. F. Mills*, Philos. Trans. R. Soc. London *B 288*, 51 (1979).

[206] *C. F. Mills, J. Bremner* in [97].

[207] *C. F. Mills*, Chem. Br. *15*, 512 (1979).

[208] *C. F. Mills*, Proc. 3rd Int. Symp. Trans. Element Metabolism in Man and Animals, München 1977.

[209] *N. J. Clarke, S. H. Laurie*, J. Inorg. Biochem. *12*, 37 (1980).

[210] *A. Müller et al.*, unpublished results.

[211] *A. Müller, E. Krickemeyer*, unpublished results.

[212] Acidification of aqueous solutions of $WS_4^{2-}$ leads very readily to formation of $W_3OS_8^{2-}$ *e.g.* after some time in a solution of 0.52 g of $(NH_4)_2WS_4$ in 50 ml of $H_2O$ treated slowly with 20 ml of 0.1 N HCl; the Cs salt precipitates after several hours upon addition of 0.17 g CsCl in 30 mL of $H_2O$. Though the exact conditions for the existence of $W_3OS_8^{2-}$ ions have not been studied, it is doubtful whether the recently published electrochemical investigations on the condensation behavior of $WS_4^{2-}$ in $H_2O$, in which no redox processes were taken into account, are completely correct, *S. Prasad*, Can. J. Chem. *59*, 563 (1981).

[213] *R. Battaglia, R. Henning, H. Kisch*, Z. Naturforsch. *B 36*, 396 (1981).

[214] The corresponding Ag complex was also obtained and structurally characterized: *A. Müller, U. Schimanski*, unpublished results.

[215] *K. Hanewald, G. Gattow*, Z. Anorg. Allg. Chem. *476*, 159 (1981).

[216] *A. Müller, W. E. Newton:* Nitrogen Fixation: Chemical, Biochemical, Genetics Interface, Plenum Press, New York 1981.

[217] *A. H. Gibson, W. E. Newton:* Current Perspectives in Nitrogen Fixation, Australian Academy of Science, Canberra 1981.

[218] For the synthesis of a multinuclear complex $[(\{SCH_2CH_2S\}MoS_3)_2Fe]^{3-}$: *P. L. Dahlstrom, S. Kumar, J. Zubieta*, J. Chem. Soc. Chem. Commun. *1981*, 411.

[219] Synthesis of a novel monocube cluster: *T. E. Wolff, J. M. Berg, P. P. Power, K. O. Hodgson, R. H. Holm*, Inorg. Chem. *19*, 430 (1980).

[220] *S. Otsuka, M. Kamota, K. Hirotsu, T. Higuchi*, J. Am. Chem. Soc. *103*, 3011 (1981).

[221] *D. Coucouvanis:* The Chemistry of the Fe—M—S Complexes (M = Mo, W) in [216].

[222] In the solid-state electronic spectrum of $(NMe_4)_2NCCu(MoS_4)\{CuCN\}$ and $(PPh_3)_3Cu_2(MoS_4)$ there is a shoulder at ca. 14000 $cm^{-1}$, which can be assigned to a $d^{10}(Cu) \rightarrow MoS_4^{2-}$ transition (see in this connection the corresponding bands in $Ag_2CrO_4$: *P. Day:* Intramolecular Interactions and Electronic Spectra of Metal Complexes in Crystals in *F. J. Comes, A. Müller, W. J. Orville-Thomas:* Spectroscopy in Chemistry and Physics: Modern Trends, Elsevier, Amsterdam 1980.

[223] *A. Müller, W. Eltzner, H. Bögge,* unpublished results.

[224] *C. F. Mills, T. T. El-Gallad, I. Bremner,* J. Inorg. Biochem. *14,* 189 (1981); *C. F. Mills, T. T. El-Gallad, I. Bremner, G. Wenham, ibid., 14,* 163 (1981).

[225] In a recently published paper (*F. Sècheresse, S. Lavigne, Y. Jeannin, J. Lefebvre,* J. Coord. Chem. *11,* 11 (1981)), the preparation and structural characterisation of $(PPh_4)_2W_3OS_8$, which contained impurities of $W_3S_9^{2-}$ (too long W=O distance) was described. According to the reported bond distances and a $\nu$(WO) at 800 $cm^{-1}$ (see also [215]) the $[N(^nC_4H_9)_4]_2W_3OS_8$ (*K. Hahnewald, G. Kiel, G. Gattow,* Z. anorg. allg. Chem. *478,* 215 (1981)) is also not pure, which leads to wrong crystallographic assumptions. However, we could obtain the pure $W_3OS_8^{2-}$ ion as the $Cs^+$ salt [212]; the crystal structure determination will be published in detail [120].

[226] $(PPh_3)_3Cu_2(WSe_4)$, having the same structure as the corresponding S analogue, could also be isdated (*A. Müller, J. Schimanski,* unpublished results).

[227] a) We have recently isolated complexes of general formula $PPh_4M'(MS_4)$, (M' = Fe, Co, Cu, Ag), which contain symmetrically coordinated $MS_4$ units, as for example in the chain-like structure of $(NH_4)(MoS_4)$ [133]. b) $[Co(WS_4)_2]^{3-}$ could also be isolated crystalline solid by us.

# COMMUNICATIONS

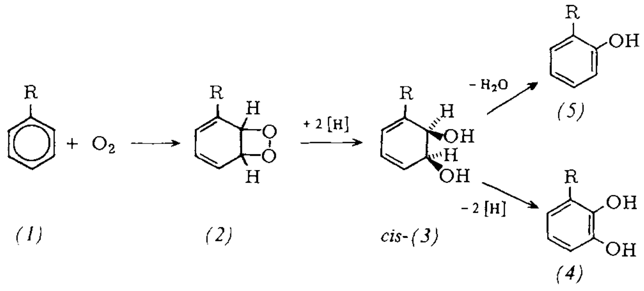
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

## Initial Steps in the Degradation of Chlorobenzene Derivatives by *Pseudomonas putida*[*]

By *Karlheinz Ballschmiter* and *Charlotte Scholz*[*]

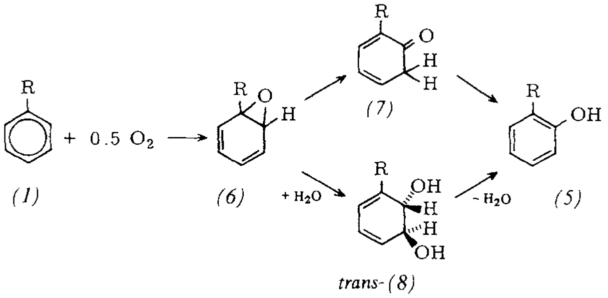
The initial step in the bacterial degradation of arenes is generally accepted to be a reaction with a dioxygenase[1].

A dioxetane *(2)*, which is presumed to be an intermediate, reacts *via* a—in many cases isolated—*cis*-cyclohexadienediol *(3)* to give the pyrocatechol *(4)*[1].



In contrast on benzene-selected mixed cultures of soil bacteria, phenols are formed from lipophilic substituted benzene- and biphenyl-derivatives[2]. 1-Naphthol is the main metabolite formed when naphthalene is treated with a species of blue algae (cyanobacterium)[3].

Phenols could be formed either by enzymatic or spontaneous dehydration of the *cis*-cyclohexadienediols *(3)*, or by transformation or hydration of arene oxides (oxiranes) following attack of monooxygenases. An indication that *(6)* is involved as a precursor is provided by the migration of substituents (NIH-shift) to cyclohexadienone *(7)*[4]. This NIH-shift was detected in the bacterial formation of chlorophenol from chlorobenzene derivatives[2a]. The hydroxylation of chlorophenols to chloropyrocatechols by *Pseudomonas sp.* has been described[2c, 5].



The three *Pseudomonas* species (see experimental), after 100 h incubation at 30°C, produced the following results: 2,3-, 3,4-, and 2,6-dichlorophenol are formed from 1,2-dichlorobenzene. Chlorophenol could not be detected. Only 2,4,6-trichlorophenol is produced from 1,3,5-trichlorobenzene, even upon incubation with a soil mixture culture which had been benzene-selected. Incubation with rat liver microsomes in a pH 7.6 buffer in the presence of NADPH under aerobic conditions, also led to formation of the same product. Dichlorophenols are not produced. When biphenyl is used as substrate in a culture medium with benzene as C source, with pentafluorobenzyl bromide as a derivatizing agent, of the three possible hydroxybiphenyl derivatives only the 2-hydroxy compound is detected, apart from phenol itself.

The $H^+$-catalyzed dehydration of a 5,6-dichlorocyclohexan-3,5-diene-1,2 diol yielded, after *ca.* 70% conversion of the diol, the 2,3-, 3,4-, and 3,5-dichlorophenols in the ratio 4 : 17 : 1.

---

[*] Prof. Dr. K. Ballschmiter, C. Scholz
Abteilung Analytische Chemie der Universität
Oberer Eselsberg, D-7900 Ulm (Germany)

[**] Microbial Degradation of Chlorinated Arenes, Part 7.—Part 6: [2c].

© *Verlag Chemie GmbH, 6940 Weinheim, 1981* *0570-0833/81/1111-0955 $ 02.50/0*

The dehydration of the dichlorocyclohexadienediol isolated from the bacterial synthesis[8] does not completely simulate the degradation of this compound by *Pseudomonas sp*. The same intermediate occurs in the dehydration of the diol from the *cis*- as well as from the *trans*-form after protonation and cleavage of $H_2O$[2c]; apart from kinetic differences in the course of the reaction, the same secondary products should be formed[1g]. The 3,5-dichlorophenol formed by dehydration could arise *via* an allyl rearrangement of the intermediate carbenium ion; it was, however, not detected in the bacterial degradation. The formation of 2,6-dichlorophenol from 1,2-dichlorobenzene in the bacterial degradation indicates a rearrangement of an α-dichloroepoxide.

Further evidence for a monooxygenase attack is provided by the formation of 2,4,6-trichlorophenol from 1,3,5-trichlorobenzene, even when no NIH-shift of the chlorine atom occurs. Moreover, the same results were obtained with pseudomonads and rat liver microsomes, indicating that the same enzymatic reactions are involved. Finally, only the direct detection of epoxides or dioxetanes would indicate that *one* primary reaction occurs—with the prerequisite that *only one* exists[1g]; even the use of $^{18}O_2$ labels in reactions having a parallel course does not enable clear statements to be made[3].

*Experimental*

Pure cultures of the arene degrader *Pseudomonas putida* (No. 50802, No. 50222, and No. 548 from the Deutsche Sammlung von Mikroorganismen, Grisebachstrasse 8, D-3400 Göttingen) were used. The degradation was performed in parallel with a benzene-selected soil mixed culture, as well as with phenobarbital-induced rat liver microsomes. 1,2-Dichlorobenzene, 1,3,5-trichlorobenzene, and biphenyl ($10^{-6}$ M) were used in conjunction with benzene as the primary C source. These compounds were introduced into the standard culture salt medium by diffusion from hard paraffin[6]. The metabolites were identified as the pentafluorophenyl ethers or acetates by comparison of the retention indices with those of authentic compounds. After high resolution capillary gas chromatography using an electron capture detector[6] reliable identification, even in the nanogram range[7] is possible.

Epoxides or cyclohexadienediols should hardly rearrange during the work-up of the culture mixtures by extractive derivatization of the phenolacetates from aqueous $K_2CO_3$ solution (0.1 M). 5,6-Dichlorocyclohexa-3,5-diene-1,2-diol—obtained by degradation of 1,2-dichlorobenzol with a *Pseudomonas* mutant[8]—was $H^+$-catalytically dehydrogenated at 23 °C in 2 M HCl within 24 h.

Received: February 6, 1980,
revised: July 17, 1981 [Z 893a IE]
German version: Angew. Chem. *93*, 1026 (1981)

CAS Registry numbers:
1,2-Dichlorobenzene 95-50-1; 1,3,5-trichlorobenzene 108-70-3; 2,3-dichlorophenol 576-24-9; 3,4-dichlorophenol 95-77-2; 2,6-dichlorophenol 87-65-0; 3,5-dichlorophenol 591-35-5; 2,4,6-trichlorophenol 88-06-2; 5,6-dichlorocyclohexan-3,5-diene-1,2-diol 79435-99-7

---

[1] a) *D. T. Gibson, J. R. Koch, C. L. Schuld, R. E. Kallio*, Biochemistry *7*, 3795 (1968); b) *D. T. Gibson*, Crit. Rev. Microbiol. *1*, 199 (1971); c) *H. J. Knackmuss*, Chem.-Ztg. *5*, 213 (1975), and cited literature; d) *K. Kieslich:* Microbial Transformations of Non-Steroid Cyclic Compounds, Thieme, Stuttgart 1976; e) *K. Haider, G. Jagnow, R. Kohnen, S. U. Lim*, Arch. Microbiol. *96*, 183 (1974); f) *W. Reineke, H. J. Knackmuss*, Biochim. Biophys. Acta *542*, 412 (1978); g) *C. E. Cerniglia, J. C. Morgan, D. T. Gibson*, Biochem. J. *180*, 175 (1979).

[2] a) *K. Ballschmiter, C. Unglert, P. Heizmann*, Angew. Chem. *89*, 680 (1977); Angew. Chem. Int. Ed. Engl. *16*, 645 (1977); b) *H. J. Neu, K. Ballschmiter*, Chemosphere *6*, 419 (1977); c) *K. Ballschmiter, C. Scholz*, *ibid. 9*, 457 (1980).

[3] *C. E. Cerniglia, C. van Baalen, G. T. Gibson*, J. Gen. Microbiol. *116*, 485 (1980).

[4] a) *J. W. Paly, D. M. Jerina, B. Witkop*, Experimentia *28*, 1129 (1972); b) *G. Bonse, M. Metzler:* Biotransformationen organischer Fremdsubstanzen, Thieme, Stuttgart 1978.

[5] *H. J. Knackmuss, M. Hellwig*, Arch. Microbiol. *117*, 1 (1978).

[6] *K. Ballschmiter, C. Unglert, H. J. Neu*, Chemosphere *6*, 51 (1977).

[7] *H. J. Neu, M. Zell, K. Ballschmiter*, Fresenius Z. Anal. Chem. *293*, 193 (1978).

[8] Prof. Dr. *G. T. Gibson*, University of Texas, Austin, USA, is thanked for a gift of cyclohexadienediol.

## Do All Eight Diastereomeric Bacteriochlorophylls Exist in Nature?

By *Bernd Scholz* and *Karlheinz Ballschmiter*[*]

Numerous anaerobic bacteria, *e.g.* the *Rhodospirillaceae*, are able to perform photosynthesis. They contain tetrahydroporphyrins; the green plant chlorophyll a and b (CHL a and b) are dihydroporphyrins. We have investigated bacteriochlorophyll ap (BCHL ap) and bacteriochlorophyll agg (BCHL agg)—together designated, in general, as BCHL a—as well as BCHL b (Fig. 1). Because of the different arrangements of substituents at C3, C4, C7, C8, and C10, eight diastereomers of BCHL a, and four diastereomers of BCHL b should occur. Until now only for BCHL a has the epimeric compound BCHL a' been detected[1]. The BCHL a epimers have—relative to the position of the substituents at C7—different configurations at C10.

The ready separation of the C10 epimers of CHL a and b by reversed phase high pressure liquid chromatography (RP-HPLC)[2] leads one to expect that the BCHL a diastereomers can also be separated using this method. The thin layer chromatographic separation of an unknown blue compound from commercial samples of BCHL ap is a further indication of other diastereomers[3].

The isolation of bacteriochlorophylls from cultures of *Rhodospirillum rubrum* (BCHL agg), *Chromatium* D, *Rhodospirillum fulvum* (BCHL ap), and *Rhodopseudomonas viridis* (BCHL b), as well as the resolution of the compounds into diastereomers by RP-HPLC are described in [4]. Under optimized separation conditions, each of BCHL ap and BCHL agg can be resolved into eight bands of largely different intensities using RP-C18 HPLC (Fig. 2A + 2C).

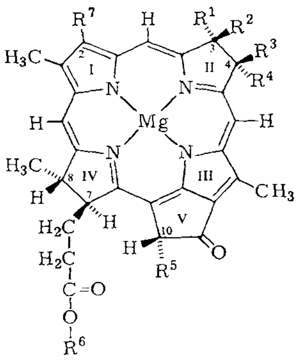
For BCHL a, the assignment of the diastereomers shown in Scheme 1 is possible. The configuration of the substituents at C7 and C8 (ring IV), as well as at C3 and C4 (ring II) is *trans* from earlier results[5]. Diastereomers which are present at the 10—20% level cannot be assigned by NMR spectroscopy[5c]. In contrast, components which are only present at the 1% level can be detected at 365 nm in the Soret region and also at 780 nm in the infrared after liquid chromatographic separation.

The isolation of the components separated by HPLC and their oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[6] enables peak 6 to be assigned to 2-devinyl-2-acetyl-proto-CHL agg (rings II and IV dehydrogenated); peak 6 is therefore not detected at 780 nm. Peaks 1—5, 7, and 8 were rearranged by treatment with DDQ to 2-devinyl-2-acetyl-CHL agg (peak 16) and by excess DDQ to

---

[*] Prof. Dr. K. Ballschmiter [+], Dr. B. Scholz
Abteilung Analytische Chemie der Universität
Oberer Eselsberg, D-7900 Ulm

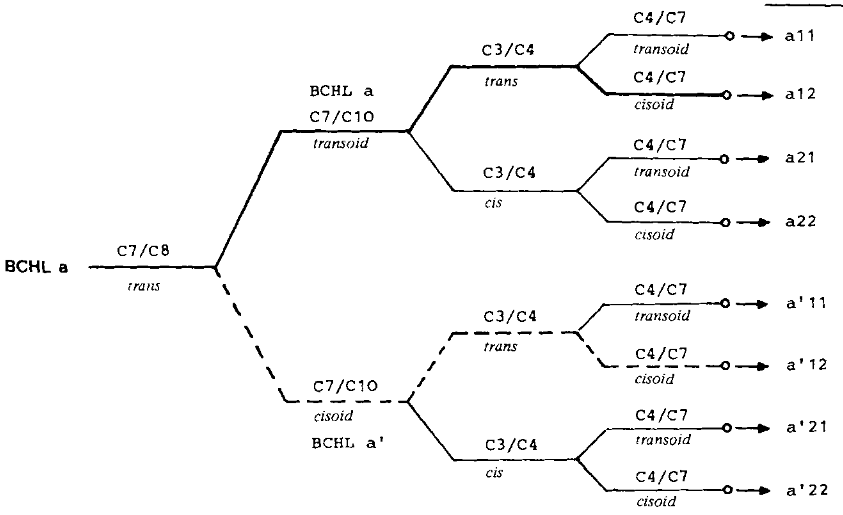
[+] Author to whom correspondence should be addressed.



| | R¹ | R² | R³ | R⁴ | R⁶ | R⁷ | Additional Compounds |
|---|---|---|---|---|---|---|---|
| CHL a | $CH_3$ | — | $C_2H_5$ | — | Phytyl | $H_2C{=}CH$ | between C3 and C4 |
| CHL b | $CH{=}O$ | — | $C_2H_5$ | — | Phytyl | $H_2C{=}CH$ | between C3 and C4 |
| BCHL ap | $CH_3$ | H | $C_2H_5$ | H | Phytyl | $H_3C{-}C{=}O$ | — |
| BCHL agg | $CH_3$ | H | $C_2H_5$ | H | Geranyl-geraniol | $H_3C{-}C{=}O$ | — |
| BCHL b | $CH_3$ | H | $={CH}{-}CH_3$ | — | Phytyl | $H_3C{-}C{=}O$ | — |
| 2-Devinyl-2-acetyl-CHL agg | $CH_3$ | — | $C_2H_5$ | — | Geranyl-geraniol | $H_3C{-}C{=}O$ | between C3 and C4 |
| 2-Devinyl-2-acetyl-proto-CHL agg | $CH_3$ | — | $C_2H_5$ | — | Geranyl-geraniol | $H_3C{-}C{=}O$ | between C3 and C4, as well as C7 and C8, (−H7, H8) |
| 2-Devinyl-2-acetyl-4-(α-hydroxyethyl)-CHL ap | $CH_3$ | — | $-\underset{\mathrm{OH}}{CH}-CH_3$ | — | Phytyl | $H_3C{-}C{=}O$ | between C3 and C4 |

Fig. 1. Structure of various chlorophylls and bacteriochlorophylls ($R^5 = CO_2CH_3$).

2-devinyl-2-acetyl-proto-CHL agg (peak 6) (Fig. 2B), *i.e.* the components 1—5, 7, and 8 are all diastereomers of BCHL agg. By analogy, these results also apply to the BCHL ap diastereomers. Furthermore, it should be noted that the *Chromatium* D bacteria, in addition to the main compound BCHL ap, contain small amounts of BCHL agg.



| | Ref. | HPLC-Peak | DC-Peak hRf-Value | DC-Peak No. |
|---|---|---|---|---|
| a11 | | 1 | 82.9 | 1 |
| a12 | [5] | 5 | 75.1 | 2 |
| a21 | | 3 | 82.9 | 1 |
| a22 | | 8 | 69.7 | 3 |
| a'11 | | 2 | 82.9 | 1 |
| a'12 | [1] | 7 | 69.7 | 3 |
| a'21 | | 4 | | n.d. |
| a'22 | | n.d. | | n.d. |

Scheme 1. Systematology of the possible diastereomers of bacteriochlorophyll ap and agg. The absolute configuration of the main component of bacteriochlorophyll agg was determined as BCHL agg12 [5a]. The C10 epimer pertaining to this is the BCHL a'gg12 [1]. By analogy the statements also apply to BCHL ap: n.d. signifies not detected; $hR_f$-value is the $R_f$ value times 100.

The DDQ oxidation of the diastereomers separated by RP-C18-HPLC also proves that the side chain at C7 is the same in both classes of compounds. In other cases, the peaks from more than each of two oxidized bacteriochlorophylls would have to appear in the chromatogram.

The combination of thin layer (TLC) distribution chromatography[3] and RP-C18-HPLC enables the assignment of the separated BCHL agg diastereomers, reproduced in Scheme 1, to be made. All the compounds contained in the three TLC spots produce the compounds devinyl-2-acetyl-CHL agg and 2-devinyl-2-acetyl-proto-CHL agg after reaction with DDQ *i.e.* intact BCHL agg diastereomers are also involved here.

From the result that $k'$ BCHL a$<k'$ BCHL a'—the $k'$ value is the quotient of the net retention time, and the retention time of the solvent front is a measure of the interaction time and hence for the interaction strength of the compounds with the stationary phase—it can be derived that in RP-C18-HPLC the retention time of diastereomers with increasing screening from both sides of the porphyrin plane is lowered with *transoid* orientated substituents. The smaller retention time of BCHL a, relative to that of BCHL a', implies a better solvation in the eluent acetonitrile/water (80:20). Generalization of this result leads *e.g.* to the expectation of a shorter retention time for BCHL a11 than for BCHL a12. Furthermore, diastereomers with *trans*-orientated groups at C3 and C4 should be preferred to those with *cis*-orientated groups, and this facilitates the assignment of the BCHL a diastereomers.

Accordingly TLC spot 1 can, at most, contain one BCHL a'. Therein, the components 1, 2, and 3, which can probably be assigned to BCHL a11, BCHL a'11, and BCHL a21, respectively, can be detected by RP-C18-

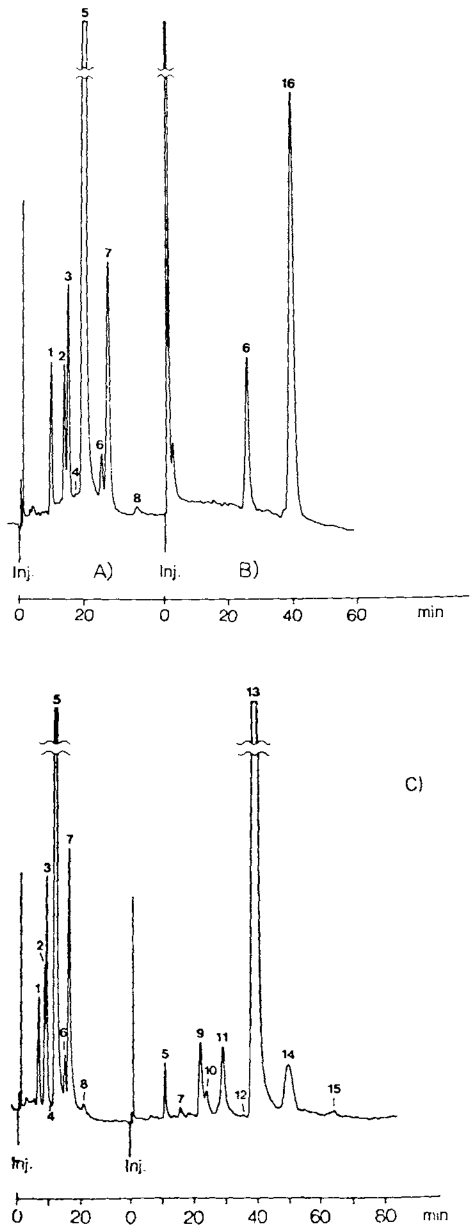


Fig. 2. A) HPLC chromatogram of BCHL agg at maximal resolution. Mobile phase: acetonitrile/water, 80/20 (V/V), stationary phase: Lichrosorb RP-18, 5 μm. Detection at 365 nm. B) HPLC chromatogram of 2-devinyl-2-acetyl-proto-CHL agg (peak 6) and 2-devinyl-2-acetyl-CHL agg (peak 16) after oxidation of the BCHL agg diastereomers (peak 1—8) with DDQ. Conditions as in A). C) HPLC chromatogram of BCHL agg (peaks 1—8) and BCHL ap (peaks 9—15). Mobile phase: acetonitrile/water 88/12 (V/V), stationary phase: Lichrosorb RP-18, 5 μm. Detection at 365 nm.

HPLC. The main peak in the HPLC chromatogram is assigned the usual structure BCHL a of the diastereomer BCHL a12. The *cisoid*-arrangement of the groups at C4/C7 also corresponds to the retention behavior in TLC (spot 2). TLC spot 3 contains the HPLC peaks 7 and 8 with a small amount of 5, *i.e.* because of its retention behavior, this compound should have an optimally unrestricted porphyrin plane. This occurs in the diastereomers BCHL a'12 and BCHL a22, as well as in BCHL a'22 and BCHL a'21. From the composition, the HPLC peak 7 corresponds to BCHL a'12; unequivocal assignment of the HPLC peak 8 cannot be made, however it probably arises from BCHL a22. The composition BCHL a11 (5.5%), a12 (71), a21 (8.5), a'11 (5.5), a'12 (8.5), a22 (0.8), a'21—peak 4—(0.2) is consistent with the assumption that by analogy to ring IV, on the basis of the biosynthesis of the bacteriochlorophylls at ring II, a *trans*-hydrogenation between C3/C4 is preferred. In an analogous way, the structural assignments also apply to the BCHL ap diastereomers (Fig. 2C), *i.e.* peak 9 = a11, 10 = a'11, 11 = a21, 12 = a'21, 13 = a12, 14 = a'12, and 15 = a22 (Scheme 1).

Although it has thus far not been possible to isolate sufficient amounts of the individual BCHL a diastereomers for an NMR-spectroscopic investigation, and final proof for the proposed structural assignment is still lacking, the presence of the different diastereomers in the photosynthetic units of the given microorganisms has been unequivocally established. The structure-related evaluation of the retentions using the combination of RP-DC and RP-C18-HPLC provide more than an indication for the correct characterization of the individual BCHL a' diastereomers.

Received: March 31, 1981,
revised: July 17, 1981 [Z 893b IE]
German version: Angew. Chem. 93, 1027 (1981)

CAS Registry numbers:
CHL a, 479-61-8; CHL b, 519-62-0; BCHL ap, 17499-98-8; BCHL agg, 40771-62-8; BCHL b, 53199-29-4; 2-devinyl-2-acetyl-CHL agg, 79448-89-8; 2-devinyl-2-acetyl-proto-CHL agg, 79448-90-1; 2-devinyl-2-acetyl-4-(a-hydroxy)-ethyl-CHL ap, 79448-91-2

[1] *J. J. Katz, G. D. Norman, W. A. Svec, H. H. Strain,* J. Am. Chem. Soc. *90,* 6841 (1968).
[2] *B. Scholz, K. Ballschmiter,* J. Chromatogr. *208,* 148 (1981).
[3] *B. Scholz, H. Müller, K. D. Willaschek, K. Ballschmiter,* J. Chromatogr. *208,* 156 (1981).
[4] *B. Scholz,* Dissertation, Universität Ulm 1981.
[5] a) *H. Brockmann, Jr.,* Angew. Chem. *80,* 234 (1968); Angew. Chem. Int. Ed. Engl. *7,* 222 (1968); *H. Brockmann, Jr., I. Kleber, ibid. 81,* 626 (1969), *8,* 610 (1969); b) *H. Scheer* in *D. Dolphin:* The Porphyrins, Vol. II, Part B, Academic Press, New York 1978, p. 1pp; c) *J. J. Katz, R. C. Dougherty, L. J. Boucher* in *L. P. Vernon, G. R. Seely:* The Chlorophylls, Academic Press, New York 1966, p. 185; *H. Scheer, J. J. Katz* in *K. M. Smith:* Porphyrins and Metalloporphyrins, Elsevier, New York 1975, p. 399 pp.
[6] *J. R. L. Smith, M. Calvin,* J. Am. Chem. Soc. *88,* 4500 (1966).

## A New Cationic Hydrido-Bridged Rhodium(I)-Iridium(III) Complex[**]

By *Alberto Albinati, Alfredo Musco, Ralph Naegeli,* and *Luigi M. Venanzi*[*]

The formation of homometallic hydrido-bridged dinuclear complexes having two alike metal atoms has frequently been observed in catalytic hydrogenations[1,2]; dinuclear species containing one five-coordinate rhodium(I) and one six-coordinate rhodium(III) of the type $[L_2Rh(\mu_2\text{-}H)_3RhHL_2]$ ($L = P(OR)_3$) have been postulated as intermediates in catalytic hydrogenation[2].

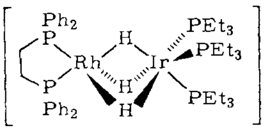
During a study of dinuclear hydrido-bridged complexes[3] we isolated complex *(1)*, which is related to the above mentioned type and contains a five-coordinate

---

[*] Prof. Dr. L. M. Venanzi, Prof. Dr. A. Musco, R. Naegeli
Laboratorium für Anorganische Chemie
der Eidgenössischen Technischen Hochschule,
ETH-Zentrum, CH-8092 Zürich (Switzerland)
Prof. A. Albinati
Istituto di Chimica, Politecnico di Milano,
Piazza Leonardo da Vinci 32, I-20133 Milano (Italy)

[**] This work was supported by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung.

rhodium(I) and a six-coordinate iridium(III). The dark green complex *(1)* was obtained by the reaction of $[Rh(diphos)(MeOH)_2][BF_4]$ with *mer*-$[IrH_3(PEt_3)_3]$ followed by



$[BPh_4]$ *(1)*

precipitation of the dinuclear cation with $Na[BPh_4]$. Whereas *(1)* in crystalline form is air-stable, its solutions decompose on exposure to air.

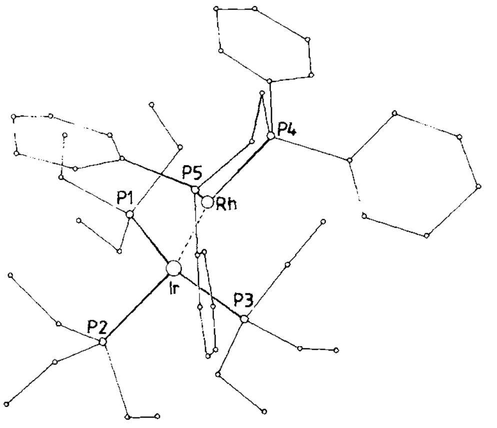


Fig. 1. Molecular structure of the cation of *(1)* in the crystal. Bond lengths [Å]: Ir···Rh 2.636(2), Ir—P1 2.352(4), Ir—P2 2.299(6), Ir—P3 2.334(4), Rh—P4 2.157(6), Rh—P5 2.194(6); Bond angles [°]: P1—Ir—P2 101.4(2), P2—Ir—P3 100.5(2), P1—Ir—P3 98.6(1), Rh—Ir—P(1) 111.6(1), Rh—Ir—P2 122.0, Rh—Ir—P3 118.9(1), P4—Rh—P(5) 83.2(2). Torsion angles [°] (ay. errors *ca.* 0.6°): P2—Ir—Rh—P4 −178.8, P2—Ir—Rh—P5 1.6, P1—Ir—Rh—P4 61.2, P3—Ir—Rh—P5 127.9.

The molecular geometry of the cation *(1)* is shown in Figure 1[4]. The hydride ligands could not be located. From the positions of the heavy atoms one can postulate a distorted octahedral coordination around the $Ir^{III}$ center with P1, P2, P3, and the three hydride ligands as donor atoms. The positions of the heavy atoms are also consistent with the presence of three bridging hydride ligands and thus a five-coordinate rhodium(I). The differences in the P—Rh—Ir and Rh—Ir—P bond angles and in the Rh—P and Ir—P bond lengths indicate that the $Rh(\mu_2\text{-}H)_3Ir$ unit is not symmetrical in the solid state.

The presence of hydride ligands in compound *(1)* is indicated by its $^1H$-NMR spectrum, which shows a complex multiplet centered at $\delta = -12.0$ (Table 1). This multiplet simplifies to a doublet of triplets on selective decoupling of P1, P2, and P3. The number of hydride ligands was confirmed by integrating the hydride region of the $^1H$-NMR spectrum of *(1)* relative to that of a known amount of *trans*-$[PtHCl(PEt_3)_2]$ which had been added to the solution. The $^1H$- and $^{31}P$-NMR spectra were unaltered by addition of this species.

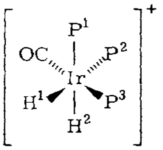
Table 1. Selected NMR data for *(1)*—*(3)*. 90 MHz $^1H$-NMR and 36.43 MHz $^{31}P$-NMR in $[D_6]$acetone.

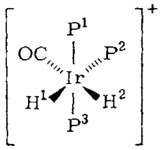
*(1)*. $^1H$-NMR: $\delta = -12.0$ (m, H 1,2,3, $^1J(Rh, H\,1,2,3) = 22$ Hz, $^2J(P4,5, H\,1,2,3) = 10$ Hz); $^{31}P\{^1H\}$-NMR: $\delta = 80.0$ (dq, P4,5, $^1J(Rh, P4,5) = 178$ Hz, $^4J(P4,5, P1,2,3) = 8.3$ Hz), −8.5 (dt, P1,2,3, $^3J(Rh, P1,2,3) = 6.8$ Hz)
*(2)*. $^{31}P$-NMR: $\delta = -16.7$ (P3, $^2J(P1, P3) = 22.3$ Hz), −27.8 (P1,2); $^1H$-NMR: $\delta = -12.4$ (H1,2, $^2J(P3, H1,2) = 7.5$ Hz)
*(3)*. $^{31}P$-NMR: $\delta = -9.6$ (P1,3, $^2J(P1,3, P2) = 15.4$ Hz), −21.7 (P2); $^1H$-NMR: $\delta = -11.3$ (H2, $^2J(P1,3, H2) = 17.0$ Hz, $^2J(P2, H2) = 17.0$ Hz, $^2J(H1, H2) = 4.5$ Hz), −12.7 (H1, $^2J(P1,3, H1) = 19.3$ Hz, $^2J(P2, H1) = 109$ Hz)

The $^{31}P\{^1H\}$-NMR spectrum of *(1)* is also consistent with the proposed structure (Table 1). The $^1H$- and $^{31}P$-NMR spectra are temperature-independent over the range 200—330 °K.

In the IR spectra (nujol) of *(1)* and of $[(diphos)Rh(\mu_2\text{-}D)_3Ir(PEt_3)_3][BPh_4]$, the H—M and D—M stretching vibrations, respectively, occur as fairly sharp, intense bands at 1686 and 1200 cm⁻¹ and broad bands centered at *ca.* 1800 and 1300 cm⁻¹.

*(2)*





*(3)*

The cation of *(1)* reacts irreversibly with CO to give *fac*-$[IrH_2(CO)(PEt_3)_3]^+$ *(2)*, which slowly rearranges to its *mer*-isomer *(3)* and an unidentified rhodium complex. Structures *(2)* and *(3)* were assigned from $^1H$- and $^{31}P$-NMR data (Table 1). The isomer with *trans*-hydride ligands has been obtained from the reaction of $[(PEt_3)PhPt(\mu_2\text{-}H)_2IrH(PEt_3)_3]^+$ with CO[6].

The isolation of a compound related to complexes of type $[L_2Rh(\mu_2\text{-}H)_3RhHL_2]$ is probably due to the inertness caused by the six-coordinate iridium(III) center in *(1)*. Preliminary investigations indicate that *(1)* is not a hydrogenation catalyst under standard conditions.

## *Experimental*

A solution of $[Rh(nbd)(diphos)][BF_4]$ (nbd = norbornadiene) (623 mg, 1 mmol) in methanol (40 mL) was hydrogenated for 2 h at atmospheric pressure. A solution of *mer*-$[IrH_3(PEt_3)_3]$ (549 mg, 1 mmol) in methanol (5 mL) was then added and a dark green color developed. *(1)* was precipitated from solution by addition of $Na[BPh_4]$ (342 mg, 1 mmol) and the solid recrystallized from acetone/methanol. Yield 1.1 g (88%).

Received: March 27, 1981 [Z 890 IE]
German version: Angew. Chem. *93*, 1018 (1981)

CAS Registry numbers:
*(1)*, 79467-02-0; *(2)*, 79467-03-1; *(3)*, 79516-93-1; $[Rh(nbd)(diphos)][BF_4]$, 60430-43-5; *mer*-$[IrH_3(PEt_3)_3]$, 27902-61-0

---

[1] *P. M. Maitlis*, Acc. Chem. Res. *11*, 301 (1978) and references quoted therein. *R. Crabtree, ibid. 12*, 331 (1979) and references quoted therein. *H. H. Wang, L. H. Pignolet*, Inorg. Chem. *19*, 1470 (1980).

[2] *E. L. Muetterties*, J. Organomet. Chem. *200*, 177 (1980) and references quoted therein.

[3] *A. Immirzi, A. Musco, P. S. Pregosin, L. M. Venanzi*, Angew. Chem. *92*, 744 (1980); Angew. Chem. Int. Ed. Engl. *19*, 721 (1980).

[4] *(1)* is monoclinic; space group $P2_1/c$; $a = 12.728(5)$, $b = 17.340(5)$, $c = 31.352(6)$ Å; $\beta = 109.3(3)°$ (least squares refined values); $Z = 4$. 6120 independent reflections were collected by automatic counter diffractometer using $Mo_{K\alpha}$ graphite-monochromated radiation up to $2\theta \leq 42°$. 4188 observed reflexions ($I_{net} > 3\sigma(I)$) were used for the structure determination. Atomic positions were obtained by Patterson and Fourier methods and refined by block diagonal least squares using anisotropic temperature factors for Rh, Ir and P atoms and isotropic for the others to $R = 5.3\%$.

[5] *A. J. Deeming, B. L. Shaw*, J. Chem. Soc. *A 1970*, 3356.

[6] *P. Boron, A. Musco, L. M. Venanzi*, Inorg. Chem., in press.

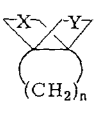
## Synthesis of Dithiapropellanes with Annelated Benzene Rings—Precursors for Molecules with the Benzene-Dewar Benzene Structure[**]

By *Klaus Weinges, Peter Günther, Wolfgang Kasel, Georg Hubertus,* and *Petra Günther*[*]

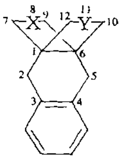
*Dedicated to Professor Karl Freudenberg on the occasion of his 95th birthday*

For some years we have investigated the thermal and photochemical behavior of 1,4-polymethylene Dewar benzene derivatives *(5)* prepared from dithiapropellanes *(1a)*[1-3]. The limit to their thermal valence isomerization is reached in the rearrangement of 1,4-hexamethylene Dewar benzene *(5)*, n = 6, to [6]paracyclophane (1,4-hexamethylenebenzene)[4]; [5]paracyclophane cannot be prepared in this way from *(5)*, n = 5[5].

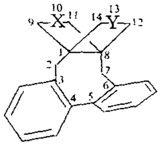
We have now prepared the hydrocarbons *(6)–(8)*, with benzene-Dewar benzene structure, using synthetic methods already tried and tested for 1,4-polymethylene Dewar benzene derivatives *(5)*, and also recently for pterodactyladiene[6]. The dithiapropellanes *(2a)–(4a)* were used as educts (Table 1). Work published by *Jamrozik*[7a] and *Ripoll*[8], who have described the dioxapropellanes *(2c)* and *(4c)*, respectively, prompted us to publish a preliminary account of our results although they are, at present, incomplete.



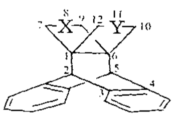
(1)



(2)

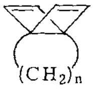


(3)

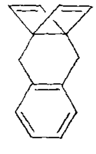


(4)

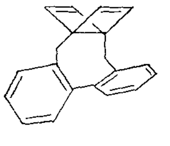
*(a)*: X, Y = S; *(b)*: X = O, Y = S; *(c)*: X, Y = O



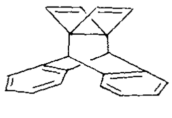
(5)



(6)



(7)



(8)

We found that 3,4-benzo[4.2.2]propella-7,9-diene *(6)* obtained from *(2a)* is stable up to 120 °C, whereas irradiation produced an isomerization product of, as yet, unknown constitution. The benzene ring must participate in this photochemical reaction, since aromatic protons can no longer be detected by $^1$H-NMR spectroscopy.

The valence isomerization of the Dewar benzene derivative *(7)*, preparable from *(3a)*, is interesting because of the effect of the cyclooctadiene ring on the previously mentioned valence isomerization of *(5)* (n = 6) to [6]paracyclophane. Moreover, the diheteropropellanes *(3)* are chiral, which is also apparent from the $^1$H- and $^{13}$C-NMR spectra of *(3a)* (see Table 1). It should be possible to separate the racemic forms present, which from a consideration of models appear to be stable, and hence to obtain the first chiral 1,4-bridged Dewar derivative *(7)* from the enantiomers of *(3a)*; however, initial attempts to resolve the racemates of *(3a–c)* on acylated cellulose[9] have been unsuccessful to date. The Dewar benzene derivative *(8)* has already been prepared by another route and ought to be stable up to *ca.* 700 °C[10]. Its photochemical behavior was not investigated.

The most important intermediate products in the synthesis of the dithiapropellanes *(2a)*, *(3a)*, and *(4a)* are the tetraethyl 1,1,2,2-tetracarboxylates *(9)*, each of which must be prepared by a different route[1,2b].

The esters *(9d)* and *(9e)*, respectively, are prepared by condensation of the disodium or dipotassium salts of tetraethyl 1,1,2,2-ethanetetracarboxylate with the corresponding bis(bromomethyl) compounds[7], whereas *(9f)* is obtained, *via* a diene synthesis, from anthracene and tetraethyl 1,1,2,2-ethenetetracarboxylate[8]. The additional reaction steps follow our previously described procedure[1,2]: LiAlH$_4$ reduction of *(9)* in tetrahydrofuran (THF) led to the tetrols *(10)*, which yielded the readily crystallizing tetrakis(methanesulfonyl) derivatives *(11)*. *(11)* is reacted with sodium sulfide nonahydrate in anhydrous dimethyl

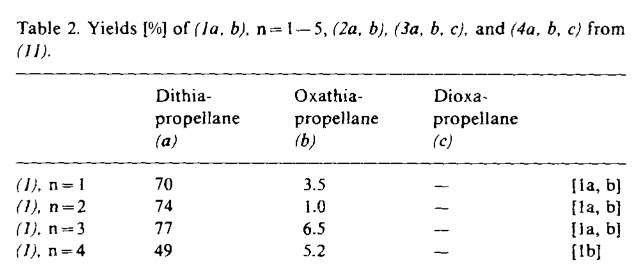


Table 1. Selected physical data for *(2a)*, *(3a)*, and *(4a)*.

*(2a)*: M.p. = 108 °C (Methanol); $^1$H-NMR (300 MHz, CDCl$_3$): $\delta = 7.08$, 7.16 (2m, 4 arom. H), 2.90 (s, H-2,5), AB signal ($\delta_A = 2.96$, $\delta_B = 2.69$, $J = 8$ Hz, H-7,9,10,12); $^{13}$C-NMR (75.46 MHz, CDCl$_3$): $\delta = 135.17$ (s, C-3,4), 128.46, 126.69 (2d, tert. arom. C), 60.57 (s, C-1,6), 43.74 (t, C-7,9,10,12), 37.72 (t, C-2,5); MS: *m/z* 248 ($M^+$, calc. 248.0693, found 248.0686), 201 ($C_{13}H_{13}S$), 181 ($C_{14}H_{13}$), 167 ($C_{13}H_{11}$), 155 ($C_{12}H_{11}$), 141 ($C_{11}H_9$), 128 ($C_{10}H_8$), 115 ($C_9H_7$), 97 ($C_5H_5S$)
*(3a)*: M.p. = 203 °C (2-propanol); $^1$H-NMR (90 MHz, CDCl$_3$): $\delta = 7.3$ (m, 8 arom. H), AB signal ($\delta_A = 3.51$, $\delta_B = 2.63$, $J = 11.1$ Hz, 4H, H-9,11,12,14), AB signal ($\delta_A = 2.93$, $\delta_B = 2.80$, $J = 11.5$ Hz, 4H, H-9,11,12,14), AB signal ($\delta_A = 2.80$, $\delta_B = 2.59$, $J = 14.2$ Hz, 4H, H-2,7); $^{13}$C-NMR (75.46 MHz, CDCl$_3$): $\delta = 140.85$ (s, C-4,5), 136.81 (s, C-3,6), 132.14, 130.40, 127.33, 126.91 (4 d, tert. arom. C), 58.44 (s, C-1,8), 44.65, 37.29 (2t, C-9,11,12,14), 39.54 (t, C-2,7); MS: *m/z* 324 ($M^+$, calc. 324.1006, found 324.1002), 179 ($C_{14}H_{11}$), 165 ($C_{13}H_9$), 97 ($C_5H_5S$)
*(4a)*: M.p. = 242–243 °C (2-Propanol); $^1$H-NMR (300 MHz, CDCl$_3$): $\delta = 7.23$ (m, 4 arom. H), 7.12 (m, 4 arom. H), 4.07 (s, H-2,5), AB signal ($\delta_A = 2.81$, $\delta_B = 2.71$, $J = 11.7$ Hz, H-7,9,10,12); $^{13}$C-NMR (75.46 MHz, CDCl$_3$): $\delta = 125.12$, 126.28 (2d, arom. C), 142.12 (s, C-3′,4′,3,4), 70.49 (s, C-1,6), 54.79 (s, C-2,5), 45.47 (t, C-7,9,10,12); MS: *m/z* 322 ($M^+$, calc. 322.0845, found 322.0853), 178 ($C_{14}H_{10}$), 97 ($C_5H_5S$)

Table 2. Yields [%] of *(1a, b)*, n = 1–5, *(2a, b)*, *(3a, b, c)*, and *(4a, b, c)* from *(11)*.

| | Dithia-propellane *(a)* | Oxathia-propellane *(b)* | Dioxa-propellane *(c)* | |
|---|---|---|---|---|
| *(1)*, n = 1 | 70 | 3.5 | – | [1a, b] |
| *(1)*, n = 2 | 74 | 1.0 | – | [1a, b] |
| *(1)*, n = 3 | 77 | 6.5 | – | [1a, b] |
| *(1)*, n = 4 | 49 | 5.2 | – | [1b] |
| *(1)*, n = 5 | 68 | 10 | – | [1b] |
| *(2)* | 25 | 2.4 | – | [7b] |
| *(3)* | 10 | 35 | 4.9 | |
| *(4)* in DMSO | 3.7 | 2.6 | 82 | |
| *(4)* in HMPA | 4.5 | 54 | 24 | |

---

[*] Prof. Dr. K. Weinges, Dipl.-Chem. P. Günther, Dipl.-Chem. W. Kasel, Dipl.-Chem. G. Hubertus, Petra Günther
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[**] Condensed Ring Systems, Part 14.—Part 13: [3b].

sulfoxide (DMSO) or hexamethylphosphoric triamide (HMPA). Whereas from *(9)*, $Z=(CH_2)_n$, in general, the dithiapropellanes *(1a)* are found as the major products, in addition to smaller amounts of the oxathiapropellanes *(1b)*, the product ratio is different from the diheteropropellanes *(2)*—*(4)* (see Table 2). In the analogous reaction starting from *(11f)* in DMSO, *Ripoll*[8] neither obtained the dithiapropellane *(4a)* nor the oxathiapropellane *(4b)*, but only the dioxapropellane *(4c)* in very high yield. The different results presumably originate from the different water contents of the solvent and reagent.

Received: December 1, 1980,
supplemented: September 1, 1981 [Z 898 IE]
German version: Angew. Chem. *93*, 1008 (1981)

CAS Registry numbers:
*(1a)* (n=1), 21533-69-5; *(1a)* (n=2), 21533-69-7; *(1a)* (n=3), 32681-86-0; *(1a)* (n=4), 50708-54-8; *(1a)* (n=5), 50708-56-0; *(1b)* (n=1), 50708-16-2; *(1b)* (n=2), 13861-82-0; *(1b)* (n=3), 24362-76-3; *(1b)* (n=4), 50708-55-9; *(1b)* (n=5), 50708-57-1; *(2a)* 79482-94-3; *(2b)* 79482-95-4; *(3a)* 79482-96-5; *(3b)* 79482-97-6; *(3c)* 79482-98-7; *(4a)* 79482-99-8; *(4b)* 79483-00-4; *(4c)* 53720-63-1; *(9d)* 76044-99-0; *(9e)* 79483-01-5; *(9f)* 53720-61-9.

---

[1] a) *K. Weinges, A. Wiesenhütter*, Justus Liebigs Ann. Chem. *746*, 70 (1971); b) *K. Weinges, K. Klessing, R. Kolb*, Chem. Ber. *106*, 2298 (1973).
[2] a) *K. Weinges, K. Klessing*, Chem. Ber. *107*, 1915 (1974); *109*, 793 (1976); *K. Weinges, K. Klessing, H. Baake, ibid. 109*, 796 (1976); b) *K. Weinges, H. Baake, ibid. 110*, 1601 (1977).
[3] a) *K. Weinges, J. Pill, K. Klessing, G. Schilling*, Chem. Ber. *110*, 2969 (1977); b) *K. Weinges, H. Baake, H. Distler, K. Klessing, R. Kolb, G. Schilling, ibid. 110*, 2978 (1977).
[4] *S. L. Kammula, L. D. Iroff, M. Jones, J. W. van Straten, W. H. de Wolf, F. Bickelhaupt*, J. Am. Chem. Soc. *99*, 5815 (1977).
[5] *H. Baake*, Dissertation, Universität Heidelberg 1977.
[6] *H.-D. Martin, B. Mayer, M. Pütter, H. Höchstetter*, Angew. Chem. *93*, 695 (1981); Angew. Chem. Int. Ed. Engl. *20*, 677 (1981).
[7] a) *J. Jamrozik*, Monatsh. Chem. *111*, 643 (1980); b) *P. Günther*, Diplomarbeit, Universität Heidelberg 1978; *L. V. Dvorken, R. B. Smith, K. Mislow*, J. Am. Chem. Soc. *80*, 486 (1958).
[8] *J. L. Ripoll*, Bull. Soc. Chim. Fr. *1974*, 2567.
[9] *G. Hesse, R. Hagel*, Justus Liebigs Ann. Chem. *1976*, 996.
[10] *G. C. Johnson, R. G. Bergman*, Tetrahedron Lett. *1979*, 2093.

---

## Decomposition of the Yellow Form of Thiamine[**]

By *Rudolf F. W. Hopmann* and *Gian Pietro Brugnoni*[*]

When thiamine (vitamin $B_1$) is dissolved in strongly alkaline media, a yellow color, which slowly fades, immediately develops; this is due to the "yellow form" $YF^{\ominus}$, which has been investigated spectroscopically[1] and kinetically[2,3]. We propose here a novel mechanism for the alkali-induced transformation of thiamine.

The decay of $YF^{\ominus}$ can be followed in the time-dependent UV spectra (Fig. 1). The spectrum of $YF^{\ominus}$ is designated as A1 and the thiol form $TS^{\ominus}$ as A9. In alkaline solution $TS^{\ominus}$ is the thermodynamically stable product of the alkali-induced transformation of thiamine, whose spectrum (curve B) is shown in Figure 1. The time-dependent UV spectra pass through isosbestic points indicating that no intermediate is formed in significant amounts.

The rearrangement from $YF^{\ominus}$ to $TS^{\ominus}$ is a pseudounimolecular reaction. A Lorentz curve is formed upon plotting the logarithm of the rate constants $k_{obs}$ against the pH value, in agreement with previous results[1] (Fig. 2, lower part). The observation that the rate of transformation at low pH is limited by the OH ion concentration and at high pH by the $H^{\oplus}$ ion concentration is not supported by the frequently investigated thiazolium hydrolysis[4] at pH values between 9.0 and 11.5 represented by the ascending branch of the Lorentz curve. The Lorentz curve must, therefore, be interpreted as indicating a change in the reaction mechanism. The only information on the decay of $YF^{\ominus}$ at high pH values that can be deduced from the decreasing branch of the Lorentz curve is a rate constant of $8\times10^9\ M^{-1}\ s^{-1}$, which would correspond to a diffusion-controlled proton transfer reaction[5]. The amplitudes observed (upper part of Fig. 2) provide no information on this reaction step, since they are assignable to the much more rapid formation of $YF^{\ominus}$.

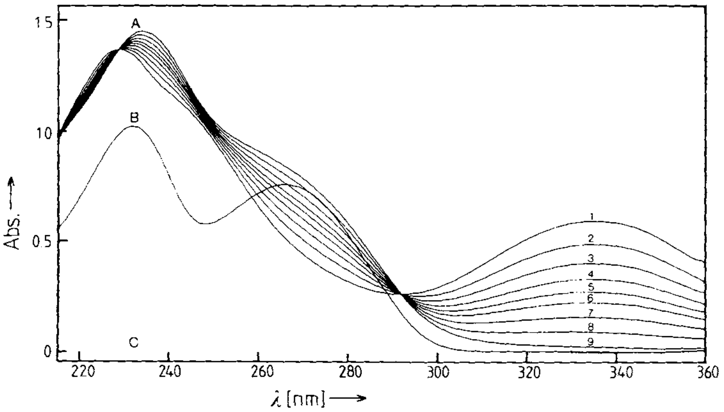


Fig. 1. Time-dependent spectra for the dissociation of the yellow form of thiamine. Thiamine concentration: $9.3\times10^{-5}$ M in 0.1 N NaOH, pH = 12.61. Curves A1—A9: recording begins after 0, 100, 200, 300, 400, 500, 700, 1000, and 1750 s, respectively (forward and reverse together take 100 s). Curve B: same concentration of thiamine in $HPO_4^{2-}/H_2PO_4^-$ buffer, pH = 6.95. Temperature: 22.5 °C, Cary 118 CX, damping 1 s, scan rate 2 nm $s^{-1}$, 0.5 mm slit width, autogain.

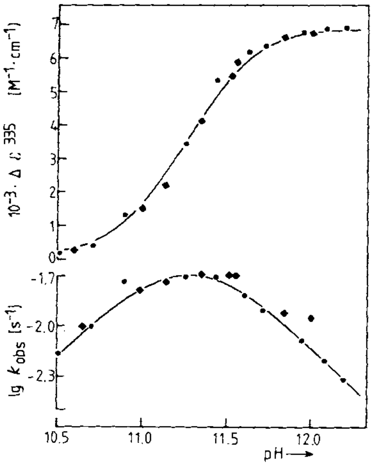


Fig. 2. pH-Rate profile and amplitudes of the decomposition of the yellow form of thiamine. Buffers: ◆ borate, ● glycinate, ionic strength 0.1 M, 22 °C. $\Delta\varepsilon^{335}$ is the change of the absorbancy ($\Delta\varepsilon=\varepsilon_{product}-\varepsilon_{educt}$) at 335 nm.

The reaction is almost independent of the buffer concentration, but depends on the ionic strength $\mu$. From the equation[6]:

$$\log k_{obs}=\log k^0+1.018\,z_A z_B A\sqrt{\mu}$$

---

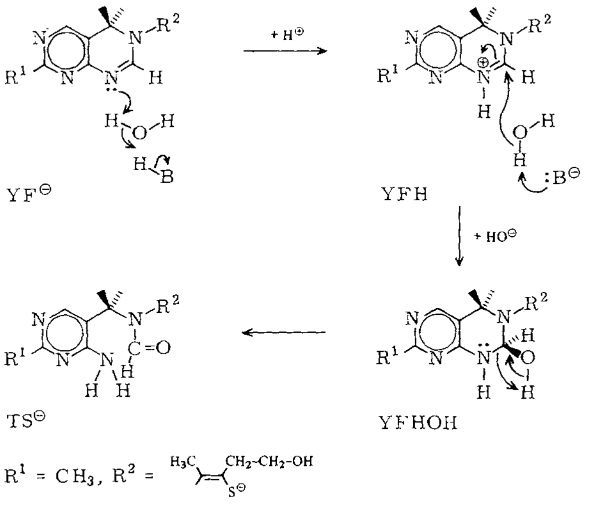
[*] Dr. R. F. W. Hopmann
Abt. Biophysikalische Chemie, Biozentrum der Universität
Klingelbergstrasse 70, CH-4056 Basel (Switzerland)
Dr. G. P. Brugnoni
Department für Pflanzenphysiologie, Ciba-Geigy AG
Schwarzwaldallee 215, CH-4058 Basel (Switzerland)

[**] Thiamine Catalysis, Part 3.—Part 2: [2].

where $k^0$ is the reaction rate extrapolated to an ionic strength of zero, $z_A$ and $z_B$ are the respective charges of the reactants, and A is a constant, we found: $k^0 = 0.0254\ s^{-1}$, $z_A \cdot z_B = -1$, and $A = 0.115$ (arsenate buffer, $4 \times 10^{-4}$ M, pH 11.55, $\mu$ adjusted with NaCl/$H_2O$ at constant buffer concentration). Since $z_A z_B$ is negative, and $YF^{\ominus}$ possesses a negative charge, the reaction partner must be positively charged: it is the proton. By synthesizing the ring skeleton of $YF^{\ominus}$ ($R^1 = R^2 = CH_3$), by its methylation, and by determining the p$K$ values of this and other compounds it was concluded that the nitrogen N1 of the dihydropyrimidine ring is probably the proton acceptor[7]. A p$K$ value of 6.38 was found, whereas the p$K$ values of the pyrimidine ring in $TS^{\ominus}$ and thiamine are 6.13[7] and 4.85[8], respectively.

It was assumed that $YF^{\ominus}$ is the product of kinetic control, and $TS^{\ominus}$ the product of thermodynamic control in the transformation, whereby thiamine exists in equilibrium with $YF^{\ominus}$ (p$K_{av}$ = 11.4), and that thiamine can rearrange to $TS^{\ominus}$ at any pH value by hydrolytic cleavage of its thiazolium ring[1]. We postulate that $YF^{\ominus}$ can be directly transformed in an acid catalyzed reaction into $TS^{\ominus}$.

A distribution of the reactants in equilibrium with each other (thiamine, $YF^{\ominus}$, and YFH) at a given pH value can be calculated from the p$K$ values of the protolytic reactions involved, and from the corresponding rate constants the rates for the pathways suggested by *Maier* and *Metzler*[1], as well as ourselves, can be estimated[9]. A ratio of *ca.* $10^{-10}:1$ results, whereby the calculated rate for the direct transformation of $YF^{\ominus}$ into $TS^{\ominus}$ is of the order of magnitude of the measured rates. This strongly supports our proposition.



Scheme 1.

Since $TS^{\ominus}$ and $YF^{\ominus}$ are negatively charged, but $YF^{\ominus}$ is protonated to yield YFH, the protonation must be followed by a deprotonation. This also formally corresponds to the addition of an $OH^{\ominus}$ ion (formation of the pseudobase YFHOH). Consequently $YF^{\ominus}$ decays *via* a similar ring opening step as the thiazolium salts. In fact, in dihydropyrimidopyrimidine, the dihydropyrimidine ring is readily opened by hydrolysis[7].

Because of the low basicity and nucleophilicity of the $NH_2$ group in $TS^{\ominus}$, the re-formation of thiamine from $TS^{\ominus}$ *via* $YF^{\ominus}$ is not possible. The sequence $YF^{\ominus} \rightarrow TS^{\ominus}$ is therefore, quasi-irreversible.

Received: December 15, 1980,
supplemented: July 29, 1981 [Z 892 IE]
German version: Angew. Chem. 93, 1005 (1981)

CAS Registry numbers:
Thiamine, 59-43-8

---

[1] *G. D. Maier, D. E. Metzler*, J. Am. Chem. Soc. *79*, 4386 (1957).
[2] *R. Hopmann, G. P. Brugnoni, B. Fol*, J. Am. Chem. Soc., in press.
[3] For structure cf. *Y. Asahi, E. Mizuta*, Talanta *19*, 567 (1972).
[4] *A. Watanabe, Y. Asahi*, J. Pharm. Soc. *75*, 1050 (1955); *P. Haake, J. M. Duclos*, Tetrahedron Lett. *1970*, 461; *Y. Asahi, M. Nagaoka*, Chem. Pharm. Bull. *19*, 1017 (1971); *H. Nogami, J. Hasegawa, T. Rikihisa*, *ibid.* *21*, 858 (1973); *J. M. Duclos, P. Haake*, Biochemistry *13*, 5358 (1974).
[5] *M. Eigen*, Angew. Chem. *75*, 489 (1963); Angew. Chem. Int. Ed. Engl. *3*, 1 (1964).
[6] *C. Capellos, B. H. J. Bielski:* Kinetic Systems, Wiley-Interscience, New York 1972, p. 119pp.
[7] *R. Hopmann, B. Fol*, unpublished results.
[8] *A. M. Chauvet-Monges, Y. Martin-Borret, A. Crevat, J. Fournier*, Biochimie *56*, 1269 (1974).
[9] *R. Hopmann*, Ann. N. Y. Acad. Sci., in press.

## $[Ga_6Se_{14}]^{10-}$: A 1900 pm Long, Hexameric Anion

By *Hans-Jörg Deiseroth* and *Han Fu-Son*[*]

The reaction of caesium with gallium monoselenide leads—similar to that which we recently found in the analogous rubidium/indium monosulfide system[1a]—to an unexpected disproportionation of the monochalcogenide. Thereby, apart from elemental gallium, a ternary selenide of trivalent gallium having the composition $Cs_{10}Ga_6Se_{14}$ forms from Cs and GaSe. The crystal structure of this solid is distinguished by the until now unknown linear, *ca.* 1900 pm long, hexameric anion $[Ga_6Se_{14}]^{10-}$ and is, to our knowledge, the first ternary compound in the Cs/Ga/Se system whose single crystal structure has been investigated.

For the preparation of the novel compound, Cs and GaSe in the molar ratio 1:1 were reacted at 200 °C (24 h)[1b] using a previously described procedure[1a]. The reaction mixture, which is liquid at 750 °C, is held at the latter temperature for 1 h to ensure complete homogenization, before being slowly cooled (2 °C/h) to 580 °C and tempered at this temperature for 24 h. The product predominantly consists of pale-yellow, transparent, leaf-shaped crystals of $Cs_{10}Ga_6Se_{14}$, which are intermingled with droplets of Ga, and decompose and turn brown in air. DTA cooling plots show a sharp signal at 610 °C (exotherm) which is assigned to the crystallization of the ternary compound. Presumably $Cs_{10}Ga_6Se_{14}$ is thermodynamically stable in the $Cs_2Se/Ga_2Se_3$ system.

The most significant structural element of this compound is the anion $[Ga_6Se_{14}]^{10-}$, which consists of six, linear, edge-linked $GaSe_4$ tetrahedra. These unusually long, discrete anions with $C_{2h}$ point group symmetry are orientated along $[10\bar{1}]$ in the crystal (Fig. 1). The bond lengths and angles of the individual $GaSe_4$ tetrahedra correspond in order of magnitude to the values found for $TlGaSe_2$[2]. The special geometry of the limited edge-coupling leads in the hexameric $[Ga_6Se_{14}]^{10-}$, however, to pronounced gradation from the center to both ends of the anion. The coordination of the cations $Cs^+$ is marked by average Cs—Se distances of between 359 and 388 pm (CN: 5—8).

---

[*] Dr. H.-J. Deiseroth [+], Dr. Han Fu-Son [++]
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)
[+] Author to whom correspondence should be addressed.
[++] Permanent address: Institute of Physics, Academia Sinica, Beijing (China).

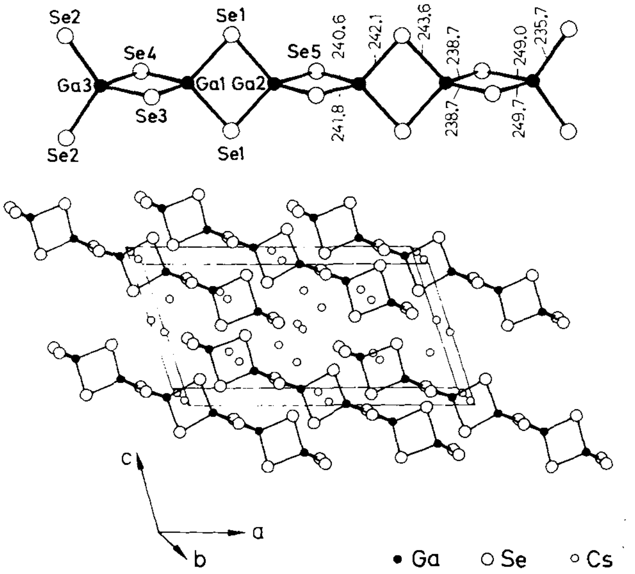


Fig. 1. $[Ga_6Se_{14}]^{10-}$ anion (distances in pm) and projection of the atomic arrangement of $Cs_{10}Ga_6Se_{14}$. Crystallographic data ($T=293$ K): C2/m, $a=1823.3(7)$, $b=1288.9(5)$, $c=966.8(3)$ pm, $\beta=108.20(3)°$, $Z=2$; $R=0.047$, $R_w=0.053$ (1907 reflections with $I>2\sigma(I)$). The Ga—Ga distances are: Ga2—Ga2 313.9, Ga1—Ga2 317.8, Ga1—Ga3 323.0 pm.

Structurally, $[Ga_6Se_{14}]^{10-}$ represents a link between the one-dimensional infinite edge-linked tetrahedral chains of type $SiS_2$ and isolated double-tetrahedra such as in $Al_2Cl_6$. Until now, the larger chalcogenic anions of elements of the third and fourth main groups have only been obtained from aqueous solutions. These possess, however, exclusively adamantane-type structures with corner-linked $MX_4$ tetrahedra, such as *e.g.* $[In_4S_{10}]^{8-}$[3], and not the limited one-dimensional edge-coupling found in $[Ga_6Se_{14}]^{10-}$. The only comparable species to $[Ga_6Se_{14}]^{10-}$ is the linear, tetrameric unit $[Zn_4O_8]^{8-}$ found in $Rb_2ZnO_2$ and $Cs_2ZnO_2$[4].

Received: March 12, 1981 [Z 900 IE]
German version: Angew. Chem. *93*, 1011 (1981)

---

[1] a) *H. J. Deiseroth*, Z. Naturforsch. *B 35*, 953 (1980); b) Herr *F. Kögel* is thanked for assistance with the preparative work.

[2] *D. Müller, H. Hahn*, Z. Anorg. Allg. Chem. *438*, 258 (1978).

[3] *B. Krebs, H. J. Wallstab, D. Voelker*, Collect. Abstr. 6th Eur. Crystallogr. Meeting, Barcelona 1980, 1-D-24.

[4] *K. R. Wambach, R. Hoppe*, Z. Anorg. Allg. Chem. *444*, 30 (1978).

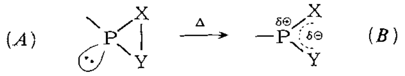
## 1,2,3λ³-Diazaphosphiridines— Synthesis, Molecular Structure and Ring Opening[**]

By *Edgar Niecke, Klaus Schwichtenhövel,*
*Hans-Günther Schäfer*, and *Bernt Krebs*[*]

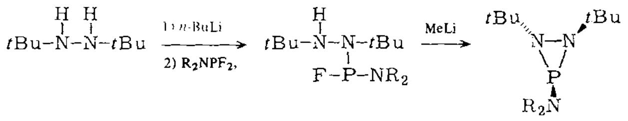
*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

Because of their high energy content, three-membered ring heterocycles (*A*) with λ³-phosphorus and heteroatoms of high electronegativity, should be good sources of the phosphorus ylides (*B*).

The combination of the elements with nitrogen ($X=Y=NR$), which through careful steering of the steric effects of the heteroatom ligands affords a sufficient kinetic stabilization of (*A*) *versus* the open ring (*B*), appeared the most promising to us.



Bearing in mind the expected thermolability of (*A*), as well as experience gained in the synthesis of 1,2λ³,3λ³-azadiphosphiridines[1], we selected as precursors the fluorophosphanes[2] *(1)*, accessible by metalation of 1,2-di-*tert*-butylhydrazine followed by reaction with amino(difluoro)phosphanes. Elimination of "HF" by methyllithium then led to the 1,2,3λ³-diazaphosphiridines *(2)*, which are colorless, remarkably air-stable solids. Their composition and constitution were confirmed by elemental analysis, mass spectroscopy[3], NMR data (Table 1), and for *(2a)* also by X-ray structural analysis (Fig. 1).



*(1)* *(2)*

*(a)*, R = *i*Pr; *(b)*, R = SiMe₃

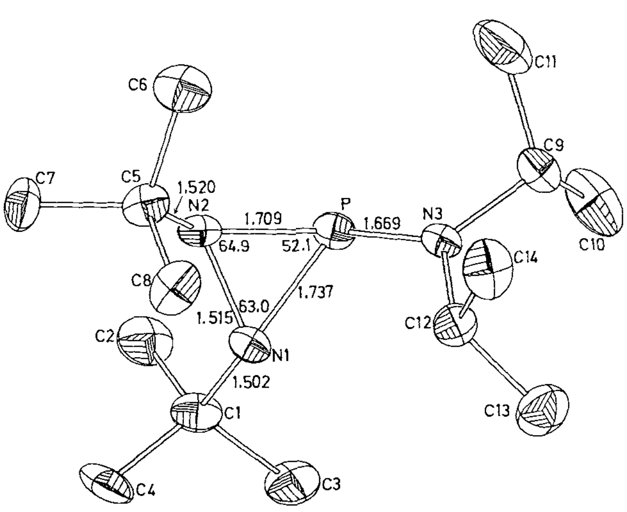


Fig. 1. Structure of *(2a)* in the crystal with the most important bond lengths [Å] and angles [°] (without H atoms). Standard errors: P—N 0.005 Å, N—N, N—C 0.007 Å.

The ¹H- and $^{13}C\{^1H\}$-NMR spectra of *(2a)* and *(2b)* at 303 K indicate free or hindered rotation, respectively, about the exocyclic PN bond, as well as groups of signals expected from the $C_2$ or $C_s$ molecular symmetry for the peripheral isopropyl- or bis(trimethylsilyl)-ligands and *tert*-butyl substituents. Lower temperatures lead in *(2a)* to a different stereochemistry for both isopropyl ligands, ($T_{c(rot)}=268\pm5$ K)[4]. Correspondingly, $^3J_{HP}$ and $^{2,3}J_{CP}$ change significantly, which by analogy to the values of $^2J_{SiP}$ and $^3J_{CP}$ in *(2b)*, respectively, arise from the different positions of these groups relative to the free electron pair on

---

[*] Prof. Dr. E. Niecke, K. Schwichtenhövel, Dipl.-Chem. H. G. Schäfer
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld
Prof. Dr. B. Krebs
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

[**] Part 22 of Phosphazenes of Coordination Number 2 and 3. This work was supported by the Fonds der Chemischen Industrie.—Part 21: [4b].

the phosphorus atom[5]. The broadening of the signals of the *tert*-butyl groups in the $^1$H-NMR, or their doubling in the $^{13}$C-NMR, indicate the *trans*-orientation of these ligands in the ground state of the molecules *(2a, b)*; the apparent stereochemistry simulated at room temperature is a consequence of a nitrogen inversion process[6] [$T_{c(inv)} = 238 \pm 5$ K *(2a)*, $240 \pm 5$ K *(2b)*]. The now chiral phosphorus atom explains the appearance of four groups of signals for the methyl ligands of the now prochiral isopropyl moieties in the $^{13}$C-NMR spectrum of *(2a)*.

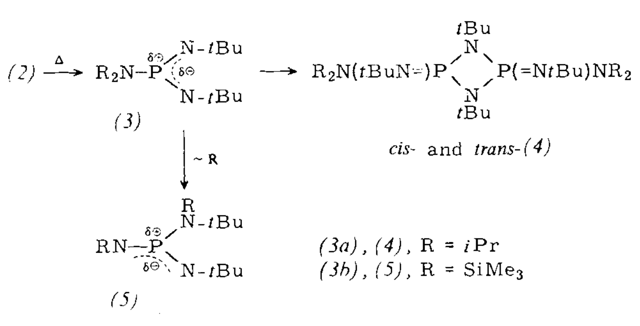
Table 1. $^1$H- and $^{13}$C-NMR data for the 1,2,3λ$^3$-Diazaphosphiridines *(2a, b)* [a, b].

| | | $^1$H-NMR | | $^{13}$C-NMR | |
|---|---|---|---|---|---|
| | | $\delta$ | $J_{HP}$ [Hz] | $\delta$ | $J_{CP}$ [Hz] |
| *(2a)* | PN(CHMe$_2$) | 1.36<br>(1.21, 1.61) | < 0.5<br>(< 0.5, <0.5) | 24.1<br>(19.5, 22.4, 24.8, [c]) | 8.6<br>(1, 2, 21, [c]) |
| | PN(CH<)$_2$ | 3.95<br>(3.40, 4.48) | 9.5<br>(±15.2, ±3.0) | 46.1<br>(42.3, 47.6) | 9.5<br>(±29.5, ∓10.2) |
| | PNCMe$_3$ | 1.50<br>(1.42) | < 0.5<br>(< 0.5) | 29.0<br>(27.4, 28.7) | 4.8<br>(±1, ±4) |
| | PNC | — | — | 55.2<br>(54.0, 54.4) | 1.2<br>(± 4.8, ∓2.5) |
| *(2b)* | PN(SiMe$_3$)$_2$ | 0.32, 0.37 | < 0.3, 2.5 | 3.1, 4.2<br>(2.7, 3.8) | 13.4, <0.5<br>(13.2, <0.5) |
| | PNCMe$_3$ | 1.16 | < 0.5 | 28.8<br>(27.7, 29.6) | 5.0<br>(±1.5, ±4) |
| | PNC | — | — | 56.2<br>(55.7, 56.6) | 1.0<br>(∓2.8, ±5) |

[a] 30% solution in CDCl$_3$ ($^1$H-NMR) or [D$_8$]toluene ($^{13}$C-NMR) with TMS as internal standard at 303 K. Values in brackets measured at 223 K. [b] $^{29}$Si-NMR: $\delta = 5.1$, 6.6, $^2J_{SiP} = 7.9$, 22.2 Hz. [c] Covered by the signal of the *tert*-butyl group at $\delta = 27.4$.

The strong deshielding of the phosphorus in the diazaphosphiridines [$\delta = -9.8$ *(2a)*; $-0.6$ *(2b)*] is surprising in view of the previously described three-membered ring systems with λ$^3$-phosphorus[7], particularly with respect to the 1,2λ$^3$-azaphosphiridine[8] ($^{31}$P-NMR: $\delta = -73.3$), which is isoelectronic to *(2a)*.

The crystal structure of *(2a)*[9] confirms the NMR spectroscopic results. Both *tert*-butyl substituents adopt the sterically favorable *trans*-positions, whereby the interaction between the "lone pairs" on the N atoms is also minimized. The almost coplanar arrangement of the atoms C5—N2—P—N3 in the crystal is possibly due to steric effects. The PN bonds in the ring are almost as long as in 1,3,2λ$^3$,4λ$^3$-diazadiphosphiridines[10]. In contrast, the NN distance of 151.5 pm is unusually large and is an indication of a high charge density at the N atoms.



In toluene at 50 °C the diazadiphosphiridines *(2)* isomerize slowly, and at 100 °C within a few minutes, to the valence isomeric diiminophosphoranes *(3)*; these react further to give the *cis*- and *trans*-[2+2]-cycloadducts *(4)* and the diiminophosphorane *(5)*, respectively[11].

The results of these investigations enable us to presume that further highly reactive phosphorus-element ylide systems are accessible *via* kinetically stabilized three-membered rings with λ$^3$-phosphorus and oxygen and/or carbon as heteroatoms by electrocyclic ring opening reactions.

## *Procedure*

*(2a, b)*: *N,N*-Di-*tert*-butylhydrazine[12] (14.4 g, 50 mmol) dissolved in *n*-hexane (100 mL) is metalated using the equivalent amount of *n*-C$_4$H$_9$Li (15% in *n*-hexane). The solution is treated dropwise with diisopropylamino(difluoro)phosphane (8.8 g, 50 mmol) or bis(trimethylsilyl)amino(difluoro)phosphane and stirred at room temperature, under $^{31}$P-NMR control, until the difluorophosphane has completely reacted (*(2a) ca.* 90 h; *(2b) ca.* 180 h).

After addition of 50 mmol of CH$_3$Li (5% in *n*-hexane), the greater part of LiF is separated off either, [*(2a)*] by filtration through a G4 frit, or [*(2b)*] using 2 equivalents of BF$_3$·Et$_2$O, bound as LiBF$_4$; solvent is thoroughly removed from the filtrate. The crude product thus obtained is recrystallized from a little *n*-hexane at 0 °C. *(2a)*: 8.2 g (60%), M.p. = 60—63 °C; *(2b)*: 4.2 g (25%), decomp. 50—55 °C.

Received: May 5, 1981,
supplemented: August 26, 1981 [Z 905 IE]
German version: Angew. Chem. *93*, 1033 (1981)

CAS Registry numbers:
*(1a)*, 79593-59-2; *(1b)*, 79593-60-5; *(2a)*, 79593-61-6; *(2b)*, 79593-62-7; *N,N'*-di-*tert*-butylhydrazine, 13952-69-7; diisopropylamino(difluoro)phosphane, 921-27-7; bis(trimethylsilyl)amino(difluoro)phosphane, 50732-22-4

---

[1] *E. Niecke, A. Nickloweit-Lüke, R. Rüger,* Angew. Chem. *93*, 406 (1981); Angew. Chem. Int. Ed. Engl. *20*, 385 (1981); Z. Naturforsch., in press.

[2] *(1a)*: $^{31}$P-NMR: $\delta = 154.8$, $^1J_{PF} = 1057$ Hz; $^{13}$C-NMR: $\delta = 23.2$ ($^3J_{CP}$, $^4J_{CF} = 4.9$, 2.3 Hz, PNC$C_2$) and 25.1 ($^3J_{CP}$, $^4J_{CF} = 10.6$, 1.4 Hz, PNC$C_2$); 30.0 ($^3J_{CP}$, $^4J_{CF} = 4.9$, 2.4 Hz, PNC$C_3$); 30.1 ($^4J_{CP}$, $^5J_{CF} = 0.5$, 2.3 Hz, PNNC$C_3$); 45.2 ($^2J_{CP} = 10.2$ Hz, PN$C$C$_2$); 53.6 ($^2J_{CP}$ or $^3J_{CF} = 1.5$ Hz, PN$C$C$_3$); 59.5 ($^3J_{CP}$ or $^4J_{CF} = 0.6$ Hz, PNN$C$C$_3$).—*(1b)*: $^{31}$P-NMR: $\delta = 170.0$ ($^1J_{PF} = 1011$ Hz); $^{13}$C-NMR: $\delta = 4.4$ ($^3J_{CP} = 9.2$ Hz, PN(SiC$_3$)$_2$) and 4.5 ($^3J_{CP} = 3.7$ Hz, PN(SiC$_3$)$_2$); 30.8 ($^3J_{CP}$, $^4J_{CF}$ = not resolved, PNC$C_3$ and PNNC$C_3$); 53.4 ($^2J_{CP}$ or $^3J_{CF} = 6.3$ Hz, PN$C$C$_3$); 60.0 ($^3J_{CP}$ or $^4J_{CF} = 1.1$ Hz, PNN$C$C$_3$).

[3] Varian 311 A, 70 eV, direct inlet, 40 °C. *(2a)*: $m/z = 273$ ($M^+$, 3%); 258 ($M^+ -$ Me, 1); 202 (2); 159 (3); 131 (53); 88 (100).

[4] For 1,2,3λ$^5$-diazaphosphiridines, the *trans*-configuration of ligands bonded to the ring-nitrogen has been established: a) *H. Quast, M. Heuschmann,* Liebigs Ann. Chem. *1981*, 967; b) *E. Niecke, H. G. Schäfer,* Chem. Ber., in press.

[5] *A. H. Cowley, M. S. J. Dewar, W. R. Jackson, W. B. Jennings,* J. Am. Chem. Soc. *92*, 1085, 5206 (1970); *M. P. Simmonin, R. M. Lequan, F. W. Wehrli,* Chem. Commun. *1972*, 1204.

[6] High temperature $^1$H-NMR studies of *(2b)* in toluene indicate no free rotation around the PN bond in the heterocycle.

[7] Reviews: *H. Quast,* Nachr. Chem. Tech. Lab. *27*, 120 (1979); *M. Baudler,* Pure Appl. Chem. *52*, 755 (1980).

[8] *E. Niecke, A. Seyer, D. A. Wildbredt,* Angew. Chem. *93*, 687 (1981); Angew. Chem. Int. Ed. Engl. *20*, 875 (1981).

[9] *(2a)* crystallizes in the monoclinic system, space group P2$_1$/c, with $a = 9.637(3)$, $b = 11.840(3)$, $c = 16.301(4)$ Å, $\beta = 107.85(3)°$, $Z = 4$. The crystal structure was determined from four-circle diffractometric data using direct methods, and refined to $R = 6.3\%$.

[10] Review: *O. J. Scherer,* Nachr. Chem. Tech. Lab. *28*, 392 (1980).

[11] The compounds *(3a, b)*, *(4)* (see [4b]) and *(5)* (*W. Flick*, Dissertation, Universität Göttingen 1975; *L. N. Markovski, V. D. Romanenko, A. V. Ruban,* Synthesis *1979*, 811) have already been prepared using other procedures.

[12] *J. C. Stowell*, J. Org. Chem. *32*, 2361 (1967).

## Structural Properties of Phosphorus Oxides in the Solid Aggregation State[**]

By *Martin Jansen, Marlen Voss,* and *Hans-Jörg Deiseroth*[*]

*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

The series of phosphorus oxides $P_4O_{6+n}$ (n = 0—4) is ideally suited for the study of the mutual influence of tri- and penta-valent phosphorus, having practically the same environment, on their bonding properties (*e.g.* by comparison of the bond lengths and angles). In this context the crystal structures of the end-members $P_4O_{10}$ and $P_4O_6$, the phosphorus(III) oxide being the last binary phosphorus oxide whose structure has not been investigated in the solid state, are of particular interest. Measurements on the $P_4O_6$ molecule in the gas phase[1] are not immediately comparable with the previously determined crystal data of $P_4O_7$[2], $P_4O_8$[3], and $P_4O_9$[4].

Single crystals of $P_4O_6$ (m. p. = 23 °C) were grown *in situ* on a diffractometer[5]. For this purpose a capillary tube (Ø = 0.3 mm) was filled with the liquid sample to a height of approximately 20 mm, under an atmosphere of dry argon, and attached to the diffractometer, which was equipped with a low temperature device. The top of the capillary protruded through a small hole at the center of a heated (+30 °C) metal screen into a cold nitrogen gas stream (−20 °C). Crystal growth was achieved by slowly moving the screen, thus introducing the whole capillary into the gas stream. Data collection was performed at −5 °C.

The crystal structure[6] consists of molecular units $P_4O_6$ with site symmetry m, having the mirror planes passing through P1, P2, O1, and O4 (cf. Fig. 1). Geometrical analysis of the molecular structure, however, reveals that within the limits of experimental error the point-group is $T_d$. The bond lengths, both uncorrected and corrected for the effect of librations of the rigid group, are significantly larger than those determined for $P_4O_6$ in the gas phase[1]. This is presumably caused by intermolecular interactions which seem to be of the van der Waals type as indicated by the smallest intermolecular contacts [$d$(O—O) = 319 pm] in the solid state. Within the series $P_4O_6$, $P_4O_7$, and $P_4O_8$ the P—O distances in the $P^{III}$—O—$P^{III}$ bridges decrease monotonically from 166 through 164 to 163 pm, and the bonds $P^V$—O (terminal) shorten similary from $P_4O_7$ (145 pm) to $P_4O_9$ (141 pm). This structural feature may be explained either in terms of increasing effective charges on the trivalent phosphorus atoms with increasing number of pentavalent phosphorus atoms in the molecule, or by decreasing effective charges on $P^V$ with increasing amounts of $P^{III}$. The interpretation suggested here is supported by $^{31}$P-NMR signals determined for the species $P_4O_6E_n$ (E = O, S, Se; n = 1—4)[7].

It is remarkable that $P_4O_6$, a perfect example of a "sheathed" compound, with its relatively low melting point and a high vapor pressure, forms no plastic phase: completely ordered $P_4O_6$ crystallizes immediately below the melting point (23 °C) This presents a marked, at first inexplicable contrast to $P_4$, which despite a higher melting point (44 °C) exists over a broad temperature range as a plastic-crystalline species.

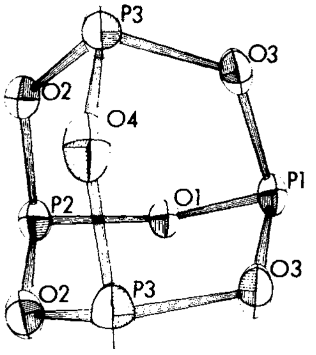


Fig. 1. Perspective view of a $P_4O_6$ molecule. Bond lengths [pm] and angles [°] in $P_4O_6$ (maximum standard deviation 0.4 pm). a) Solid state: P1—O1(O3) = 165.8 (165.8); P2—O1 (O2) = 165.9 (165.9); P3—O2 (O3) = 165.9 (164.6); P3—O4 = 165.6 (corrected for rigid body motion); P—O—P 127.0, O—P—O 99.5.—b) Gaseous state [1]: P—O = 163.8; P—O—P = 126.4; O—P—O = 99.8.

Received: March 2, 1981 [Z 899 IE]
German version: Angew. Chem. *93*, 1023 (1981)

CAS Registry numbers:
$P_4O_6$, 10248-58-5.

---

[1] *B. Beagley, D. W. J. Cruickshank, T. G. Hewitt, K. H. Jost,* Trans. Faraday Soc. *65*, 1219 (1969).
[2] *M. Jansen, M. Voss,* Angew. Chem. *93*, 120 (1981); Angew. Chem. Int. Ed. Engl. *20*, 100 (1981). *K. H. Jost, M. Schneider,* Acta Crystallogr. *B37*, 222 (1981).
[3] *K. H. Jost,* Acta Crystallogr. *21*, 34 (1966).
[4] *K. H. Jost,* Acta Crystallogr. *17*, 1593 (1964); *B. Beagley, D. W. J. Cruickshank, T. G. Hewitt, A. Halland,* Trans. Faraday Soc. *63*, 836 (1967).
[5] *A. Simon, H. J. Deiseroth, E. Westerbeck, B. Hillenkötter,* Z. Anorg. Allg. Chem. *423*, 203 (1976).
[6] $P2_1/m$, $a = 643.0$, $b = 788.7$, $c = 681.2$, $\beta = 106.01°$, $Z = 2$, 1277 observed reflexions (diffractometer data), $R = 0.087$.
[7] *M. Walker, D. Reckenpaugh, J. Mills,* Inorg. Chem. *18*, 2792 (1979).

---

[*] Prof. Dr. M. Jansen [+], Dipl.-Chem. M. Voss
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)
Dr. H. J. Deiseroth
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)

[+] Author to whom correspondence should be addressed. New address:
Institut für Anorganische Chemie der Universität
Callinstrasse 9, D-3000 Hannover 1 (Germany)

[**] The authors thank the Deutsche Forschungsgemeinschaft and Fonds der Chemie for financial support and the Hoechst AG (Werk Knapsack) for supplying a sample of $P_4O_6$.

---

## CC Bond Formation Between "Electron-Rich" and "Electron-Deficient" Alkenes[**]

By *Bernd Giese* and *Gerhard Kretzschmar*[*]

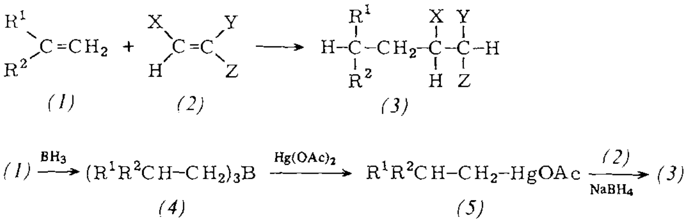
*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

Formation of CC bonds is an important synthetic procedure in organic chemistry. We have now succeeded in reductively coupling "electron-rich" alkenes *(1)* with "electron-deficient" alkenes *(2)*, in a one-pot process using mild conditions, to give the products *(3)*. The synthesis proceeds *via* the steps 1. Hydroboration of the alkenes *(1)* to the trialkylboranes *(4)*[1], 2. Mercuration of *(4)* to form the organomercury salts *(5)*[2], and 3. Reduction of *(5)* with sodium tetrahydridoborate in the presence of the alkenes *(2)*, whereby the products *(3)* are formed *via* a radical chain reaction[3].

---

[*] Prof. Dr. B. Giese, Dipl.-Ing. G. Kretzschmar
Institut für Organische Chemie und Biochemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.



(1), (2), (3), (4), (5)

$$(1) \xrightarrow{BH_3} (R^1R^2CH{-}CH_2)_3B \xrightarrow{Hg(OAc)_2} R^1R^2CH{-}CH_2{-}HgOAc \xrightarrow[NaBH_4]{(2)} (3)$$

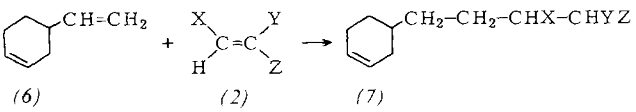
Alkyl-, aryl-, and alkoxy-groups serve as suitable substituents $R^1$ and $R^2$ for the "electron-rich" alkenes *(1)*; halogen atoms, carboxylic acid esters, sulfonic acid esters, hydroxy[4], and vinyl groups that are less reactive in hydroboration reactions[1] remained unchanged.

In order to direct the attack of the boron with >98% regioselectivity towards the vinylic $CH_2$ group of *(1)*, $(cC_6H_{11})_2BH$ (Method A) was used for the hydroboration instead of $BH_3$/THF (Method B), particularly with monosubstituted alkenes ($R^1 = H$). The regioisomers of *(4)* do not lead to impurities in the reaction products *(3)*, because only bonds between primary alkyl groups and boron are cleaved by $Hg(OAc)_2$[2].

For acrylonitrile, the total yields over the three reaction steps in this one-pot synthesis vary between 50 and 70% (Table 1). Cyano groups, as well as carboxylic acid ester-, ketone-, anhydride-, and imide-moieties prove to be highly suitable X-, Y-, and Z-substituents for the "electron deficient" alkenes *(2)*; yields are considerably lower with chlorine atoms and phenyl groups (Table 2)[5]. This reflects the reactivity gradation of the alkenes *(2)* in reactions with alkyl radicals[6].

Table 1. Reductive CC coupling of alkenes *(1)* with acrylonitrile to give products *(3)*, X = Y = H, Z = CN.

| Educt *(1)* | | Product *(3)* | |
|---|---|---|---|
| $R^1$ | $R^2$ | Yield [%] | Method |
| H | $C(CH_3)_3$ | 47 | A |
| H | $C_6H_4$-4-$CH_3$ | 50 | A |
| H | $CH_2$—$C_6H_4$-2-OAc | 65 | A |
| H | $CH_2$—$C_6H_4$-2-OH [4] | 48 | A |
| H | $CH_2CH_2Br$ | 53 | A |
| H | $CH_2OAc$ | 51 | A |
| H | $CH_2CH_2OTos$ | 71 | A |
| H | $(CH_2)_8CO_2C_2H_5$ | 57 | A |
| H | $OC_2H_5$ | 55 | B |
| H | $CH_2OC_6H_5$ | 55 | A |
| $CH_3$ | $C_2H_5$ | 65 | B |
| $CH_3$ | $C_3H_7$ | 57 | B |
| $CH_3$ | $CH_2Cl$ | 50 | A |
| β-Pinene | | 53 | B |



(6) (2) (7)

Table 2. Coupling of the diene *(6)* with the alkenes *(2)* to give products *(7)* (Method A).

| Alkene *(2)* | | | Product *(7)* |
|---|---|---|---|
| X | Y | Z | Yield [%] |
| H | H | CN | 54 |
| H | H | $CO_2CH_3$ | 47 |
| H | H | $COCH_3$ | 44 |
| H | Cl | CN | 52 |
| H | Cl | Cl | 28 |
| H | $CH_3$ | $C_6H_5$ | 13 |
| CN | $CH_3$ | CN | 37 |
| O=C—O—C=O | | H | 53 |
| O=C—NH—C=O | | H | 50 |

## *Procedure*

*Method A:* A solution of cyclohexene (1.81 g, 22 mmol) in 5 mL of tetrahydrofuran (THF) is added over 5—20 min to a solution of $BH_3$ (11 mmol, 11 mL of a 1 M solution in THF) under $N_2$ at 0 °C. After 2 h, alkene *(1)* or *(6)* (10 mmol) is added, left to react for 12 h at 20 °C, and the mixture then treated with $Hg(OAc)_2$ (3.18 g, 10 mmol). The resulting mixture is stirred for 5—30 min and mixed with alkene *(2)* (20—50 mmol). Rapid addition of $NaBH_4$ (450 mg, 12 mmol), suspended in 1 mL of water, leads to precipitation of metallic mercury within 5 min. Separation of the organoboron compounds follows by chromatography on silica gel, or by oxidation with $H_2O_2$[1]. The analytically pure products *(3)* and *(7)*, respectively, are obtained by distillation.

*Method B:* $BH_3$ (3.5 mmol, 3.5 mL of a 1 M solution in THF) is added to a solution of alkene *(1)* (10 mmol) in 10 mL of THF under $N_2$ at 0 °C. After 45 min, $Hg(OAc)_2$ (3.18 g, 10 mmol) is added, and the mixture allowed to react for 30 min at 20 °C. The resulting mixture is diluted with $CH_2Cl_2$ (20 mL) and mixed with alkene *(2)* (20—50 mmol). Rapid addition of $NaBH_4$ (450 mg, 12 mmol) suspended in 1 mL of water leads to precipitation of metallic mercury within 5 min. Analytically pure *(3)* is obtained by distillation.

Received: March 13, 1981 [Z 901a IE]
German version: Angew. Chem. *93*, 1015 (1981)

CAS Registry numbers:
*(1)* (R′ = H, $R^2 = C(CH_3)_3$), 558-37-2; *(1)* (R′ = H, $R^2 = C_6H_4$-*p*-$CH_3$), 622-97-9; *(1)* (R′ = H, $R^2 = CH_2C_6H_4$-*o*-OAc), 4125-54-6; *(1)* (R′ = H, $R^2 = CH_2C_6H_4$-*o*-OH), 1745-81-9; *(1)* (R′ = H, $R^2 = CH_2CH_2Br$), 5162-44-7; *(1)* (R′ = H, $R^2 = CH_2OAc$), 591-87-7; *(1)* (R′ = H, $R^2 = CH_2CH_2OTos$), 778-29-0; *(1)* (R′ = H, $R^2 = (CH_2)_8CO_2C_2H_5$), 692-86-4; *(1)* (R′ = H, $R^2 = OC_2H_5$), 109-92-2; *(1)* (R′ = H, $R^2 = CH_2OC_6H_5$), 1746-13-0; *(1)* (R′ = $CH_3$, $R^2 = C_2H_5$), 563-46-2; *(1)* (R′ = $CH_3$, $R^2 = C_3H_7$), 763-29-1; *(2)* X, Y = H, Z = CN), 107-13-1; *(2)* (X, Y = H, Z = $CO_2CH_3$), 96-33-3; *(2)* (X, Y = H, Z = $COCH_3$), 78-94-4; *(2)* (X = H, Y = Cl, Z = CN), 920-37-6; *(2)* (X = H, Y, Z = Cl), 75-35-4; *(2)* (X = H, Y = $CH_3$, Z = $C_6H_5$) 98-83-9; *(2)* (X, Z = CN, Y = $CH_3$), 70240-55-0; *(2)* X, Z = COOCO, Z = H), 108-31-6; *(2)* (X, Y = CONHCO, Z = H), 541-59-3; *(3)* (R′ = H, $R^2 = C(CH_3)_3$, X, Y = H, Z = CN), 30616-89-8; *(3)* (R′ = H, $R^2 = C_6H_4$-*p*-$CH_3$, X, Y = H, Z = CN), 79593-79-6; *(3)* (R′ = H, $R^2 = CH_2C_6H_4$-*o*-OAc, X, Y = H, Z = CN), 79593-80-9; *(3)* (R′ = H, $R^2 = CH_2C_6H_4$-*o*-OH, X, Y = H, Z = CN), 79593-81-0; *(3)* (R′ = H, $R^2 = CH_2CH_2Br$, X, Y = H, Z = CN), 20965-27-9; *(3)* (R′ = H, $R^2 = CH_2OAc$, X, Y = H, Z = CN), 34957-71-6; *(3)* (R′ = H, $R^2 = CH_2CH_2OTos$, X, Y = H, Z = CN), 79593-82-1; *(3)* (R′ = H, $R^2 = (CH_2)_8CO_2C_2H_5$, X, Y = H, Z = CN), 36665-53-9; *(3)* (R′ = H, $R^2 = OC_2H_5$, X, Y = H, Z = CN), 6067-01-2; *(3)* (R′ = H, $R^2 = CH_2OC_6H_5$, X, Y = H, Z = CN), 16728-57-7; *(3)* (R′ = $CH_3$, $R^2 = C_2H_5$, X, Y = H, Z = CN), 79593-83-2; *(3)* (R′ = $CH_3$, $R^2 = C_3H_7$, X, Y = H, Z = CN), 79593-84-3; *(3)* (R′ = $CH_3R^2 = CH_2Cl$, X, Y = H, Z = CN), 79593-85-4; *(6)*, 766-03-0; *(7)* (X, Y = H, Z = CN), 79593-86-5; *(7)* (X, Y = H, Z = $CO_2CH_3$), 79593-87-6; *(7)* (X, Y = H, Z = $COCH_3$), 79593-88-7; *(7)* (X = H, Y = Cl, Z = CN), 79593-89-8; *(7)* (X = H, Y, Z = Cl), 79593-90-1; *(7)* (X = H, Y = $CH_3$, Z = $C_6H_5$), 79593-91-2; *(7)* (X, Z = CN, Y = $CH_3$), 79593-92-3; *(7)* (X, Y = COOCO, Z = H), 79593-93-4; *(7)* (X, Y = CONHCO, Z = H), 79593-94-5; β-pinene, 127-91-3; 4-(6,6-dimethylbicyclo[3.1.1]hept-2-yl)butanenitrile, 79593-95-6; *1* (R′ = $CH_3$, $R^2 = CH_2Cl$), 563-47-3.

---

[1] *H. C. Brown:* Boranes in Organic Chemistry, Cornell University Press, Ithaca, New York 1972.

[2] *R. C. Larock, H. C. Brown,* J. Am. Chem. Soc. *92*, 2467 (1970).

[3] *B. Giese, J. Meister,* Chem. Ber. *110*, 2588 (1977); *B. Giese, G. Kretzschmar, J. Meixner, ibid. 113*, 2787 (1980).

[4] In the presence of acidic groups, correspondingly greater amounts of boron hydrides are required.

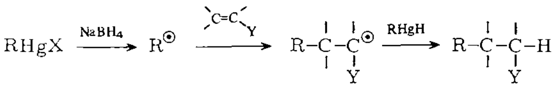
[5] The method of CC bond formation developed by ***Brown*** can only be performed with alkenes *(2)* which bear a keto group (Y = COR); cf. [1].

[6] *B. Giese, J. Meixner,* Angew. Chem. *92*, 215 (1980); Angew. Chem. Int. Ed. Engl. *19*, 206 (1980); Polymer Bull. *2*, 805 (1980).

## Steric Effects in the Addition of Alkyl Radicals to Alkenes[**]

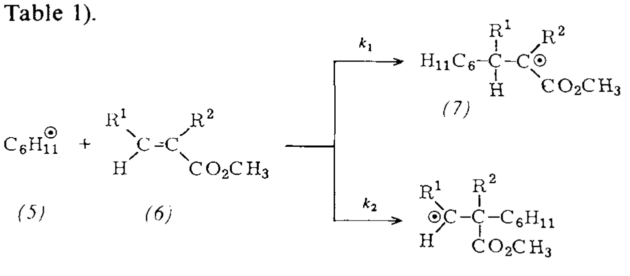
By *Bernd Giese* and *Stephen Lachhein*[*]

The alkyl radicals *(2)*[1], generated by reduction of alkylmercury salts *(1)* with sodium tetrahydridoborate, form the adduct radicals *(3)* in the presence of "electron-deficient" alkenes[2]. The complete reaction of *(3)* to the H-captured products *(4)* enables the relative rate constants to be determined using the competitive kinetic method[3]. Steric effects, which have a considerable influence on the reactivity and selectivity of addition of alkyl radicals to alkenes in polymerizations, can, therefore, be quantitatively measured for the first time[4].



*(1)* *(2)* *(3)* *(4)*

If the cyclohexyl radicals *(5)* are generated from cyclohexylmercury salts[2,3] in the presence of pairs of acrylates *(6)*, the relative rate constants $k_1$ and $k_2$ can be determined from the products formed by the radicals *(7)* and *(8)* (see Table 1).



*(5)* *(6)* *(7)* *(8)*

Table 1. Influence of the alkyl substituents R$^1$ and R$^2$ on the relative rate constants $k_1$ and $k_2$ (average error ± 10%) for the reaction of cyclohexyl radicals *(5)* with acrylate esters *(6)* in $CH_2Cl_2$ at 293 K.

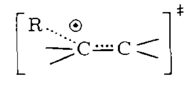
| | R$^1$ | R$^2$ | $10^3\,k_1$ | $10^3\,k_2$ | $k_1 : k_2$ |
|---|---|---|---|---|---|
| *(a)* | H | H | ≡1000 | 2.0 | 99.8 : 0.2 |
| *(b)* | $CH_3$ | H | 11 | 1.0 | 92 : 8 |
| *(c)* | $C_2H_5$ | H | 6.6 | 0.9 | 88 : 12 |
| *(d)* | $i C_3H_7$ | H | 1.5 | 0.5 | 75 : 25 |
| *(e)* | H | $CH_3$ | 710 | [a] | |
| *(f)* | H | $C_2H_5$ | 550 | [a] | |
| *(g)* | H | $i C_3H_7$ | 430 | [a] | |
| *(h)* | H | $t C_4H_9$ | 250 | [a] | |

[a] $k_2$ is smaller than $10^{-3}$ and could not be measured.

Alkyl groups having similar polarity but substantially different steric effects were selected as substituents R$^1$ and R$^2$ for the alkenes *(6)*. The data in Table 1 show that steric influences depend markedly on the position of the shielding group on the alkene *(6)*. A substituent at the vinylic C atom undergoing attack reduces the rate from $R^1 = H$ *via* $CH_3$ to $iC_3H_7$ by factors of 90 and 670, respectively (α-effect). In contrast, the same variation at the C atom not undergoing attack only produces factors of 1.4 and 2.3, respectively (β-effect). From the correlation with steric substituent parameters[5] the nonmeasurable effect of a *tert*-butyl group can be estimated as 3000, whilst its β-effect is only 4 (Table 1).

The small β-effect is also reflected in the rate constants $k_2$ shown in Table 1. Hence, the isopropyl derivative *(6d)* is only attacked 4-times slower at the methoxycarbonyl-substituted vinylic C atom than the unsubstituted acrylate *(6a)*. In consequence, the regioselectivity decreases with increasing bulkiness of the alkyl moiety R$^1$ from 99.8 : 0.2%, in unsubstituted acrylate esters *(6a)* *via* 92 : 8% ($R^1 = CH_3$, $R^2 = H$), and 88 : 12% ($R^1 = C_2H_5$, $R^2 = H$), to 75 : 25% for the isopropyl derivative *(6d)* (Table 1).

The vast difference between the steric α- and β-effects can be viewed as experimental confirmation of calculations[6] in which an unsymmetrical transition state *(9)* for the addition of alkyl radicals to alkenes was postulated.



*(9)*

In contrast to electrophilic addition, nucleophilic alkyl radicals do not initially attack alkenes at the center of the double bond, but approach the π-system from the side. This can be understood in terms of the Frontier Orbital theory[3b,7] for addition of nucleophilic alkyl radicals, since the overlap of the singly occupied orbital of the radical (SOMO) with the unoccupied orbital of the alkene (LUMO) is decisive. An approach of the radical from the side is, however, only hampered by substituents which are located at the vinylic C atom being attacked. This difference in magnitude of the steric α- and β-effects is of decisive importance for the regioselectivity of radical additions[8].

Received: March 13, 1981 [Z 901b IE]
German version: Angew. Chem. *93*, 1016 (1981)

CAS Registry numbers:
*(5)*, 3170-58-9; *(6a)*, 96-33-3; *(6b)*, 18707-60-3; *(6c)*, 818-59-7; *(6d)*, 50652-78-3; *(6e)*, 80-62-6; *(6f)*, 2177-67-5; *(6g)*, 3070-67-5; *(6h)*, 79593-50-3.

---

[1] *D. J. Pasto, J. A. Gontarz*, J. Am. Chem. Soc. *91*, 719 (1969); *G. M. Whitesides, J. San Filippo Jr., ibid. 92*, 6611 (1970); *R. P. Quirk, R. E. Lea*, Tetrahedron Lett. *1974*, 1925.

[2] *B. Giese, J. Meister*, Chem. Ber. *110*, 2588 (1977).

[3] a) *B. Giese, J. Meister*, Angew. Chem. *89*, 178 (1977); Angew. Chem. Int. Ed. Engl. *16*, 178 (1977); b) *B. Giese, G. Kretzschmar, J. Meixner*, Chem. Ber. *113*, 2787 (1980).

[4] *C. Rüchardt*, Top. Curr. Chem. *88*, 1 (1980); *J. M. Tedder, J. C. Walton*, Tetrahedron *36*, 701 (1980).

[5] *T. Fujita, C. Takayama, M. Nakajima*, J. Org. Chem. *38*, 1623 (1973); *H.-D. Beckhaus*, Angew. Chem. *90*, 633 (1978); Angew. Chem. Int. Ed. Engl. *17*, 593 (1978).

[6] *S. Nagase, K. Takatsuka, T. Fueno*, J. Am. Chem. Soc. *98*, 3838 (1976); *V. Bonacic-Koutecky, L. Salem, ibid. 99*, 842 (1977); *M. J. S. Dewar, S. Olivella, ibid. 100*, 5290 (1978); *E. Gey, W. Kühnel*, Collect. Czech. Chem. Commun. *44*, 3649 (1979).

[7] *I. Fleming:* Frontier Orbitals and Organic Chemical Reactions, Wiley, New York 1976; *J. Sorba, J. Fossey, D. Lefort*, Bull. Soc. Chim. Fr. *1977*, 967; *A. Citterio, F. Minisci, O. Porta, G. Sesana*, J. Am. Chem. Soc. *99*, 7960 (1977); *B. Giese, J. Meixner*, Angew. Chem. *91*, 167 (1979); Angew. Chem. Int. Ed. Engl. *17*, 154 (1978).

[8] *C. Walling:* Free Radicals in Solution, Wiley, New York 1957.

---

[*] Prof. Dr. B. Giese, Dipl.-Chem. S. Lachhein
Institut für Organische Chemie und Biochemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

---

## *t*Bu$_4$P$_6$, a Novel Bicyclic Organophosphane[**]

By *Marianne Baudler, Yusuf Aktalay,*
*Karl-Friedrich Tebbe,* and *Thomas Heinlein*[*]

*Dedicated to Professor Herbert Grünewald on the occasion of his 60th birthday*

Organo(dichloro)phosphanes react with metals to form monocyclic organophosphanes (RP)$_n$ of various ring

---

[*] Prof. Dr. M. Baudler, Dipl.-Chem. Y. Aktalay, Prof. Dr. K.-F. Tebbe, Dipl.-Chem. T. Heinlein
Institut für Anorganische Chemie der Universität
Greinstrasse 6, D-5000 Köln 41 (Germany)

[**] Contributions to the Chemistry of Phosphorus, Part 107. This work was supported by the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen and by the Fonds der Chemischen Industrie.— Part 106: *M. Baudler, F. Saykowski*, Z. Anorg. Allg. Chem., in press.

sizes[1a,b]. In the presence of $PCl_3$, polycyclic organophosphanes $P_mR_n$ ($n < m$)[2a,b] are formed. We report here the synthesis and properties of tetra-*tert*-butylhexaphosphane *(1)*, a bicycle having an unexpected structure.

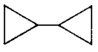
*(1)* is formed by dehalogenating a mixture of *tert*-butyl(dichloro)phosphane and $PCl_3$ with magnesium using widely variable mixture ratios of both phosphorus-halogen compounds

$$4\,t\mathrm{BuPCl_2} + 2\,\mathrm{PCl_3} + 7\,\mathrm{Mg} \rightarrow \underset{(1)}{t\mathrm{Bu_4P_6}} + 7\,\mathrm{MgCl_2}$$

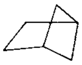
In addition, $t\mathrm{Bu_6P_8}$[2b], $(t\mathrm{BuP})_4$[3a], and $(t\mathrm{BuP})_3$[3b] are formed together with small amounts of the polycyclic phosphanes $t\mathrm{Bu_3P_9}$[3c], $t\mathrm{Bu_5P_9}$, $t\mathrm{Bu_5P_7}$, $t\mathrm{Bu_4P_8}$, and $t\mathrm{Bu_6P_{10}}$. The product distribution is strongly dependent on the reaction conditions: the best initial yield of *(1)* is obtained by performing the reaction rapidly, and using a molar ratio $t\mathrm{BuPCl_2} : \mathrm{PCl_3} = 3:2$ (not 2 : 1!) in boiling tetrahydrofuran (THF). Analytically pure *(1)* can be isolated by column chromatography.

The hexaphosphane *(1)* forms colorless, lamellar crystals (m.p. = 121 °C, sealed tube) which are stable under inert gas at room temperature, and can be sublimed in high vacuum. They are readily soluble in hydrocarbons and THF, but, in contrast, only moderately soluble in methanol. In the solid state at room temperature, *(1)* is stable for some time against atmospheric oxygen, but in solvents is rapidly oxidatively attacked. In the mass spectrum (field ionization, 100 °C), apart from $M^+$ ($m/z$) = 414; rel. int. 100), a single fragment $M^+ - C_4H_9$ (357; 2) appears. The vibrational spectra show bands in the P—P stretching- and deformation-regions[4].

The NMR data (Table 1) unequivocally show that of the four possible structures for the phosphorus skeleton, *(1a)*—*(1d)*[5], the structure assigned as *(1d)* is present; *(1)* is therefore a 2,3,4,6-tetra-*tert*-butylbicyclo[3.1.0]hexaphosphane.


*(1a)*


*(1b)*


*(1c)*

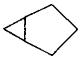
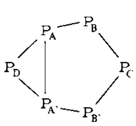

*(1d)*

Table 1. $^{31}$P-, $^{1}$H-, and $^{13}$C-NMR data of *(1d)* [a].



| | | | | | |
|---|---|---|---|---|---|
| $\delta(^{31}P)$ | A = A' | = −48.4 | $J_{PP}$ [Hz] | AA' | = −212.9 |
| | B = B' | = 115.6 | | AB = A'B' | = −324.3 |
| | C | = 143.6 | | BC = B'C | = −328.4 |
| | D | = −136.9 | | AD = A'D | = −175.2 |
| | | | | AB' = A'B | = 18.3 |
| | | | | AC = A'C | = −16.3 |
| | | | | BB' | = −23.2 |
| | | | | BD = B'D | = 118.1 |
| | | | | CD | = −1.7 |
| $\delta(^{1}H)$ [b] | $P_BCMe_3$ | = 1.42 | | | |
| | $P_CCMe_3$ | = 1.33 | | | |
| | $P_DCMe_3$ | = 0.94 | | | |
| $\delta(^{13}C)$ [b] | $P_BC$ | = 32.89 | | $P_BCC$ | = 31.97 |
| | $P_CC$ | = 30.23 | | $P_CCC$ | = 33.58 |
| | $P_DC$ | = 29.17 | | $P_DCC$ | = 29.83 |

[a] 30% solution in $C_6H_6/C_6D_6$ at 303 K ($^{31}$P) and 306 K ($^{1}$H, $^{13}$C). [b] The assignment follows from the relative intensities and the characteristic high-field of the signals for the substituents on the three-membered ring; the results were confirmed by $^{31}$P-partial decoupling experiments.

The $^{31}P\{^1H\}$-NMR spectrum (four complex multiplets in the ratio 1 : 2 : 2 : 1 at $\delta \approx +145, +115, -45$, and $-135$) establishes that the signal group at high-field stems from $P_D$ in the three-membered ring, and that both closely neighboring low-field signal groups stem from $P_B$ and $P_C$ in the five-membered ring. The configuration follows from the chemical equivalence of $P_A$ and $P_{A'}$, as well as $P_B$ and $P_{B'}$; moreover, the large $^2J_{P_BP_D}$ coupling constant[6] indicates that the lone pairs of electrons at $P_B$ and $P_D$ are directed towards each other. In consequence, the three-membered ring is strongly inclined relative to the five-membered ring, and the arrangement of the substituents is *all-trans*. In contrast to other polycyclic organophosphanes, further configurational isomers do not occur[2a,7]. The X-ray structural analysis[8] (Fig. 1) confirms that *(1d)* has a chair-like phosphorus skeleton. Because of the influence of the substituents, the five-membered ring adopts an unusually flat, only slightly twisted envelope conformation in the crystal; the endocyclic bond angles are comparatively large. The slightly distorted three-membered ring stands almost at right angles to the five-membered ring.

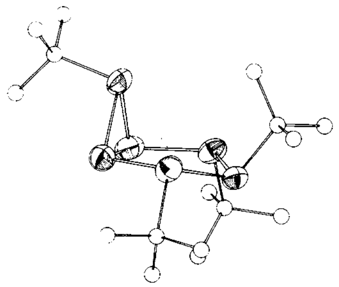
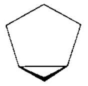
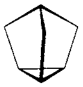


Fig. 1. Molecular structure of *(1)* in the crystal; values and average values of important bond lengths [pm], bond angles and torsional angles [°]: $d$(P—P) = 219.2, 220.2, 220.8, 219.5 (five-membered ring); 219.5 (zero bridge); 217.8, 219.2 (three-membered ring); $\sigma$(P—P) = 0.4; $\varphi$(P—P—P) = 108.4, 106.7, 107.4, 106.8, 107.7 (five-membered ring); 99.6, 97.9 (three-membered ring/five-membered ring); 60.2, 60.3, 59.5 (three-membered ring); $\sigma$(P—P—P) = 0.2; $\tau$(P—P—P—P) = −1.8, 11.7, −17.3, 16.2, −8.9 (five-membered ring); 88.9, −90.7 (five-membered ring/three-membered ring over the zero bridge); $\sigma$(P—P—P—P) = 0.2; $\bar{d}$(P—C) = 189.5(6); $\bar{d}$(C—C) = 153.2(10); $\bar{\varphi}$(P—P—C) = 102.1(18); $\bar{\varphi}$(P—C—C) = 105.9(9) (twice respectively), 115.5(12) (once respectively); $\bar{\varphi}$(C—C—C) = 109.8(12).

The ring system *(1d)* formally arises from the particularly stable $P_7$-cage *(2)*[7,9] when one of the three one-atom bridges is removed.


*(1d)*


*(2)*

A consideration of molecular models indicates that $t\mathrm{Bu_4P_6}$ does not adopt the framework *(1b)* or *(1c)* with a four-membered ring because of the strong transannular interactions between the *tert*-butyl groups. With smaller substituents, *(1d)* could be destabilized relative to *(1b)* and *(1c)*.

### Procedure

A solution of $t\mathrm{BuPCl_2}$ (31.8 g, 0.20 mol) and $PCl_3$ (18.3 g, 0.13 mol) in 60 mL of THF is added dropwise, with rigorous stirring, over 30 min to a suspension of magnesium turnings (10.0 g, 0.41 mol), which had been etched by evaporating a few grains of iodine, in 400 mL of boiling THF. The yellow mixture is refluxed for 30 min, whereby it turns dark red-brown. Finally, the solvent is completely removed under reduced pressure at room temperature. The residue is taken up in 500 mL *n*-pentane and the undissolved material filtered off, washed with pentane (4 x 20 mL), and the solvent removed from the combined filtrates. The yellow, viscous residue is dissolved in the minimum amount of pentane and chromatographed on $Al_2O_3$ using pentane with $^{31}P\{^1H\}$-NMR spectroscopic control (column length: 50 cm; inner diameter: 5.8 cm; filling material: $Al_2O_3$ neutral according to *Brockmann*, particle size 0.063—0.200 mm, thoroughly heated *in vacuo*, and gassed with Ar; amount of solvent: 4500 mL; duration: 10—12 h). The fractions having the highest content of *(1)* are combined, the pentane is removed, and the white residue is taken up in 50 mL of boiling methanol (made absolute over Mg). After rapidly filtering off the undissolved part while still warm, and allowing the filtrate to slowly cool to room temperature, large, translucent crystals of *(1)* precipitate out; yield 3.3 g (16%). If necessary, ($^{31}P$-NMR spectroscopic control of purity) they can be recrystallized again.

Received: July 10, 1981 [Z 906 IE]
German version: Angew. Chem. *93*, 1020 (1981)

CAS Registry numbers:
*(1)*, 79593-41-2; *t*-$BuPCl_2$, 25979-07-1; $PCl_3$, 7719-12-2.

---

[1] a) *L. Maier* in *G. M. Kosolapoff, L. Maier:* Organic Phosphorus Compounds, Vol. 1, Wiley-Interscience, London 1972, p. 340; b) *M. Baudler*, Pure Appl. Chem. *52*, 755 (1980).

[2] a) *M. Baudler, Y. Aktalay, J. Hahn, E. Därr*, Z. Anorg. Allg. Chem. *473*, 20 (1981); b) *M. Baudler, J. Hellmann, P. Bachmann, K.-F. Tebbe, R. Fröhlich, M. Fehér*, Angew. Chem. *93*, 415 (1981); Angew. Chem. Int. Ed. Engl. *20*, 406 (1981).

[3] a) *K. Issleib, M. Hoffmann*, Chem. Ber. *99*, 1320 (1966); b) *M. Baudler, J. Hahn, H. Dietsch, G. Fürstenberg*, Z. Naturforsch. *B 31*, 1305 (1976); *M. Baudler, C. Gruner, ibid. B 31*, 1311 (1976); c) *W. Hölderich, G. Fritz*, Z. Anorg. Allg. Chem. *457*, 127 (1979).

[4] IR ($< 500\ cm^{-1}$, KI disc): 494 (vw), 458 (vw), 438 (w), 393 (m), 374 (w), 361 (m), 355 (w, sh), 316 (vw) $cm^{-1}$; Raman ($< 500\ cm^{-1}$, Krypton): 495 (w), 460 (vw), 438 (w), 402 (m), 377 (m), 310 (w), 288 (w), 247 (m), 220 (w), 191 (s), 162 (s), 141 (s), 112 (s) $cm^{-1}$.

[5] Isomers with exocyclic $tBu_{n+1}P_n$ groups are unlikely to be formed in this synthetic route.

[6] In this content see also the analysis of the $^{31}P\{^1H\}$-NMR spectrum of $P_7Me_5$; *M. Baudler, E. Därr, J. Hahn*, Z. Naturforsch., in press.

[7] *M. Baudler, W. Faber, J. Hahn*, Z. Anorg. Allg. Chem. *469*, 15 (1980).

[8] Space group $P2_1/n$ (No. 14); $a = 912.0(3)$, $b = 1383.8(2)$, $c = 1951.4(5)$ pm, $\beta = 90.93(2)°$; $V = 2462.4 \times 10^6\ pm^3$, $Z = 4$, $\rho_{X\text{-ray}} = 1.117\ g \cdot cm^{-3}$. $\mu(Mo_{K\alpha}) = 4.26\ cm^{-1}$. CAD4-Diffractometer (ENRAF Nonius), $Mo_{K\alpha}$ irradiation, $2\theta \leq 32.5°$; 1375 reflections (hkl), of which 860 with $|F_0| \geq 4 \cdot \sigma(F_0)$. Solution (direct methods) with the SHELX76 program; refinement (P and C anisotropically, H in rigid methyl groups with $d(C—H) = 108$ pm) to $R = 0.033$, $R_w = 0.037$; *T. Heinlein, K.-F. Tebbe*, unpublished results.

[9] a) *G. Fritz, W. Hölderich*, Naturwissenschaften *62*, 573 (1975); b) *H. G. von Schnering*, Angew. Chem. *93*, 44 (1981); Angew. Chem. Int. Ed. Engl. *20*, 33 (1981), and literature cited therein; c) *M. Baudler, T. Pontzen, J. Hahn, H. Ternberger, W. Faber*, Z. Naturforsch. *B35*, 517 (1980).

---

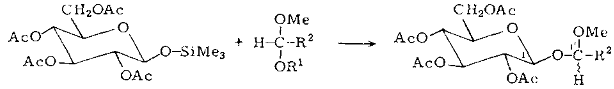
# Stereoselective Synthesis of β-Glucosides with 1,1'-Diacetal Structure[**]

By *Lutz-F. Tietze* and *Roland Fischer*[*]

*Dedicated to Professor George Büchi on the occasion of his 60th birthday*

The stereoselective preparation of glycosides is one of the most exacting synthetic tasks in natural product chemistry[1]. Particularly difficult is the synthesis of glucosides having 1,1'-diacetal structure, such as those present in the 1,1-coupled disaccharides or iridoid glycosides[2]. We have now found a simple, highly stereoselective method for the synthesis of this type of compounds.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-trimethylsilyl-β-D-glucopyranose *(1)*[3] is used as educt for the synthesis of β-glucosides. Reaction of *(1)* with the acetals *(2a—h)* in the presence of catalytic amounts of trimethylsilyl trifluoromethanesulfonate[4] at −70 °C affords the β-glucosides *(3a, c—h)* in very good yields. α-Glucosides are not formed at all under these conditions. As expected, in the reaction with formaldehyde acetal *(2a)* the homogeneous product *(3a)* is obtained, whereas reaction with the prochiral acetals *(2c—h)* leads to a *ca.* 1 : 1 mixture of the C-1' epimers. In the case of the methyl(phenyl) acetal *(2b)*, exclusive cleavage of the phenoxy group takes place (Table 1).



*(1)* *(2)* *(3)*

Table 1. Synthesis of the β-glucosides *(3)* from the educts *(1)* and *(2)*.

| Educts *(1)*+*(2)* | $R^1$ | $R^2$ | Products *(3)* | Yield [%] | $^1H$-NMR [a] *(3)*, H instead of Ac |
|---|---|---|---|---|---|
| *(2a)* | Me | H | *(3a)* | 75 | 4.58 |
| *(2b)* | Ph | H | | 88 | |
| *(2c)* | Me | $CH_2—Ph$ | *(3c)* [b] | 84 | 4.57, 4.67 |
| *(2d)* | Me | *n*-$C_3H_7$ | *(3d)* [b] | 78 | 4.47, 4.59 |
| *(2e)* | Me | $CH_2—CH(OMe)_2$ | *(3e)* [b] | 79 | 4.63, 4.71 |
| *(2f)* | Me | $CH_2—OMe$ | *(3f)* [b] | 77 | 4.57, 4.67 |
| *(2g)* | Me | $CH_2—Cl$ | *(3g)* [b] | 75 | 4.63, 4.71 |
| *(2h)* | Me | $CH_2—Br$ | *(3h)* [b] | 78 | 4.63, 4.71 |
| *(2i)* | Me | Ph | — | | |

[a] $[D_6]$Acetone/$D_2O$, δ-values for 1-H; $J_{1,2} = 7.5$ Hz. [b] Mixture of the C-1' epimers (*ca.* 1 : 1).

We assume that the reaction proceeds *via* a silylation of one acetal oxygen of *(2)* with formation of an oxonium ion[5], which then undergoes a kind of $S_N2$ reaction[6] with the trimethylsilylglucoside *(1)* at −70 °C with retention of configuration at C-1. Ketals such as cyclohexanone- and acetonedimethyl acetal, as well as the dimethyl acetals of aromatic aldehydes [*e.g.* *(2i)*][7], do not react with *(1)*.

The work-up and purification of the products is accomplished by chromatography on silica gel. For determination of the selectivity of the reaction and of the configuration at C-1 the glucosides were liberated from the unpurified and purified acetyl derivatives *(3)* by solvolysis with methanol/sodium methoxide (yield >90%).

## *Procedure*

A 0.1 M solution of trimethylsilyl trifluoromethanesulfonate (0.2 mL) in $CH_2Cl_2$ is added to a solution of *(1)* (105 mg, 0.25 mmol) and *(2c)* (83.0 mg, 0.50 mmol) in anhydrous $CH_2Cl_2$ (3 mL) under inert gas at −70 °C and the mixture stirred at this temperature (TLC monitoring; silica gel, hexane/ethyl acetate = 1 : 1) for *ca.* 20 h. After addition of 0.1 mL triethylamine the reaction mixture is washed with saturated $NaHCO_3$ and NaCl solutions and dried over $Na_2SO_4/Na_2CO_3$ (1 : 1). Removal of the solvent *in vacuo* affords 115 mg (95%) of crude product which is almost homogeneous. Further purification can be achieved by chromatography on silica gel; yield 101 mg (84%) *(3c)*.

Received: March 31, 1981 [Z 889a IE]
German version: Angew. Chem. *93*, 1002 (1981)

---

[*] Prof. Dr. L.-F. Tietze, Dipl.-Chem. R. Fischer
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

CAS Registry numbers:
*(1)*, 19126-95-5; *(2a)*, 109-87-5; *(2b)*, 824-91-9; *(2c)*, 101-48-4; *(2d)*, 4461-87-4; *(2e)*, 102-52-3; *(2f)*, 24332-20-5; *(2g)*, 65652-26-8; *(2h)*, 7252-83-7; *(2i)*, 1125-88-8; *(3a)*, 79435-86-2; *(3c)* isomer *1*, 79435-87-3; *(3c)* isomer 2, 79435-91-*(3d)* isomer *1*, *79435-89-5*; *(3d)* isomer 2, 79435-90-8; *(3e)* isomer *1*, 79435-91-9; *(3e)* isomer 2, 79435-92-0; *(3f)* isomer *1*, 79448-87-6; *(3f)* isomer 2, 79448-88-7; *(3g)* isomer *1*, 79435-93-1; *(3g)* isomer 2, 79435-94-2; *(3h)* isomer *1*, 79435-95-3; *(3h)* isomer 2, 79435-96-4

---

[1] *G. Wulff, G. Röhle*, Angew. Chem. *86*, 173 (1974); Angew. Chem. Int. Ed. Engl. *13*, 157 (1974).

[2] *L.-F. Tietze, U. Niemeyer*, Chem. Ber. *111*, 2423 (1978); *L.-F. Tietze, U. Niemeyer, P. Marx, K.-H. Glüsenkamp, L. Schwenen*, Tetrahedron *36*, 735 (1980); *L.-F. Tietze, U. Niemeyer, P. Marx, K.-H. Glüsenkamp, ibid. 36*, 1231 (1980).

[3] *L. Birkofer, A. Ritter, F. Bentz*, Chem. Ber. *97*, 2196 (1964); preparation analogous to the synthesis of the α-compound (*A. Klemer, E. Buhe, R. Kutz*, Justus Liebigs Ann. Chem. *739*, 185 (1970)). *(1)*: m.p. 104.7 °C, $[\alpha]_D^{20}$ −6.8 ($c=1$ in $CHCl_3$).

[4] For the use of trimethylsilyl trifluoromethanesulfonate in nucleoside synthesis see *H. Vorbrüggen, K. Krolikiewicz*, Angew. Chem. *87*, 417 (1975); Angew. Chem. Int. Ed. Engl. *14*, 421 (1975); *T. Azuma, K. Isono*, Chem. Pharm. Bull. *25*, 3347 (1977).

[5] Cf. *S. Murata, M. Suzuki, R. Noyori*, J. Am. Chem. Soc. *102*, 3248 (1980); *T. Tsunoda, M. Suzuki, R. Noyori*, Tetrahedron Lett. *1980*, 71.

[6] It cannot be ruled out that the reaction may proceed *via* an ion-pair. This problem should be checked with chiral acetals.

[7] Use of the method for the synthesis of α-glycosides: *L.-F. Tietze, R. Fischer*, Tetrahedron Lett. *1981*, 3239.

---

## Synthesis of [10-$^{13}$C]Secologanin[**]

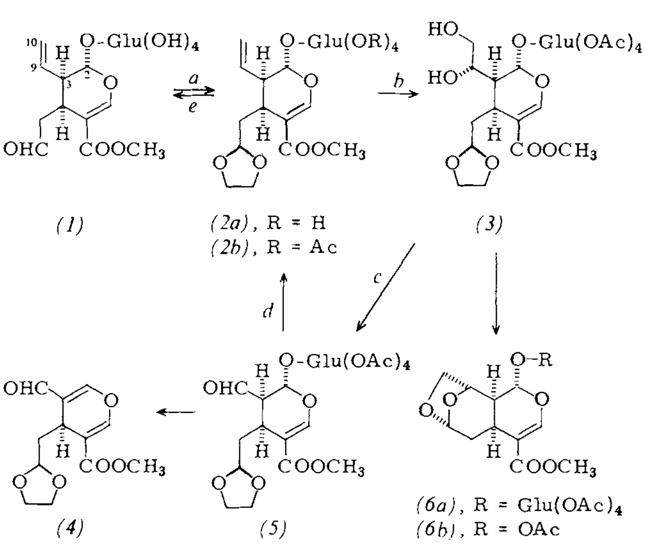
By *Lutz-F. Tietze* and *Stephan Henke*[*]

*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

The monoterpeneglycoside secologanin *(1)* assumes a key position in the biogenesis of the indole, cinchona, ipecacuanha and pyrroloquinoline alkaloids[1] and the secoiridoids[2]. Most biosynthetic investigations in this field have been carried out with [$^{3}$H]- and [$^{14}$C]-labeled precursors. However, identification of unisolated intermediates is generally impossible by this method. This necessitates monitoring the reactions of [$^{13}$C]-labeled precursors with cell-free enzyme systems or isolated enzymes by means of $^{13}$C-NMR spectroscopy[3].

We now describe a method for the synthesis of [10-$^{13}$C]secologanin [10-$^{13}$C]-*(1)* from natural secologanin *(1)*[4]. C-10 was chosen for labeling, since this center participates in most biological transformations of *(1)*.

Acid-catalyzed reaction of *(1)* with ethylene glycol to give *(2a)*, followed by acetylation with acetic anhydride/pyridine, affords almost quantitative yields of the peracetylated acetal *(2b)*. The analogously prepared dimethyl acetal is not stable enough for the following reactions. Oxidation of *(2b)* with equimolar amounts of osmium tetraoxide[5] in pyridine leads to the diol *(3)* in 31% yield. The other diastereomer is not formed. Other products of the reaction include tetraacetylglucose[6] (30%) and *(6a)* together with educt *(2b)* (29%). For determination of the configuration at C-9, *(3)* is converted with perchloric acid/acetic acid into the tricyclic compound *(6a)*, which, on solvolysis, glycoside-cleavage and acetylation, affords the acetate *(6b)* (m.p. 119 °C) in 82% overall yield. *(6b)* is identified by comparison with authentic material[7].



Scheme 1. *a*: 1. $HOCH_2CH_2OH$, $CH_3CN$, IR 120 ($H^{\oplus}$), $Na_2SO_4$, 5 °C/24 h, 94% *(2a)*; 2. $Ac_2O$/pyridine, 20 °C/24 h, 91% *(2b)*, m.p. 131.5 °C.—*b*: $OsO_4$/pyridine, 20 °C/72 h; $NaHSO_3$, 5 min, 31% *(3)*, m.p. 138 °C; 30% tetraacetylglucose; 29% *(2b)*; 3% *(6a)*.—*c*: $Pb(OAc)_4$, $CHCl_3$, 60 °C, 30 min, 96% *(5)*, m.p. 145 °C.—*d*: $Ph_3\overset{\oplus}{P}CH_3$ $I^{\ominus}$, *n*BuLi, THF, −30 °C/30 min, 20 °C/3 h, 60 °C/12 h, 20% *(2b)*, m.p. 131.5 °C; 48% *(4)*.—*e*: 1. MeOH/NaOMe, 20 °C/6 h, 96% *(2a)*; 2. $H_2O$, $CH_3CN$, IR 120 ($H^{\oplus}$), 5 °C/6 d, 81% *(1)*.—The yields refer to isolated and analytically pure products.

Oxidative cleavage of *(3)* with lead tetraacetate furnishes the aldehyde *(5)* in 96% yield, which very readily loses tetraacetylglucose with formation of the pyran *(4)*. For introduction of the labeled C$_1$-unit, *(5)* is allowed to react with (triphenylphosphonio)[$^{13}$C]methanide, which can be easily prepared from triphenylphosphane and [$^{13}$C]$H_3I$[8]. The desired [10-$^{13}$C]-*(2b)* can be obtained under a wide variety of reaction conditions, albeit in only 20% yield; the pyran *(4)* is always the main product. Base-solvolysis of the acetate groups in [10-$^{13}$C]-*(2b)* and subsequent acid-catalyzed cleavage of the acetal affords [10-$^{13}$C]secologanin [10-$^{13}$C]-*(1)* in 78% yield (Scheme 1).

Introduction of the C$_1$-unit[9] into *(5)* can also be accomplished in 45% yield *via* a Grignard reaction with methylmagnesium iodide. The secondary alcohol formed, however, reacts after conversion into the methanesulfonate with 1,5-diazabicyclo[4.3.0]non-5-ene to give an *E*-configurated isomer of *(2b)* having a double bond between C-3 and C-9 (38% yield).

Received: March 31, 1981 [Z 889b IE]
German version: Angew. Chem. *93*, 1005 (1981)

CAS Registry numbers:
*(1)*, 19351-63-4; *(2a)*, *79409-45-3*; *(2b)*, 79409-46-4; *(3)*, 79409-47-5; *(4)*, 79409-48-6; *(5)*, 79420-93-2; *(6a)*, 79409-49-7; *(6b)*, 79409-50-0.

---

[*] Prof. Dr. L.-F. Tietze, Dipl.-Chem. S. Henke
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *G. A. Cordell*, Lloydia *37*, 219 (1974), and references cited therein; *A. R. Battersby, R. J. Parry*, J. Chem. Soc. Chem. Commun. *1971*, 901; *C. R. Hutchinson, A. H. Heckendorf, P. E. Daddona, E. Hagaman, E. Wenkert*, J. Am. Chem. Soc. *96*, 5609 (1974).

[2] *H. Inouye, S. Ueda, Y. Takeda*, Heterocycles *4*, 527 (1976).

[3] *U. Séquin, A. I. Scott*, Science *186*, 101 (1974); *M. Tanabe*, Spec. Period. Rep. Biosynthesis *4*, 204 (1976), Chem. Soc. London.

[4] Secologanin was isolated from *Symphoricarpus rivularis*.

[5] Oxidation with catalytic amounts of $OsO_4$ in the presence of $KClO_3$ led to only 11% of *(3)*.

[6] The formation of tetraacetylglucose can be explained in terms of a reaction of $OsO_4$ at the CC double bond in the dihydropyran ring. Tetraacetylglucose could be detected only with difficulty, since it gave the same $R_f$ value as *(2b)* in almost all eluents on chromatography on silica gel. Separation was accomplished with *tert*-butyl methyl ether/cyclohexane (3 : 1).

[7] *L.-F. Tietze, K.-H. Glüsenkamp*, unpublished results.

[8] For refinement of the method methyltriphenylphosphonium iodide containing natural isotopes was employed.

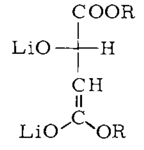
[9] Attempts to introduce the C$_1$-unit with metalated chloromethyltrimethylsilane did not give the desired products; *D. J. Peterson*, J. Org. Chem. *33*, 780 (1968); *T. H. Chan, E. Chang, ibid. 39*, 3264 (1974).

# Alkylation of Amino Acids without Loss of Optical Activity: α- and β-Alkylation of an Aspartic Acid Derivative

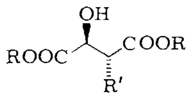
By *Dieter Seebach* and *Daniel Wasmuth*[*]

*Dedicated to Professor Leopold Horner on the occasion of his 70th birthday*

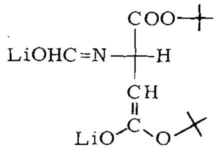
Double deprotonation of dimethyl or diethyl malate by two equivalents of lithium diisopropylamide (LDA) generates the dilithio derivative *(1)*, which is converted into *erythro*-products *(2)* with a variety of electrophiles[1]. We have now tried to extend this *α-alkylation of β-heterosubstituted carbonyl compounds* to di-*tert*.-butyl (*S*)- or L-(+)-*N*-formyl-aspartate[2]. Unlike LDA, lithium diethylamide effected a clean double deprotonation (THF, −78 °C, 2 h) to give *(3)*, which was alkylated by iodomethane, iodoethane, allyl bromide, or benzyl bromide (−78 °C, 12 h) to furnish a mixture of β- and α-substituted aspartic acid derivatives *(4)* and *(5)* in the ratio of *ca.* 7 : 2 and in total yields ranging from 60 to 70%. The pairs of isomers *(4)/(5)* can be separated chromatographically (silica gel, diethyl ether/pentane). According to their chromatographic behavior, to their melting points and/or their specific rotations, and to their $^1$H- and $^{13}$C-NMR spectra, the β-alkylated α-amino acid esters *(4b)—(4e)* thus obtained are diastereomerically and enantiomerically pure. However, their solutions, like those of the starting material *(4a)* itself, contain two rotamers[3].—To our surprise, the α-alkylated α-amino acid derivatives *(5b)—(5e)* are also optically active. Enantiomeric enrichment by fractional crystallization was possible with *(5c)—(5e)*. From the highest specific rotations thus observed, and from $^1$H-NMR measurements with chiral shift reagent Eu(tfc)$_3$ we deduce enantiomeric excesses of *ca.* 60% in the originally formed samples of *(5)*.—Table 1 lists some characteristic data of the products *(4)* and *(5)*.



*(1)*

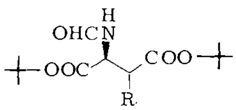


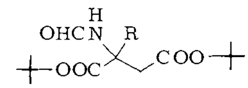
*(2)*



*(3)*

*(4)*





*(5)*

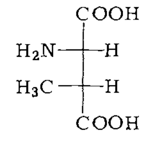
*(a)*, R = H; *(b)*, R = CH$_3$; *(c)*, R = C$_2$H$_5$; *(d)*, R = CH$_2$CH=CH$_2$; *(e)*, R = CH$_2$C$_6$H$_5$

Table 1. Characteristic physical data of the analytically pure β- and α-alkylated aspartates *(4)* and *(5)*, respectively, after crystallization or distillation. Except in the case of *(5b)*, the specific rotations are given of products *(5) after* separation of the racemic components.

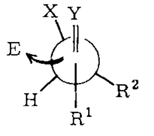
| Compound | B.p./torr [a] or M.p. [°C] | $[\alpha]_D^{20}$ (*c*, CHCl$_3$) |
|---|---|---|
| *(4a)*≡*(5a)* | 130/0.01 | +44.4 (1.14) |
| *(4b)* | 84—85 | +16.8 (1.22) |
| *(5b)* | 140/0.01 | −15.3 (1.27) [b] |
| *(4c)* | 150/0.005 | + 1.0 (1.36) |
| *(5c)* | 150/0.01 | −17.0 (1.07) |
| *(4d)* | 140/0.005 | +24.6 (1.05) |
| *(5d)* | 77—78 | +17.2 (1.00) |
| *(4e)* | 102—103 | +43.0 (1.45) |
| *(5e)* | 106 | +61.1 (1.05) |

[a] Air bath temperatures during Kugelrohr distillations. [b] As obtained as a colorless oil by chromatography, *without* enrichment of the enantiomeric purity.

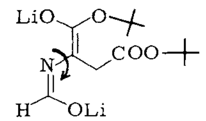
The configuration of *one* of the products *(4)*, the methyl derivative *(4a)*, was established by hydrolysis of the ester and amide groups to give *erythro*- or (2*S*,3*R*)-3-methylaspartic acid *(6)* ($[\alpha]_D^{20}$ = +38.7 (*c* = 1.83, 5 N HCl; ref.[4] $[\alpha]_D^{24}$ = +35 (*c* = 2, 5 N HCl)). We tentatively assign *erythro*-configuration to *all* alkylation products *(4)*. This is compatible with the rule (cf. *(7)*, R$^1$ = H, R$^2$ = CO$_2$*t*Bu, X = NCHOLi, Y = C(OLi)(O-*t*Bu)), proposed previously for reactions of other donor double bonds[1a,5].—The α-alkylation of the *N*-formyl-aspartate shows that the dilithio-derivative *(8)* has been formed besides the desired enolate *(3)*. Further experiments will be necessary to decide, why *(8)* leads to optically active α-alkylated products; two possibilities are: (a) the 6-atom-8-electron π-system[6] is axially chiral [see the bond emphasized by an arrow in *(8)*], (b) the achiral *(8)* forms mixed aggregates[7] with the chiral dilithio-derivative (3). If the interpretation (a) should turn out to be valid, simple amino acids might also be alkylated *via* derivatives of type *(8)* (R instead of CH$_2$CO$_2$-*t*Bu) without racemization[8].



*(6)*



*(7)*



*(8)*

Received: June 19, 1981 [Z 894 IE]
German version: Angew. Chem. *93*, 1007 (1981)

CAS Registry numbers:
*(4a)*, 79435-77-1; *(4b)*, 79435-78-2; *(4c)*, 79435-79-3; *(4d)*, 79435-80-6; *(4e)*, 79435-81-7; *(5b)*, 79435-82-8; *(5c)*, 79435-83-9; *(5d)*, 79435-84-0; *(5e)*, 79435-85-1; *(6)*, 7298-96-6.

---

[*] Prof. Dr. D. Seebach, Dipl. sc. nat. D. Wasmuth
Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

[1] a) *D. Seebach, D. Wasmuth*, Helv. Chim. Acta *63*, 197 (1980); *M. Züger, T. Weller, D. Seebach, ibid. 63*, 2005 (1980).—b) cf. also: *G. Fráter, ibid. 62*, 2825 and 2829 (1979); 1383 (1980); Tetrahedron Lett. *1981*, 425.

[2] The compound was obtained by formylation of commercial di-*tert*.-butyl aspartate dibenzene sulfimide salt (DBSI-salt) with CH$_3$—CO—O—CHO (*L. I. Krimen*, Org. Synth. *50*, 1 (1970)).

[3] The ratio (>9 : 1) of rotamers can be determined from the NMR spectra; it is unchanged after purification steps such as chromatography, distillation, or recrystallization. Most likely, we are dealing with conformational diastereomerism around the N—CHO-formamide bond.

[4] *M. Bodanzky, G. G. Marconi*, J. Antibiot. *23*, 238 (1970); *H. A. Barker, R. D. Smyth, R. M. Wilson, H. Weissbach*, J. Biol. Chem. *234*, 320 (1959).

[5] *D. Seebach, A. K. Beck, F. Lehr, T. Weller, E. W. Colvin*, Angew. Chem. *93*, 422 (1981); Angew. Chem. Int. Ed. Engl. *20*, 397 (1981).

[6] See the references cited in the Section "redox umpolung" of the following article on umpolung of reactivity: *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979).—Cf. the discussion in: *D. Seebach, W. Wykypiel, W. Lubosch, H.-O. Kalinowski*, Helv. Chim. Acta *61*, 3100 (1978).—*B. W. Metcalf, P. Casara*, J. Chem. Soc. Chem. Commun. *1979*, 119.

[7] Formation of aggregates in solution: *L. M. Jackman, B. C. Lange*, Tetrahedron *33*, 2737 (1977).

[8] It was reported recently that the α-alkylation of benzal-tryptophane ester is feasable without racemization: *M. F. Braña, M. Garrido, M. L. López, A. M. Sanz*, J. Heterocycl. Chem. *17*, 829 (1980).

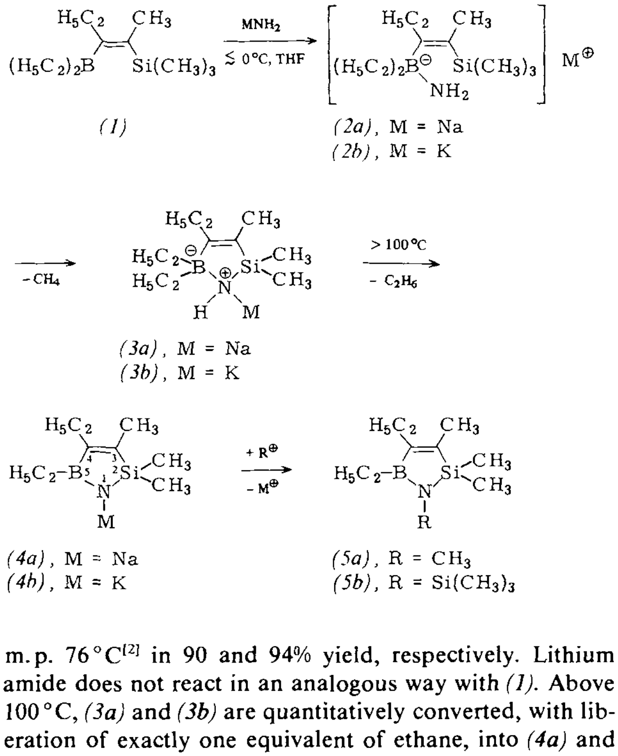
*0570-0833/81/1111-0971 $ 02.50/0*

## Novel Five-Membered $C_2BNSi$-Rings[**]

By *Roland Köster* and *Günter Seidel*[*]

We have prepared novel five-membered ring heterocycles by a new type of ring-closure reaction. The (*E*)-diethyl(2-trimethylsilyl-2-penten-3-yl)borane *(1)*[1], which is readily accessible by reaction of sodium triethyl-1-propynylborates with chloro(trimethyl)silane, can easily be converted into the *N*-metalated pentaalkyl-$\Delta^3$-1,2,5-azasilaborolines *(4)* and the *N*-methylated or *N*-trimethylsilylated $\Delta^3$-1,2,5-azasilaborolines *(5a)* or *(5b)*, respectively.

Reaction of *(1)* in toluene or tetrahydrofuran (THF) at $\leq 0\,^\circ C$ with sodium or potassium amide leads to formation of the thermally unstable, $^{11}$B-NMR spectroscopically detectable alkali-metal amino(triorgano)borates *(2a)* or *(2b)*. In THF solution, aminolysis of a methyl residue of the trimethylsilyl group leads to loss of exactly one equivalent of methane, in the case of *(2a)* at 25 °C, in the case of *(2b)* already at 0 °C. This unexpected, rapid and completely smooth reaction affords the previously unknown five-membered ring heterocycles *(3a)*, m.p. > 120 °C (dec.) and *(3b)*, m.p. 76 °C[2] in 90 and 94% yield, respectively. Lithium amide does not react in an analogous way with *(1)*. Above 100 °C, *(3a)* and *(3b)* are quantitatively converted, with liberation of exactly one equivalent of ethane, into *(4a)* and *(4b)*[2], which are colorless solids that melt without decomposition at 154–156 and 262 °C, respectively. The intramolecular aminolysis of the borates *(2)* takes place exclusively at the SiC bond and not—as is otherwise usual—at the BC bond. The regiospecificity of the aminolysis can be ascribed to the *cis* orientation of the trimethylsilyl group in the borates *(2)*, for dialkyl(amino)-substituted vinyl borates free of silyl groups are thermally preferably cleaved at the $BC_{vinyl}$ bond[3]. *(4a)* and *(4b)* readily react with electrophiles, *e.g.* with iodomethane or chloro(trimethyl)silane to give very good yields (80–90%) of the heterocycles *(5a)* and *(5b)*, which can be distilled without decomposition[2].



*(4)* and *(5)* are suitable for the preparation of a variety of transition metal complexes[3].

*Procedure*

*(3a)*: *(1)*[1] (8 g, 38 mmol) is added dropwise within 0.5 h at 0 °C to a suspension of sodium amide (1.9 g, 49 mmol) in THF (80 mL) and the mixture stirred for *ca.* 1 h [*(2a)* $^{11}$B-NMR: $\delta = -7.8$] before removing the cooling-bath. On warming to over 25 °C (up to boiling) 852 mL (100%) methane is evolved within 1.5 h. After removal of *ca.* 0.9 g of $NaNH_2$ (excess) by filtration, evaporation to dryness at 12 torr, and drying ($10^{-3}$ torr/60 °C), 8 g (90%) of *(3a)* is obtained.—IR (Nujol): $\nu_{NH} = 3355, 3300$, $\nu_{C=C} = 1535$ cm$^{-1}$; $^{11}$B-NMR: $\delta = -2.3$ ($\Delta = 65$ Hz).

*(4a)*: *(3a)* (50.8 g, 218 mmol) is heated to 120–130 °C; 4.8 L (98%) of ethane is liberated within *ca.* 2 h. There remain 44 g (98%) of *(4a)*.—IR (Nujol): $\nu_{C=C} = 1550$ cm$^{-1}$; $^{11}$B-NMR: $\delta = 48$.

*(5a)*: Iodomethane (24.2 g, 171 mmol) is added dropwise within *ca.* 50 min to a solution of *(4a)* (30.3 g, 149 mmol) in THF (250 mL), whereupon the mixture warms to *ca.* 45 °C. After 4 hours boiling under reflux and removal of 18.2 g of NaI by filtration, the solvent is distilled off at 12 torr. 5.3 g of residue and 25.2 g (87%) of *(5a)* are obtained. *(5a)*: b.p.$_{12}$ = 67–68 °C.—IR: $\nu_{C=C} = 1560$ cm$^{-1}$; $^{11}$B-NMR: $\delta = 46.4$ ($\Delta = 190$ Hz).

Received: March 11, 1981 [Z 896 IE]
German version: Angew. Chem. *93*, 1009 (1981)

CAS Registry numbers:
*(1)*, 79483-02-6; *(2a)*, 79483-25-3; *(2b)*, 79483-26-4; *(3a)*, 79483-27-5; *(3b)*, 79499-31-3; *(4a)*, 79483-03-7; *(4b)*, 79483-04-8; *(5a)*, 79483-05-9; *(5b)*, 79483-06-0.

---

[1] *P. Binger, R. Köster*, Synthesis *1973*, 309; *R. Köster, L. A. Hagelee, ibid. 1976*, 118.

[2] Composition and structure of the compounds *(3)*, *(4)* and *(5)* are confirmed by elemental analysis, mass spectrum and NMR spectra.

[3] *R. Köster, G. Seidel*, unpublished results.

---

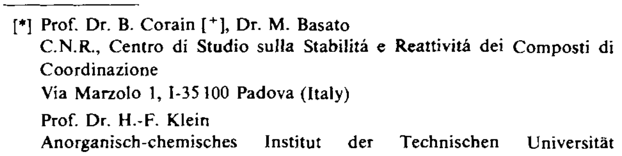
[*] Prof. Dr. R. Köster, Chem.-Ing. G. Seidel
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim an der Ruhr (Germany)

[**] Boron compounds, Part 51.—Part 50: *R. Köster, W. Fenzl, F. J. Levelt*, Liebigs Ann. Chem. *1981*, 734.

## Simple Metal-Catalyzed Synthesis of Functionalized Pyrimidines from Dicyanogen and 1,3-Dicarbonyl Compounds[**]

By *Benedetto Corain, Marino Basato,* and *Hans-Friedrich Klein*[*]

Conventional pyrimidine syntheses are based on the ring closure reactions A—C[1], the desired functionalization generally being carried out in the synthetic building blocks *prior to* cyclization—which occasionally meets with difficulties.

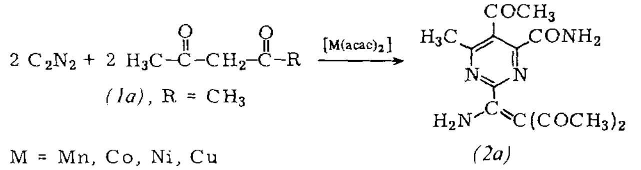


---

[*] Prof. Dr. B. Corain [+], Dr. M. Basato
C.N.R., Centro di Studio sulla Stabilitá e Reattivitá dei Composti di Coordinazione
Via Marzolo 1, I-35100 Padova (Italy)
Prof. Dr. H.-F. Klein
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Fonds der Chemischen Industrie and by the Alexander-von-Humboldt-Stiftung (Grant for *B. C.*).

We have recently reported the preparation of the highly functionalized pyrimidine derivative *(2a)*[2] by reaction of dicyanogen and 2,4-pentanedione under mild conditions in the presence of catalytic amounts of metal acetylacetonate.

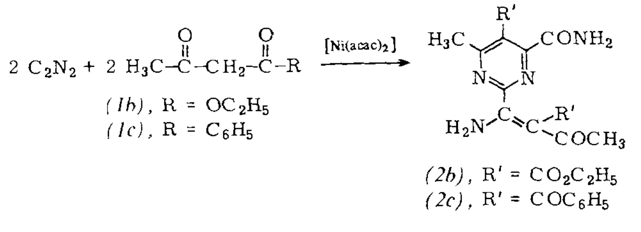

*(1a)*, R = $CH_3$

M = Mn, Co, Ni, Cu

*(2a)*

In the new pyrimidine synthesis, which is carried out as a one-pot reaction under mild conditions, the heterocycle is formed by way of the schematic ring-closure reaction D.

We have found that other readily accessible 1,3-dicarbonyl compounds can also be used for the preparation of functionalized pyrimidines. The simplicity of the procedure and the high yields make the catalytic pyrimidine synthesis a very promising method (Table 1).


*(1b)*, R = $OC_2H_5$

*(1c)*, R = $C_6H_5$

*(2b)*, R' = $CO_2C_2H_5$

*(2c)*, R' = $COC_6H_5$

Table 1. Conditions, yields, and conversions for the synthesis of pyrimidine derivatives *(2)* in 1,2-dichloroethane.

| Educt *(1)* [a] | Catalyst [b] | *t* [h] | Yield of *(2)* [%] [c] |
|---|---|---|---|
| *(a)* | $Ni(acac)_2$ | 24 | 78 (100) |
| | | 140 | 100 (100) |
| *(a)* | $Cu(acac)_2$ | 24 | 58 (100) |
| | | 288 | 100 (100) |
| *(b)* | $Cu(acac)_2$ | 288 | 20 (44) |
| *(b)* | $Ni(acac)_2$ | 288 | 41 (49) |
| *(c)* | $Ni(acac)_2$ | 288 | 22 — |

[a] 0.35 mol $L^{-1}$; $[(CN)_2]$ 0.40 mol $L^{-1}$. [b] $1.2\times10^{-3}$ mol $L^{-1}$. [c] Isolated product. In brackets: yields with respect to converted educt.

The new pyrimidine derivatives are characterized by elemental analysis, NMR, IR, UV/VIS, and mass spectra. In the case of *(2a)* and *(2b)* the structure could also be determined by an X-ray structure analysis.

*(1b)* and *(1c)* cyclize with dicyanogen in the presence of Cu and Ni complexes more slowly and less selectively than *(1a)* (Table 1). If the yield of *(2)* with respect to initial amount of educt used in the presence of $Ni(acac)_2$ is higher than in the case of $Cu(acac)_2$ then it is of about the same order of magnitude with respect to amount of educt converted. Hence, longer reaction times are necessary in order to obtain high yields of pyrimidines.

*(2a)* is formed particularly rapidly (80% conversion after 1 h) at the following concentrations: 2 mmol $Cu(acac)_2$ in 20 mL 1,2-dichloroethane, 0.30 mol $L^{-1}$ acacH, and 0.80 mol $L^{-1}$ $(CN)_2$; vigorous stirring is necessary and the reaction must be interrupted after 1 h, because otherwise a secondary precipitation of green bis[1-cyano-2-(1-iminoethyl)-1,3-butanedionato]copper will contaminate the product *(2a)*.

The catalytic pyrimidine synthesis proceeds in two steps: base-catalyzed addition of dicyanogen to the 1,3-dicarbonyl compounds[3]—which can also be carried out with malonic esters—followed by the metal-catalyzed cyclization, which only takes place if at least one keto-function is present in the substrate.

### *Procedure*

*(2b):* $Ni(acac)_2$ (10 mg) is dissolved with stirring in 40 mL of a standardized 0.6 M solution of dicyanogen in 1,2-dichloroethane. *(1b)* (2.5 mL, 19.2 mmol) is pipetted into the orange colored solution and the mixture stirred slowly (*ca.* 100 r.p.m.) at 20 °C. After 12 d the resulting yellow precipitate is filtered off from the supernatant red solution, washed twice with 10 mL of 1,2-dichloroethane, and air-dried. Yield: 1.5 g of yellow powder, 41% referred to *(1b)*. Recrystallization from 100 mL of hot 1,2-dichloroethane affords 1.3 g of analytically pure *(2b)*, m.p. 206–208 °C. IR (nujol, $cm^{-1}$): 3485, 3450, 3345, 3245 $\nu_{NH}$; 1740, 1705, 1680, 1610 $\nu_{C=O}$, $\nu_{C=C}$, $\nu_{NH_2}$.

Received: March 24, 1981 [Z 907 IE]
German version: Angew. Chem. *93*, 1034 (1981)

CAS Registry numbers:
*(1a)*, 123-54-6; *(1b)*, 141-97-9; *(1c)*, 93-91-4; *(2a)*, 77097-65-5; *(2b)*, 79593-42-3; *(2c)*, 79593-43-4; dicyanogen, 460-19-5; $Ni(acac)_2$, 3264-82-2; $Cu(acac)_2$, 13395-16-9.

---

[1] *R. Fusco, V. Rosnati, G. Bianchetti:* Chimica Organica, Vol. 2, Guadagni, Milano 1975, p. 557.

[2] *B. Corain, C. Crotti, A. Del Pra, F. Filira, G. Zanotti,* Inorg. Chem. *20*, 2044 (1981).

[3] *W. Traube,* Chem. Ber. *31*, 2938 (1898).

[4] *B. Corain, M. Basato, G. Bontempelli,* Anal. Chem. *53*, 124 (1981).

## A New Onium Salt: Synthesis and Characterization of the Difluorophosphonium Ion, $PH_2F_2^+$ [**]

By *Herbert W. Roesky, Karl-Ludwig Weber,* and *Jürgen Schimkowiak*[*]

*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

Ammonium salts have been known since the 14th century[1]. The homologous cation of phosphorus, first prepared in 1870 as $PH_4I$[2], is stable only with large anions. $NF_4^+$ salts[3] are also thermally more stable than $PF_4^+$ salts[4]. By way of contrast, we have now found that $PH_2F_2^+$, which, unlike $NH_2F_2^+$ does not decompose explosively at room temperature[5], can be isolated in the reaction

$$PH_2F_3 + AsF_5 \rightarrow PH_2F_2^+AsF_6^- \qquad (1)$$

in high yields as the hexafluoroarsenate.

The new salt *(1)*, a finely crystalline, colorless solid, decomposes on warming, with elimination of HF and formation of red phosphorus. The compound cannot be stored for longer than 12 h at room temperature in glass vessels; in polyethylene vessels no noticeable decomposition occurs, even after several days. In contrast to $PF_4^+Sb_3F_{16}^-$[4], *(1)* shows no measurable decomposition pressure at 20 °C in a vacuum.

---

[*] Prof. Dr. H. W. Roesky, Dipl.-Chem. K.-L. Weber, J. Schimkowiak
Anorganisch-chemisches Institut der Universität
Tammannstr. 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by Hoechst AG.

*0570-0833/81/1111-0973 $ 02.50/0*

We assume the $PH_2F_2^+$ cation to have a tetrahedral skeletal structure ($C_{2v}$ point group). The nine normal vibrations are classified as $4A_1+A_2+2B_1+2B_2$. Apart from the torsional vibration $\nu_5(A_2)$, which is only Raman-active, all other vibrations should appear in both the IR as well as the Raman spectrum. The bands of the antisymmetric ($\nu_6$) and symmetric ($\nu_1$)$PH_2$ valence vibrations at 2600 and 2538 $cm^{-1}$, respectively, can be assigned by comparison with the valence vibrations of the isoelectronic compound $SiH_2F_2$[6]; tentative assignment of the remaining bands [$cm^{-1}$]: $\delta$(HPH) 1096 w, $\delta$(HPF) 1055 s, $\nu_{as}$(PF) 1010 s, $\nu_s$(PF) 950 s, $\delta$(HPF) 885 w, $\delta$(FPF) 835 s. Absorptions were observed at 695 and 645 $cm^{-1}$ for the $AsF_6^-$ anion. NMR investigations have so far proved impossible, since no suitable solvent for *(1)* has yet been found.

## *Experimental*

$H_2PF_3$[7] (0.64 g, 7 mmol) and $AsF_5$ (1.2 g, 7 mmol) are condensed together at − 196 °C in a metal apparatus. The mixture is allowed gradually to warm to room temperature and the volatile components are removed by suction, leaving behind 1.7 g (6.5 mmol) (93%) as crystalline, analytically pure salt *(1)*.

Received: March 13, 1981 [Z 909a IE]
German version: Angew. Chem. *93*, 1017 (1981)

CAS Registry numbers:
*(1)*, 79593-53-6; $H_2PF_3$, 13659-65-9; $AsF_5$, 7784-36-3.

---

[1] *R. D. Young* in Kirk-Othmer: Encyclopedia of Chemical Technology, 3rd Ed., Vol. *2*, Wiley-Interscience, New York 1978, p. 518.
[2] *A. v. Baeyer*, Liebigs Ann. Chem. *159*, 269 (1870).
[3] *K. O. Christe, J. P. Guertin, A. E. Pavlath*, Inorg. Nucl. Chem. Lett. *2*, 83 (1966); *W. E. Talberg, R. T. Rewick, R. S. Stringham, M. E. Hill, ibid. 2*, 79 (1966); *K. O. Christe, W. W. Wilson, R. D. Wilson*, Inorg. Chem. *19*, 3254 (1980).
[4] *G. S. H. Chen, J. Passmore*, J. Chem. Soc. Chem. Commun. *1973*, 559.
[5] *K. O. Christe*, Inorg. Chem. *14*, 2821 (1975).
[6] *S. Cradock, E. A. V. Ebsworth, A. G. Robiette*, Trans. Faraday Soc. *60*, 1502 (1964).
[7] *B. Blaser, K.-H. Worms*, DBP 1106736 (1962).

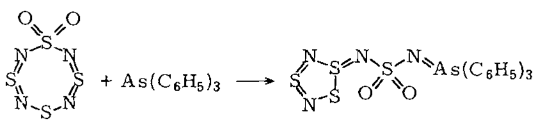
---

# Synthesis and Structure of a Non-Polymeric Molecule Containing Eleven Alternating Sulfur- and Nitrogen-Atoms[**]

By *Michael Witt, Herbert W. Roesky, Mathias Noltemeyer, William Clegg, Martin Schmidt,* and *George M. Sheldrick*[*]

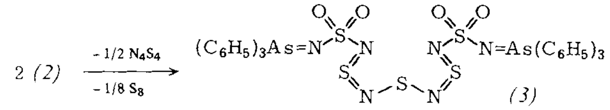
*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

We recently reported[1] a ring contraction in the eight-membered ring $S_4N_4O_2$ *(1)*, which leads to the five-membered ring system *(2)*, a triphenylarsane adduct, in high yields.



*(1)* *(2)*

*(2)* forms crystals (space group $P2_1/n$) which are stable towards air and hydrolysis. We have now found that *(2)* slowly loses $S_4N_4$ and sulfur in acetone solution, and is converted into the condensation product *(3)*.



*(3)*

This reaction can be explained mechanistically in terms of an intermediate formation of a dimer of *(2)* containing a central ten-membered ring system $S_6N_4$.

The molecular structure of *(3)* was determined by X-ray diffraction analysis on a single crystal[2]. *(3)* proves to be the longest non-polymeric sulfur-nitrogen chain synthesized so far, with eleven alternating atoms. The compound cannot be sublimed without decomposition. The largest fragment appearing in the mass spectrum is $(C_6H_5)_3AsS$ at $m/z=338$.

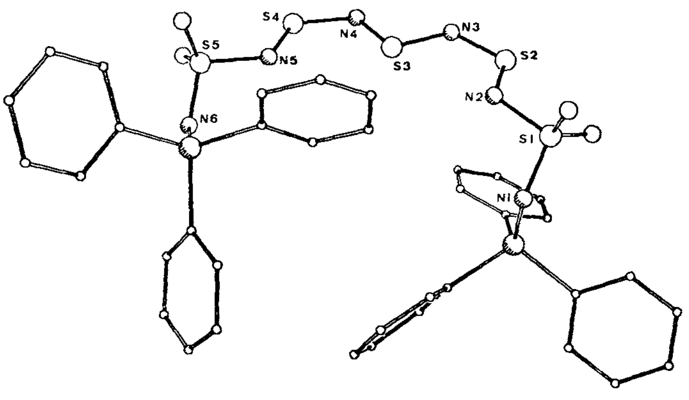


Fig. 1. Structure of the molecule *(3)* in the crystal.

Bond lengths [Å]: N1—S1 1.576(10), S1—N2 1.684(10), N2—S2 1.544(10), S2—N3 1.574(11), N3—S3 1.632(11), S3—N4 1.645(13), N4—S4 1.602(11), S4—N5 1.629(12), N5—S5 1.655(11), S5—N6 1.559 (11); N1—As1 1.756(12), N6—As2 1.779(13), S—O (mean value) 1.438(12), As—C (mean value) 1.892, C—C (mean value) 1.376

Bond angles [°]: As1—N1—S1 120.8(7), N1—S1—N2 105.1(6), S1—N2—S2 116.1(5), N2—S2—N3 110.4(6), S2—N3—S3 119.5(7), N3—S3—N4 96.3(6), S3—N4—S4 117.0(8), N4—S4—N5 113.7(7), S4—N5—S5 115.3(8), N5—S5—N6 104.3(6), S5—N6—As2 118.9(9)

The SN bond lengths (and angles) in the two halves of the molecule of *(3)* differ considerably; the average SN bond length 1.602 Å, however, is similar to the corresponding value of 1.611 in $(SN)_x$[3]. Nevertheless, shorter and longer SN bonds occur in *(3)* than in $(SN)_x$ (1.593 and 1.628 Å). The greater variation in the bond lengths in *(3)* appears to be a result of arbitrary folding of the molecule in the solid state.

## *Procedure*

A solution of $AsPh_3$ (7.6 g, 25 mmol) in benzene (50 mL) is added dropwise to a solution of *(1)* (5.4 g, 25 mmol) in benzene (100 mL) and the mixture briefly heated to boiling. After cooling, the intense yellow precipitate is filtered off, dried, and extracted with acetonitrile. At room temperature, blood-red crystals of *(2)* precipitate out from the extract. After filtration, the mother liquor is stored for a few

---

[*] Prof. Dr. H. W. Roesky, M. Witt, Prof. Dr. G. M. Sheldrick, Dr. W. Clegg, Dr. M. Noltemeyer, M. Schmidt
Anorganisch-chemisches Institut der Universität
Tammannstr. 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and by Hoechst AG.

days in a refrigerator. A mixture of sulfur, $S_4N_4$ and *(3)* separates out on the wall of the flask; after decanting off the solvent, the crystals of *(3)* can be separated manually from the mixture and recrystallized from $CH_3CN$ or benzene. *(3)* crystallizes from benzene with 3 molecules of solvation (m.p. 87 °C, dec.), from $CH_3CN$ without any molecules of solvation (m.p. 146 °C, dec.), as translucent orange needles.

Received: May 14, 1981 [Z 909b IE]
German version: Angew. Chem. *93*, 1017 (1981)

CAS Registry numbers:
*(1)*, 57932-64-6; *(2)*, 75768-56-8; *(3)*, 79593-51-4; Asfh$_3$, 603-35-0.

---

[1] *H. W. Roesky, M. Witt, W. Clegg, W. Isenberg, M. Noltemeyer, G. M. Sheldrick*, Angew. Chem. *92*, 959 (1980); Angew. Chem. Int. Ed. Engl. *19*, 943 (1980).

[2] Space group $P\bar{1}$, $a=10.987(4)$, $b=12.521(6)$, $c=15.976(13)$ Å, $\alpha=69.15(5)$, $\beta=80.66(5)$, $\gamma=73.69(4)°$, $Z=2$; four-circle diffractometer data, $R=6.2\%$.

[3] *C. M. Mikulski, P. J. Russo, M. S. Saran, A. G. MacDiarmid, A. F. Garito, A. J. Heeger*, J. Am. Chem. Soc. *97*, 6358 (1975); *C. M. Mikulski, M. S. Saran, J. Kleppinger, ibid. 98*, 3844 (1976).

## Synthesis of Dithiophosphinato Complexes with Bis(diorganothiophosphoryl)disulfanes: $Mo_3S_7$-Cluster Dithiophosphinates

By *Helmut Keck, Wilhelm Kuchen, Jürgen Mathow, Beate Meyer, Dietrich Mootz,* and *Hartmut Wunderlich*[*]

Dithiophosphinate ions *(1)* reduce some metals according to eq. (a); simultaneously, they are themselves oxidized according to eq. (b) to bis(diorganothiophosphoryl)disulfanes *(2)*. $Cu^{2+}$ reacts analogously to give $R_2PS_2Cu$. Presumably, dithiophosphinato chelates of the higher valence metal $R_2PS_2M/m$[1] are formed as intermediates. On the other hand, the disulfanes *(2a)* and *(2b)* can oxidize metals according to reversed eq. (b), being themselves reduced to chelate ligands *(1)*. Thus, *e.g.*, on heating *(2a)* with $Cr(CO)_6$, tris(diethyldithiophosphinato)chromium(III)[2a] is formed according to

$$3\ \underset{(1)}{R_2PS_2^-} + M^{m+} \longrightarrow R_2PS_2M/n + R_2P(S){-}S_2{-}P(S)R_2 \qquad \text{(a)}$$

$$(2a),\ R = C_2H_5$$
$$(2b),\ R = n\text{-}C_3H_7$$

e.g. M = Au, Tl: m = 3, n = 1

$$2\ R_2PS_2^- \underset{+2e}{\overset{-2e}{\rightleftharpoons}} R_2P(S){-}S_2{-}P(S)R_2 \qquad \text{(b)}$$

$$Cr(CO)_6 + 3/2\,(2a) \rightarrow (Et_2PS_2)_3Cr + 6\,CO$$

$Ni(CO)_4$ and $Fe(CO)_5$ react analogously to give $(Et_2PS_2)_2Ni$[2b] and $(Et_2PS_2)_3Fe$[2b], respectively; $SnCl_2$ is oxidized to $(Et_2PS_2)_2SnCl_2$[2c].

We have found that this reaction of the disulfanes can be used for the synthesis of $Mo_3S_7$-cluster chelates of type *(3)*, and of dinuclear tungsten(V) complexes *(4)*. On reaction with carbonyl complexes $M(CO)_6$ of these metals they additionally act as sulfur transferring agents with conversion into monosulfanes $R_2P(S){-}S{-}P(S)R_2$.

Thus, reaction of $Mo(CO)_6$ with *(2a)* or *(2b)* affords the $Mo^{IV}$ compounds *(3a)* and *(3b)*, respectively:

$$[Mo_3S_7(R_2PS_2)_3]^+[R_2PS_2]^-$$

*(3a)*, R = Et, orange-red, decomp. above 260 °C
*(3b)*, R = *n*Pr, copper-red needles, decomp. above 200 °C

The cluster structure of the 1 : 1 electrolytes *(3a)* follows from the elemental analysis, the $^{31}P\{^1H\}$-NMR spectrum ($\delta_P = 110.1$ and 73.5; intensity ratio 3 : 1, saturated solution in $CH_2Cl_2$, relative to 85% $H_3PO_4$), the field-desorption (FD) mass spectrum ($[Mo_3S_7(Et_2PS_2)_3]^+$ $m/z$ 977, ref. to $^{98}Mo$), and the X-ray structure analysis (Fig. 1). *(3b)* exhibits similar properties and a better solubility in many organic solvents. Reaction of *(3a)* with triphenylphosphane affords the sulfur-deficient chelate complex $Mo_3S_4(Et_2PS_2)_4$, a non-electrolyte, which forms deep-black, shiny crystals.

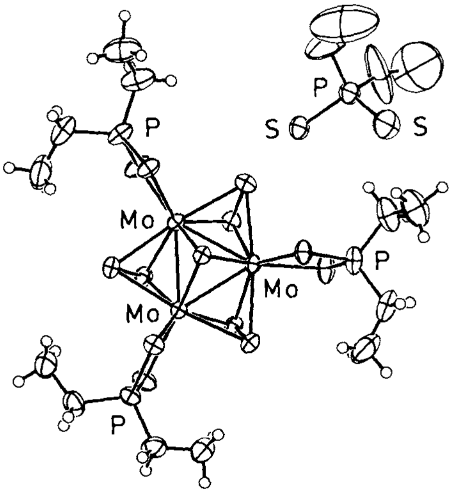


Fig. 1. Crystal Structure of the $Mo^{IV}$ cluster *(3a)* [6]. The orientation and assignment of cation and anion are arbitrary. A disorder in the anion cannot be ruled out. *(3a)* crystallizes in two modifications with the lattice constants $a=2065.1(3)$, $b=1015.2(2)$, $c=1901.9(2)$ and $a=2012.8(2)$, $b=1565.5(2)$, $c=1260.8(1)$ pm, respectively. The corresponding orthorhombic space groups are $Pca2_1$ and Pnma, each with $Z=4$. The structure determinations with 2886 and 3414 significant measured diffraction intensities (ω-scan, $Mo_{K\alpha}$, $2\theta_{max}=54°$) lead to $R$ values of 0.058 and 0.045, respectively. In the latter case anion and cation have a crystallographic mirror plane. In both structures the Mo atoms form an equilateral triangle with an average bond length of 273.7 pm. Each of these bonds is bridged by a vertically oriented $S_2$-dumbbell on one side of the triangle, a single S atom trigonal-pyramidally coordinates the Mo triangle from the other side. This $Mo_3S_7$ cluster was first observed in $Mo_3S_7Cl_4$ [4a]. To each of the three Mo atoms a dithiophosphinato ligand is bonded *via* both S atoms. The two modifications differ in the conformation of the organic moiety and in the arrangement of anions and cations.

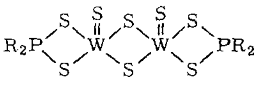
Molybdenum-sulfur clusters are of topical interest because of their importance as model substances in bioinorganic chemistry[3]. The method described here provides the first convenient access to $Mo_3S_7$ clusters modified by organo groups[4]. Thus, not only a high solubility in organic solvents is achieved, but the functionalization of these compounds by suitable choice of substituents R is also possible.

Reaction of $W(CO)_6$ with *(2)* affords the tungsten complexes *(4a, b)*.

We postulate a dinuclear structure for these non-electrolytes. *(4a)*: $^{31}P\{^1H\}$-NMR: $\delta_P = 135.6$ (saturated solution in 1,2-dichloroethane); electron-impact induced (EI) MS:

---

[*] Prof. Dr. W. Kuchen, Dr. H. Keck, Dipl.-Chem. J. Mathow, cand. rer. nat. B. Meyer, Prof. Dr. D. Mootz, Dr. H. Wunderlich
Institut für Anorganische Chemie und Strukturchemie der Universität
Universitätsstr. 1, D-4000 Düsseldorf (Germany)



(4a), R = $C_2H_5$, bordeaux red, m.p. 238 °C (dec.)
(4b), R = $n$-$C_3H_7$, cinnabar red, m.p. 248 °C (dec.)

$m/z$ 802 ($M^+$, ref. to $^{184}W$); IR (Nujol): $\nu_{W=S} = 528$ $cm^{-1}$[5]. *(4b):* $^{31}P\{^1H\}$-NMR: $\delta_P = 130.3$ (saturated solution 1,2-dichloroethane); EIMS: $m/z$ 858 ($M^+$ ref. to $^{184}W$); IR (Nujol): $\nu_{W=S} = 530$ $cm^{-1}$. Accordingly, *(2)* also functions here as an oxidizing agent under chelate formation and sulfur transfer.

*Procedure*

*(3a):* A mixture of $Mo(CO)_6$ (2.6 g, 10 mmol), disulfane *(2a)* (9.2 g, 30 mmol), and toluene (50 mL) is heated under reflux in an argon atmosphere. The initial clear, colorless solution turns dark-brown with evolution of CO. After *ca.* 1 h an orange-yellow precipitate is formed which after 4 h is filtered off and washed with toluene and ether. For further purification, *(3)* is precipitated from boiling $CH_2Cl_2$ by slow addition of $CH_3OH$. Yield 65%, soluble in $CHCl_3$ and $CH_2Cl_2$, air-stable.

*(4a):* A mixture of $W(CO)_6$ (8.8 g, 25 mmol), disulfane *(2a)* (19.2 g, 63 mmol) and 1,2,4-trimethylbenzene is heated under reflux for 2 h. On addition of 400 mL of ligroin (100—120 °C) to the red-brown solution a red solid is precipitated, which is washed several times with hot methanol. Yield 82%; the bordeaux-red crystals (1,2-dichloroethane) are moderately soluble in acetone, chloroform or benzene.

Received: February 18, 1981 [Z 904 IE]
German version: Angew. Chem. *93*, 1019 (1981)

CAS Registry numbers:
*(2a)*, 24057-20-3; *(2b)*, 40292-59-9; *(3a)*, 79594-15-3; *(3b)*, 79594-18-6; *(4a)*, 79594-19-7; *(4b)*, 79594-20-0; $Mo(CO)_6$, 13939-06-5; $W(CO)_6$, 14040-11-0.

---

[1] *W. Kuchen, H. Mayatepek,* Chem. Ber. *101*, 3454 (1968).
[2] a) *W. Kuchen, J. Metten, A. Judat,* Chem. Ber. *97*, 2306 (1964); b) *W. Kuchen, A. Judat, ibid. 100*, 991 (1967); c) *W. Kuchen, A. Judat, J. Metten, ibid. 98*, 3981 (1965).
[3] *A. Müller,* Nachr. Chem. Tech. Lab. *28*, 452 (1980).
[4] a) *J. Marcoll, A. Rabenau, D. Mootz, H. Wunderlich,* Rev. Chim. Miner. *11*, 607 (1974); b) *A. Müller, R. Jostes, F. A. Cotton,* Angew. Chem. *92*, 921 (1980); Angew. Chem. Int. Ed. Engl. *19*, 875 (1980).
[5] *K. H. Schmidt, A. Müller,* Coord. Chem. Rev. *14*, 115 (1974).
[6] *C. K. Johnson* (1976); Programm ORTEP II, ORNL-5138, Oak Ridge National Laboratory, Tennessee, USA.

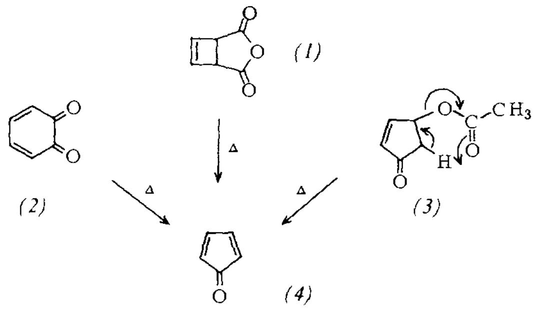
---

## Trimethylsilylated Cyclopentadienones[**]

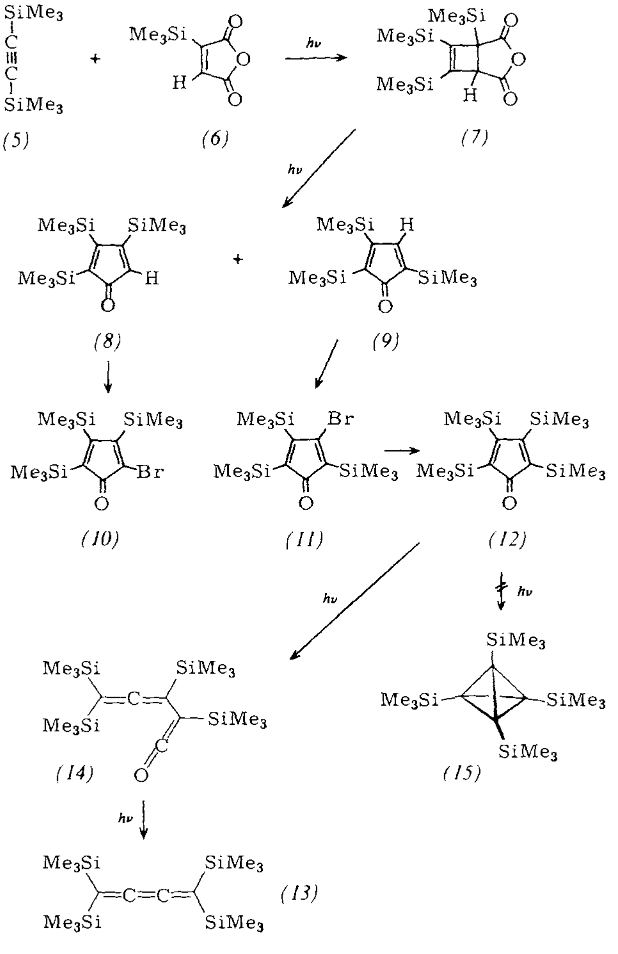
By *Günther Maier, Hans Werner Lage,* and
*Hans Peter Reisenauer*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

The use of cyclopentadienone *(4)* in syntheses is rendered difficult by its strong tendency to dimerize. Monomeric *(4)* is obtainable in substance only by matrix isolation[1]—*e.g.* in combination with the vacuum flash pyrolysis of *(1)*, *(2)*, or *(3)*[2]. Trimethylsilylated derivatives of *(4)*, whose protective groups can easily be cleaved at a later stage, should be far more suitable as synthetic building blocks. A recent publication on this topic prompted us to report the results of our experiments, in which we attempt to open up an entry to unsubstituted tetrahedrane[5] *via* silylated precursors.



Trimethylsilylmaleic anhydride *(6)* is accessible by addition of trimethylsilane to di-*tert*-butyl acetylenedicarboxylate[6a] in the presence of $PdCl_2(PPh_3)_2$[6b] and heating the primary adduct to 190 °C. Photolysis of *(6)* and bis(trimethylsilyl)acetylene *(5)*[7a] in acetone smoothly affords the [7b] anhydride *(7)*. On direct irradiation, photofragmentation of *(7)* leads to the structurally isomeric tris(trimethylsilyl)cyclopentadienones *(8)* and *(9)*[8] (Table 1). *(8)* completely dimerizes within a week at room temperature, whereas *(9)* is stable under these conditions.



---

[*] Prof. Dr. G. Maier, Dipl.-Chem. H. W. Lage, Dr. H. P. Reisenauer
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Table 1. Data for compounds *(6)*—*(12)*: Yields, physical and spectroscopic properties. IR [cm$^{-1}$]; NMR (CDCl$_3$): $\delta$ values rel. TMS (all signals are singlets); UV (cyclohexane) [nm] ($\varepsilon$). All substances gave correct elemental analyses.

*(6)*: 65%; colorless oil, b.p. 50 °C/10$^{-2}$ torr.—IR (Film): 1853, 1815, 1760 (anhydride); $^1$H-NMR: −0.13 (9H), 6.72 (1H); $^{13}$C-NMR: 2.42, 145.28, 157.54, 166.98, 169.80

*(7)*: 80%; colorless crystals, m.p. 54 °C.—IR (Film): 1840, 1760 (anhydride); $^1$H-NMR: 0.24 (27H), 3.72 (1H); $^{13}$C-NMR: 0.77, 2.36, 2.60, 55.55, 58.80, 170.35, 172.58, 177.16 (2C); UV: 220 (1290), 240 (850)

*(8)*: 32%; red-orange oil.—IR (Film): 1690 (C═O); $^1$H-NMR: 0.27 (18H), 0.35 (9H), 5.80 (1H); $^{13}$C-NMR: 0.47, 1.38, 1.61, 133.30, 143.61, 169.18, 174.87, 210.16; UV: 230 (sh), 395 (190)

*(9)*: 13%; red-orange crystals, m.p. 36—37 °C.—IR (Film): 1690 (C═O), 1570 (C═C); $^1$H-NMR: 0.16 (9H), 0.22 (9H), 0.28 (9H), 7.28 (1H); $^{13}$C-NMR: −1.28, −0.15, 0.84, 133.23, 145.86, 160.60, 167.61, 210.61; UV: 227 (1040), 400 (180)

*(10)*: 17%; red crystals, m.p. 81—83 °C.—IR (CDCl$_3$): 1700 (C═O), 1530 (C═C); $^1$H-NMR: 0.25 (9H), 0.35 (9H), 0.40 (9H); $^{13}$C-NMR: 0.31, 0.76, 1.64, 129.13, 145.65, 162.66, 181.34, 198.31; UV: 250 (sh), 445 (350)

*(11)*: 41%; yellow-orange crystals, m.p. 50 °C.—IR (CDCl$_3$): 1685 (C═O), 1545 (C═C); $^1$H-NMR: 0.30 (18H), 0.46 (9H); $^{13}$C-NMR: 0.77, 1.66, 2.23, 130.65, 148.57, 161.49, 168.40, 206.06; UV: 250 (6590), 405 (495)

*(12)*: 49%; orange crystals, m.p. 132—133 °C.—IR (KI): 1670 (C═O); $^1$H-NMR: 0.24 (18H), 0.35 (18H); $^{13}$C-NMR: 1.13, 2.36, 146.82, 181.09, 204.81; UV: 423 (290)

Bromination of *(8)* with pyridinium perbromide at −78 °C in pentane and subsequent dehydrobromination with 1,5-diazabicyclo[5.4.0]undec-5-ene affords 2-bromo-3,4,5-tris(trimethylsilyl)cyclopentadienone *(10)*, while bromination of *(9)* at 0 °C followed by HBr-elimination furnishes the structurally isomeric bromodienone *(11)*.

The fourth trimethylsilyl group can be incorporated by reaction of the reactive Michael acceptor *(11)*[9a] with LiSiMe$_3$ in the presence of CuI[9b].

The resulting tetrakis(trimethylsilyl)cyclopentadienone *(12)* behaves completely different compared to the analogous fourfold *tert*-butyl substituted derivative[5b] on photochemical excitation. The final product of the photolysis (Hg low-pressure lamp, Rigisolve matrix, 77 K, 200 h) is not the tetrahedrane *(15)*[10], but tetrakis(trimethylsilyl)butatriene *(13)* (65%)[11]. On irradiation in an argon matrix (10 K, 35 h) with 313-nm light, the allenylketene *(14)* (IR: 1890, 2080 cm$^{-1}$) can be detected as intermediate. Further irradiation at a wavelength of 254 nm (10 K, 10 h) leads to loss of CO and formation of the butatriene *(13)* (1543 cm$^{-1}$).

The new trimethylsilyl compounds *(9)* and *(12)* constitute the first cyclopentadienone-equivalents available as synthons, which are stable at room temperature.

Received: January 22, 1981 [Z 908 IE]
supplemented: May 29, 1981
German version: Angew. Chem. *93*, 1010 (1981)

---

[1] *G. Maier, H. P. Reisenauer, L. H. Franz*, unpublished. IR spectrum of *(4)*: 1727, 1724, 1332, 1136, 822, 632 cm$^{-1}$ (cf. *G. Maier, H.-G. Hartan, T. Sayraç*, Angew. Chem. *88*, 252 (1976); Angew. Chem. Int. Ed. Engl. *15*, 226 (1976): footnote [13]). UV spectrum: $\lambda_{max}$ = 195 (s), 360 (vw) nm.

[2] *K. Hafner, K. Goliasch*, Chem. Ber. *94*, 2909 (1961); *V. Osterthun, E. Winterfeldt*, ibid. *110*, 146 (1977).—We thank Prof. *Winterfeldt* for a sample of *(3)*.

[3] Cyclopentadienone *(4)* already dimerizes on thawing the argon matrix. We were unable to confirm earlier data (*O. L. Chapman, C. L. McIntosh*, J. Chem. Soc. Chem. Commun. *1971*, 770), according to which *(4)* was obtained in the condensed phase at 77 K. Isolation on a cold (10 K) window, without argon, yielded monomeric *(4)*, but mainly the dimer was recorded at 77 K.

[4] *E. R. F. Gesing, J. P. Tane, K. P. C. Vollhardt*, Angew. Chem. *92*, 1057 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1023 (1980).

[5] In analogy to a) *G. Maier, S. Pfriem*, Angew. Chem. *90*, 551 (1978); Angew. Chem. Int. Ed. Engl. *17*, 519 (1978); b) *G. Maier, S. Pfriem, U. Schäfer, R. Matusch*, ibid. *90*, 552 (1978) and *17*, 520 (1978).

[6] a) *I. Böhm, H. Herrmann, K. Menke, H. Hopf*, Chem. Ber. *111*, 523 (1978); b) *H. Okinoshima, K. Yamamoto, M. Kumada*, J. Organomet. Chem. *86*, C27 (1975).

[7] a) Preparation according to the method of *D. R. M. Walton, F. Waugh*, J. Organomet. Chem. *37*, 45 (1972); b) Addition of *(5)* to maleic anhydride: *K. Birkofer, D. Eichstädt*, ibid. *145*, C29 (1978).

[8] A corresponding photoreaction in the tri-*tert*-butyl series has already been reported: *G. Maier, A. Alzérreca*, Angew. Chem. *85*, 1056 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1015 (1973).

[9] a) *G. Stork, B. Ganam*, J. Am. Chem. Soc. *95*, 6152 (1973); b) *D. J. Alger, I. Fleming*, J. Chem. Soc. Chem. Commun. *1978*, 177.

[10] Force-field calculations show that the "corset effect" [5b] for the stabilization of the tetrahedrane skeleton no longer suffices in the case of fourfold substitution with trimethylsilyl groups. The trimethylsilyl group is larger than the *tert*-butyl group, but the decisive factor is the distance between Si and the ring C-atom (*K. Mislow*, private communication).

[11] Identified by comparison with authentic substance: *J. R. Fritch, K. P. C. Vollhardt, M. R. Thompson, V. W. Day*, J. Am. Chem. Soc. *101*, 2768 (1979).

## Enantioselective Synthesis of (*R*)-α-Vinylamino Acids[**]

By *Ulrich Schöllkopf* and *Ulrich Groth*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

α-Vinylamino acids of type *(6)* have gained increasing importance as potential enzyme inhibitors[1]. Although several methods are available for their preparation in racemic form[2], enantioselective syntheses, which would provide access to these compounds in, if possible, the most optically pure form and with defined configuration have so far not been described in the literature.

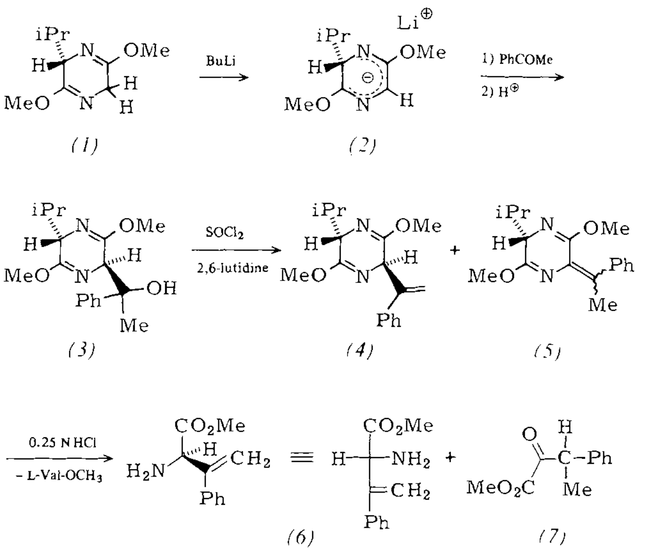
We describe here the enantioselective synthesis of almost optically pure (*R*)-2-amino-3-phenyl-3-butenoic acid methyl ester *(6)* (β-methylenephenylalanine methyl ester), which has previously been prepared in racemic form[3]. This demonstrates that our bislactim-ether method[4] is also suitable for the asymmetric synthesis of α-vinylamino acids. The bislactim ether *(1)*[5] of cyclo-(L-Val-Gly) is converted with butyllithium into its lithium derivative *(2)*, which on reaction with acetophenone affords the adduct *(3)* (*ca.* 90% yield) with extremely high diastereoselectivity. The carbonyl compound enters *trans* to the isopropyl group at C-6, *i.e.* the (*R*)-configuration is induced at C-3 (use of D-valine would result in the (*S*)-configuration). The configuration was assigned on the basis of the $^1$H-NMR spectrum. Since the adduct *(3)* has the "aryl-inner" conformation[6], the hydrogen atom 6-H falls into the shielding anisotropic region of the phenyl ring and its NMR signal experiences a strong upfield shift.

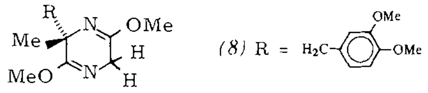
Reaction of thionyl chloride/2,6-lutidine with *(3)* affords a mixture (80:20) of the two olefins *(4)* and *(5)*, which on hydrolysis with hydrochloric acid give, aside from L-Val-OCH$_3$, the (*R*)-α-vinylamino acid ester *(6)* and the α-keto ester *(7)*. The keto ester *(7)* can be extracted from the acidic aqueous solution. The amino acid ester *(6)*, which can be separated from L-Val-OCH$_3$ by distillation, is >95% optically pure[7].

---

[*] Prof. Dr. U. Schöllkopf, Dipl.-Chem. U. Groth
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] Asymmetric Synthesis *via* Heterocyclic Intermediates, Part 9.—Part 8: [4].





The bislactim ether *(8)*[8] of [(*S*)-(*O,O*-dimethyl-α-methyldopa)-Gly] is also suitable as starting compound for the enantioselective synthesis of α-vinylamino acids. Reaction of the lithium compound of *(8)* with acetone, followed by elimination of water and hydrolysis, affords the (*R*)-2-amino-3-methyl-3-butenoic acid methyl ester (type *(6)*, Me instead of Ph)[9] with *e.e.* ≈ 88% (determined $^1$H-NMR spectroscopically with Eu(hfc)$_3$ on the OCH$_3$ signal.

### *Procedure*

*(3)*: A 1.55 N solution of *n*-butyllithium (4.2 mmol) in hexane (2.7 mL) was added dropwise (under $N_2$, injection needle) at −70 °C to a solution of *(1)*[5] (0.74 g, 4 mmol) in dimethoxyethane (8 mL). The mixture was stirred for *ca.* 10 min at −70 °C and then treated with the solution of acetophenone (0.50 g, 4.2 mmol) in dimethoxyethane (5 mL). After *ca.* 4 h the mixture was rendered neutral with a solution of glacial acetic acid (0.25 g, 4.2 mmol) in dimethoxyethane (2 mL), allowed to warm to room temperature, and the solvent removed under reduced pressure. The residue was taken up in *ca.* 10—15 mL of ether, washed with about 20 mL of water, and the aqueous phase extracted twice with 20 mL of ether. The combined ether extracts were dried over $MgSO_4$, the ether removed under reduced pressure, and *(3)* was distilled in a Kugelrohr apparatus. Yield 1.1 g (91%) *(3)*, b.p. 140—150 °C/0.1 torr.

*(4)* and *(5)*: A solution of $SOCl_2$ (0.37 g, 3.1 mmol) in toluene (4 mL) was added to a solution of *(3)* (0.91 g, 3 mmol) and 2,6-lutidine (0.66 g, 6.2 mmol) in toluene (10 mL) at room temperature. After 16 h the mixture was treated with *ca.* 20 mL of ether, washed with *ca.* 15—20 mL of water, dried over $MgSO_4$, the solvent removed under reduced pressure, and the residue distilled in a Kugelrohr apparatus. Yield 0.75 g (88%) *(4)* and *(5)* in the ratio 80 : 20, b.p. 130—140 °C/0.1 torr.

*(6)*: A solution of *(4)* plus *(5)* (0.52 g, 1.8 mmol) in 0.25 N HCl (14.4 mL, 3.6 mmol) was stirred for 30 h and then extracted with ether. The aqueous phase was evaporated down under reduced pressure to *ca.* 1-2 mL (bath temperature 60—80 °C), covered with *ca.* 10 mL ether, and treated with conc. ammonia solution with vigorous shaking until the pH was 8—10. The ether phase was separated off and the aqueous phase extracted a further three times with ether. The combined ether extracts were dried over $MgSO_4$, the ether removed under reduced pressure, and *(6)* distilled in a Kugelrohr apparatus. Yield 0.22 g (64% referred to the isomeric mixture of *(4)* and *(5)*), b.p. 100—110 °C/0.1 torr, $[\alpha]_D^{20} = -62.1°$ ($c = 0.6$, ethanol), enantiomeric purity >95%[7]; $^1$H-NMR ($CDCl_3$): $\delta = 1.83$ (s, $NH_2$), 3.71 (s, $OCH_3$), 4.54 (s, α-H), 5.34 and 5.43 (2 s, C=$CH_2$), 7.25—7.49 (m, $C_6H_5$).

Received: April 10, 1981 [Z 891 IE]
German version: Angew. Chem. *93*, 1022 (1981)

CAS Registry numbers:
*(1)*, 78342-42-4; *(3)*, 79435-70-4; *(4)*, 79435-71-5; *(5)*, 79435-72-6; *(6)*, 79435-73-7; *(8)*, 79448-86-5; methyl (*R*)-2-amino-3-methyl-3-butenate, 79435-74-8; PhCOMe, 98-86-2

---

[1] *B. W. Metcalf, K. Jund*, Tetrahedron Lett. *1977*, 3689; *R. R. Rando*, Acc. Chem. Res. *8*, 281 (1975); *G. Nass, K. Poralla, H. Zähner*, Naturwissenschaften *58*, 603 (1971); *W. Trowitzsch, H. Sahm*, Z. Naturforsch. *32c*, 78 (1977); *R. H. Abeles*, Pure Appl. Chem. *53*, 149 (1980).

[2] Cf. *W. J. Greenlee, D. Taub, A. A. Patchett*, Tetrahedron Lett. *1978*, 3999; *B. W. Metcalf, E. Bonilavri*, J. Chem. Soc. Chem. Commun. *1978*, 914; *W. Steglich, H. Wegmann*, Synthesis *1980*, 481; *I. Hoppe, U. Schöllkopf*, *ibid. 1981*, 646.

[3] *R. V. J. Chari, J. Wemple*, Tetrahedron Lett. *1979*, 111.

[4] *U. Schöllkopf, U. Groth, K.-O. Westphalen, C. Deng*, Synthesis *1981*, 969, and earlier communications of this series.

[5] *U. Schöllkopf, U. Groth, C. Deng*, Angew. Chem. *93*, 793 (1981); Angew. Chem. Int. Ed. Engl. *20*, 798 (1981).

[6] Cf. *U. Schöllkopf, W. Hartwig, U. Groth, K.-O. Westphalen*, Liebigs Ann. Chem. *1981*, 696; *U. Schöllkopf, W. Hartwig, U. Groth*, Angew. Chem. *91*, 922 (1979); Angew. Chem. Int. Ed. Engl. *18*, 863 (1979); *A. K. Bose, M. S. Manhas, R. V. Tawares, J. M. van der Veen, H. Fujiwara*, Heterocycles *7*, 1227 (1977).

[7] We assume >95%, if only one enantiomer is detectable $^1$H-NMR spectroscopically on the basis of its $OCH_3$ signal using Eu(hfc)$_3$.

[8] *U. Schöllkopf, W. Hartwig, K.-H. Pospischil*, Synthesis *1981*, 966.

[9] For the synthesis of this amino acid (D-isodehydrovaline) from methyl 2-aminoacrylate with isomerization and its use in penicillin synthesis cf. *J. E. Baldwin, M. A. Christie, S. B. Haber, L. I. Kruse*, J. Am. Chem. Soc. *98*, 3045 (1976).

## CC-Coupling and Reversible γ-H Abstraction in the Tantalum Complex Cl($\eta^5$-Cp)($\eta^3$-$C_9H_7$)Ta(CHCMe$_3$)

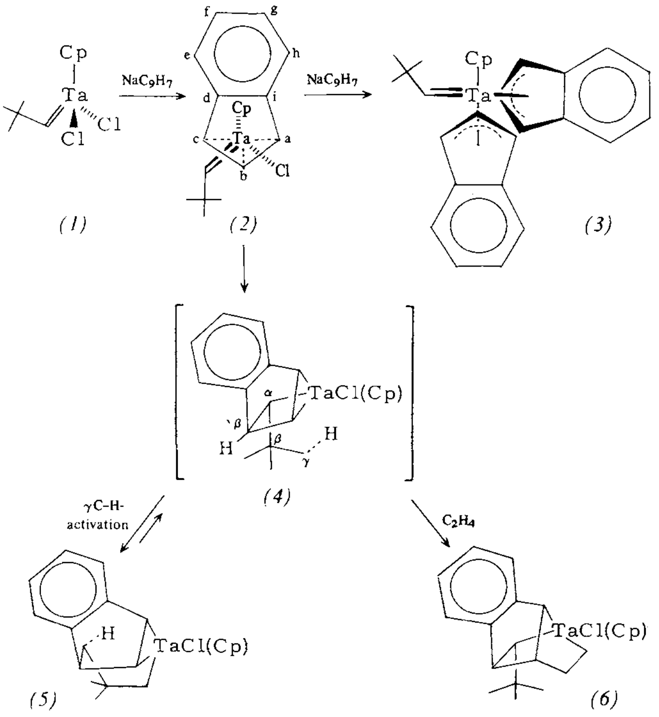
By *Anton W. Gal* and *Harry van der Heijden*[*]

Coordinatively unsaturated cyclopentadienyl(Cp)-tantalum-neopentylidene complexes have been shown to be useful precursors for reactive tantalum olefin compounds[1a]. They generally react with olefins to give tantalacyclobutane intermediates, which rearrange *via* β,α hydrogen migration to give the corresponding tantalum olefin complexes[1a,c]. However, coordinatively saturated neopentylidene complexes, such as Cl($\eta^5$-Cp)$_2$Ta(CHCMe$_3$)[1d], do not react with olefins. In an attempt to enhance the reactivity of Cl($\eta^5$-Cp)$_2$Ta(CHCMe$_3$) we have now replaced one $\eta^5$-Cp group by an $\eta^3$-indenyl group ($\eta^3$-$C_9H_7$) to obtain Cl($\eta^5$-Cp)($\eta^3$-$C_9H_7$)Ta(CHCMe$_3$) *(2)*[2].

The $\eta^3$-indenyl complex *(2)* is prepared by reaction of one equivalent of indenylsodium with $Cl_2$CpTa(CHCMe$_3$) *(1)* (molar ratio 1 : 1) in benzene[3]. If excess of indenylsodium (>2 : 1) is used *(3)* is the only product (Scheme 1).

---

[*] Dr. A. W. Gal, H. van der Heijden
Koninklijke/Shell-Laboratorium, Amsterdam (Shell Research B.V.)
Badhuisweg 3, NL-1031 CM Amsterdam (The Netherlands)



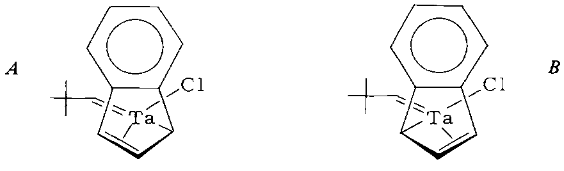
Scheme 1.

The structures assigned to *(2)* and *(3)*, are based on their $^1$H- and $^{13}$C-NMR spectra. The $^{13}$C-NMR signals ($C_6D_6$, TMS) of the bridgehead carbon atoms $C_d$ and $C_i$ in both *(2)* ($\delta = 129.8$)[3] and *(3)* (137.0 and 140.4) are shifted downfield relative to those for $C_d$ and $C_i$ in $\eta^5$-($C_9H_7$) complexes (*e.g.* ($\eta^5$-$C_9H_7$)$_2$Fe: $\delta = 87.0$)[4a]. Comparison of the chemical shifts of $C_a$, $C_b$, and $C_c$ in compounds *(2)* ($\delta = 82.9$, 118.0, and 98.7 resp.) and *(3)* (77.1, 134.4, and 97.2 resp.) with those of the corresponding carbon atoms in Ni($\eta^3$-$C_9H_7$)$_2$ (67.6, 106.6, and 67.6 resp.)[4a] and $Me_3Sn$($\eta^1$-$C_9H_7$) (45.8, 135.3 126.6 resp.)[4b] clearly indicates that the indenyl group is $\eta^3$-coordinated. The $^{13}$C-NMR spectrum of compound *(3)* at room temperature shows broad resonances due to carbon atoms $C_a$, $C_b$, $C_c$, $C_d$, and $C_i$, which are thought to represent the collapsed signals due to two rapidly exchanging nonequivalent $C_9H_7$ groups.

The coordinatively saturated 18e species *(3)* can be formally considered as a pseudo-octahedral complex in which each of the asymmetrically coordinated[5] $\eta^3$-$C_9H_7$ groups occupies two coordination sites. As expected, *(3)* does not react with ethylene. The coordinatively unsaturated 16e species *(2)* can be regarded as a pseudo-tetragonal pyramidal complex. It reacts slowly with ethylene in benzene at room temperature. $^1$H-NMR spectroscopy indicates that the neopentylidene originally present in *(2)* is quantitatively converted within 2.5 h into the homologous olefins 4,4-dimethyl-1-pentene and *trans*-4,4-dimethyl-2-pentene in a molar ratio of 1 : 1[6].

In the absence of ethylene, compound *(2)* has a half-life of *ca.* 1 d at room temperature, and is quantitatively converted to the tantalum bicycloheptane derivative *(5)* (Scheme 1). We presume that this reaction occurs *via* the tantalum bicyclopentane derivative *(4)* as intermediate. The structure assigned to compound *(5)* is based on $^1$H- and $^{13}$C-NMR spectroscopic evidence. The most salient features in the $^1$H-NMR spectrum, on going from *(2)* to *(5)*, are the disappearance of the singlet of the *tert*-butyl group ($\delta = 1.20$) in *(2)* accompanied by the simultaneous appearance of both singlets of the methyl groups of *(5)* (1.64 and 1.31). This clearly demonstrates the involvement of the *tert*-butyl group in the reaction.

CC bond formation in *(2)* can only occur when the two carbon atoms involved are in a *cis*-position to each other.

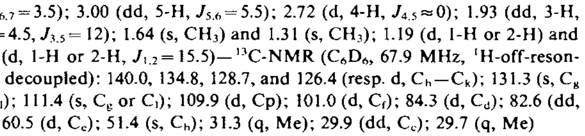


Scheme 2. Two resonance structures of *(2)*; Cp is not shown.

Dependent on the relative contributions of resonance structures *A* and *B*, the coupling between the neopentylidene and the asymmetrically coordinated $\eta^3$-$C_9H_7$ ligand can be formulated in two ways: 1) coupling of the neopentylidene fragment and the $\pi$-coordinated double bond to give a tantalacyclobutane ring; 2) insertion of the neopentylidene fragment into the Ta—$C_9H_7$ $\sigma$-bond. At present we cannot discriminate between the two possibilities. Both types of reaction have their precedents in tantalum chemistry[1a, b].

Dreiding molecular models of intermediate *(4)* suggest that the isomer shown in Scheme 1 is the most attractive one from the point of view of steric interactions. This isomer has to arise from the conformer of *(2)* containing an *endo*-oriented $\eta^3$-$C_9H_7$[7a, b] and an *exo*-oriented neopentylidene ligands[7c] (Scheme 1). The geometrical constraints in the highly coordinatively unsaturated 14e species *(4)* prevent $\beta$-H abstraction ($C_{\beta'}$—H) from the indenyl skeleton and provoke $\gamma$-H abstraction from a methyl in the *tert*-butyl group. This $\gamma$-H abstraction is unique in the sense that a

Table 1. $^1$H- and $^{13}$C-NMR data for *(5)* and *(6)* [a, b].



*(5)*: $^1$H-NMR ($C_6D_6$, 270 MHz): 7.36, 6.88 (2 d, 11-H, 8-H, $J_{8,9} \approx J_{10,11} = 8$); 7.01, 6.64 (2 dd, 10-H, 9-H, $J_{9,10} = 8$); 5.28 (s, Cp); 4.87 (d, 7-H); 4.06 (dd, 6-H, $J_{6,7} = 3.5$); 3.00 (dd, 5-H, $J_{5,6} = 5.5$); 2.72 (d, 4-H, $J_{4,5} \approx 0$); 1.93 (dd, 3-H, $J_{3,4} = 4.5$, $J_{3,5} = 12$); 1.64 (s, $CH_3$) and 1.31 (s, $CH_3$); 1.19 (d, 1-H or 2-H) and 1.02 (d, 1-H or 2-H, $J_{1,2} = 15.5$)—$^{13}$C-NMR ($C_6D_6$, 67.9 MHz, $^1$H-off-resonance decoupled): 140.0, 134.8, 128.7, and 126.4 (resp. d, $C_h$—$C_k$); 131.3 (s, $C_g$ or $C_l$); 111.4 (s, $C_g$ or $C_l$); 109.9 (d, Cp); 101.0 (d, $C_f$); 84.3 (d, $C_d$); 82.6 (dd, $C_a$); 60.5 (d, $C_e$); 51.4 (s, $C_h$); 31.3 (q, Me); 29.9 (dd, $C_c$); 29.7 (q, Me)
*(6)*: $^1$H-NMR ($CD_2Cl_2$, 90 MHz): 6.9—7.6 (complex, 9-H—12-H); 5.22 (s, Cp); 4.33 (ddd, 5-H, $J_{5,6} = 4.5$, $J_{5,7} = 5.0$); 4.03 (dd, 2-H, $J_{2,3} = 9$, $J_{2,4} \approx 0$); 3.68 (dd, 4-H, $J_{4,5} \approx 0$); 3.66 (s, 8-H); 3.46 (d, 6-H); 2.95 (d, 7-H, $J_{7,8} \approx 0$); 2.2 (m, 3-H, $J_{3,4} = 13.5$, $J_{3,5} = 4.5$); 1.04 (s, $C(CH_3)_3$); 0.5 (m, 1-H, $J_{1,2} = 12.5$, $J_{1,3} = 10$, $J_{1,4} = 6.5$)—$^{13}$C-NMR ($C_6D_6$, 67.9 MHz, $^1$H-gated decoupled): 140.4, 134.3, 129.0 and 124.8 (resp. d, $C_i$—$C_l$, $J_{C—H} = 163$); 128.6 (s, $C_h$ or $C_m$); 118.4 (s, $C_h$ or $C_m$); 109.2 (d, Cp, $J_{C—H} = 179$); 99.0 (d, $C_f$, $J_{C—H} = 153$); 87.7 (d, $C_d$, $J_{C—H} = 145$); 63.9 (dd, $C_a$, $J_{C—H^1} = 110$, $J_{C—H^2} = 132$); 58.7 (d, $C_c$, $J_{C—H} = 126$); 53.4 (d, $C_e$, $J_{C—H} = 122$); 40.6 (dd, $C_b$, $J_{C—H^3} = 124$, $J_{C—H^4} = 125$); 31.3 (s, $C_g$); 29.7 (q, Me, $J_{C—H} = 122$)

[a] $\delta$-Values relative to TMS; $J$ in Hz. Signals were assigned by selective proton decoupling of the $^1$H- and $^{13}$C-NMR spectra. [b] *(5)*: 7,8-benzo-2-chloro-2-cyclopentadienyl-4,4-dimethyl-2-tantalatricyclo[4.3.0.0$^{2,9}$]non-7-ene; *(6)*: 4,5-benzo-2-*endo-tert*-butyl-1-chloro-1-cyclopentadienyl-1-tantalatricyclo-[4.3.0.0$^{3,7}$]non-4-ene.

*0570-0833/81/1111-0979 $ 02.50/0*

γ-H is abstracted by $C_\alpha$ of the same alkyl group[8]. Whether this "γ,α-hydrogen shift" actually involves oxidative addition of $C_\gamma$-H to a Ta atom, followed by reductive elimination of $C_\alpha$-H[8], or a four centered transition state (see α-H abstraction in $ClTa(CH_2CMe_3)_4$)[1d] remains to be determined.

The result of the hydrogen shift is an expansion of the tantalacyclobutane ring to a less strained tantalacyclohexane ring in the boat conformation (*(5)*, Scheme 1). In this conformation the C—H bond formed is still close to the metal center and γ-H abstraction and ring expansion should be easily reversible. Several conformers of *(5)* can be envisaged. Dreiding molecular models reveal that of all the possible conformations, the skew boat form of *(5)* (Table 1) is the only one that involves both the energetically favored coordination of the double bond of the indenyl fragment parallel to the Cp group[6a] *and* a dihedral angle of *ca.* 90° between $C_c$—$H^4$ and $C_d$—$H^5$, since $J_{H^4H^5} \approx 0$ (Table 1). This conformation may well be the one prevailing in solution at room temperature.

The reversibility of the γ-H abstraction discussed above is shown by the reaction of *(5)* with ethylene in toluene at 70 °C: within 3 h, compound *(5)* is quantitatively converted into the tantalanorbornane derivative *(6)* *via* incorporation of 1 mol of ethylene (Scheme 1). The most striking change in the $^1$H-NMR spectrum upon conversion of *(5)* into *(6)* is the reappearance of a *tert*-butyl singlet: ($\delta = 1.04$) since $J_{H^7H^x} = 0$ (Table 1) the *tert*-butyl group must be in the *endo*-position, in accordance with the proposed mechanism. Treatment of *(5)* with $C_2D_4$ indicates that no significant H/D exchange occurs during $C_2D_4$ incorporation: only the signals and couplings due to $H_1$, $H_2$, $H_3$, and $H_4$ disappear in the $^1$H-NMR spectrum.

Both conversions *(2)→(5)* and *(5)→(6)*, described above, are highly specific and quantitative. They clearly demonstrate the high potential of organotantalum complexes in the C—C coupling and hydrogen-shift reactions involved in rearrangements of complex, unsaturated hydrocarbons.

### *Procedure*

*(2):* Solid $NaC_9H_7$ (360 mg, 2.6 mmol) was added over 1 h to a stirred solution of *(1)* (1.00 g, 2.6 mmol) in 20 mL of $C_6D_6$ at 6—10 °C. After warming up to room temperature over 30 min and filtration to remove the precipitate of NaCl, the solution was concentrated by partial evaporation of $C_6D_6$. The $^1$H-NMR spectrum indicated virtually quantitative conversion of *(1)* to *(2)*, with small amounts of *(1)* and *(3)* present.

*(3):* Solid $NaC_9H_7$ (0.10 g, 0.72 mmol) was added to a stirred solution of *(1)* (0.07 g, 0.18 mmol) in 4 mL of $C_6D_6$. After 1 h, the solution was filtered to remove NaCl and excess $NaC_9H_7$. The $^1$H-NMR spectrum of a sample of this solution indicated that quantitative conversion of *(1)* to *(3)* had occurred. Evaporation of the $C_6D_6$ resulted in formation of a brown oil, which we have not been able to crystallize.

*(5):* A sample of the crude solution of *(2)* was allowed to stand for 3 d at room temperature. The $^1$H-NMR spectrum indicated complete conversion of *(2)* into *(5)*. The brown oil obtained upon evaporating $C_6D_6$ was dissolved in *n*-hexane, and activated carbon added. After being stirred for 1 h and filtration, the solution was concentrated. Cooling at −20 °C gave brownish purple needles of *(5)*.

*(6):* A solution of *(5)* (1.5 g, 3.2 mmol) in 150 mL of toluene was heated at 70 °C under an ethylene pressure of 0.3 bar. The color of the solutions slowly changed from brown to red. After 3 h the solution was concentrated to 20 mL, and 35 mL of hexane and activated carbon were added. After being stirred, filtration of the mixture resulted in a clear red solution. Evaporation of the solvents produced *(6)* as a red oil. Upon recrystallization of this oil from hexane, analytically pure solid *(6)* was obtained.

Received: January 8, 1981,
in altered form: September, 1981 [Z 887 IE]
German version: Angew. Chem. *93*, 1029 (1981)

CAS Registry numbers:
*(1)*, 63312-60-7; *(2)*, 79483-58-2; *(3)*, 79483-59-3; *(5)*, 79467-00-8; *(6)*, 79483-60-6

---

[1] a) *R. R. Schrock, S. J. McLain, J. Sancho*, Pure Appl. Chem. *52*, 729 (1980); b) *P. R. Sharp, R. R. Schrock*, J. Organomet. Chem. *171*, 43 (1979); c) *J. H. Wengrovius, R. R. Schrock, M. R. Churchill, J. R. Missert, W. J. Youngs*, J. Am. Chem. Soc. *102*, 4515 (1980); d) *R. R. Schrock*, Acc. Chem. Res. *12*, 98 (1979).

[2] *A. J. Hart-Davis, R. J. Mawby*, J. Chem. Soc. *A 1969*, 2403; *P. Caddy, M. Green, E. O'Brien, L. E. Smart, P. Woodward*, Angew. Chem. *89*, 671 (1977); Angew. Chem. Int. Ed. Engl. *16*, 648 (1977).

[3] One of the signals from $C_d$ and $C_i$ in *(2)* is hidden by $C_6D_6$ signals.

[4] a) *F. H. Köhler*, Chem. Ber. *107*, 570 (1974); b) *G. A. Taylor, P. E. Rakita*, J. Org. Magn. Reson. *6*, 644 (1974).

[5] In *(2)* and *(3)*, the different ligands which are *trans* to $C_a$ and $C_c$ of the allylic part of the indenyl ligand cause a localization of the π-electron density between either $C_a$ and $C_b$ or $C_b$ and $C_c$, which is clearly shown in the $^{13}$C-NMR spectrum (see text).

[6] a) This ratio is different from that observed in the reaction of *(1)* with $C_2H_4$. 4,4-Dimethyl-1-pentene : *trans*-4,4-dimethyl-2-pentene = 0.97 : 0.03 (*S. J. McLain, C. B. Wood, R. R. Schrock*, J. Am. Chem. Soc. *101*, 4558 (1979)); b) we have been unable to characterize the Ta complexes formed, since they are difficulty soluble and their NMR spectra exhibit broad lines (probably due to the formation of paramagnetic compounds).

[7] a) *exo-* and *endo*-Indenyl are defined by analogy to *exo-* and *endo*-allyl (*B. E. R. Schilling, R. Hoffman, J. W. Faller*, J. Am. Chem. Soc. *101*, 592 (1979); b) a single crystal X-ray study of the pseudo-tetragonal pyramidal species $(\eta^5\text{-}C_9H_7)(\eta^3\text{-}C_9H_7)W(CO)_2$ revealed a dihedral angle of 26° between the allylic part ($C_a$, $C_b$, $C_c$) and the aromatic ring of the *exo*-coordinated $\eta^3$-indenyl ring. *endo*-Coordination of the $\eta^3\text{-}C_9H_7$ ligand is prevented since the six-membered rings of $\eta^3\text{-}C_9H_7$ and $\eta^5\text{-}C_9H_7$ would then be extremely close together. *J. A. N. Nesmeyanov, N. A. Ustynyuk, L. G. Makarova, V. G. Andrianov, Yu. T. Struchkov, S. Andrea, Yu. A. Ustynyuk*, and *S. G. Malyugina*, J. Organometal. Chem. *159*, 189 (1978). *endo*-$\eta^3\text{-}C_9H_7$ coordination would however be feasible if, as is the case for *(2)*, $\eta^5$-Cp were present instead of $\eta^5\text{-}C_9H_7$. c) In *exo*-neopentylidene the *tert*-butyl group is directed away from the Cp fragment; in *endo*-neopentylidene the *tert*-butyl group is turned towards the Cp fragment.

[8] In $(Et_3P)_2Pt(CH_2CMe_3)_2$ a γ-H atom of one neopentyl group is abstracted by the $C_\alpha$ atom of the second neopentyl group. γ-H abstraction by $C_\alpha$ of the same neopentyl group was not observed; *P. Foley, G. M. Whitesides*, J. Am. Chem. Soc. *102*, 6713 (1980).

## Palladation of sp$^3$-Carbon Atoms: Preparation of *N*-Palladiomethylthioamides[**]

By *Yoshinao Tamaru, Masahiro Kagotani*, and *Zen-ichi Yoshida*[*]

Many studies on the *ortho*-palladation of aromatics which possess a benzylic heteroatom (N, P, S, *etc.*) substituent have been reported[1]. Although the reaction of *N,N*-dimethylthiobenzamide *(1a)* with $PdCl_2$ in refluxing $CH_3OH$ is analogous to the *ortho*-palladation of thiobenzophenone[2a] and thiopivaloylferrocene[2b], the product *(2a)* which is C-metalated at the N—$CH_3$ group is quantitatively formed; no *ortho*-palladation product was detected.

---

[*] Prof. Dr. Z. Yoshida, Dr. Y. Tamaru, M. Kagotani
Department of Synthetic Chem., Kyoto University
Yoshida, Kyoto 606 (Japan)

[**] Reactions of Organosulfur Compounds with Palladium, Part 2.—Part 1: *Y. Tamaru, M. Kagotani, Z. Yoshida*, J. Org. Chem. *44*, 2816 (1979). This work was supported by the Ministry of Education, the Japanese Government (Grant-in-Aid for Scientific Research No. 203014).

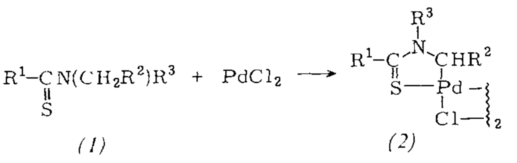


Table 1. Cyclic *N*-palladiomethylthioamides *(2) via* palladation of thioamides *(1)* in methanol at 60 °C.

| | R$^1$ | R$^2$ | R$^3$ | *t* [h] | *(2)* Yield [%] |
|---|---|---|---|---|---|
| *(a)* | Ph | H | $CH_3$ | 10 | 94 |
| *(b)* | Ph | $CH_3$ | $C_2H_5$ | 20 | 13 |
| *(b)* [a] | Ph | $CH_3$ | $C_2H_5$ | 1 | 46 |
| *(c)* | Ph | H | $C_2H_5$ | 7 | 91 |
| *(d)* | $CH_3$ | H | $CH_3$ | 10 | 49 |
| *(e)* | $CH(CH_3)_2$ | H | $CH_3$ | 4 | 82 |
| *(f)* | $C(CH_3)_3$ | H | $CH_3$ | 1 | 94 |
| *(g)* | $CH(CH_3)_2$ | $-(CH_2)_3-$ | | 10 | 94 |
| *(h)* | $C(CH_3)_3$ | $-(CH_2)_4-$ | | 1 | 96 |
| *(i)* [a] | PhCH=CH | H | $CH_3$ | 1.5 | 94 |
| *(j)* [a] | Cyclohexenyl | H | $CH_3$ | 1 | 83 |

[a] In HMPA in 80 °C.

The structure of *(2a)* (acac complex), which is characterized by its five-membered ring (Pd—C($sp^3$)—N—C=S), follows from IR- and $^1$H-NMR spectra, and X-ray crystal structure analysis (Fig. 1)[3]. *(2a)* is thermally stable and does not decompose in air or in the presence of moisture.

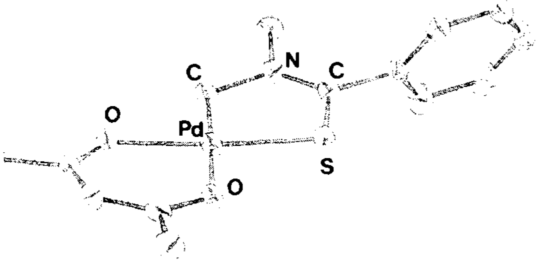


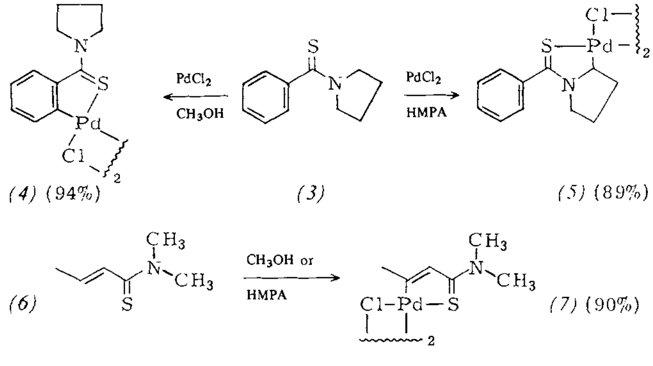
Fig. 1. ORTEP plot of *(2a)* (acac complex) in the crystal.

The reaction *(1)*→*(2)* is reminiscent of the lithiation of the $NCH_3$ groups of *N,N*-dimethylthioamides[4a] or *N,N*-dimethylcarbamates[4b]. While metalation with Li is restricted to compounds whose thiocarbonyl groups are protected against attack of organolithium compounds, the present metalation with Pd indicates the high structural flexibility of many thioamides[5].

Selected results are summarized in Table 1, which reveals that not only thiobenzamides but also thioalkylamides can react to give *N*-palladiomethyl derivatives *(2)* with similar ease: hereby thioalkylamides with bulky alkyl groups react particularly easily (Table 1)[6].

The *N*-methyl group is much more reactive than the *N*-ethyl or pyrrolidino groups, as shown *e.g.* by the selective palladation of the $NCH_3$ group in *(1c)*. The *N*-isopropyl group could not be metalated with Pd. Hexamethylphosphoric triamide (HMPA) is found to be a better solvent for less reactive substrates.

The regioselectivity (palladation of the *N*-alkyl group in the α-position *versus ortho*-palladation) largely depends on the reaction conditions and/or the structural features of the thioamides. While *N*-thiobenzoylpyrrolidine *(3)* is metalated by $PdCl_2$ at the $CH_2$ group neighboring the nitrogen in HMPA to give *(5)*, the similar reaction in $CH_3OH$ leads to a selective *ortho*-palladation producing *(4)* in quantitative yield. Similarly *N,N*-dimethylthiocrotonamide *(6)* reacts both in HMPA and in $CH_3OH$, whereby an $sp^2$-C atom is also metalated; this is in marked contrast to the selective palladation of *N,N*-dimethylthiocinnamamide *(1i)* and *N,N*-dimethyl-1-cyclohexenethioamide *(1j)* (where only an $sp^3$-C atom is attacked.



## *Procedure*

*(2a):* A suspension of $PdCl_2$ (1 mmol) and *1a* (1.2 mmol) is magnetically stirred and refluxed in $CH_3OH$ for 10 h, during which time a pale yellow solid gradually precipitates. When the reaction mixture has cooled to room temperature, the precipitate is filtered and washed with ether. Yield 90—100% (based on Pd). The acetylacetonato complex of *(2a)* is obtained as follows: A solution of *(2a)* (1 mmol) in 20 mL of $CH_3CN$ is treated with Tl(acac) (1.2 mmol) at room temperature for 4 h. After evaporation of the solvent, the residue is dissolved in benzene, filtered through a 2 cm long cellulose column, and then chromatographed on a silica gel column ($C_6H_6/CH_2Cl_2$). Recrystallization (EtOH/$CH_2Cl_2$) provides a pale yellow solid (50—60%). IR (KBr disk): 1595 (s), 1575 (s), 1520 (s), 1405 (br. s), 764 (m), and 604 (m); $^1$H-NMR ($CDCl_3$): $\delta = 1.97$ (s, 6 H), 3.13 (s, 3 H), 4.56 (s, 2 H), 5.30 (s, 1 H), and 7.47 (br. s, 5 H).

Received: December 17, 1979
revised: September 22, 1981 [Z 888 IE]
German version: Angew. Chem. *93*, 1031 (1981)

CAS Registry numbers:
*(2a)*, 74790-33-3; *(2b)*, 79467-04-2; *(2c)*, 79467-05-3; *(2d)*, 79467-06-4; *(2e)*, 79467-07-5; *(2f)*, 79467-08-6; *(2g)*, 79467-09-7; *(2h)*, 79467-10-0; *(2i)*, 79467-11-1; *(2j)*, 79467-12-2; *(4)*, 79467-13-3; *(5)*, 79467-14-4; *(7)*, 79467-15-5; *2a* (acac complex), 76791-93-0

---

[1] *M. I. Bruce*, Angew. Chem. *89*, 75 (1977); Angew. Chem. Int. Ed. Engl. *16*, 73 (1977).

[2] a) *H. Alper*, J. Organomet. Chem. *61*, C62 (1973); b) *80*, C29 (1974).

[3] The authors are indebted to Prof. *N. Kasai* and Dr. *K. Miki* for the X-ray crystal structure analysis of *2a* (acac complex). For the structural details, see *K. Miki, N. Tanaka, N. Kasai*, Acta Crystallogr. *B37*, 447 (1981).

[4] a) *D. Seebach, W. LuBosch*, Angew. Chem. *88*, 339 (1976); Angew. Chem. Int. Ed. Engl. *15*, 313 (1976); b) *D. Seebach, T. Hassel, ibid. 90*, 296 (1978); *17*, 274 (1978).

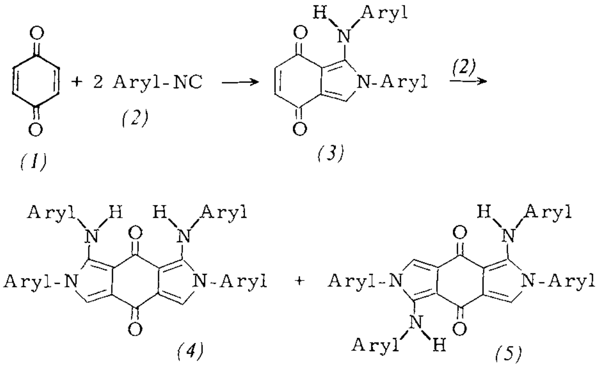
[5] For palladation of $sp^3$-C atoms, see *A. J. Deeming, I. P. Rothwell*, J. Chem. Soc. Chem. Commun. *1978*, 344; *A. G. Constable, W. S. McDonald, L. C. Sawkins, B. L. Shaw, ibid. 1978*, 1061; *S.-I. Murahashi, T. Yano, ibid. 1979*, 270.

[6] For the steric acceleration of C-palladation see *A. J. Cheney, B. L. Shaw*, J. Chem. Soc. Dalton Trans. *1973*, 2394.

# Addition of Aryl Isocyanides to 1,4-Quinones: Synthesis of Novel Deep-Blue Dyes

By *Walter Ott* and *Victor Formacek*[*]

Although quinones and isocyanides have each been the subject of numerous investigations, nothing has so far been mentioned about how they react with each other[1-3]. We have now found that on heating a mixture of 1,4-benzoquinone *(1)* and 2.5 equivalents of 4-methylphenyl isocyanide *(2)* in toluene, a deep-blue solution is obtained from which the products *(3)*, *(4)*, and *(5)* can be isolated. *(3)* is apparently a precursor of *(4)* and *(5)*, since reaction of pure *(3)* with *(2)* under the same conditions also affords *(4)* and *(5)*. According to elemental analyses and mass spectra *(3)* is a 1:2 adduct, *(4)* and *(5)* are 1:4 adducts of the quinone *(1)* and the isocyanide *(2)*.



Aryl = 4-Methylphenyl

Table 1. Melting points and spectroscopic data of the compounds *(3)*, *(4)*, and *(5)*.

| Cpd. | M.p. [°C] | Spectroscopic data |
|---|---|---|
| *(3)* | 162 | UV/VIS [a]: $\lambda_{max}=604$ ($\lg\varepsilon=3.85$), 404 (3.32), 296 (4.15), 245 (sh, 4.36)<br>IR [b]: $\nu=1600, 1640, 1657$ cm$^{-1}$<br>$^1$H-NMR [c]: $\delta=8.03$ (s), 7.2 (m), 7.11 (s), 6.58 (m), 2.44 (s), 2.31 (s)<br>$^{13}$C-NMR [d]: $\delta=184.26$ (s), 174.96 (s), 139.41 (s), 139.16 (s), 138.70 (d), 136.67 (d), 135.82 (s), 132.92 (s), 131.07 (s), 130.03 (2 d), 129.64 (2 d), 125.32 (2 d), 124.82 (s), 117.50 (2 d), 114.54 (d), 113.76 (s), 21.21 (q), 20.64 (q) |
| *(4)* | 242 | UV/VIS [a]: $\lambda_{max}=608$ ($\lg\varepsilon=4.25$), 376 (sh, 3.16), 297 (4.44), 250 (4.60)<br>IR [b]: $\nu=1600, 1627$ cm$^{-1}$<br>$^1$H-NMR [c]: $\delta=8.21$ (s), 7.15 (m), 6.82 (s), 2.38 (s), 2.31 (s)<br>$^{13}$C-NMR [d]: $\delta=182.26$ (s), 165.76 (s), 140.14 (s), 138.35 (s), 136.73 (s), 131.90 (s), 129.92 (s), 129.86 (2 d), 129.39 (2 d), 127.31 (s), 125.64 (2 d), 116.81 (2 d), 114.89 (s), 114.38 (d), 21.14 (q), 20.58 (q) |
| *(5)* | 305 | UV/VIS [a]: $\lambda_{max}=602$ ($\lg\varepsilon=4.30$), 293 (4.54)<br>IR [b]: $\nu=1595, 1625$ cm$^{-1}$<br>$^1$H-NMR [c]: $\delta=8.14$ (s), 7.2 (m), 7.04 (s), 2.27 (s), 1.58 (s)<br>$^{13}$C-NMR [d]: $\delta=174.02$ (s), 139.98 (s), 138.92 (s), 136.60 (s), 133.14 (s), 130.17 (s), 128.95 (s), 129.85 (2 d), 129.61 (2 d), 125.70 (2 d), 117.20 (2 d), 115.39 (s), 114.01 (d), 21.31 (q), 20.59 (q) |

[a] In 1,2-dichloroethane. [b] In Nujol. [c] In $CDCl_3$, 250 MHz. [d] In $CDCl_3$, 62.89 MHz. Quoted multiplicities taken from the off-resonance decoupled $^{13}$C-NMR spectra.

The spectra of *(3)*, *(4)* and *(5)* verify the close similarity of the compounds (see also Table 1). According to the $^1$H-NMR spectrum *(3)* contains two different aryl moieties and two *cis*-vinyl protons, which are absent in the case of *(4)* and *(5)*. All spectroscopic data of the 1:2 adduct are consistent with it being the 4,7-dioxo-4,7-dihydroisoindole *(3)*. According to the $^{13}$C-NMR spectra, *(4)* has $C_{2h}$ symmetry (16 $^{13}$C-NMR signals) and *(5)* has $C_{2v}$ symmetry (15 $^{13}$C-NMR signals). It follows, therefore, that the 1:4 adducts, which are also formed from *(3)*, must have the structures *(4)* and *(5)*, the basic skeletal unit of which was recently synthesized *via* an alternative route[4]. Noteworthy is the deep-blue color of the compounds *(3)*, *(4)* and *(5)*, which is reminiscent of the color of the diamino-1,4-benzoquinones[5]. Annelation of the second pyrrole ring on *(3)* hardly influences the position of the longest wave absorption maximum, only the extinction becomes larger.

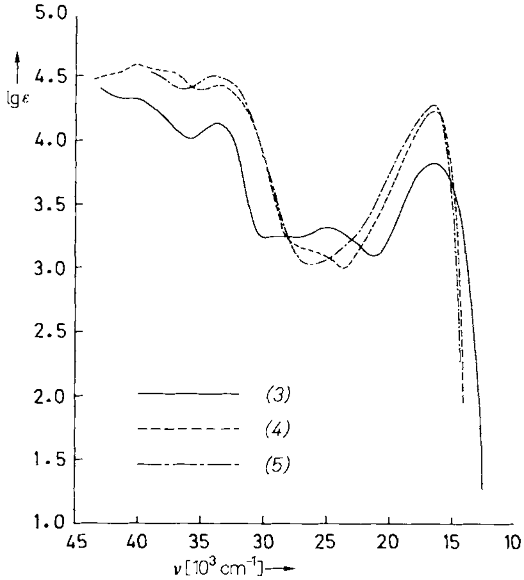
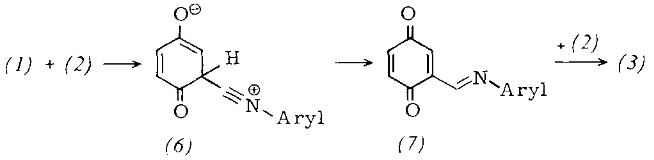


Fig. 1. UV/VIS spectra of the dyes *(3)*, *(4)* and *(5)* in 1,2-dichloroethane.

We assume the first step of the reaction sequence leading to *(3)* to be a formal insertion of the isocyanide C atom into a CH bond of *(1)*, in which the dipole *(6)* occurs as intermediate. [4+1]-Cycloaddition of a second isocyanide molecule to the heterodiene *(7)* and stabilization of the cycloadduct by prototropy leads to the 1:2 adduct. [4+1]-Cycloadditions of isocyanides to electron-deficient heterodienes have been described on numerous occasions[6]. Phenyl isocyanide and 4-substituted aryl isocyanides containing residues other than methyl likewise give 1:2 and 1:4 adducts.



### *Procedure*

A solution of *(1)* (1.08 g, 10 mmol) and *(2)* (2.93 g, 25 mmol) in toluene (30 mL) was heated under reflux until no more *(1)* was present (4 h, TLC monitoring, silica gel, chlo-

---

[*] Dr. W. Ott
Institut für Organische Chemie der Universität
Heinrichstrasse 28, A-8010 Graz (Austria)
Dr. V. Formacek
Bruker Analytische Messtechnik
Silberstreifen, D-7512 Rheinstetten (Germany)

roform). The solvent was removed by distillation under reduced pressure and the oily residue was chromatographed on silica gel with chloroform, *(5)*, *(4)* and *(3)* being eluted one after the other as zones of almost the same color, which after evaporation and crystallization from ethanol furnished 0.14 g of *(5)*, 0.14 g of *(4)* and 0.9 g of *(3)* as bluish-black crystals.

Received: August 1, 1980 [Z 897 IE]
supplemented: February 23, 1981
German version: Angew. Chem. *93*, 1014 (1981)

CAS Registry numbers:
*(1)*, 106-51-4; *(2)*, 7175-47-5; *(3)*, 79482-91-0; *(4)*, 79482-92-1; *(5)*, 79482-93-2

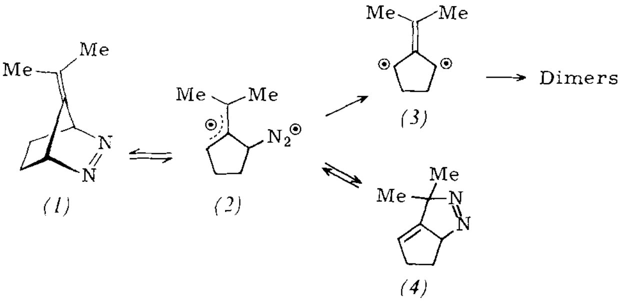
---

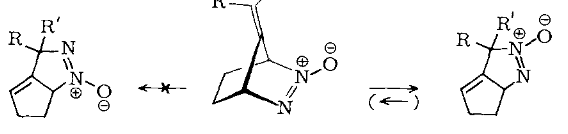
[1] *S. Yamada, K. Takashima, T. Sato, S. Terashima*, Chem. Commun. *1969*, 811.
[2] *I. Ugi*: Isonitrile Chemistry, Academic Press, New York 1971.
[3] *H. Ulrich, R. Richter* in *Houben-Weyl-Müller*: Methoden der Organischen Chemie, 4th edit., Vol. VII/3a, Thieme, Stuttgart 1977, p. 647ff.
[4] *J. A. Myers, L. D. Moor, W. L. Whitter, S. L. Council, R. M. Waldo, J. L. Lanier, B. U. Omoji*, J. Org. Chem. *45*, 1202 (1980).
[5] *S. Dähne, D. Leupold*, Angew. Chem. *78*, 1029 (1966); Angew. Chem. Int. Ed. Engl. *5*, 984 (1966).
[6] *G. Kollenz, W. Ott, E. Ziegler, K. Peters, H. G. von Schnering, H. Quast*, Liebigs Ann. Chem. *1980*, 1801.

## Rearrangement of Bridged Diazene *N*-Oxides: Selective Cleavage of the C—NO Bond[**]

By *Henrik Olsen* and *Jean F. M. Oth*[*]

It has been shown recently by *Berson et al.* that thermal loss of $N_2$ from the bridged diazene *(1)* is accompanied by a rearrangement to the isomer *(4)*[1a]. Kinetic investigations combined with MO calculations suggest that the thermolysis proceeds *via* the diradical *(2)*[1]. We report here on the thermal isomerization of the analogous diazene *N*-oxides *(5)*—*(7)*.





*(8b)*, R = R' = Me
*(5)*, R = R' = Me
*(6a)*/*(6b)*, R = Me/Ph, R' = Ph/Me
*(7)*, R = R' = Ph
*(8a)*, R = R' = Me
*(9a)*/*(9b)*, R = Me/Ph, R' = Ph/Me
*(10)*, R = R' = Ph

Pyrolysis of degassed solutions of *(5)* in sealed pyrex ampules yielded quantitatively the isomer *(8a)*, the structure of which was established unequivocally by an X-ray analysis[2]. A mixture of the diastereomers *(6)* underwent thermal rearrangement to give a mixture of the diastereomers *(9)*[3]. Although the spatial arrangement of the phenyl and methyl groups in *(6)* and *(9)* could not be specified, the $^1$H-NMR spectra recorded before and after thermolysis indicate that each stereoisomer rearranges to give a single product: in all cases the molar ratio of the products was found to be identical to the molar ratio of the educts. In contrast, thermolysis of *(7)* yields equilibrium mixtures of *(7)* and *(10)*[3] ($K_{(10)/(7)} = 1.75$ at 134.6 °C).

Table 1. Rate constants and free energies of activation for the isomerization of *(5)*—*(7)* in $[D_8]$dioxane at 134.6 °C.

| Compound | $k \times 10^5$ [s$^{-1}$] | $\Delta G^{\neq}$ [kcal/mol] |
|---|---|---|
| *(5)* | 2.6 | 32.6 |
| *(6a)* | 3.8 | 32.3 |
| *(6b)* | 4.9 | 32.1 |
| *(7)* | 9.6 | 31.6 |

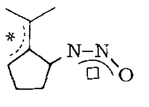
Table 2. The effect of solvent and temperature on the thermal Rearrangement of *(5)*.

| Solvent | $E_t$ | $k \times 10^5$ [s$^{-1}$] [a] | $\Delta H^{\neq}$ [kcal/mol] [b, c] | $\Delta S^{\neq}$ [cal mol$^{-1}$K$^{-1}$] [b, c] |
|---|---|---|---|---|
| $[D_8]$toluene | 33.9 | 21.6 | — | — |
| $[D_8]$dioxane | 36 | 12.0 | 33.6 ± 1.9 | 8.9 ± 4.4 |
| $CD_3CN$ | 46 | 4.5 | — | — |

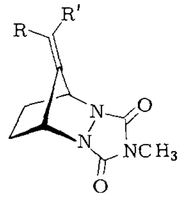
[a] At 150.5 °C. [b] At 25 °C. [c] The values are given with standard deviations.

The rate constants for the rearrangements of *(5)*—*(7)* were determined at 134.6 °C in $[D_8]$dioxane; the effects of temperature and solvent on the isomerization *(5)*→*(8a)* are shown in Table 2. The rate of disappearence of the substrate was found to be first order by $^1$H-NMR spectroscopy.

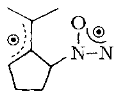
Several pathways for the rearrangement are conceivable: apart from a concerted process, diradical *(11a)* or zwitterionic intermediates *(11b)* and *(11c)*, respectively, deserve consideration. However, the following evidence makes it probable that the diradical *(11a)* is involved: 1) isomerization of *(5)* is insensitive to solvent polarity *i.e.* zwitterionic intermediates are improbable; 2) the entropy of activation for the rearrangement of *(5)* is strongly positive ($\Delta S^{\neq} = 8.7$ cal mol$^{-1}$K$^{-1}$); this is more consistent with a flexible,



*(11a)*, *, □ = ⊙, ⊙
*(11b)*, *, □ = ⊕, ⊖
*(11c)*, *, □ = ⊖, ⊕



*(12)*, R = R' = Me
*(13)*, R = Me, R' = Ph
*(14)*, R = R' = Ph



*(15)*

---

[*] Dr. H. Olsen[+], and Prof. J. F. M. Oth
Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätsstrasse 16, CH-8006 Zürich (Switzerland)

[+] Present address:
Teknologisk Institut
Gregersensvej, DK-2630 Tåstrup (Denmark)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung.

than with a pericyclic transition state; 3) finally, the rates of rearrangement (at 140 °C) of *(5)*—*(7)* are practically the same as those of the triazolidinedione derivatives *(12)*—*(14)*, thus indicating a similar mechanism. The isomerizations of *(12)*—*(14)*, which are also first order reactions, leads *via* a common diradical intermediate to two products: a fused isomer and an isomer formed by H-abstraction[4].

All NMR data recorded during the thermal isomerization of *(5)* indicate that only *(8a)* is formed; if *(8b)* is also formed its yield must be less than 1%. This implies that the rate of cleavage of the C—NO bond is at least 100 times faster than the rate of cleavage of the C—N bond ($\Delta\Delta G^{+} = \Delta G^{+}(\text{C—N}) - \Delta G^{+}(\text{C—NO}) > 3.9$ kcal/mol at 150.0 °C). Preferential cleavage of the C—NO bond may be attributable to the differences in stability between the two diradicals *(11a)* and *(15)*. *(11a)* is stabilized by the "three-electron-bonding" effect, which is precluded in *(15)*. This effect has recently been invoked by *Greene et al.* as an important factor in the stabilization of diazenoxyl radicals[5].

Comparison of the rearrangement of the diazene *(1)* with that of the analogous *N*-oxide *(5)* is instructive. The ratio of the rate constants[6] $k_{\text{diazene}}/k_{\text{diazene }N\text{-oxide}} = 44000$ (at 50 °C), corresponding to $\Delta\Delta G^{+} \simeq 7$ kcal/mol. This difference in reactivity between *(1)* and *(5)* is considerably smaller than the observed difference between $N_2$ and $N_2O$ extrusion in diazenes and their corresponding *N*-oxides: diazenes normally eliminate $N_2$ *ca.* $10^{17}$ times faster than the rate at which the related *N*-oxides extrude $N_2O$ ($\Delta\Delta G^{+} > 26$ kcal/mol)[7]. This dramatic difference in reactivity has been related to the fact that loss of $N_2$ is much more exothermic than loss of $N_2O$ ($\Delta\Delta H_{\text{react.}} = \Delta H_{\text{react.}}$(diazene) $- \Delta H_{\text{react.}}$(diazene *N*-oxide) $= -32$ kcal/mol; $\Delta H_f^0(N_2O, g) = 19.4$ kcal/mol)[7]. The enthalpy of reaction for the *(1)*→*(4)* and *(5)*→*(8a)* transformations should be very similar. Since the group increment for the enthalpy of formation of the *cis*-azoxy group is 13 kcal/mol smaller than that of the *cis*-azo group[7], the energy profiles for the reactions *(1)*→*(2)* and *(5)*→*(8a)* would be expected to be mutually displaced by this amount. Actually the transition states differ by 6 kcal/mol[7]. Hammond's postulate[8] suggests that the resemblance between the diazenyl diradical and the transition state leading to it is closer than the resemblance between the diazenoxyl diradical *(11a)* and its corresponding transition state.

Received: July 4, 1980,
in altered form October 5, 1981 [Z 903a IE]
German version: Angew. Chem. 93, 1024 (1981)

---

[1] a) *D. Cichra, M. S. Platz, J. A. Berson*, J. Am. Chem. Soc. 99, 8507 (1977); b) *R. Siemionko, A. Shaw, G. O'Connell, R. D. Little, B. K. Carpenter, L. Shen, J. A. Berson*, Tetrahedron Lett. *1978*, 3529.

[2] *A. W. Maverick, E. F. Maverick, H. Olsen*, Helv. Chim. Acta *63*, 1304 (1980).

[3] The proposed structures for *(9a, b)* and *(10)* are based on the unequivocal structure of *(8a)* and on their ¹H- and ¹³C-NMR spectra.

[4] *H. Olsen*, unpublished results.

[5] *F. D. Greene, J. D. Burrington, A. M. Karkowsky* in *W. A. Pryor:* Organic Free Radicals. ACS Symp. Ser. 69, Washington 1978, p. 122.

[6] A statistical factor of two has to be introduced because either of the two equivalent CN-bonds may be cleaved.

[7] *J. F. M. Oth, H. Olsen, J. P. Snyder*, J. Amer. Chem. Soc. 99, 8505 (1977) and references therein.

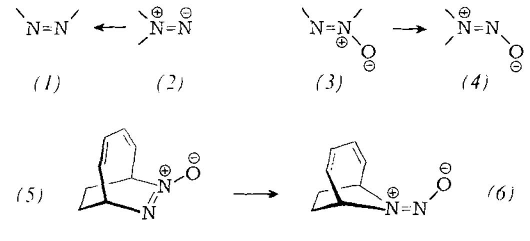
[8] *D. Farcasiu*, J. Chem. Educ. *52*, 76 (1975).

---

# Valence Isomerization of a *cis*-Diazene-/Isodiazene-*N*-Oxide: Thermolysis of 7,8-Diazabicyclo[4.2.2]deca-2,4,7-triene *N*-Oxide[**]

By *Henrik Olsen*[*]

Both experimental evidence[1a] and *ab initio* calculations[1b] indicate that *cis*-1,2-diazenes *(1)* are thermodynamically more stable than their 1,1-isomers *(2)*. *cis*-1,2-Diazene *N*-oxides, on the other hand, are expected to be less stable than their 1,1-isomers [*(3)*: $\Delta H_f^0 \simeq 35-40$ kcal/mol[2a]; *(4)*: $\Delta H_f^0 \simeq 30$ kcal/mol[2b]]. However, no evidence for the occurrence of the rearrangements *(2)*→*(1)* and *(3)*→*(4)* has, to date, been found[3]. We now wish to report on the thermolysis of 7,8-diazabicyclo[4.2.2]deca-2,4,7-triene *N*-oxide *(5)*, which to our knowledge represents the first example of an isomerization of the type *(3)*→*(4)*.



Pyrolysis of degassed solutions of *(5)*[4] in toluene sealed in pyrex ampules yielded, after 500 min at 185 °C, isomer *(6)*[5] (65%, m.p. = 61—62°, lit.[6] 62—63 °C). The rate of disappearence of *(5)*—a first order reaction—was studied at different temperatures and in different solvents by ¹H-NMR spectroscopy (Table 1). However, the formation of *(6)* was not strictly first order, since it slowly decomposes at the temperatures at which the isomerization *(5)*→*(6)* can be observed ($k_6 = 1.15 \times 10^{-5}$ s$^{-1}$; $k_5 = 2.04 \times 10^{-4}$ s$^{-1}$ at 184.6 °C)[7].

Table 1. Influence of solvent and temperature on the thermal isomerization *(5)*→*(6)*.

| Solvent | $E_t$ | $\delta$ | $k \times 10^5$ [s$^{-1}$] [a] | $k_{\text{rel}}$ [a] | $\Delta G^{+}$ [kcal/mol] [a] | $\Delta H^{+}$ [kcal/mol] [b, c] | $\Delta S^{+}$ [cal mol$^{-1}$ K$^{-1}$] [b, c] |
|---|---|---|---|---|---|---|---|
| [D₈]Toluene | 33.9 | 8.9 | 5.24 | 4.6 | 34.9 | 36.8 ± .8 | 4.2 ± 1.8 |
| [D₈]Dioxane | 36 | 9.8 | 3.10 | 2.7 | 35.4 | 38.0 ± .6 | 6.0 ± 1.4 |
| $CD_3CN$ | 46 | 11.8 | 1.15 | 1.0 | 36.2 | | |

[a] At 169.9 °C. [b] At 25 °C. [c] Tolerances given are standard deviations.

*A priori* two mechanistic pathways must be considered for the rearrangement *(5)*→*(6)*: a) a one-step concerted 1,2-sigmatropic shift, which according to frontier orbital considerations[8] is a forbidden reaction, and b) a two-step sequence *via* the diradical *(7)* or the zwitterions *(8a)* or *(8b)*.

The following arguments indicate that the isomerization probably proceeds *via* the intermediate diradical *(7)*: 1)

---

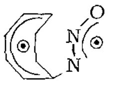
[*] Dr. H. Olsen,
Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Present adress:
Teknologisk Institut
Gregersensvej, DK-2630 Tåstrup (Denmark).

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung.

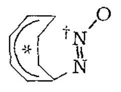
The observed rate dependence on solvent polarity (Table 1) is consistent with a polar ground state which rearranges *via* a less polar transition state, suggesting a concerted or diradical process. 2) Solvent effects are also to be expected if the substrate molecular volume changes on moving from the ground to the transition state. According to *Abraham*[9] the volume of activation $\Delta V^{\neq}$ can be estimated by fitting the data to a linear equation of the form

$$\ln k_{rel} = -(\Delta V^{\neq}/RT)\delta^2 + c_0$$

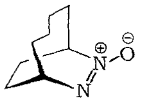
where $\delta$ is the Hildebrand solubility parameter. The dependence of the rate constant on $\delta^2$ ($r=0.996$) is consistent with a positive value for $\Delta V^{\neq}$ and is therefore in agreement with a two-step process. 3) The positive entropy of activation (Table 1) is more consistent with a flexible than with a pericyclic transition state. 4) Finally, replacement of the butadiene bridge by a tetramethylene group decreases the rate dramatically. The relative rate of decomposition $k_5/k_9$ is 1750 at 250°C ($\Delta\Delta G^{\neq}=7.8$ kcal/mol)[10]. Since the pentadienyl radical has a stabilization energy of *ca.* 20 kcal/mol[11] the observed $k_5/k_9$ ratio constitutes further evidence for a diradical mechanism.



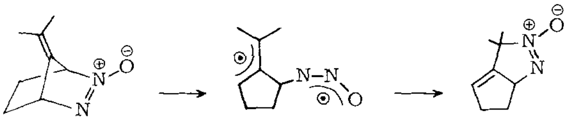
*(7)*



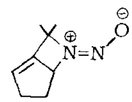
*(8a)*, *, † = ⊕, ⊖
*(8b)*, *, † = ⊖, ⊕



*(9)*



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



*(13)*

Thermolysis of the bridged diazene *N*-oxide *(10)* leads, *via* the diradical *(11)*, to isomer *(12)*[12]. The ring closure of *(11)*→*(12)* is preferred, since the 1,1-diazene *N*-oxide *(13)* is thermodynamically unstable (ring strain). The relative rate of rearrangement of *(10)* and *(5)* in toluene at 150°C is 28 ($\Delta\Delta G^{\neq}=2.8$ kcal/mol). These values suggest that release of strain, together with stereoelectronic factors appear to strongly influence the reactivity[13].

Received: February 3, 1981 [Z 903b IE]
German version: Angew. Chem. *93*, 1025 (1981)

CAS Registry numbers:
*(5)*, 65115-46-0; *(6)*, 51787-57-6

---

[1] a) *W. D. Hinsberg, III, P. B. Dervan*, J. Am. Chem. Soc. *101*, 6142 (1979); b) *C. J. Casewit, W. A. Goddard, III, ibid. 102*, 4057 (1980).

[2] a) *J. F. M. Oth, H. Olsen, J. P. Snyder, ibid. 99*, 8505 (1977). b) The group increment for the *N*-nitrosoamine group is based on the reported standard heat of formation of *N*-nitrosodimethylamine (l) ("Selected Values of Chemical Thermodynamic Properties", Circular 270—3 of the National Bureau of Standards, U.S. Government Printing Office, Washington D.C., 1968, pp. 161), *Benson*'s group increment for the C—(H)$_3$(C)-group (*S. W. Benson:* Thermochemical Kinetics, 2nd ed., Wiley, New York 1976), and the assumption that $\Delta H_v$(*N*-nitrosodimethylamine) ≃ 10 kcal/mol.

[3] The *(2)*→*(1)* isomerization has only previously been observed when it is accompagnied by aromatization, see *e.g. D. J. C. Adams, S. Bradbury, D. C. Horwell, M. Keating, C. W. Rees, R. C. Storr*, Chem. Commun., 828 (1971).

[4] *H. Olsen, J. P. Snyder*, J. Am. Chem. Soc. *100*, 285 (1978).

[5] $^1$H-NMR (300 MHz, CDCl$_3$/Me$_4$Si): $\delta=6.11$ (H-1, A-part of an ABX-system, $J_{1,3}=11.7$, $J_{1,5}=5.5$ Hz), 6.05 (H-2, dd, $J_{2,4}=10.7$, $J_{2,6}=6.5$ Hz), 5.87 (H-3, B-part of an ABC-system, $J_{3,4}=7.3$ Hz), 5.69 (H-4, B-part of an ABX-system), 5.30 (H-5, m), 5.05 (H-6, m), 2.35 (2H, m), and 2.26 (2H, m); $^{13}$C-NMR (CDCl$_3$/Me$_4$Si): $\delta=132.8$ (d), 132.6 (d), 124.6 (d), 124.5 (d), 61.8 (d), 53.0 (d), 38.9 (t), and 34.3 (t).—IR (KBr): $\nu=1410$, 1350 cm$^{-1}$. UV (96% EtOH): $\lambda_{max}=233$ nm ($\varepsilon=8600$), 351 nm (55).

[6] *A. G. Anastassiou, H. Yamamoto*, J. Chem. Soc. Chem. Commun. *1973*, 840.

[7] At this temperature or at higher temperatures *(6)* was converted into a complex mixture of products. Similar behavior has been reported for the related *N*-nitroso-9-azabicyclo[4.2.1]nona-2,4,7-triene, see *W. L. Mock, P. A. H. Isaac*, J. Amer. Chem. Soc. *94*, 2749 (1972).

[8] *I. Fleming:* Frontier Orbitals and Organic Chemical Reactions. Wiley, London 1976.

[9] *M. H. Abraham*, Prog. Phys. Org. Chem. *11*, 1 (1974).

[10] The rate of decomposition of *(9)* was measured in [D$_8$]toluene at 249.5°C by $^1$H-NMR spectroscopy ($k_9=1.95\times10^{-5}$ s$^{-1}$).

[11] *H. M. Frey, A. Krantz*, J. Chem. Soc. *A 1969*, 1159; *K. W. Egger, M. Jola*, Int. J. Chem. Kinet. *2*, 265 (1970).

[12] *H. Olsen, J. F. M. Oth*, Angew. Chem. *93*, 1024 (1981); Angew. Chem. Int. Ed. Engl. *20*, 983 (1981).

[13] The reverse rate ratio is predicted alone from the difference in resonance stabilization energy between the allyl (*K. W. Egger, D. M. Golden, S. W. Benson*, J. Am. Chem. Soc. *86*, 5420 (1973) and the pentadienyl radicals [11].

---

# Chemical Applications of NMR Isotope Effects: Ring Inversion and Conformational Equilibrium in [$^2$H$_1$]Cyclohexane[**]

By *Rafet Aydin* and *Harald Günther*[*]

Secondary isotope effects of heavy nuclei on the NMR chemical shift of neighboring nuclides have been known for some time[1], however, chemical applications of this parameter are, until now, rare. In particular, the $^1$H/$^2$H isotope effect on the chemical shift of the $^{13}$C nucleus is of interest to the organic chemist, not least because the vicinal isotope effects ($^3\Delta$) are stereospecific[3a]. Since NMR isotope effects can be relatively easily determined using high-field NMR spectrometers, structurally interesting information thus becomes readily accessible.

We report here the possibility of detecting dynamic phenomena by means of stereospecific $^1$H/$^2$H isotope effects through *one* bond ($^1\Delta$), and of investing these kinetically with the aid of $^{13}$C-NMR spectroscopy. At high field, the $^1$H-decoupled $^{13}$C-NMR spectrum of [$^2$H$_1$]cyclohexane *(1)*[3b] shows the expected triplet for C-1, ($\Delta\delta=0.41$ ppm relative to C-4) caused by $^1J(^{13}\text{C},^2\text{H})$ coupling, whose lines broaden upon coaling and which below −80°C—the ring inversion process *(1a)*⇄*(1b)* is slow on the NMR time scale—Split into doublets (Fig. 1). The superposition of *two* triplets observed at this temperature signifies that the situation $^1\Delta_a \neq {}^1\Delta_e$ must apply to the isotope effect (Table 1). The assignment $^1\Delta_a > {}^1\Delta_e$ is based on the coupling constants $^1J(^{13}\text{C},^2\text{H})$, for which we found values of 18.89 and 19.49 Hz for the axial (a) and equatorial (e) C—$^2$H bonds, respectively. According to the results of *Sergeyev* on [$^2$H$_1$]cyclohexane, the larger coupling originates from the equatorial deuterium[4].

---

[*] Prof. Dr. H. Günther, Dipl.-Chem. R. Aydin
Universität—Gesamthochschule, FB 8, OC II
Postfach 210209, D-5900 Siegen 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie. We are indebted to Dr. *J. R. Everett* for helpful comments.

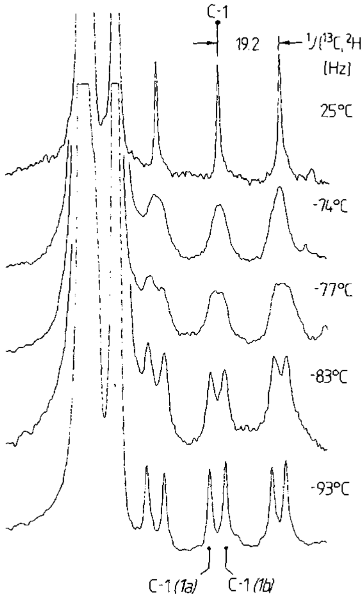
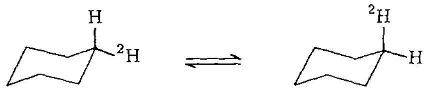


Fig. 1. $^{13}$C-NMR spectrum of [$^{2}H_{1}$]cyclohexane *(1)* at different temperatures; measuring frequency 100.61 MHz, $^{1}$H-broad-band decoupling, Bruker WH-400 FT spectrometer.

Table 1. $^{1}H/^{2}H$ Isotope effects $^{n}\Delta$ through n bonds (in Hz at 100.61 MHz measuring frequency) for the $^{13}$C resonances in [$^{2}H_{1}$]cyclohexane *(1)* and [1,1,$^{2}H_{2}$]cyclohexane *(2)*.

| Comp. | $T$ [°C] | $^{1}\Delta$ | $^{2}\Delta$ | $^{3}\Delta$ | Measuring conditions [a] |
|---|---|---|---|---|---|
| *(1a)* | −80 | 39.64 | — | — | $CS_2/CD_2Cl_2$ (4:1) |
| *(1b)* | −80 | 44.49 | — | — | 1 M; exp. error ±0.04 Hz |
| *(1)* | *ca.* 20 | 42.02 | 10.41 | 2.50 | as above; exp. error ±0.02 Hz |
| *(1)* | *ca.* 20 | 41.32 | 10.47 | 2.56 | $CCl_4$, 1 M; $^{19}$F lock |
| *(2)* | *ca.* 20 | 82.98 | 21.07 | 5.07 | $C_6F_6$ int.; exp. error ±0.02 Hz [b] |

[a] The experimental errors were determined from the digital resolution using error propagation for difference measurements; upper limit values are therefore involved. [b] As shown by measurements with internal $^{19}$F lock ($C_6F_6$), solvent effects of 1–2% can occur in the $^{1}\Delta$-values.



*(1a)* $\rightleftarrows$ *(1b)*

The coalescence of the two C-1 triplets is observed over a narrow temperature range of *ca.* 4° (Fig. 1). Since the frequency difference between the triplet components for the same $^{2}$H spin state differ because of the different couplings[5], the individual doublets merge successively; the reaction rate constants $k$ and the $\Delta G^{+}$ values can be determined from the coalescence temperatures using known methods[6a]. At −75°C we obtained $\Delta G^{+} = 42.68$ kJ/mol, which is in excellent agreement with the best literature value (42.85 kJ/mol)[6b].

For the equilibrium *(1a)*$\rightleftarrows$*(1b)* it is interesting whether an isotope effect on the position of the equilibrium (isotopic perturbation of degeneracy[2a]) can be determined. This would not be unexpected[7] in view of the different sizes of the C-$^{2}$H and C-$^{1}$H groups[6c].

From the isotope effects measured for *(1a)* and *(1b)* at low temperatures (for experimental errors, see Table 1) an average value of 42.07 Hz for $^{1}\Delta$ is calculated for an equilibrium constant $K = 1.0$ at room temperature. Experimentally we found 42.02 Hz. It must however, be borne in mind that $^{1}\Delta$ increases with temperature[8a]. The effect of temperature on $^{1}\Delta$ was determined on [1,1-$^{2}H_{2}$]cyclohexane *(2)*[8b] at −80 and +25°C. Using the value of $+0.07 \pm 0.03$ Hz thus obtained, $^{1}\Delta$ (corrected) is found to be 41.95 Hz and is hence smaller than the average value expected for $K = 1.0$ Accordingly, conformer *(1a)* predominates in the equilibrium.

Independent confirmation of this result, which was desirable because of the small magnitude of the effect, was achieved by studying a mixture of cyclohexane, [$^{2}H_{1}$]cyclohexane, and [1,1-$^{2}H_{2}$]cyclohexane. From the simplified spectrum obtained by $^{1}$H- and $^{2}$H broad-band decoupling[8c], we measured the following $^{1}\Delta$-values [relative to $\delta(C_6H_{12})$]: *(1)* 41.32 Hz; *(2)* 82.98 Hz. Since isotope effects are additive[8a,9], we would have expected a value of 82.98/2 = 41.49 Hz for *(1a)*$\rightleftarrows$*(1b)* with $K = 1.0$. Finally, additional confirmation of the result was possible from $^{2}$H-NMR low-temperature measurements on *(1)*. Integration and line-shape analysis of the signals observed for the equatorial and axial deuterium atoms at −88°C (measurement frequency 61.42 MHz, $\Delta\nu$ 29.4 Hz) produced $K = 1.060 \pm 0.014$, which is consistent with the other results. On the other hand, from the $^{1}\Delta$-values we obtained $K = 1.100 \pm 0.037$. In consequence, the conformation *(1a)* is favored by *ca.* 200 J/mol at room temperature.

Our result can be understood if it is assumed that the vicinal *gauche*-$^{1}$H, $^{1}$H-, and $^{1}$H,$^{2}$H-interactions are decisive for the relative energies of conformers *(1a)* and *(1b)*[10]. In order to avoid unfavorable H,H-interactions, the system takes up conformation *(1a)*, and the C—$^{1}$H group, *i.e.* the "larger substituent", preferentially adopts the axial position by way of exception.

Received: August 20, 1980 [Z 701 IE]
German version: Angew. Chem. *93*, 1000 (1981)

---

[1] a) *H. Batiz-Hernandez, R. A. Bernheim*, Prog. Nucl. Magn. Reson. Spectrosc. *3*, 63 (1967); b) *W. T. Raynes*, Spec. Period. Nucl. Magn. Reson. *8*, 12 (1979) and earlier volumes in this series.

[2] a) *M. Saunders, L. Telkowski, M. R. Kates*, J. Am. Chem. Soc. *99*, 8070 (1977); b) *J. M. Risley, R. L. van Etten, ibid. 101*, 252 (1979); c) *M. Schlosser, M. Stähle*, Angew. Chem. *92*, 497 (1980); Angew. Chem. Int Ed. Engl. *19*, 487 (1980).

[3] a) *R. Aydin, H. Günther*, Z. Naturforsch. *B 34*, 528 (1979); b) Synthesized from cyclohexylmagnesium bromide and $^{2}H_{2}O$.

[4] *N. A. Chertkov, N. M. Sergejev*, J. Am. Chem. Soc. *99*, 6750 (1977); the relationship $^{n}J(^{13}C,^{2}H) = {}^{n}J(^{13}C,^{1}H)/6.5144$ applies to the conversion. [Cf. *P. Diehl, Th. Leipert*, Helv. Chim. Acta *47*, 545 (1964) and *T. F. Wimett*, Phys. Rev. *91*, 499 (1953).]

[5] At −93°C we found 5.42, 4.83 and 4.30 Hz in the direction of the field.

[6] a) *H. Günther:* NMR-Spektroskopie. Thieme, Stuttgart 1973; b) *F. A. L. Anet, R. Anet* in *L. M. Jackman, F. A. Cotton:* Dynamic NMR-Spectroscopy. Academic Press, New York 1975; c) *W. A. Van Hook* in *C. J. C. Collins, N. S. Bowman:* Isotope Effects in Chemical Reactions. Van Nostrand Reinhold, New York 1970, p. 60; d) *F. A. L. Anet, A. H. Dekmezian*, J. Am. Chem. Soc. *101*, 5449 (1979).

[7] The perturbation of a degenerate conformational equilibrium by deuterium substitution was, to our knowledge, first observed NMR-spectroscopically for [7-$^{2}$H]cycloheptatriene [*F. R. Jensen, L. A. Smith*, J. Am. Chem. Soc. *86*, 956 (1964)].

[8] a) *C. S. Jameson*, J. Chem. Phys. *66*, 4983 (1977); b) Synthesized by Li[Al$^{2}H_{4}$] reduction of cyclohexanone, HBr bromination of the alcohol, Grignard reaction, and treatment with $^{2}H_{2}O$; c) *H. Günther, H. Seel, H. Schmickler*, J. Magn. Reson. *28*, 145 (1977).

[9] *M. Alei, Jr., W. E. Wageman*, J. Chem. Phys. *68*, 783 (1978). We found a convincing example for the additivity of the NMR isotope effects in [1,1′-$^{2}H_{2}$]-1,1′-dicyclohexyl, which is a by-product of the synthesis of *(2)*. Values of the sums $^{1}\Delta + {}^{2}\Delta = 51.82$ and $^{2}\Delta + {}^{3}\Delta = 13.03$ Hz were measured. Values of 51.79 and 13.03 Hz were predicted from the results on *(1)*.

[10] *D. H. Wertz, N. L. Allinger*, Tetrahedron *30*, 1579 (1974).

# Cleavage of Water by Visible-Light Irradiation of Colloidal CdS Solutions; Inhibition of Photocorrosion by $RuO_2$[**]

By *Kuppuswamy Kalyanasundaram, Enrico Borgarello, Dung Duonghong,* and *Michael Grätzel*[*]

The conversion of light into electricity or chemical fuels in photoelectrochemical devices equipped with semiconductor electrodes is of great current interest[1]. A serious problem associated with the use of materials with valence-band gaps appropriate for solar energy exploitation, is their inherent instability. For example, n-type CdS or GaP are subject to undesirable decomposition upon irradiation[2]. Holes ($h^+$) produced in the valence band upon irradiation migrate to the surface where photocorrosion occurs:

$$CdS + 2h^+ \rightarrow Cd^{2+} + S \qquad (1)$$

$$GaP + 3H_2O + 8h^+ \rightarrow Ga^{3+} + PO_3^- + 6H^+ \qquad (2)$$

This undesired process may be prevented in the presence of suitable reducing agents such as, $Fe(CN)_6^{4-}$, $S^{2-}$, $SO_3^{2-}$, or hydroquinone[3] which scavenge the hole at the semiconductor/electrolyte interface before lattice dissolution can occur. However, in order to be effective, the hole-transfer across the interface requires a large driving force which consumes a significant fraction of the absorbed light energy.

In investigations of microheterogeneous systems capable of decomposing water into $H_2$ and $O_2$ by visible light[4a], we discovered that ultrathin layers of $RuO_2$ on CdS inhibit photocorrosion[4b]: reaction *(1)* is replaced by oxidation of water.

$$4h^+(CdS) + 2H_2O \xrightarrow{RuO_2} O_2 + 4H^+ \qquad (3)$$

We now describes the design and performance of *colloidal* CdS microelectrodes which exhibit surprisingly high activity as water-cleaving catalysts.

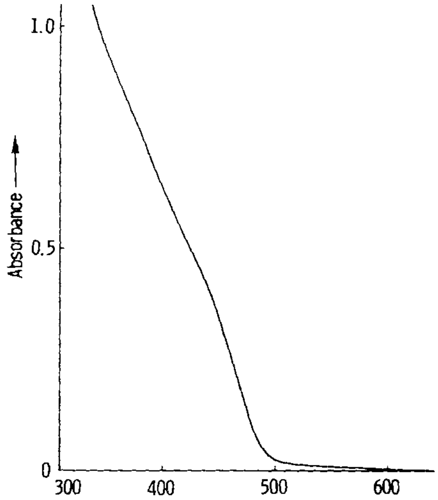


Fig. 1. Absorption spectrum of the colloidal CdS solution (330 mg/L), optical path length 0.2 cm.

Precipitation of CdS from aqueous solutions of $Cd^{2+}$ and $(NH_4)_2S$ in the presence of maleic anhydride/styrene copolymer produces a perfectly transparent, intensely yellow colored sol, whose absorption spectrum is shown in Figure 1. Noteworthy is the upper band limit at 520 nm, whose position coincides with the 2.4 eV band gap of CdS. The band rises towards the UV in a very steep fashion, typical of electronic transitions in semiconductors[5]. From these characteristics it is concluded that microcrystalline CdS particles of colloidal dimensions are present in solution.

The CdS particles themselves do not afford photodecomposition of water. Active catalysts are obtained only after they have been loaded with Pt and $RuO_2$[6]. Sustained water cleavage by visible light ($\lambda > 400$ nm) was observed with such colloidal solutions, *e.g.* from a 25 mL solution (2.75 mg of CdS, 1 or 0.5 mg of Pt and 0.2 mg of $RuO_2$) a total of 2.8 mL of $H_2$ and 1.4 ml of $O_2$ was produced after 44 h of irradiation (cf. Fig. 2); this corresponds to turnover numbers of 6, 25, and 85 for CdS, Pt, and $RuO_2$, respectively. Clearly the reaction is catalytic with respect to all three constituents. In particular, no appreciable photodegradation of CdS occurs. To further confirm this surprising and important effect we examined carefully the $Cd^{2+}$ concentration before and after 72 h of photolysis. Polarographic analysis showed no detectable increase in ion concentration during this period, which precludes any significant contribution of the anodic dissolution reaction (1) to the overall photoprocess. Since, on the other hand, the generation of oxygen by photolysis can be demonstrated readily and unambiguously it can be inferred that oxidation of water occurs exclusively, and at the expense of photocorrosion.

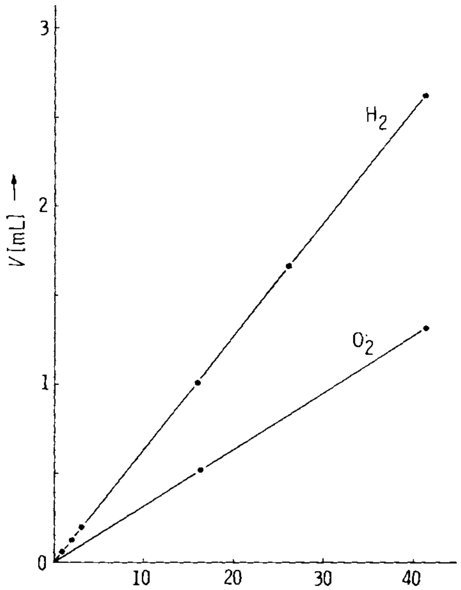


Fig. 2. Production of $H_2$ and $O_2$ by irradiation of a $8.4 \times 10^{-4}$ M CdS sol at room temperature. Particles loaded with Pt and $RuO_2$. $O_2$ determined by flow procedures [11].

Further experiments established that the stabilization of CdS is brought about by the $RuO_2$ catalyst. Particles only loaded with Pt decompose rapidly under illumination with formation of sulfur. A similar observation was made with dispersions of commercial CdS powders[4b].

---

[*] K. Kalyanasundaram, E. Borgarello, D. Duonghong, M. Grätzel
Institut de Chimie Physique, Ecole Polytechnique Fédérale Ecublens
CH-1015 Lausanne (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds and by Ciba-Geigy, Basel.

*0570-0833/81/1111-0987 $ 02.50/0*

The reaction temperature has a decisive influence on the efficiency of the light induced water cleavage. Thus, at 75 °C the rate of $H_2$ formation (0.1 mL/h) is approximately twice as fast than at room temperature.

Compared to a macrodispersion, decreasing the particle size to colloidal dimensions increases the yield of $H_2$ per unit mass of catalyst by a factor of 50. These observations may be rationalized in terms of electron/hole pair-formation in the colloidal CdS particles under band gap excitation. The electrons migrate to Pt sites where $H_2$ production from water occurs. The flat band potential of CdS is located at *ca.* −900 mV (*vs.* standard $H_2$ electrode at pH = 7), which is sufficiently cathodic for water reduction. On the other hand the valence band edge of n-type CdS is *ca.* + 1.5 V and holes trapped by $RuO_2$ sites on the surface are subsequently used to produce oxygen from water: since the driving force for water oxidation is therefore more than 600 mV this process is sufficiently fast[7] to compete with surface corrosion. Thus, the role of the $RuO_2$ is to promote the transfer of holes from the valence band to the aqueous solution where $O_2$ evolution occurs.

Moreover, we have found that the catalytic properties of the CdS sols (also *without* Pt!) described here are also particularly suitable for the photolytic decomposition of $H_2S$ into $H_2$ and sulfur[9b].

Our results clearly identify the decisive influence of $RuO_2$ on valence band processes in irradiated semiconductor particles. In the case of CdS a striking augmentation of the photoactivity is observed when the particle size is reduced to colloidal dimensions[8]. Work is now in progress to substitute these microsystems by polycrystalline semiconductor electrodes by covering the electrode with an ultrathin layer of $RuO_2$ and by coupling it to a Pt counterelectrode, such a device should afford local separation of the $H_2$- and $O_2$-generating reactions[9a].

## *Experimental*

100 mg of maleic anhydride/styrene copolymer (50/50, TNO, Utrecht) is dissolved in 100 mL of alkaline water (pH = 10, adjusted with 1 N NaOH) under constant stirring at 50 °C for several hours. When dissolution is complete, 0.15 mL of a 10% (W/V) solution of $(NH_4)_2S$ is added. A stock solution of $CdSO_4$ (2 g/L) is prepared, and 10 mL is slowly (microsyringe!) injected. After being stirred for *ca.* 1 h the appearance of an intense yellow color indicates formation of the CdS sol. The pH of the solution is subsequently adjusted to 3 (HCl), and excess sulfide removed as $H_2S$ by slushing the solution with $N_2$ overnight. The final concentration is 110 mg CdS/L ($8.4 \times 10^{-4}$ M).

CdS is loaded with $RuO_2$ *via* decomposition of $RuO_4$ ($RuO_4 \rightarrow RuO_2 + O_2$) by injecting 0.5 mL of a stock solution of $RuO_2$ in water (0.5 g/L) into 20 mL of the CdS solution. An ultrathin deposit of $RuO_2$ is formed when the mixture is stirred for 30 min. $H_2PtCl_2$ (3 mg) and 1 mL of a 40% aqueous solution of formaldehyde are subsequently directly added to the CdS/$RuO_2$ solution. After deoxygenation, Pt is deposited onto the CdS particles *via* photoplatinization[4, 10] and excess formaldehyde is subsequently removed under *in vacuo*. The final concentrations are 40 mg/L Pt, 8 mg/L $RuO_2$, and 110 mg CdS/L.

Photolysis experiments were carried out with a xenon lamp (Osram XBO-450W; filter for IR region and $\lambda < 400$ nm) in a pyrex flask (25 mL of solution) equipped with optically flat entry- and exit-windows. $H_2$ production was monitored by gas chromatography (GOW MAC, carbosieve column, 35 °C, $N_2$ carrier gas). $O_2$ was analyzed using a Teledyne $B_1$ oxygen specific microfuel cell[11].

Received: January 28, 1981,
publication delayed at the authors' request [Z 820 IE]
German version: Angew. Chem. *93*, 1012 (1981)

---

[1] *A. J. Nozik*, Ann. Rev. Phys. Chem. *21*, 189 (1978); *R. Memming*, Philips Techn. Rev. *38*, 160 (1978/79); *A. Heller, B. Miller*, Electrochim. Acta *25*, 24 (1980); Faraday Discuss. Photoelectrochemistry, Oxford, September 1980.

[2] *R. Williams*, J. Chem. Phys. *32*, 1505 (1960); *H. Gerischer*, J. Electroanal. Chem. Interfacial Electrochem. *58*, 263 (1975); *M. Matsumura, K. Yamamoto, H. Tsubomura*, J. Chem. Soc. Japan *1976*, 399.

[3] *H. Gerischer, E. Meyer*, Z. Phys. Chem. (Frankfurt am Main) *74*, 302 (1971); *A. Fujishima, E. Sugiyama, K. Honda*, Bull. Chem. Soc. Jpn. *44*, 304 (1971); *F. Sitabkhan*, Ber. Bunsenges. Phys. Chem. *76*, 389 (1972); *A. B. Ellis, S. W. Kaiser, M. S. Wrighton*, J. Am. Chem. Soc. *98*, 1635 (1976); *G. Hodes, J. Manassen, D. Cohen*, Nature *261*, 403 (1976); *B. Miller, A. Heller*, Nature *262*, 680 (1976); *T. Inone, T. Watanabe, A. Fumishima, K. Honda, K. Kohayakawa*, J. Electrochem. Soc. *12*, 719 (1977).

[4] a) *K. Kalyanasundaram, M. Grätzel*, Angew. Chem. *91*, 759 (1979); Angew. Chem. Int. Ed. Engl. *18*, 701 (1979); *J. Kiwi, E. Borgarello, E. Pelizzetti, M. Visca, M. Grätzel, ibid. 92*, 663 (1980); *19*, 646 (1980); *E. Borgarello, J. Kiwi, E. Pelizzetti, M. Visca, M. Grätzel*, Nature *289*, 158 (1981); J. Am. Chem. Soc., in press; b) *K. Kalyanasundaram, E. Borgarello, M. Grätzel*, Helv. Chim. *64*, 362 (1981).

[5] *P. Salvador*, Solar Energy Mat. *2*, 413 (1980).

[6] The loading does not significantly change the absorption behavior of the CdS sol.

[7] $RuO_2$ is known to be an excellent electrocatalyst for water oxidation: *S. Trasatti, G. Buzzanca*, Electroanal. Chem. *29*, App. 1 (1971); *D. Galizzioli, F. Tantardine, S. Trasatti*, J. Appl. Electrochem. *4*, 57 (1974); *D. Galizzioli, F. Tantardini, S. Trasatti*, J. Appl. Electrochem. *5*, 203 (1975); *G. Lodi, G. Zucchini, A. de Battisti, E. Sivieri, S. Trasatti*, Mater. Chem. *3*, 179 (1978).

[8] *Darwent* and *Porter* have observed light-induced $H_2$ evolution on Pt-loaded CdS particles. In this case ethylenediaminetetracetic acid (EDTA) instead of water is oxidized. We thank these authors for communicating their results prior to publication. Cf. *F. D. Saeva, G. R. Olin, J. R. Harbour*, J. Chem. Soc. Chem. Commun. *1980*, 401, and references cited therein.

[9] a) *M. Neumann-Spallart, K. Kalyanasundaram, M. Grätzel*, unpublished results. b) *M. Grätzel, E. Borgarello, K. Kalyanasundaram, E. Pelizzetti*, unpublished results.

[10] *B. Kraeutler, A. J. Bard*, J. Am. Chem. Soc. *100*, 4318 (1978).

[11] *D. Duonghong, E. Borgarello, M. Grätzel*, J. Am. Chem. Soc. *103*, 4685 (1981).

**An Introduction to Synthesis Using Organocopper Reagents.** By *G. H. Posner*. J. Wiley & Sons, Chichester 1980. xvii, 140 pp., bound, £ 12.50.

The subject of the monograph and the author's name could give rise to misunderstanding: it is in no way a review like *Posner*'s two contributions that appeared in "Organic Reactions" [*19*, 1 (1972) and *22*, 253 (1975)]. The principal aim here is to show how an organic synthesis is planned and on what basis a choice between several possible solutions is made. The reader takes part in a course of instruction organized from beginning to end on the basis of practical examples. About 30 syntheses of aromas and flavors, growth substances, pheromones, alkaloids, sugars, phenols, lactones, sesquiterpenes, prostaglandins, and steroids are dealt with one by one. The copper reagents enjoy a privileged role as a means to this end, but occasionally another organometal compound may prove to be more useful and often in fact a quite different approach may well be superior.

The examples have been carefully chosen and are expertly explained. Slight uncertainties appear to exist on stereochemical questions. Thus, in connection with a synthesis of muscalure, the sex attractant of the housefly, it is assumed that the Wittig reaction permits its preparation only with *Z/E* ratios of about 85 : 15 (p. 69), while since 1966 a procedure has been known which ensures more than 99% *cis*-selectivity. In discussing manicon, an ant pheromone, an important point is left unmentioned (p. 81): the compound contains an asymmetric carbon atom. Any synthesis will be judged beforehand on how it handles the problem of leading to a pure enantiomer.

To stimulate the reader toward more basic reading and independent study, about a dozen references are given at the end of each example. No single synthesis is given in all its details; in each case only the basic features of possible strategies are explained. In view of this policy, it is surprising to find at the end of the monograph, as an appendix, four small detailed experimental procedures. The historical review given in the introduction also falls somewhat outside the framework of the book. With a length of under ten lines, it is not exhaustive. Several studies that together with others probably gave the impetus to the later extensive systematic investigation of copper reagents have passed unquoted (*e.g. G. Köbrich et al.*, J. Organomet. Chem. *6*, 194 (1966); *T. Kaufmann et al.*, Angew. Chem. *79*, 101 (1967); Angew. Chem. Int. Ed. Engl. *6*, 85 (1967); *G. Wittig et al.*, Justus Liebigs Ann. Chem. *704*, 91 (1967)).

The monograph is short but lively, careful, and intelligent. An exhaustive subject and author index facilitates reference to the literature. With excellent presentation and illustrations, the publishers have done their part toward contributing to the great pleasure with which one leafs through the book. It will please anyone who can wax enthusiastic about synthesis, and it will probably prove particularly suitable as a basis for group seminars.

*Manfred Schlosser* [NB 547 IE]

---

**Recent Books**

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Makromoleküle.** By *H.-G. Elias*. Hüthig & Wepf Verlag, Heidelberg 1981. 4th edit. xxxvii, 1097 pp., bound, DM 192.00.—ISBN 3-7785-0677-3

**Elements of Quantum Chemistry.** By *R. Zahradnik* and *R. Polák*. Plenum Press, New York 1980. 462 pp., bound, $ 39.50.—ISBN 0-306-31093-7

**Solid State Reactions.** By *H. Schmalzried*. Verlag Chemie, Weinheim 1981. 2nd edit. x, 254 pp., bound, DM 98.00.—ISBN 3-527-25872-8

**Biochemistry of Antimicrobial Action.** By *T. J. Franklin* and *G. A. Snow*. Chapman and Hall, London 1981. 3rd edit. xi, 217 pp., bound, £ 7.50.—ISBN 0-412-22450-X

**Nutzpflanzenkunde.** Nutzbare Gewächse der gemäßigten Breiten, Subtropen und Tropen. By *W. Franke*. Thieme Verlag, Stuttgart 1981. 2nd edit. x, 470 pp., bound, *ca.* DM 30.00.—ISBN 3-13-530402-7

**Schwingungsfrequenzen I.** Hauptgruppenelemente. By *J. Weidlein, U. Müller,* and *K. Dehnicke*. Thieme Verlag, Stuttgart 1981. xii, 339 pp., bound, DM 88.00.—ISBN 3-13-567201-8

**Genitourinary Reconstruction with Prostheses.** By *L. V. Wagenknecht, W. L. Furlow,* and *J. Auvert*. Thieme Verlag, Stuttgart 1981. *ca.* 256 pp., bound, *ca.* DM 80.00.—ISBN 3-13-588401-5

**Fachstudium Chemie—Arbeitsbuch 6.** Chemische Kinetik. By *R. Ebisch, E. Fanghänel, W.-D. Habicher, R. Hahn,* and *K. Unverferth*. Verlag Chemie, Weinheim 1981. 212 pp., bound, DM 36.00.—ISBN 3-527-25000-0

**Insulin**— Chemistry, Structure and Function of Insulin and Related Hormones. Edited by *D. Brandenburg* and *A. Wollmer*. de Gruyter, Berlin 1980. xviii, 752 pp., bound, DM 170.00.—ISBN 3-11-00-81-56-3

**Aspekte von Kraftfeldrechnungen.** By *O. Ermer*. W. Baur Verlag, München 1981. 619 pp., bound, DM 48.00.—ISBN 3-88410-006-8

**Surfactant Science Series—Vol. 11. Anionic Surfactants.** Physical Chemistry of Surfactant Action. Edited by *E. H. Lucassen-Reynders*. Marcel Dekker, Basel 1981. xi, 412 pp., bound, SFr 148.00.—ISBN 0-8247-1017-7

**Organic Synthesis—Today & Tomorrow.** Edited by *B. M. Trost* and *C. R. Hutchinson*. Pergamon Press, New York 1981. x, 354 pp., bound, $ 90.00.—ISBN 0-08-025268-0

**Surfactant Science Series—Vol. 5. Detergency.** Theory and Test Methods. Part III. Edited by *W. G. Cutler* and *R. C. Davis*. Marcel Dekker, Basel 1981. x, p. 729—p. 1060, bound, SFr. 118.00.—ISBN 0-8247-6982-1

**Chemistry and Physics of Carbon. Vol. 17.** Edited by *P. L. Walker, Jr.* and *P. A. Thrower*. Marcel Dekker, Basel 1981. xii, 304 pp., bound, SFr. 120.00.—ISBN 0-8247-1209-9

**Inorganic Chemistry.** By *A. G. Sharpe*. Longman, London 1981. xv, 682 pp., bound, £ 11.95.—ISBN 0-582-45080-2

**Organic Photochemistry.** Edited by *A. Padwa*. Marcel Dekker, Basel 1981. x, 502 pp., SFr. 160.00.—ISBN 0-8247-1345-5

**Polymer Chemistry.** An Introduction. By *R. B. Seymour* and *C. E. Carraher, Jr.* Marcel Dekker, Basel 1981. xvi, 564 pp., bound, SFr. 80.00.—ISBN 0-8247-6979-1

**Synthetic Reagents. Vol. 4.** Mercuric Acetate, Periodic Acid and Periodates, Sulfuryl Chloride. Edited by *J. S. Pizey*. John Wiley & Sons, Chichester 1981. 426 pp., bound, £ 32.50.—ISBN 0-470-27133-7

**Progress in Pesticide Biochemistry. Vol. 1.** Edited by *D. H. Hutson* and *T. R. Roberts*. John Wiley & Sons, Chichester 1981. xi, 346 pp., bound, £ 24.00.—ISBN 0-471-27290-X

**Handbuch der Präparativen Anorganischen Chemie, Vol. 3.** Edited by *G. Brauer*. Enke Verlag, Stuttgart 1981. 3rd Edit. xiv, pp. 1407–2113, bound, DM 288.00 (all three volumes must be ordered). — ISBN 3-432-87823-0

**Oxygen and Life. Second BOC Priestley Conference.** Issued by The Royal Society of Chemistry, London 1981. Special Publication No. 39. xii, 224 pp., bound, £ 11.00.—ISBN 0-85186-825-8

**Aliphatic and Related Natural Product Chemistry. Vol. 2.** Senior Reporter: *F. D. Gunstone*. The Royal Society of Chemistry, London 1981. xiii, 265 pp., bound, £ 40.00.—ISBN 0-85186-652-2.—A volume of the series "Specialist Periodical Reports"

**Inorganic Biochemistry. Vol. 2.** Senior Reporter: *H. A. O. Hill*. The Royal Society of Chemistry, London 1981. xiv, 347 pp., bound, £ 40.00.—ISBN 0-85186-555-0.—A volume of the series "Specialist Periodical Reports"

**Messen, Steuern und Regeln in der Chemischen Technik.** Edited by *J. Hengstenberg, B. Sturm,* and *O. Winkler*. Springer-Verlag, Berlin 1981. 3rd revised edit. xii, 500 pp., bound, DM 210.00.—ISBN 3-540-10092-X

**Methoden der Organischen Chemie. In sechzehn Bänden.** Band IV/1d: Reduktion, Teil II. Edited by *H. Kropf*. Thieme Verlag, Stuttgart 1981. 4th completely new edit. *Ca.* 1000 pages, bound, *ca.* DM 780.00.—ISBN 3-13-201104-5

**Elektrochemie II.** Elektrodenprozesse, Angewandte Elektrochemie. Taschentext 42. By *C. H. Hamann* and *W. Vielstich*. Verlag Chemie, Weinheim 1981. xv, 428 pp., bound, DM 52.00.—ISBN 3-527-21081-4

**Lexikon alchemistisch-pharmazeutischer Symbole.** By *W. Schneider*. Verlag Chemie, Weinheim 1981. 2nd edit. 140 pp., bound, DM 38.00.—ISBN 3-527-25898-1

**Polarographische Analyse.** By *M. Geißler*. Verlag Chemie, Weinheim 1981. 1st edit. 194 pp., bound, DM 73.00.—ISBN 3-527-25887-6

**Hazards in the Chemical Laboratory.** Edited by *L. Bretherick*. The Royal Society of Chemistry, London 1981. 3rd edit. xxi, 567 pp., bound, £ 15.00.—ISBN 0-85186-419-8

**Reactivity of Metal-Metal Bonds.** ACS Symposium Series No. 155. Edited by *M. H. Chisholm*. American Chemical Society, Washington 1981. 327 pp., bound, $ 39.00.—ISBN 0-8412-0624-4

**Handbook of Automated Analysis.** Continuous Flow Techniques. By *W. A. Coakley*. Marcel Dekker, Basel 1981. xii, 144 pp., loose-leaf SFr. 55.00.—ISBN 0-8247-1392-3

**Dielectric Properties of Binary Solutions.** A Data Handbook. By *Y. Y. Akhadov*. Pergamon Press, New York 1981. 475 pp., bound, $ 112.50.—ISBN 0-08-023600-6

**Analytical Chemistry of Polycyclic Aromatic Compounds.** By *M. L. Lee, M. V. Novotny,* and *K. D. Bartle*. Academic Press, New York 1981. xi, 462 pp., bound, $ 60.00.—ISBN 0-12-440840-0

**Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden. Anleitungen für die chemische Laboratoriumspraxis, Band 15.** By *E. Pretsch, T. Clerc, J. Seibl,* and *W. Simon*. Springer-Verlag, Berlin 1981. 2nd edit. ix, 316 pp., bound, DM 39.80.—ISBN 3-540-10556-5

---

**Editorial office:** Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 602-1, Telex 465516 vchwh d.

**Editor:** *O. Smrekar*, **Translation Editors:** *I. G. Neil* and *A. Stimson*.

**Publishers:** Verlag Chemie GmbH. (Managing Director *Dr. Helmut Grünewald*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany, Telephone Weinheim (06201) 602-1, Telex 465516 vchwh d.

ANGEWANDTE
CHEMIE

Volume 20 · Number 12
December 1981
Pages 991-1066

International Edition in English

# Pyramidal Carbocations[**]

By Helmut Schwarz[*]

*Dedicated to Professor Ferdinand Bohlmann on the occasion of his 60th birthday*

Pyramidal cations are discussed with reference to their role as the connecting link between organic and inorganic chemistry. The electronic structure of these ions is treated with respect to their physical and chemical properties, namely charge distribution, geometry, and quenching reactions with nucleophiles. The chemistry in the gas phase of certain carbenium ions, in particular the scrambling of carbon atoms, is readily explicable by invoking transition states or intermediates of pyramidal structure. Moreover, the behavior of unimolecular processes can be understood in terms of transition states in which a hydrogen molecule is positioned as a "side-on" or an "end-on" ligand.

## 1. Introduction

Carbocations are now seen as *the* logical bridge between organic and organometallic chemistry[1]. Although as hydrocarbons, carbocations are unquestionably organic, nonetheless their valence properties and structural features, not least of which is the coordination number of carbon, owe much to organometallic compounds. In most organic compounds the coordination number is never greater than *four*. However, in carbaboranes and cluster compounds[2], a central carbon atom having *five* or *six* ligands is not unusual and carbonium ions are, by definition, at least *penta*coordinate. *Wilson et al.*[3] first suggested that a C atom could also be pentacoordinated. Subsequently, *Winstein*[4], *Olah*[5], *Hogeveen*[1a,6], and others[7] developed and refined the theory of carbocations. Experimental confirmation for it was forthcoming from studies on protonated alkanes—such as $CH_5^\oplus$ *(1)*—in both the gas phase[8] and in superacid media[9], as well as by indications of the existence of nonclassical carbenium ions *e.g.* the norbornyl cation *(2)*[10] and other ions such as *(3)*[11] and *(4)*[12]. These cations can be adequately described in terms of 2-center/2-electron (2z/2e) and 3z/2e bonds[13]. Examples of 3c/2e bonds are provided *e.g.* by the boranes[14]. The structural similarity between carbocations and organometallic compounds is even more apparent in the *pyramidal* carbocations $(CH)_5^\oplus$ *(5)* and $(CH)_6^{2\oplus}$ *(6)*. In these species the C atoms of interest are not only five- and six-coordinated, respectively, but the structural topology of the $(CH)_n^\oplus$ compounds finds its counterpart in organometallic chemistry. Consequently, compounds *(5)* and *(6)* are analogous to ferrocene *(7)*, since they both have semisandwich structures. Following the more general approach to cluster theory formulated by *Wade*[2c], *Williams*[2d], and *Rudolph*[2e] compounds *(5)* and *(6)* could be described as *nido*-clusters since they have the same topology and are isoelectronic with the carbaboranes[2]. For example, formal replacement of the apical cationic $C^\oplus$ ion of *(5)* by the isoelectronic B atom, and exchange of the four basal C atoms by the isoelectronic BH fragment produces, directly, the known borane $B_5H_9$ *(8)*[15]. Similarly, the carbaborane *(9)* can be generated from the dication *(6)* by replacement of the apical and one basal C atom by two B atoms. In fact, the hexamethyl derivatives of *(6)* and *(9)* have been identified[16,17], while the unsubstituted *(9)* has been characterized by its

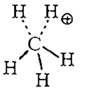
---

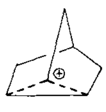
[*] Prof. Dr. H. Schwarz
Institut für Organische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

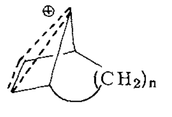
[**] This article is based on the Otto-Klung-Preis lecture presented in January 1981 at the Freie Universität Berlin.

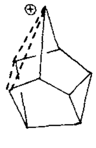
0570-0833/81/1212-0991 $ 02.50/0

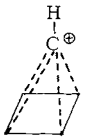
microwave spectrum[18]. As we will see in Section 2, the bonding in pyramidal cations *(5)* and *(6)*, unlike cations *(1)*–*(4)*, can no longer be described by a set of 2c/3e or 3c/2e bonds, but requires a more complex description. Recourse to graph theory[19] has recently provided a useful general model for seemingly different types of complexes.

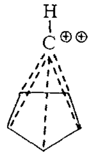

*(1)*

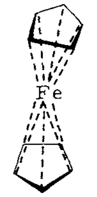

*(2)*

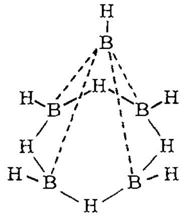

*(3)*, n = 1, 2

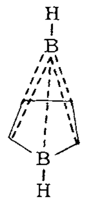

*(4)*


*(5)*


*(6)*


*(7)*


*(8)*

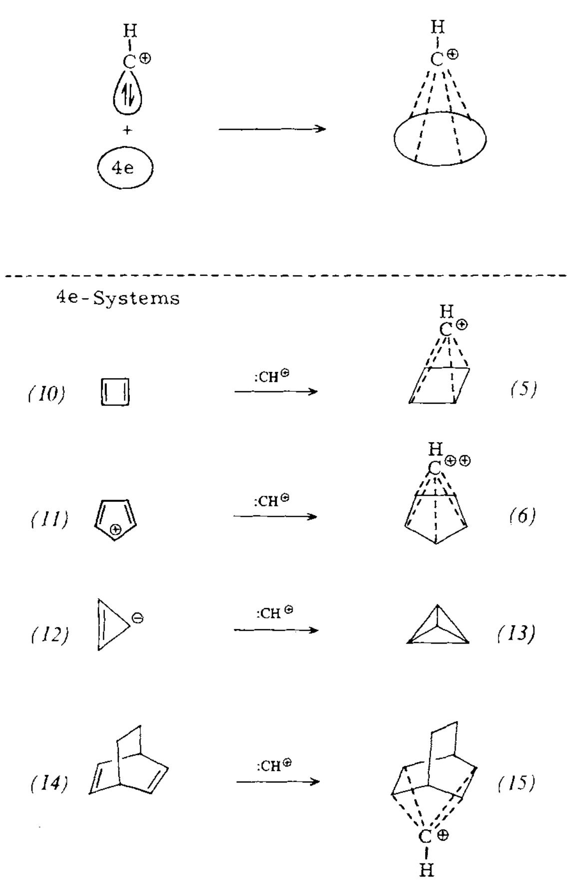

*(9)*

## 2. Bonding Properties and Theoretical Aspects

### 2.1. Formal Construction of Pyramidal Ions from $CH^\oplus$ and 4e Systems

Pyramidal cations such as *(5)* can formally be considered as being the result of the interaction of the $CH^\oplus$ fragment (protonated C atom) with a 4e system such as cyclobutadiene *(10)*[20]. The only requirements are that the interacting orbitals of the molecular fragments be of similar energy and of appropriate symmetry. Furthermore, the segment forming the base must supply *four* electrons while the $CH^\oplus$ fragment provides *two* electrons and two empty orbitals[20,21]. The interaction diagram (Fig. 1a), which should not be mistaken for a correlation diagram for the central linear approach of $CH^\oplus$ to cyclobutadiene, clearly describes the electronic nature of *(5)*. The $a_1$ and e orbitals of $CH^\oplus$ on combination with *(10)* furnish three bonding molecular orbitals containing *six* electrons (two from $CH^\oplus$ and four from *(10)*). In analogous fashion, the pyramidal dication *(6)* may be described as a *nido*-cluster resulting from combination of $CH^\oplus$ and the antiaromatic cyclopentadienyl cation *(11)* (Fig. 1b). Here again, six electrons are accomodated in three stabilized molecular orbitals[22].

The foregoing treatment also accounts for the fact that certain carbocations and carbanions cannot be stable if pyramidal geometry is adopted. Thus, the pyramidal $C_5H_5^\ominus$ anion *(16)* requires that the extra pair of electrons be placed in an antibonding orbital (Fig. 1a). This constitutes an unfavorable situation, and in fact there is neither theoretical nor experimental evidence for the existence of *(16)*[20]. Similarly, the pyramidal $C_7H_7^\oplus$ cation *(20)* is unstable[26], although it has been postulated as an intermediate in the solvolysis of C7-substituted norbornadienyl derivatives *(17)*[27] and in the carbon scrambling of the benzyl *(19)* and tropylium cations *(21)*[28], and contains *eight* electrons, (six from benzene and two from the $CH^\oplus$ fragment, two of which have to be placed in orbitals of high energy). Nature arranges things differently; solvolysis of *(17)* generates a cation which is better described by *(18)*, in which 3c/2e bonding occurs, than by *(20)*[29]. Carbon atom scrambling between *(19)* and *(21)* proceeds *via* a sequence of orbital symmetry allowed isomerizations in which *(20)* is not involved[26]. In principle, structures of type *(20)* are possible, provided they possess two electrons less, as exemplified by the $C_7H_7^{3+}$ cation *(22)*. Obviously, structure *(22)* is unredistic for electrostatic reasons[30]. Nonetheless, the structurally analogous carbaborane $C_4B_3H_7$ *(23)* should be an excellent candidate for a neutral molecule possessing a ***heptacoordinated*** apical carbon atom[31].



Scheme 1. Formal construction of pyramidal cations from 4e systems and $CH^\oplus$.

If the 4e component of the diene is unsymmetric, then interaction with the $CH^\oplus$ cap does not create a cation of pyramidal structure, but gives instead an ion with 3c/2e bonds. Examples are provided by *Coates'* $C_9H_9^\oplus$ cation *(4)* which must have $C_{3v}$ symmetry: the pyramidal alternative *(24)* should not be favored[12]. However, the isomeric $C_9H_9^\oplus$ ion *(26)* ought to be pyramidal as it is lower in energy than the 3c/2e structure *(28)*, which according to MINDO/3 calculations does not correspond to a minimum on the energy hypersurface[24]. Similarly, cation *(3)*[1a] and the bishomocyclopropenyl cation *(33)*[32] are better described by 3c/2e bonding than by the greater charge delocalization needed for the pyramidal cations *(29)* and *(31)*.

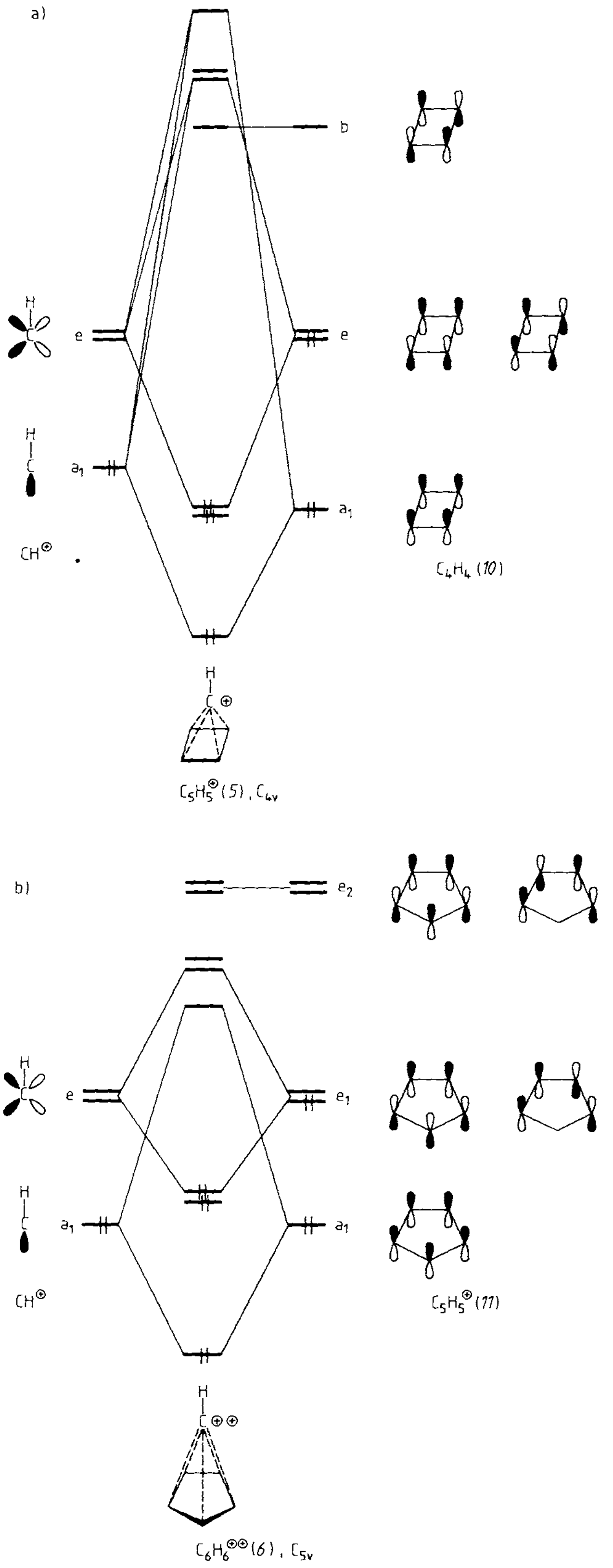
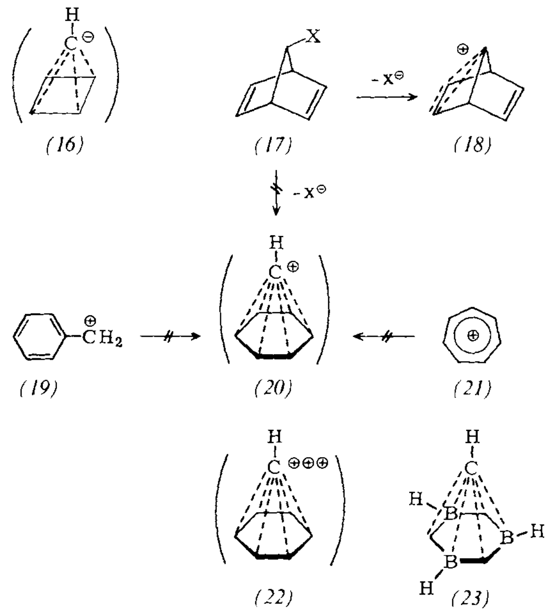
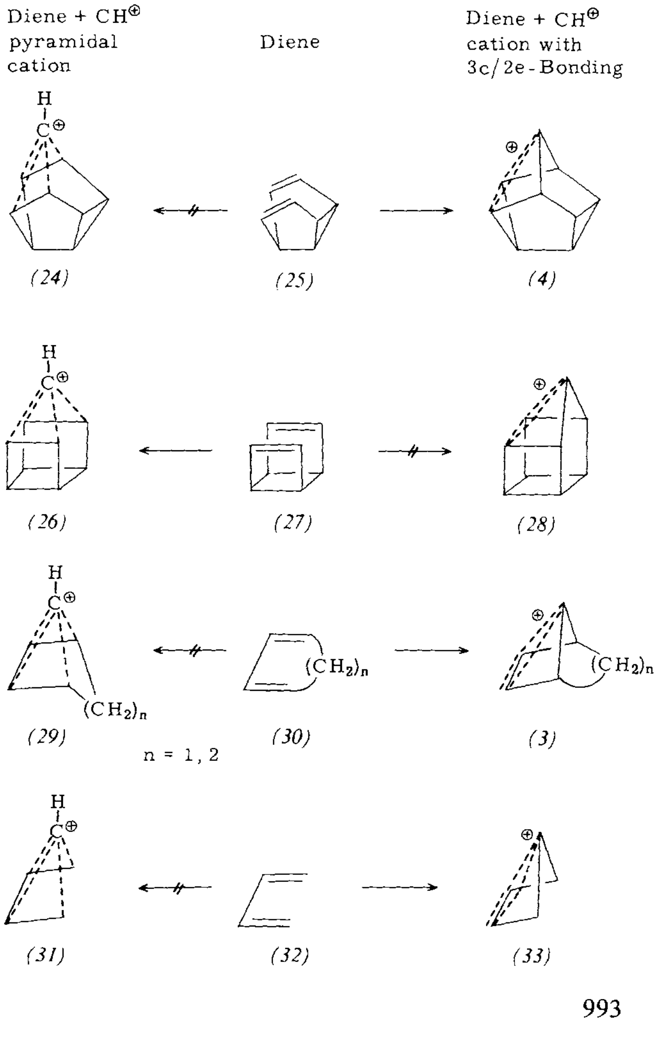


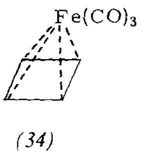
Fig. 1. Interaction diagram for the construction of a) $C_5H_5^{\oplus}$ *(5)* from $CH^{\oplus}$ and cyclobutadiene, b) $C_6H_6^{2+}$ *(6)* from $CH^{\oplus}$ and $C_5H_5^{\oplus}$.



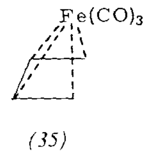
The reason why 3c/2e bonds contend energetically with pyramidal structures is that cations such as *(26)*, and others, contain a diene component *(27)* which is symmetrically substituted. On the other hand, cations such as *(3)*, *(4)*, and *(33)* require unsymmetric diene components *(30)*, *(25)*, and *(32)*, respectively. Presumably in the case of unsymmetrically substituted dienes the interaction of $CH^{\oplus}$ is more favorable with one set of terminal carbon atoms than with



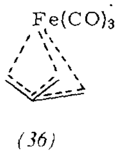
the other, thereby leading to a less symmetric distribution of charge. This suggests that transitions between classical 3c/2e bonding and that required by pyramidal ions can be brought about with the proper choice of diene. It is entirely possible that the $C_5H_7^{\oplus}$ ion (formed under the conditions of ion cyclotron resonance by β-protonation of cyclopentadiene) possesses a structure which can be considered as a 3c/2e system or an *arachno*-cluster ion *(31)*[32].



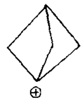
*(34)*



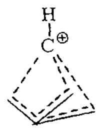
*(35)*



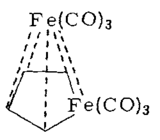
*(36)*



*(37)*

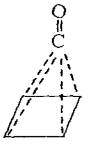


*(38)*

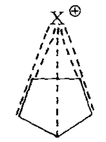


*(39)*

The idea that pyramidal cations are made up of molecular fragments allows us to replace $CH^{\oplus}$ by similar fragments which are *isolobal* with $CH^{\oplus}$, namely fragments X having the same or similar properties regarding the number, symmetry, shape, and energy of the relevant frontier orbitals[33], *e.g.* BH and $Fe(CO)_3$. Consequently, it is not surprising that clusters of $Fe(CO)_3$ combined with 4e systems are well known[34]. Of the many examples it is sufficient to mention only the complexes of $Fe(CO)_3$ with cyclobutadiene *(34)*[34], butadiene *(35)*[35], and trimethylenemethane *(36)*[36]. *(34)* and *(35)* correspond to the pyramidal cations *(5)* and *(31)*, whereas *(36)* finds its carbocation counterpart in the 1-bicyclo[1.1.1]pentyl cation *(37)*. The latter can also be considered as a $CH^{\oplus}$-trimethylenemethane cluster *(38)*[37]. The pyramidal dication *(6)* also has an organometallic cluster counterpart, namely compound *(39)*[33,34]. This complex is formally obtained by replacing the apical and one basal $CH^{\oplus}$ group of *(6)* by the *isolobal* $Fe(CO)_3$.



*(40)*



*(41)*, X = Sn, Ge

The structure of the carbonylcyclobutadiene cluster *(40)* is readily obtained by the interaction of CO and cyclobutadiene[20]: the appropriate interaction diagram resembles Figure 1a. In *(40)* the HOMO of carbon monoxide, in which the lone pair of electrons is more or less localized axially on the carbon atom, replaces the axial lone pair of $CH^{\oplus}$. The role of the p-orbitals of the $CH^{\oplus}$ is taken up by the π* orbitals of the carbonyl group. In other words, *(40)* is the carbonyl complex of cyclobutadiene.

Clusters can also be constructed having a metal ion such as $Sn^{2+}$ or $Ge^{2+}$ at the apex. Unambiguously characterized examples have been obtained from the cyclopentadienyl *anion* and its permethyl derivative *(41)*[38]. The cations *(41)* can also be considered as *nido*-clusters of pentagonal pyramidal symmetry in which the electronic and orbital requirements are completely fulfilled. The MO diagram (Fig. 2) shows that in *(41)*, X = Sn, the interaction of the orbitals of the apical metal atom with the π MOs of the cyclopentadienyl moiety gives a typical closed-shell electronic structure. Apart from the six electrons located in the $1a_1$ and $1e_1$ molecular orbitals, the "lone pair" is essentially localized in a high lying orbital on the Sn atom having considerable p-character. An octet of electrons formally fills the valence shell of the main group element, thereby occupying the $1a_1$ to $2a_1$ molecular orbitals of *(41)*. This description satisfactorily accounts for the unusual stability of these cations.

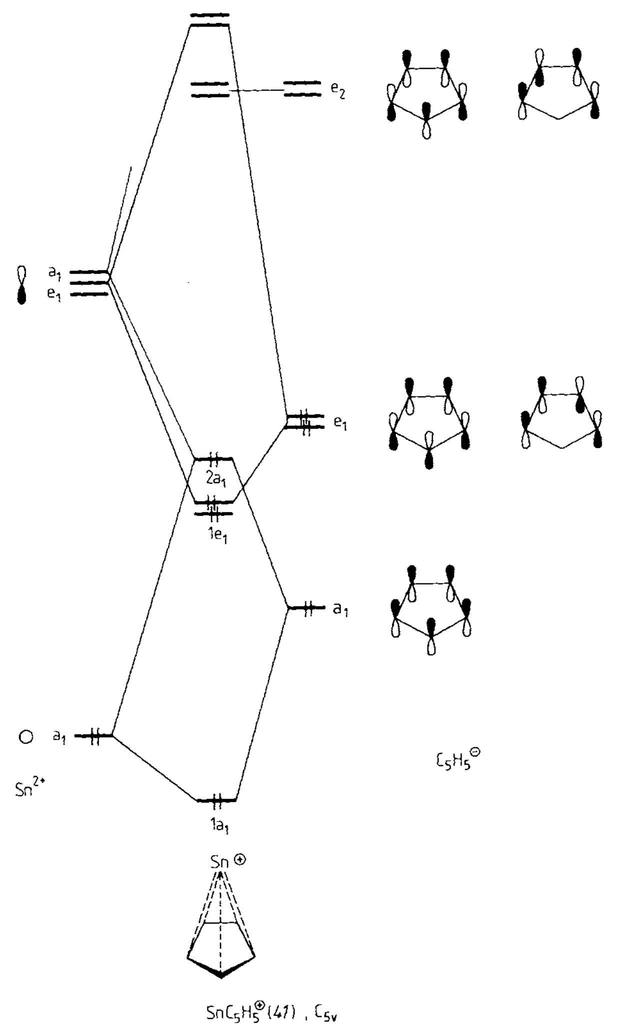


Fig. 2. MO diagram for the interaction of $Sn^{2+}$ with $C_5H_5^{\ominus}$ to form *(41)*.

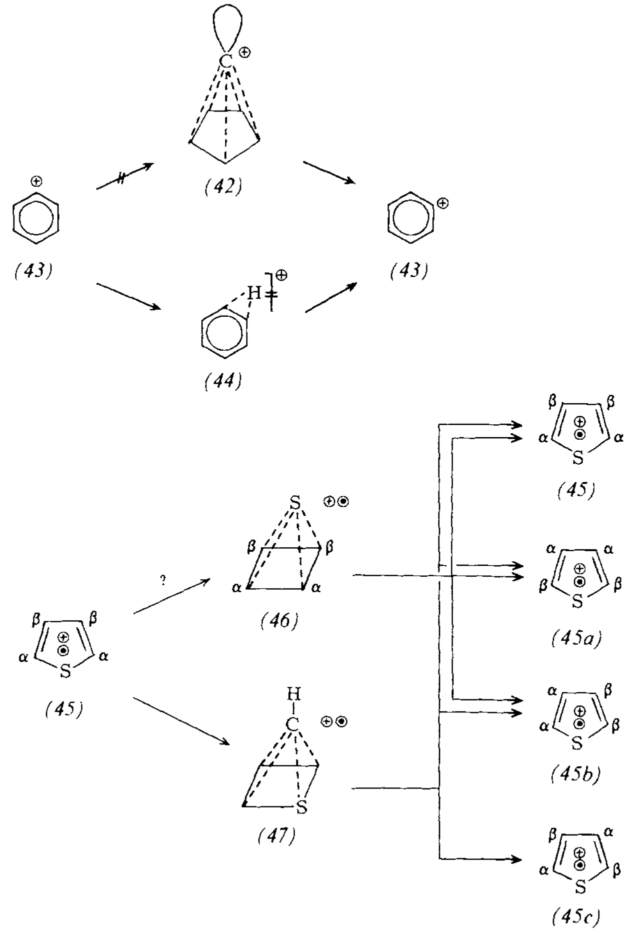
From studies of the gas phase automerization of *(43)* *via* H-migration[39a], it can safely be concluded that the pyramidal cation *(42)* is not involved. The degenerate isomerization of *(43)* presumably proceeds *via* *(44)* (Scheme 2)[*]. However, MINDO/3 calculations[39b] clearly reveal that

---

[*] In this article, the symbol ‡ is used in formulas, schemes, and figures to denote the transition state.

*(42)* is involved in the dissociation of the phenyl cation *(43)* to $C_4H_3^{\oplus}$ and $C_2H_2$. The activation energy for the process *(43)*→*(42)* has been calculated to be 69 kcal/mol, which is substantially lower than the activation energy for loss of $C_2H_2$ from *(43)* (108 kcal/mol). In consequence it is to be expected that *(43)* undergoes complete carbon scrambling prior to dissociation: this is in fact observed[39c].

Further studies are needed to decide whether the partial scrambling of carbon atoms preceding the molecular decay of the radical cation of thiophene *(45)* passes through the *nido*-cluster intermediate *(46)* having sulfur at the apex. Intermediate *(46)* cannot account for complete scrambling of carbon since the fourth product *(45c)* is inaccessible from *(46)*. A possible intermediate, which has not been considered or detected so far, is *(47)* which could decay to all four degenerate thiophene radical cations.



Scheme 2. Examples of automerization reactions which do *not* [in *(43)*] or only probably [*(45)*] involve pyramidal intermediates.

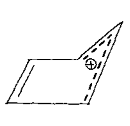
## 2.2. Quantum Mechanical Calculations on the Pyramidal $(CH)_5^{\oplus}$ Ion

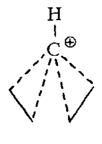
Many of the current quantum chemical methods for calculating the stability of pyramidal carbocations give widely different results. The pyramidal cation *(5)* provides a typical illustration. Extended Hückel calculations[20] show that *(5)* constitutes the global minimum on the energy hypersurface for the family of $C_5H_5^{\oplus}$ ions. These findings were confirmed by CNDO/2[41] and by modified CNDO calculations[42]. Calculations by *Smith et al.*[42] further showed that structure *(48)* also constitutes a minimum, but that it is located some 45 kcal/mol higher in energy than the minimum for *(5)*. MINDO/3 calculations[43] confirm that both *(5)* and *(48)* lie at minima on the energy hypersurface, but that *(5)* is *ca.* 14 kcal/mol less stable than *(48)*[44]. *Ab initio* calculations at the STO-3G/4-31G level indicate that *(48)* is more stable than *(5)* by *ca.* 55 kcal/mol[45]. This enormous difference in stability is understandable in view of the electronic structure of the pyramidal cation *(5)* in which three pairs of electrons are spacially closely packed together, holding the $CH^+$ and cyclobutadiene fragments in place. The difference between the enthalpies of formation of *(5)* and *(48)* should be substantially smaller in *ab initio* calculations when the effects of electron correlation are accounted for. When these are taken into account[46], enthalpy differences between *(5)* and *(48)* agree fairly well with those computed by MINDO/3.

Despite the discrepancies concerning the absolute stability of $C_5H_5^{\oplus}$ isomers, all methods indicate that *(5)* and *(48)* are separated by high potential barriers. For example, the barrier for the isomerization *(5)*→*(48)* according to MINDO/3 calculations, amounts to 43 kcal/mol[43], which indicates that the pyramidal cation *(5)*, once formed, should enjoy considerable stability.

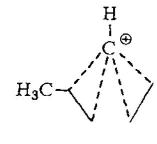
## 2.3. Substituent Effects

The effect of methyl and phenyl groups on the relative stability of structures *(5)* and *(48)* was estimated by *ab initio* calculations using isodesmic reactions[*][45]. It was found that phenyl substituents stabilize the cyclopentadienyl structure *(48)* over the pyramidal form *(5)*. Moreover, substitution by phenyl and methyl groups at the base of *(5)* turned out to be more favorable than at the apex. This difference *vide infra* is due to the charge distribution in the pyramidal cations. Calculations reveal that placing both methyl groups on the base, rather than one on the base and one at the apex, is energetically more favorable by 1.7 kcal/mol. This result is consistent with the findings for mono-substitution of pyramidal cations. However, neither Hückel calculations[47] nor experiment[21,48] confirm this tendency. Complete substitution by methyl, exemplified by the permethyl derivatives of *(5)* and *(49)*, results in stabilization of both structures with a slight preference for the pyramidal form. MINDO/3 and MNDO calculations indicate that pyramidal cations of type *(48)*, $C_5H_9^{\oplus}$[49], prefer to be substituted by methyl at the base *(50)* rather than at the apex *(51)*. (MINDO/3: $\Delta\Delta H_f^0 = 18$ kcal/mol, MNDO = 9 kcal/mol)[49-50].

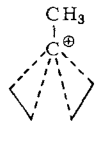

(48)



(49)



(50)

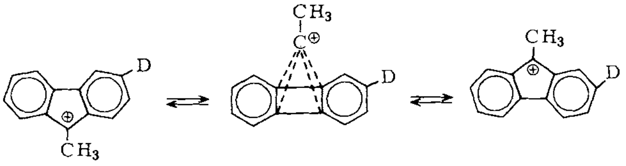


(51)

---

[*] For definition of isodesmic, see *W. J. Hehre, R. Ditchfield, L. Radom, J. A. Pople*, J. Am. Chem. Soc. 92, 4796 (1970), as well as *L. Radom, J. A. Pople, P. von R. Schleyer, ibid. 94*, 5935 (1972).

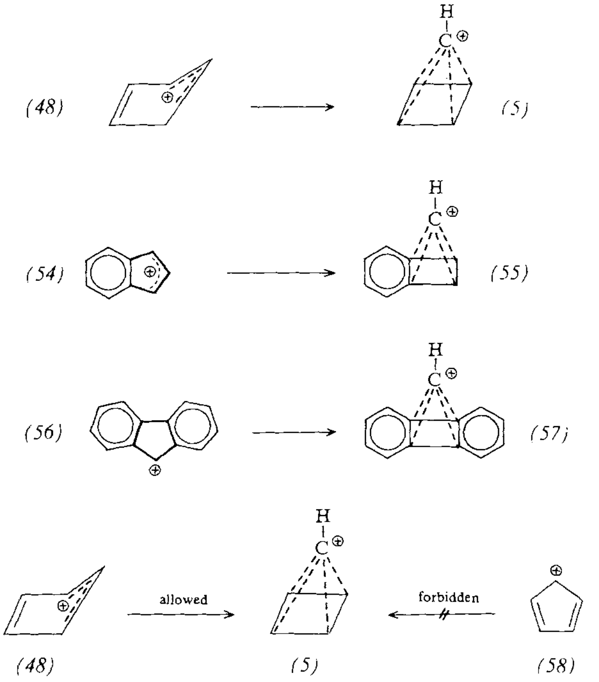
The influence of benzannelation on the relative stabilities of classical *versus* pyramidal cations has been discussed by *Olah* and *Schleyer et al.*[52] in relation to whether 9-substituted 9-fluorenyl cations, *e.g.* *(52)* undergo degenerate isomerization [*(52)*⇄*(52a)*] *via* intermediates having pyramidal structures such as *(53)*.



(52) (53) (52a)

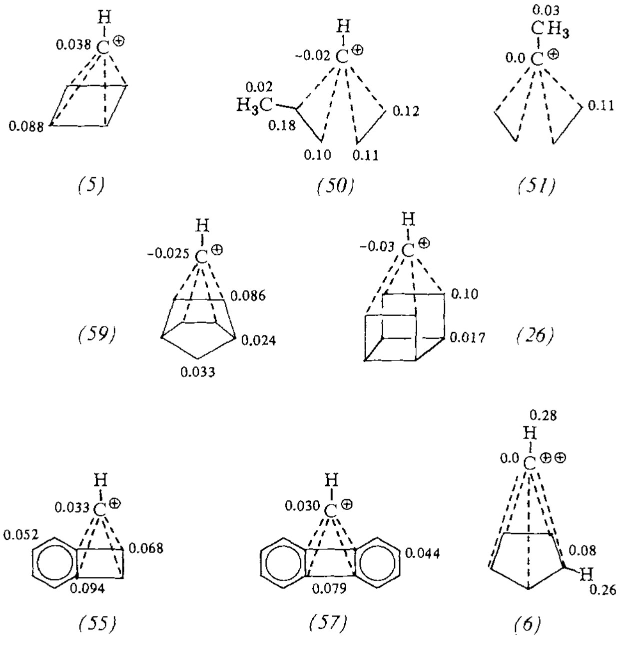
Scheme 3. Degenerate isomerization of the 3-deuterio-9-methyl-9-fluorenyl cation.

Numerous MINDO/3 calculations[52] clearly show that the pyramidal structures *(5)*, *(55)*, and *(57)* are destabilized upon increasing annelation compared to the classical structures *(48)*, *(54)*, and *(56)*, ($\Delta\Delta H_f^0$ = 14.4, 49.1, and 73.0 kcal/mol, respectively). There are two reasons for this substantial increase in energy difference. Firstly, the antiaromatic character of the classical structures is diminished upon increasing benzannelation, *i.e.* *(56)* is more stable than *(54)*, which is in turn more stable than *(48)*. Secondly, the stability of the pyramidal structures decreases in the order *(5)*>*(55)*>*(57)*. The differences are readily apparent from the "complexation energies" arising from the hypothetical reaction: olefin + $CH^{\oplus}$ → pyramidal cation. The relevant values for the formation of *(5)*, *(55)*, and *(57)* are −176.2, −153, and −131.9 kcal/mol, respectively[52]. As the complexation energy arises from the interaction of the doubly degenerate p-LUMO of the $CH^{\oplus}$ fragment with the π orbital of the diene, the observed trend becomes understandable; increasing annelation diminishes the π energy and at the same time decreases the coefficients of the carbon centers involved in the coordination. Another factor responsible for the non-occurrence of the reaction *(52)*⇄*(53)*⇄*(52a)* is the electronic situation in *(56)* and *(57)*. Although the process *(48)*→*(5)* is symmetry allowed, the reaction *(56)*→*(57)* is forbidden, the reason being that the electronic structure of *(56)* is not comparable to that of *(48)*, but rather to that of *(58)*. Furthermore *(58)*, which is a lumomer[*] of *(48)*, cannot isomerize to *(5)* for symmetry reasons[20].



## 2.4. Charge Distribution in Pyramidal Cations

For many pyramidal carbocations it has been found that the apical C atoms bear only a small positive charge or even a slight negative charge (Scheme 4)[54]. The apical C atom in *(5)* carries only 3.8% of the total charge, whereas the basal C atoms carry 35%[52]. Similar distributions have been obtained for cations *(50)* and *(51)*[50]. The apical C atom in *(50)* is slightly negative (−2%), whereas in *(51)* it is almost charge-free. As far as the H atoms are concerned, computation reveals that the basal part of *(50)* supports 99% of the charge and the apex only 1%. In the case of *(51)* the base possesses 91% of the charge and the $CH_3C$ apex 9%. In the pyramidal $C_8H_9^{\oplus}$ and $C_9H_9^{\oplus}$ ions *(59)*[55] and *(26)*[24] a slightly negative charge is found at the apical C atoms (−2.5 and −3%, respectively), whereas the basal C atoms share 34.4 and 40% of the positive charge, respectively. In *(59)* the H atoms carry a total of 59.7% of the charge and 56.3% in *(26)*. These results mean that the carbyne carbon atom is practically neutral, with the charge being strongly deflected to the periphery. This is an electrostatically favorable state of affairs which is a characteristic of the polyhedral structure. The analogy with the distribution of charge on a spherical surface is obvious.



Scheme 4. Charge distribution on the carbon atoms of pyramidal cations [54]. For the dication *(6)*, the charge distribution on C and H atoms is given.

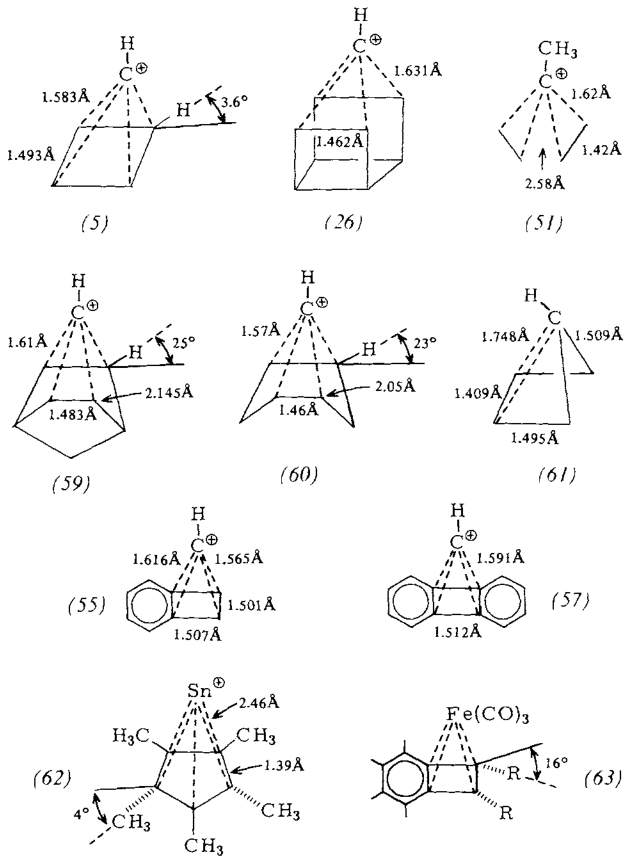
---

[*] Lumomers are isomers which are predominantly distinguished from each other by their LUMO.

The apical C atoms in the ions *(55)* and *(57)* are also only partially charged (3.3 and 3.0%, respectively)[52]. The dication *(6)* presents an interesting case. Its charge distribution was computed by *ab initio* methods[56] and it was found that the apical CH group only possesses 0.29 charge units (corresponding to 14.5%), whereas the entire basal region possesses 1.71 units (85.5%). An interesting insight into the nature of the electronic interaction underlying the formal combination of the $CH^{\oplus}$ and $C_5H_5^{\oplus}$ fragments is provided by analysis of the valence configuration of $CH^{\oplus}$. Starting from a $\sigma_{CH}^2\pi^2\sigma^0$ configuration for the free $CH^{\oplus}$ fragment, a $\sigma_{CH}^2\pi^{1.76}\sigma^{0.96}$ configuration is obtained for the CH-partial structure in *(6)*. This can be interpreted as follows. The five-membered ring donates 0.96 electrons to the empty σ orbital of $CH^{\oplus}$, whereas 0.24 electrons from the π orbital of $CH^+$ are donated back to the five-membered ring. This type of bonding is commonplace for organometallic compounds[33,34b].

### 2.5. Geometry of Pyramidal Ions

Only the more significant structural parameters of pyramidal cations will be discussed here. 1) The distance between the apical C atom and the basal C atoms corresponds to that of an elongated CC-single bond (1.6 Å). 2) The original CC-double bonds of the diene moiety are lengthened from 1.35 to *ca.* 1.48 Å on complexing with $CH^{\oplus}$. 3) The four basal atoms interact with each other in such a way as *not* to form a substituted cyclobutane ring. In fact, the distance between the opposing $C_2$ units is 2.58 Å in *(51)*[50], 2.15 Å in *(59)*[55], and amounts to 2.05 Å[21,57] in the analogously substituted $C_7H_9^{\oplus}$ ion *(60)* (Scheme 5). Similar results have been obtained for *(49)* and *(50)*[49,50]. For unsymmetrically substituted cations such as *(55)*[52], *(31)*, and *(33)*[32] the situation is more complicated: the single bonds in the basal region and those to the apical C atom differ in length. This is exemplified by the bishomocyclopropenyl cation *(61)*. This cation is intermediate in structure between 3c/2e bond species *(33)* and a distorted pyramid[32]. It is worth mentioning that the SnC separation in the cluster ion *(62)*, as determined by X-ray analysis, is significantly shorter compared to that of the $(Cp)_2Sn$ derivatives (from *ca.* 2.6 to 2.46 Å. 4) Pyramidal cations have similar shapes. The basal CH bonds of cations *(5)*, *(59)*, and *(60)* are all bent upwards towards the apex[20,21,41,43,45,55,57]. This probably allows better overlap of the molecular orbitals of the diene with those of the $CH^{\oplus}$ fragment. An analogous conformation is found in $B_5H_9$ *(8)*[15a]. On the other hand, the methyl groups on the five-membered ring of the permethyl-substituted cluster *(62)* are bent out of the plane of the five-membered ring by 4° *away* from the metal[38]. This out-of-plane bending is also encountered in the $Fe(CO)_3$ complex of benzocyclobutadiene derivatives *(63)*. X-ray analysis reveals that the plane of the annelated benzene ring and the two substituents ($R = t\text{-}C_4H_9$) are bent away from the $Fe(CO)_3$ center by 5° and 16°, respectively[58]. A satisfactory explanation of these configurational differences between carbocations and boranes on one hand, and organometallic cluster compounds on the other has recently been provided[83].



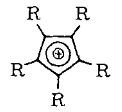
Scheme 5. Some geometric data of pyramidal cations.

## 3. Studies of Pyramidal Cations in the Condensed Phase

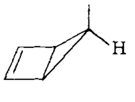
### 3.1. $(CX)_5^{\oplus}$ Derivatives (X = H, Cl, Ph, Aryl)

All attempts to generate and characterize the prototype of pyramidal cations *(5)* have, so far, been unsuccessful. The unsubstituted $C_5H_5^{\oplus}$ ion *(65a)* obtained from *(64)*, according to low temperature ESR studies, exists as a triplet[59]. A triplet state has also been assigned to the perchlorinated ion $C_5Cl_5^{\oplus}$ *(65b)*[60], whereas the derivatives *(65c)* exist as singlets in their ground states[60b,61]. It is no surprise that *(64)* gives the cyclopentadienyl derivative *(65a)* and not the pyramidal structure *(5)*. Theory[42,43] indicates that *(64)* and *(66)* should give *(65a)* or its lumomer *(48)*, respectively. Potential precursors for the pyramidal cation *(5)* are *(67)* and *(68)*. Unfortunately, experimental confirmation is still lacking.

*(64)*

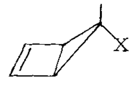


*(65a)*, R = H
*(65b)*, R = Cl
*(65c)*, R = Ph, Aryl

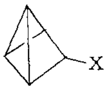


*(66)*

X = Cl, Br



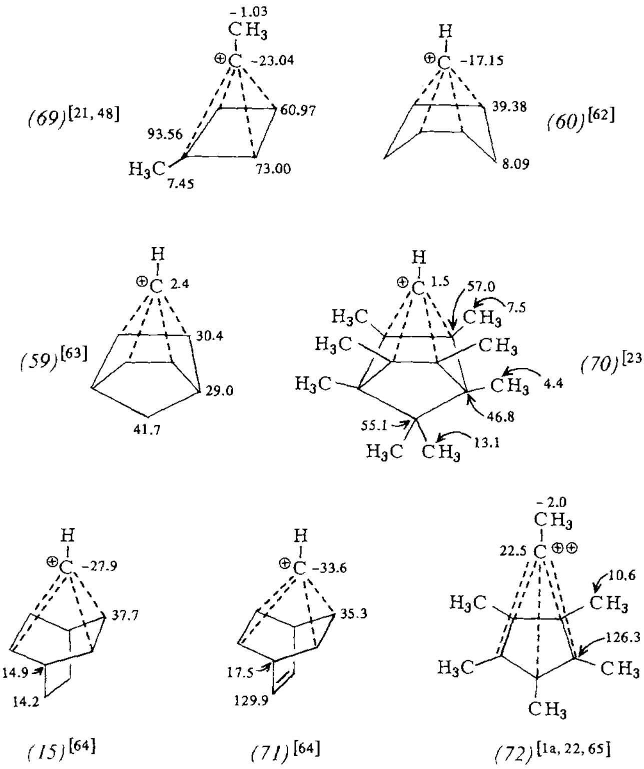
*(67)*



*(68)*

### 3.2. $^{13}$C-NMR Spectroscopic Investigations

Several cations *(15)*, *(59)*, *(60)*, *(69)*-*(72)* have been generated in superacid media and characterized as stable species. The dominant feature of the $^{13}$C-NMR spectra of these cations is the appearance of the resonance of the apical C atom at unusually high field (Scheme 6). Although the shift is certainly influenced by strain effects and steric crowding—*e.g.* in *(70)*—its value essentially arises because the apical C atom hardly bears any positive charge and that it is largely sp-hybridized. Most of the charge (see Section 2.4) is delocalized on the basal region and, in consequence, these atoms display a corresponding downfield shift. The sp-hybridization of the apical C atom is also evident from the $^{13}$C—$^{1}$H coupling constants, these being sensitive to hybridization[66]. The apical C atom in *(70)* has a $^{13}$C—$^{1}$H coupling constant of 220±5 Hz[67]: This value is entirely characteristic of a pyramidal structure and an sp-hybridized apical center[68].



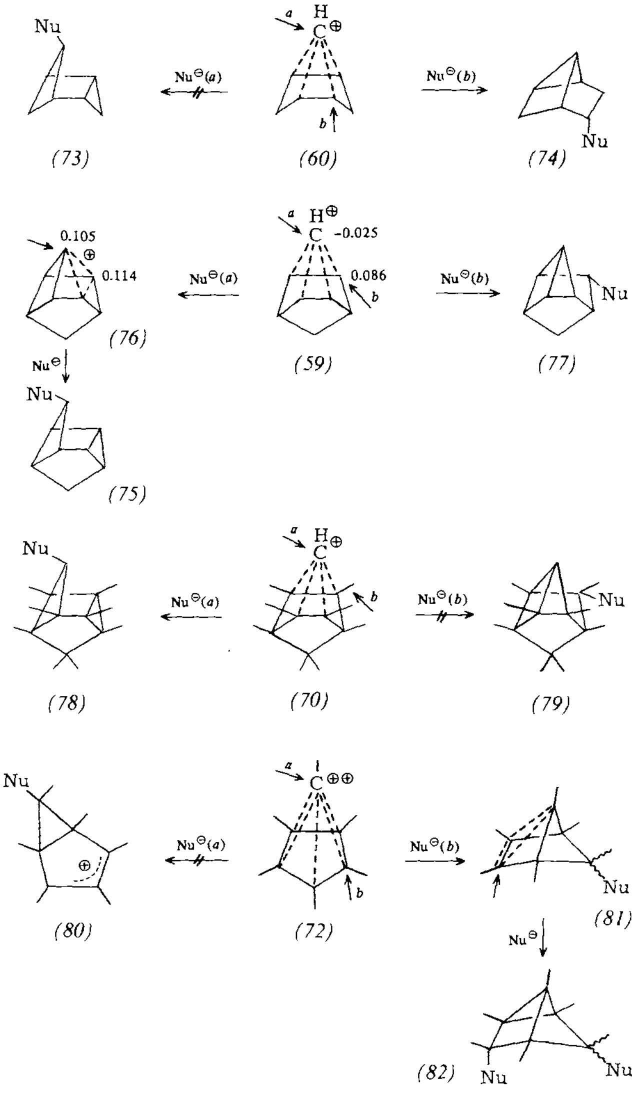
Scheme 6. $^{13}$C-NMR data (δ-values) of some pyramidal cations.

### 3.3. Quenching by Nucleophiles Nu$^{\ominus}$

The charge distribution discussed in Section 2.4 leads one to expect that attack by nucleophiles Nu$^{\ominus}$ under conditions of kinetic control should occur preferentially at the basal center. Indeed, Nu$^{\ominus}$ attacks *(60)* exclusively from the *endo*-side yielding *(74)*[21,62]. Attack at the apex to give *(73)* is not observed. A similar pattern of reactivity is to be expected for the homologous $C_8H_9^{\oplus}$ ion *(59)*. Almost equal amounts of *(75)* and *(77)* are formed[62,69], *i.e.* *(59)* is nucleophilically attacked at both the base and apex. This result can be rationalized if the principle of microscopic reversibility is taken into account[55], and if the reaction course is examined in more detail.

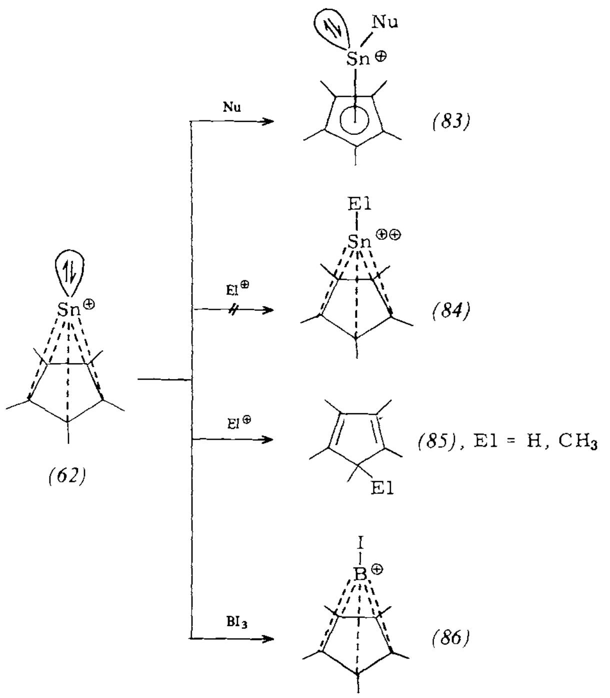
Reaction of *(75)* (Nu = OTs) with $CH_3CO_2H$[69a] and its solvolysis (Nu = Cl) in superacidic media[70] lead to the trishomocyclopropenyl cation *(76)*, which according to MINDO/3 calculations[55] is separated from the pyramidal cation *(59)* by a barrier of only 0.2 kcal/mol. A nucleophile could therefore "displace" the apical carbon atom away from the $C_2$ axis of *(59)*. This distortion redistributes the charge in *(76)*, thereby favoring attack at the apical C atom. Clearly, other factors may be important in controlling the approach of the nucleophile, *inter alia* different substitution patterns at the basal and apical carbon atoms. This is clearly seen by comparing *(59)* with its permethylated derivative *(70)* which reacts exclusively with nucleophiles at the apical C atom [*(70)*→*(78)*]. The product expected from *endo*-attack at the base, *viz.* *(79)*, was not detected[23,72].

Interestingly, the dication *(72)* undergoes nucleophilic attack exclusively at the basal C atom. *(72)*→*(82)* is unfavorable for steric and electronic reasons[1a,16,65]. Reaction of *(72)* with Nu$^{\ominus}$ occurs *via* the intermediate configurationally unstable monocation *(81)* to give the tricycle *(82)* (Scheme 7).



Scheme 7. Quenching of pyramidal cations by nucleophiles Nu$^{\ominus}$.

The behavior of the organometallic cation *(62)* towards electrophiles and nucleophiles is worth mentioning[38b]. Despite their topological similarity, *(62)* and the pyramidal cation *(72)* have completely different chemistries (Scheme 8). Nucleophiles attack the cluster at the tin atom [*(62)*→*(83)*]. Although the cluster-type bonding is lost, the *pentahapto*-structure *(83)* nevertheless remains intact. Electrophiles $El^{\oplus}$ do not attack the lone pair of the tin atom. In contrast to the formation of $(CCH_3)_6^{2+}$ *(72)* from the corresponding monocation, the dication $(CCH_3)_5SnR^{2+}$ *(84)* is not detected. Instead, the cluster either undergoes degradation [*(62)*→*(85)*], exchange of the apical tin atom [*(62)*→*(86)*], or attack of $El^{\oplus}$ at the counterion[38b].



Scheme 8. Reactions of the cluster ion *(62)* with nucleophiles (Nu) and electrophiles (El).

## 4. Pyramidal Carbocations in the Gas Phase

### 4.1. Carbon Atom Scrambling and Alkene Elimination

An increasing number of theoretical and experimental studies in recent years have shown that pyramidal cations play a central role in gas phase reactions of cations. The following examples are typical.

Metastable $C_5H_9^{\oplus}$ ions, generated from several precursors by dissociative ionization, lose ethylene in a unimolecular fashion to give an allylic cation. $C_5H_9^{\oplus}$ ions doubly labeled with $^{13}C$ have been shown to undergo complete scrambling of their C atoms prior to elimination of ethylene[49].

Model studies and quantum mechanical calculations[49] show that C atom scrambling in the cyclopentyl ion *(90)* can be accounted for in two ways; either by a bisected cyclobutylcarbinyl cation *(91)* or by the pyramidal cation *(49)*. Ethylene elimination, however, occurs only with the pyramidal cation *(49)*. Electronic reorganization in *(49)* leads to a transition state $TS_3$, whose structure *(92)* corresponds to a partially opened cyclopropyl cation "solvated" by an ethylene molecule[74].

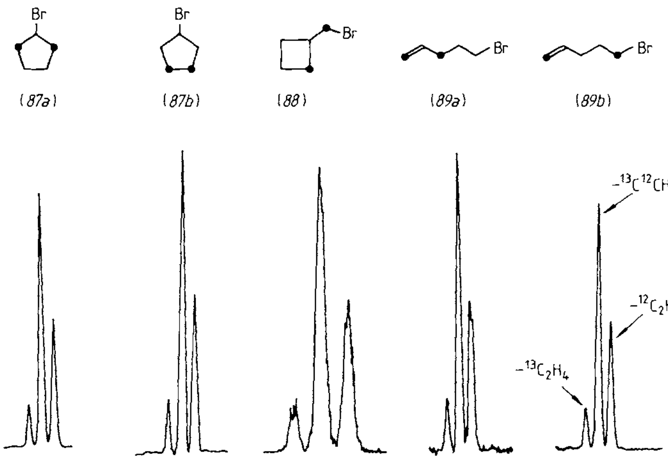


Fig. 3. Unimolecular ethylene elimination from the $[M-Br]^{\oplus}$ ions of *(87)*—*(89)*. $^{13}C$ label indicated by (•). Spectra were recorded by the MIKES method[73]. For complete C atom equilibration, the relative intensities for fragments obtained by loss of $^{13}C_2H_4$, $^{13}C^{12}CH_4$, and $^{12}C_2H_4$ are respectively 10%, 60%, and 30%, respectively.

Alternative mechanisms for the process $C_5H_9^{\oplus} \rightarrow C_3H_5^{\oplus}$ *(93)* $+ C_2H_4$, the cycloreversion [*(91)*→*(93)*] or two-step reactions involving acyclic $C_5H_9^{\oplus}$ ions, have been found by calculation to be energetically unfavorable.

Similar results were obtained for the homologuous $C_6H_{11}^{\oplus}$ ion which decomposes unimolecularly to the 1-methylallyl cation and ethylene[50]. It is seen from the doubly $^{13}C$-labeled $C_6H_{11}^{\oplus}$ cations, generated from *(94)*—*(97)* by

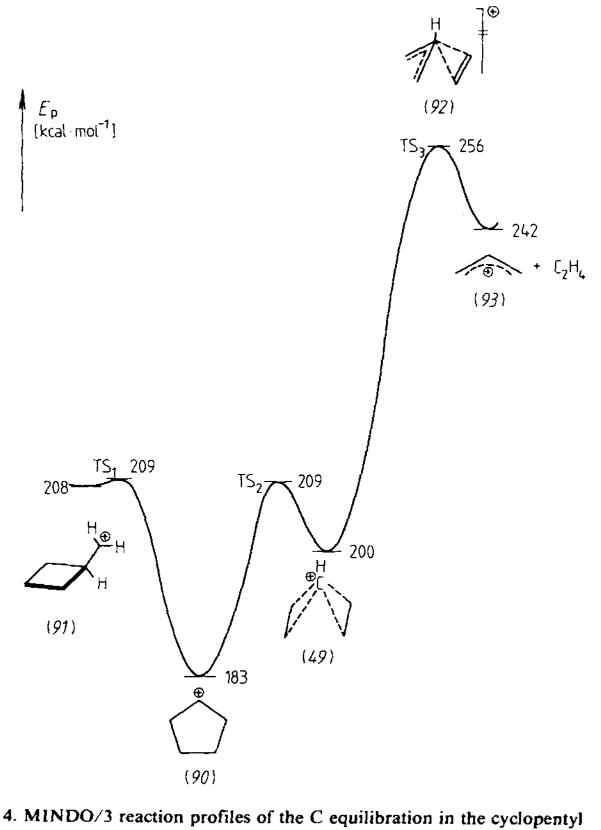


Fig. 4. MINDO/3 reaction profiles of the C equilibration in the cyclopentyl cation *(90)* and for the reaction $C_5H_9^{\oplus} \rightarrow C_3H_5^{\oplus} + C_2H_4$.

dissociative ionization, that complete C scrambling occurs (Fig. 5). Moreover, the constitution of the molecular ions (five- or six-membered ring derivatives) has no effect on the scrambling pattern. The nature of the neutral part X to be eliminated (X = COOH or Br) and the initial position of the $^{13}C$ label (1,2- or 1,3-assignment) are also without effect. Accordingly, the scrambling of C atoms is best described by an equilibrium between the cyclohexyl *(98)* and the 1-methylcyclopentyl cations *(99)*, involving both protonated cyclopropane derivatives *(100)*[75] and the pyramidal cations *(50)* and *(51)* (Scheme 9)[50]. Ethylene elimination, however, proceeds most favorably from the transition state *(101)*. According to MNDO calculations[50], *(101)* is at least 11 kcal/mol more stable than its isomeric form *(103)*, and is expected to decay to ethylene and $C_4H_7^{\oplus}$ (Scheme 10). Numerous experimental methods confirm that the $C_4H_7^{\oplus}$ ion has the 1-methylallylic structure *(102)* and not the 2-methylallyl cation structure *(104)*[50,76].

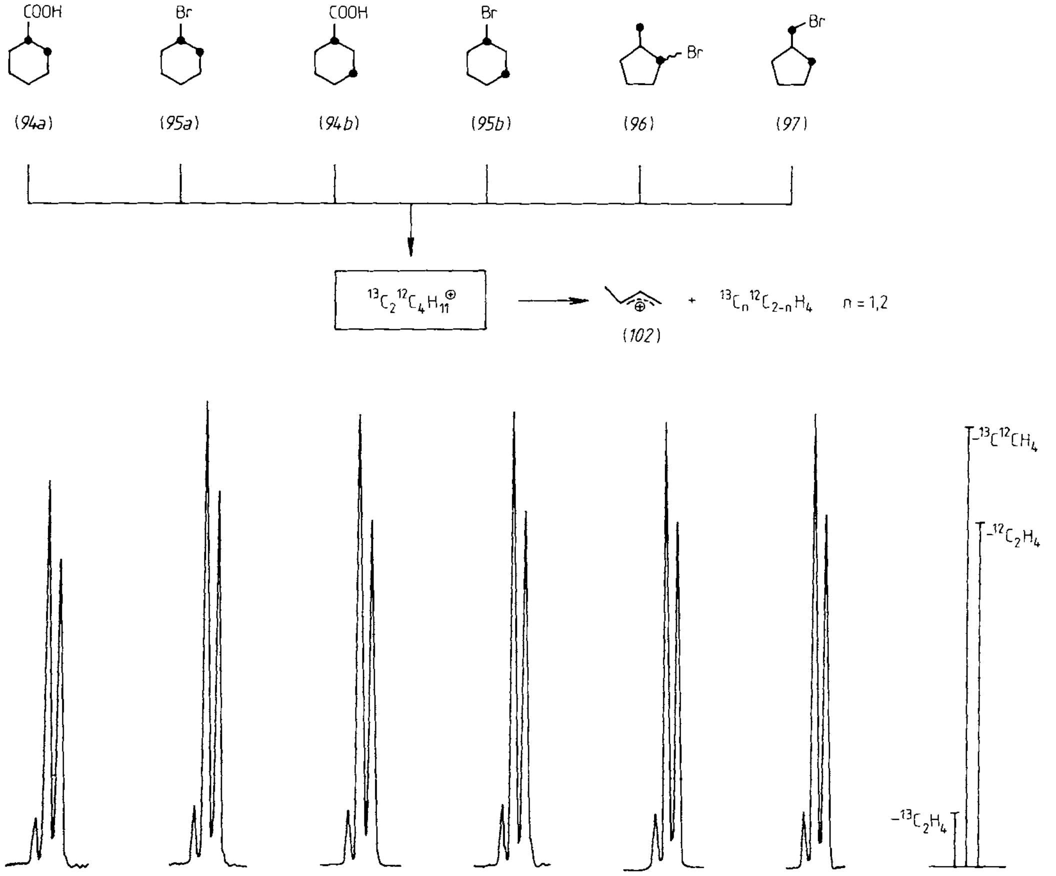
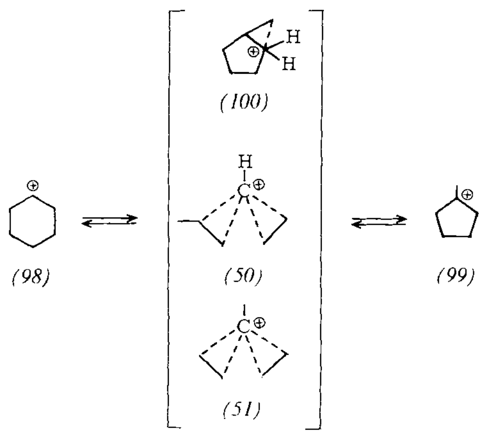
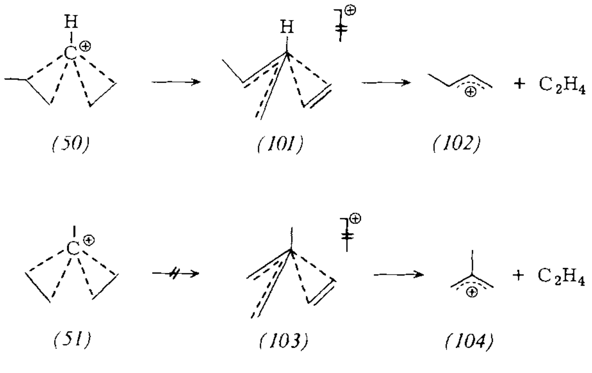


Fig. 5. MIKE spectra of the unimolecular ethylene elimination from doubly $^{13}C$ labeled $C_6H_{11}^{\oplus}$ ions obtained from *(94)*–*(97)*. $^{13}C$ label indicated by (●).

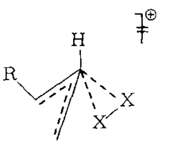


Scheme 9. Isomerization of the cyclohexyl- *(98)* and 1-methylcyclopentyl-cations *(99)*.



Scheme 10. Unimolecular ethylene elimination from $C_6H_{11}^{\oplus}$.

Elimination of $C_2H_4$ from $C_5H_9^{\oplus}$ and $C_6H_{11}^{\oplus}$ is mechanistically similar to the unimolecular elimination of $H_2$ from



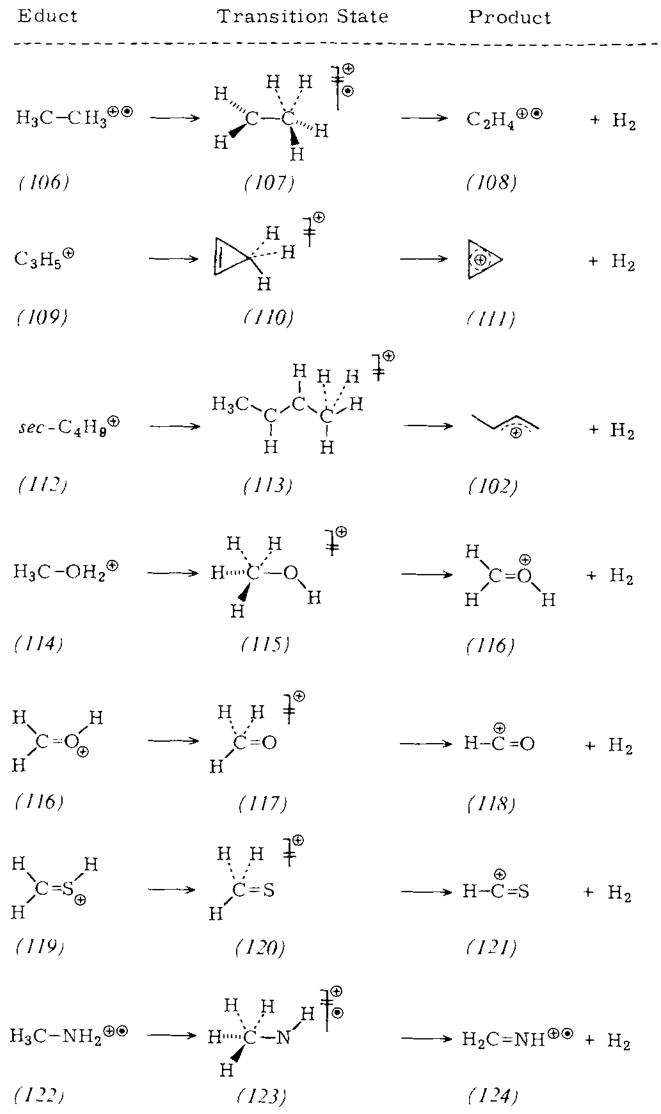
(105)

| R | X | Reaction | Lit. |
|---|---|---|---|
| H | H | $C_3H_7^{\oplus} \rightarrow C_3H_5^{\oplus} + H_2$ | [77] |
| H | $CH_2$ | $C_5H_9^{\oplus} \rightarrow C_3H_5^{\oplus} + C_2H_4$ | [49] |
| $CH_3$ | $CH_2$ | $C_6H_{11}^{\oplus} \rightarrow C_4H_7^{\oplus} + C_2H_4$ | [50] |

$C_3H_7^{\oplus}$, which also produces the allyl cation[77]. Once again, experiments and calculations both show that the transition state *(105)* (X = H, R = H) exhibits the properties of a partially opened cyclopropyl cation which is "solvated" by $H_2$. Indeed, the reaction $C_3H_7^{\oplus} \rightarrow C_3H_5^{\oplus} + H_2$ is the first example of *two* coupled symmetry allowed processes, namely the opening of a cyclopropyl cation to the allyl cation and the simultaneous cheletropic elimination of hydrogen[77].

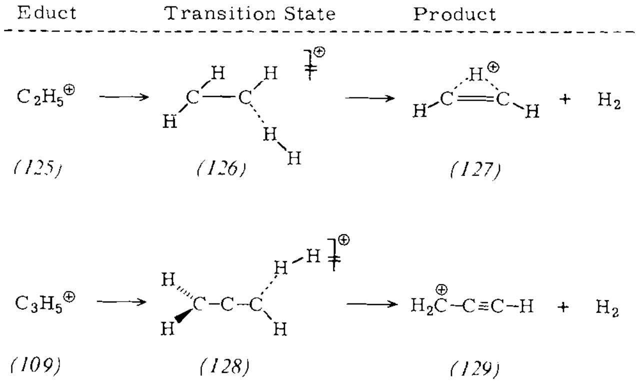
### 4.2. $H_2$ "Solvated" Transition States

Transition states like *(105)* represent the formal "solvation" of cations by $H_2$ and have been discussed for numerous unimolecular gas-phase reactions[79]. The unimolecular decomposition of such solvated cations displays a common feature, a [1,2] $H_2$ shift combined with a [1,1] elimination of $H_2$ (Scheme 11). The transition state for elimination can be described by a side-on complexation of the cation with $H_2$. The resulting species correspond to deformed derivatives of the methonium ion $CH_5^{\oplus}$ (with the exception of *(117)* and *(120)*). In all these processes (Scheme 11) the translational energy ($E_T$)[79], released in the unimolecular decomposition process, is found to represent a substational fraction of the energy of activation of the reverse reaction[79b–d, 80]. This is probably a direct consequence of the repulsive nature[81] of the corresponding transition states and the inefficient coupling of the imaginary normal vibrational modes between the ionized and neutral parts of the complex.



Scheme 11. Unimolecular elimination of $H_2$ from side on complexed transition states.

Transition states leading to the vinyl cation *(127)* and the propargylium ion *(129)* are completely different from the side-on coordinated transition states discussed in Scheme 11. Instead of a pentacoordinated C atom, a complex in which the hydrogen molecule is positioned end-on is necessary[78] (Scheme 12).

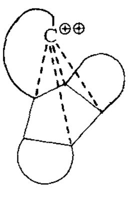


Scheme 12. Unimolecular elimination of $H_2$ from end-on complexed transition states.

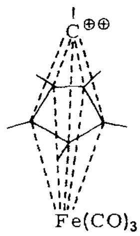
## 5. Future Prospects

There is considerable support for the view that pyramidal cations constitute *the* essential bridge between organic and inorganic chemistry. By an appropriate choice of conditions these ions can be prepared either as stable species in superacid media, where they can be conveniently studied by spectroscopic methods, or as transient species formed by solvolysis. Lastly, and perhaps most importantly, they can be easily prepared in the gas phase. Under these latter conditions, the polyhedral shape and the associated favorable "spherical" charge distribution clearly make these pyramidal cations sufficiently long-lived and hence amenable to study. Carbon atom scrambling reactions of several carbocations, which were previously not properly understood, can now be conveniently rationalized in terms of pyramidal cations. For example, seemingly different processes such as the unimolecular elimination of σ (such as $H_2$) or π ligands (alkenes) are seen to have much in common if intermediates and transition states involving pyramidal structures are admitted.

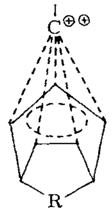
There is no doubt that these novel pyramidal structures provide a stimulus to the ingenuity of chemists. As examples of compounds which have not been synthesized up to now we may cite the neutral carbaboranes containing hypervalent carbon, *e.g. (23)*[31], futuristic structures possessing polycyclic skeletons, *e.g. (130)* and inverted sandwich structures *(131)*[1,82], and to complete the list of this exotic series, pyramidal dications having fluxional properties, *e.g. (132)*[19] (R=CH=CH, *o*-$C_6H_4$, *etc.*).



*(130)*



*(131)*



*(132)*

Although not all carbocations have pyramidal structures neither do they have "rococo" topology[15], which has aroused the skepticism of some chemists. Analysis by graph theory has already predicted that no *closo-* or *arachno* clusters are to be expected for carbonium ions. Moreover, calculation[24] has demonstrated that the stability order for pyramidal *versus* classical structures can be easily upset by solvation by the simple act of passing from the gas to the condensed phase. In other words, from the ideal solvent-free state to the real situation.

*I wish to acknowledge the generous support by the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft (project Schw 221/5, 6-2), the Gesellschaft von Freunden der Technischen Universität Berlin, and Schering AG. Work in our laboratory has been accomplished essentially by my co-worker Dipl.-Chem. Wilfried Franke, to whom I express my gratitude. An Overseas Fellowship awarded by Churchill College, Cambridge, England (1981) allowed me to write this report. I also greatly appreciate many stimulating discussions with R. G. Cooks (Purdue), T. Gäumann (Lausanne), P. von R. Schleyer (Erlangen), and D. H. Williams (Cambridge). Translated from the German by Drs C. W. Jefford and U. Burger, Université de Genève, Switzerland.*

Received: July 8, 1981 [Z 390 IE]
German version: Angew. Chem. *93*, 1046 (1981)

---

[1] a) *H. Hogeveen, P. W. Kwant*, Acc. Chem. Res. *8*, 413 (1975); b) *H. C. Brown* (with comments by *P. von R. Schleyer*): The Nonclassical Ion Problem, Plenum Press, New York 1977, Chap. 1, p. 17.

[2] a) *R. N. Grimes:* Carboranes, Academic Press, New York 1970; b) *W. N. Lipscomb*, Acc. Chem. Res. *7*, 257 (1973); c) *K. Wade*, Chem. Br. *11*, 177 (1975); Adv. Inorg. Chem. Radiochem. *18*, 1 (1976); New Sci. *1974*, 615; d) *R. E. Williams*, Inorg. Chem. *10*, 210 (1971); e) *R. W. Rudolph*, Acc. Chem. Res. *9*, 446 (1976).

[3] *T. P. Nevell, E. de Salas, C. L. Wilson*, J. Chem. Soc. *1939*, 1188.

[4] a) *S. Winstein, D. S. Trifan*, J. Am. Chem. Soc. 71, 2953 (1949); b) *S. Winstein*, Q. Rev. Chem. Soc. *23*, 1411 (1969).

[5] *G. A. Olah*, Angew. Chem. *85*, 183 (1973); Angew. Chem. Int. Ed. Engl. *12*, 173 (1973).

[6] a) *D. M. Brouwer, H. Hogeveen*, Prog. Phys. Org. Chem. *9*, 179 (1972); b) *H. Hogeveen*, Adv. Phys. Org. Chem. *10*, 29 (1973); c) *H. Hogeveen, E. M. G. A. van Kruchten*, Top. Curr. Chem. *80*, 89 (1979).

[7] *G. A. Olah, P. von R. Schleyer:* Carbonium Ions, Vol. I–IV, Wiley-Interscience, New York 1968.

[8] a) *V. L. Tal'rose, A. K. Lyubimova*, Dokl. Akad. Nauk SSSR *86*, 909 (1952); b) *V. L. Tal'rose, E. L. Frankevitch*, J. Am. Chem. Soc. *80*, 2344 (1958); c) *F. H. Field, M. S. B. Munson, ibid. 87*, 3289 (1965); d) *K. Hiraoka, P. Kebarle, ibid. 98*, 6119 (1976); e) *R. Houriet, G. Parisod, T. Gäumann, ibid. 99*, 3599 (1977).

[9] a) *G. A. Olah:* Carbocations and Electrophilic Reactions, Wiley-Interscience, New York 1974; b) *G. A. Olah, R. H. Schlosberg*, J. Am. Chem. Soc. *90*, 2726 (1968).

[10] a) See *e.g. M. Saunders, M. R. Kates*, J. Am. Chem. Soc. *102*, 6867 (1980); b) *W. Kirmse*, Top. Curr. Chem. *80*, 125 (1979).

[11] a) *G. A. Olah, A. M. White, J. R. DeMember, A. Commeyras, C. Y. Lui*, J. Am. Chem. Soc. *92*, 4627 (1970); b) *R. K. Lustgarten, M. Brookhart, S. Winstein, P. G. Gassman, D. S. Patton, H. G. Richey, J. D. Nichols*, Tetrahedron Lett. *1970*, 1699; c) *S. Masamune, E. N. Cain, R. Vukov, S. Takada, N. Nakatsuka*, Chem. Commun. *1969*, 243.

[12] a) *R. M. Coates, E. R. Fretz*, J. Am. Chem. Soc. *97*, 2538 (1975); b) *W. L. Jorgensen*, Tetrahedron Lett. *1976*, 3033; c) *H. C. Brown, M. Ravindranathan*, J. Am. Chem. Soc. *99*, 299 (1977); d) *R. M. Coates, E. R. Fretz, ibid. 99*, 297 (1977).

[13] See *e.g.* a) *S. Yoneda, Z. Yoshida, S. Winstein*, Tetrahedron *28*, 2395 (1972); b) *M. D. Sefcik, J. M. S. Henis, P. P. Gaspor*, J. Chem. Phys. *61*, 4321 (1974); c) *W. Th. A. M. van der Lugt, P. Ros*, Chem. Phys. Lett. *4*, 389 (1969); d) *H. Kollmar, H. O. Smith, ibid. 5*, 7 (1970); e) *V. Dyczmos, V. Staemmler, W. Kutzelnigg, ibid. 5*, 361 (1970).

[14] *W. N. Lipscomb:* Boron Hydrides, Benjamin, New York 1963.

[15] *W. N. Lipscomb*, J. Chem. Phys. *22*, 985 (1954).

[16] a) *H. Hogeveen, P. W. Kwant*, J. Am. Chem. Soc. *96*, 2208 (1974); b) *H. Hogeveen, E. M. G. A. van Kruchten*, J. Org. Chem. *46*, 1350 (1981).

[17] *J. Hasse*, Z. Naturforsch. *A 28*, 785 (1973).

[18] *J. P. Pasinski, R. A. Beandet*, J. Chem. Soc. Chem. Commun. *1973*, 928.

[19] *A. T. Balaban, D. H. Rouvray*, Tetrahedron *36*, 1851 (1980).

[20] *W. D. Stohrer, R. Hoffmann*, J. Am. Chem. Soc. *94*, 1661 (1972).

[21] *S. Masamune*, Pure Appl. Chem. *44*, 861 (1975).

[22] *Hart* [23] suggests that the interaction of $CH^{\oplus}$ with any 4e system might generally produce a "stable" molecular arrangement. Tetrahedrane *(13)* could be considered as the covalent form of the interaction of $CH^{\oplus}$ with the antiaromatic cyclopropenyl anion *(12)*. Further, the $C_{4v}$ symmetry of the methonium in *(1)* might result from the interaction of $CH^{\oplus}$ with two $\sigma_{H-H}$ bonds.
The rules which have been suggested for the nomenclature of pyramidal cations suggested by *Jorgensen* [24] follow closely those proposed by *Cotton* [25] for use with organometallic complexes. For example, the positions of the $CH^{\oplus}$ groups are followed by the term *"tetrahapto"* ($\eta^4$), then the name of the 4e system, finally followed by the name of the apical fragments. *(5)* is therefore named the tetrahaptocyclobutadienemethinyl cation. Similarly, *(6)* is termed the *pentahapto*-cyclopentadienylmethinyl cation. The cluster *(15)*, obtained from $CH^{\oplus}$ and bicyclo[2.2.2]octadiene *(14)* would be termed 2,3,5,6-*tetrahapto*-bicyclo[2.2.2]octadienemethinyl cation.

[23] *H. Hart, M. Kuznya*, J. Am. Chem. Soc. *96*, 6436 (1974).

[24] *W. L. Jorgensen*, J. Am. Chem. Soc. *99*, 4272 (1977).

[25] *F. A. Cotton*, J. Am. Chem. Soc. *90*, 6230 (1968).

[26] *C. Cone, M. J. S. Dewar, D. Landman*, J. Am. Chem. Soc. *99*, 372 (1977).

[27] *S. Winstein, C. Ordronneau*, J. Am. Chem. Soc. *82*, 2084 (1960).

[28] a) *K. L. Rinehardt, Jr., A. C. Buchholz, G. E. van Lear, H. L. Cantrill*, J. Am. Chem. Soc. *90*, 2983 (1968); b) *K. L. Rinehardt, A. Siegel*, 158. Nat. Meet. Am. Chem. Soc., New York 1969, Abstr. ORG N 66.

[29] a) *R. K. Lustgarten, M. Brookhart, S. Winstein*, J. Am. Chem. Soc. *94*, 2347 (1972); b) *P. R. Story, L. C. Snyder, D. C. Douglas, E. W. Anderson, R. L. Kornegay, ibid. 85*, 3630 (1963).

[30] a) Ref. [1a]; b) ref. [1b], Chap. 14.5.

[31] *P. von R. Schleyer* in Ref. [1b], p. 18.

[32] *R. Houriet, H. Schwarz, W. Zummack, J. G. Andrade, P. von R. Schleyer*, Nouv. J. Chim., in print.

[33] *M. Elian, M. M. L. Chen, D. M. P. Mingos, R. Hoffmann*, Inorg. Chem. *15*, 1148 (1976).

[34] For reviews see: a) ref. [2c]; b) *M. Elian, R. Hoffmann*, Inorg. Chem. *14*, 1058 (1975); c) *R. Pettit*, Pure Appl. Chem. *17*, 253 (1968); d) *A. Efraty*, Chem. Rev. *77*, 691 (1977).

[35] *M. L. H. Green, L. Pratt, G. Wilkinson*, J. Chem. Soc. London *1959*, 3753.

[36] a) *M. R. Churchill, K. Gold*, Chem. Commun. *1968*, 693; Inorg. Chem. *8*, 401 (1969); b) *A. Almenniagen, A. Haaland, K. Wahl*, Acta Chem. Scand. *23*, 1145 (1969); c) *D. C. Andrews, G. Davidson*, J. Organomet. Chem. *43*, 393 (1972); d) *D. C. Andrews, G. Davidson, D. A. Duce, ibid. 97*, 95 (1975); e) *E. S. Magyar, C. P. Lillya, ibid. 116*, 99 (1976).

[37] a) *J. J. Gajewski, M. J. Chang*, J. Org. Chem. *43*, 765 (1978); b) *J. Chandrasekhar, P. von R. Schleyer, H. B. Schlegel*, Tetrahedron Lett. *1978*, 3393.

[38] a) *P. Jutzi, F. Kohl, P. Hofmann, C. Krüger, Y. H. Tsay*, Chem. Ber. *113*, 757 (1980); b) *P. Jutzi* in Festschrift: 30 Jahre Fonds der Chemischen Industrie, Verband der Chemischen Industrie, Frankfurt 1980, p. 37.

[39] a) *M. Speranza*, Tetrahedron Lett. *1980*, 1983; b) *M. Tasaka, M. Ogata, H. Ichikawa*, J. Am. Chem. Soc. *103*, 1885 (1981); c) *R. Dichinson, D. H. Williams*, J. Chem. Soc. *B 1971*, 249.

[40] a) *A. S. Siegel*, Tetrahedron Lett. *1970*, 4113; b) *H. Wynberg, R. M. Kellog, H. Van Driel, G. E. Berkhuis*, J. Am. Chem. Soc. *89*, 3501 (1967); c) *F. De Jong, H. J. M. Sinnige, M. J. Janssen*, Org. Mass Spectrom. *3*, 1539 (1970).

[41] *S. Yoneda, Z. Yoshida*, Chem. Lett. *1972*, 607.

[42] *H. Kollmar, H. O. Smith, P. von R. Schleyer*, J. Am. Chem. Soc. *95*, 5834 (1973).

[43] *M. J. S. Dewar, R. C. Haddon*, J. Am. Chem. Soc. *95*, 5836 (1973).

[44] True only for singlet states; triplet state *(48)* is more stable by 1.6 kcal/mol than the singlet state *(48)*, according to MINDO/3 calculations.

[45] *W. J. Hehre, P. von R. Schleyer*, J. Am. Chem. Soc. *95*, 5837 (1973).

[46] *H. J. Köhler, H. Lischka*, J. Am. Chem. Soc. *101*, 3479 (1979).

[47] *R. Hoffmann*, personal communication cited in [48].

[48] *S. Masamune, M. Sakai, H. Ona, A. J. Jones*, J. Am. Chem. Soc. *94*, 8956 (1972).

[49] a) *W. Franke, H. Schwarz, H. Thies, J. Chandrasekhar, P. von R. Schleyer, W. J. Hehre, M. Saunders, G. Walker*, Angew. Chem. *92*, 488 (1980); Angew. Chem. Int. Ed. Engl. *19*, 485 (1980); b) Chem. Ber. *114*, 2808 (1981).

[50] *W. Franke, G. Frenking, H. Schwarz, R. Wolfschütz*, Chem. Ber. *114*, Heft Nr. 11 (1981).

[51] In our experience [50], the enthalpies of formation computed for pyramidal cations (ground or transition state) from MNDO are found to be 25-36 kcal/mol *above* the MINDO/3 values.

[52] *G. A. Olah, G. K. S. Prakash, G. Liang, P. W. Westerman, K. Kunde, J. Chandrasekhar, P. von R. Schleyer*, J. Am. Chem. Soc. *102*, 4485 (1980).

[53] For "antiaromaticity" see: *R. Breslow*, Acc. Chem. Res. *6*, 393 (1973).

[54] These results are independent of the computational method used. Deviations concern only the absolute values. The charges cited here were, however, computed by MINDO/3, with the exception of those for dication *(6)*.

[55] *C. W. Jefford, J. Mareda, J.-C. Perlberger, U. Burger*, J. Am. Chem. Soc. *101*, 1370 (1979).

[56] *H. T. Jonkman, W. C. Nieuwport*, Tetrahedron Lett. *1973*, 1671.

[57] *K. Morio, S. Masamune*, Chem. Lett. *1974*, 1107.

[58] *H. Straub, G. Döring, W. Winter*, Z. Naturforsch. *B 34*, 125 (1979).

[59] *M. Saunders, R. Berger, A. Jaffe, J. M. McBride, J. O'Neill, R. Breslow, J. M. Hoffman, Jr., C. Perchonock, E. Wasserman, R. S. Hutton, V. J. Kuck*, J. Am. Chem. Soc. *95*, 3017 (1973).

[60] a) *R. Breslow, R. Hill, E. Wasserman*, J. Am. Chem. Soc. *86*, 5349 (1964); b) *R. Breslow, H. W. Chang, R. Hill, E. Wasserman, ibid. 89*, 1112 (1967).

[61] a) *R. Breslow, H. W. Chang, W. A. Yager*, J. Am. Chem. Soc. *85*, 2033 (1963); b) *W. Broser, H. Kurreck, P. Siegle*, Chem. Ber. *100*, 788 (1967); c) *W. Broser, P. Siegle, H. Kurreck, ibid. 101*, 69 (1968).

[62] *S. Masamune, M. Sakai, A. V. Kemp-Jones, H. Ona, A. Venot, T. Nakashima*, Angew. Chem. *85*, 829 (1973); Angew. Chem. Int. Ed. Engl. *12*, 769 (1973).

[63] *A. V. Kemp-Jones, N. Nakamura, S. Masamune*, J. Chem. Soc. Chem. Commun. *1974*, 109.

[64] *R. M. Coates, E. R. Fretz*, Tetrahedron Lett. *1977*, 1955.

[65] *H. Hogeveen, P. W. Kwant*, Tetrahedron Lett. *1973*, 1665.

[66] *J. B. Stothers:* Carbon-13 NMR Spectroscopy, Academic Press, New York 1972, p. 331. $^{13}C$—$^{1}H$ coupling constants for $sp^3$, $sp^2$ and sp centers are respectively 125 Hz, 160 Hz and 250 Hz. See also *W. A. Bingel, W. Lüttke*, Angew. Chem. *93*, 944 (1981); Angew. Chem. Int. Ed. Engl. *20*, 899 (1981).

[67] *H. Hart, R. Willer*, Tetrahedron Lett. *1978*, 4189.

[68] We wish to mention that a *few* spectroscopic observations could well be compatible with the existence of rapidly equilibrating systems. However, rigorous analysis of *all* experimental and spectroscopic data, and inclusion of theoretical results allows the conclusion to be made that all ions *(15)*, *(59)*, *(60)*, *(69)*, *(70)*, *(71)*, and *(72)* correspond to potential minima.

[69] a) *R. M. Coates, K. Yano*, Tetrahedron Lett. *1972*, 2289; b) *W. Kirmse, T. Olbricht*, Chem. Ber. *108*, 2616 (1975); c) *X. Creary*, J. Org. Chem. *40*, 3326 (1975).

[70] a) *S. Masamune, M. Sakai, A. V. Kemp-Jones, T. Nakashima*, Can. J. Chem. *52*, 855, 858 (1974); b) *W. L. Jorgensen*, Tetrahedron Lett. *1976*, 3029.

[71] *(59)* according to MINDO/3 is more stable by 2.8 kcal/mole than *(77)* [55].

[72] *H. Hart, M. Kuzuya*, J. Am. Chem. Soc. *94*, 8958 (1972).

[73] MIKES (acronym for Mass Analyzed Ion Kinetic Energy Spectroscopy); for the method see: a) *J. H. Beynon, R. G. Cooks, J. W. Amy, W. E. Baitinger, T. Y. Ridley*, Anal. Chem. *45*, 1023 A (1973); b) *U. P. Schlunegger*, Angew. Chem. *87*, 731 (1975); Angew. Chem. Int. Ed. Engl. *14*, 679 (1975); c) *K. Levsen, H. Schwarz, ibid. 88*, 589 (1976), *15*, 509 (1976).

[74] a) *U. Schöllkopf, K. Fellenberger, M. Patsch, P. von R. Schleyer, T. Su, G. W. van Dine*, Tetrahedron Lett. *1967*, 3639; b) *G. A. Olah, D. B. Ledlie, M. G. Costopolous*, J. Am. Chem. Soc. *99*, 4196 (1973); c) *U. Schöllkopf*, Angew. Chem. *80*, 603 (1968); Angew. Chem. Int. Ed. Engl. *7*, 588 (1968); d) *W. Kutzelnigg*, Tetrahedron Lett. *1967*, 4965; e) *D. T. Clark, G. Smale*, Tetrahedron *25*, 13 (1969); f) *W. Kirmse, T. Engbert*, Angew. Chem. *91*, 240 (1979); Angew. Chem. Int. Ed. Engl. *18*, 228 (1979); g) Ref. [50].

[75] *M. Saunders, P. Vogel, E. L. Hagen, J. Rosenfeld*, Acc. Chem. Res. *6*, 53 (1973).

[76] *B. J. Stapleton, R. D. Bowen, D. H. Williams*, Tetrahedron *34*, 259 (1978).

[77] *H. Schwarz, W. Franke, J. Chandrasekhar, P. von R. Schleyer*, Tetrahedron *35*, 1969 (1979).

[78] a) *M. J. S. Dewar, H. S. Rzepa*, J. Am. Chem. Soc. *99*, 7432 (1977); b) *D. A. Krause, R. J. Day, W. L. Jorgensen, R. G. Cooks*, Int. J. Mass Spectrom. Ion Phys. *27*, 227 (1978); c) *R. J. Day, D. A. Krause, W. L. Jorgensen, R. C. Cooks, ibid. 30*, 83 (1979); d) *R. J. Day, R. G. Cooks, ibid. 35*, 293 (1980).

[79] a) *R. G. Cooks, J. H. Beynon, R. M. Caprioli, G. R. Lester:* Metastable Ions, Elsevier, Amsterdam 1973; b) *D. H. Williams*, Acc. Chem. Res. *10*, 280 (1977); c) *R. D. Bowen, D. H. Williams, H. Schwarz*, Angew. Chem. *91*, 484 (1979); Angew. Chem. Int. Ed. Engl. *18*, 451 (1979).

[80] a) *J. L. Holmes, A. D. Osborne, G. M. Weese*, Org. Mass Spectrom. *10*, 867 (1975); b) *G. Hvistendahl, D. H. Williams*, J. Chem. Soc. Perkin Trans. II *1975*, 881; c) J. Am. Chem. Soc. *96*, 6753, 6755 (1974); d) *W. T. Huntress, Jr., D. K. Sen Sharma, K. R. Jennings, M. T. Bowers*, Int. J. Mass Spectrom. Ion Phys. *24*, 25 (1977).

[81] a) *J. C. Polanyi*, Acc. Chem. Res. *5*, 161 (1972); b) *T. Carrington, J. C. Polanyi* in *J. C. Polanyi:* MTP Int. Rev. Sci. Phys. Chem., Ser. I, Vol. 9, University Park Press, Baltimore 1972; c) *N. W. Cole, G. J. Rickard, J. R. Christie, P. J. Derrick*, Org. Mass Spectrom. *14*, 337 (1979).

[82] For organometallic compounds related to *(131)* see: a) *V. R. Müller, L. G. Sneddon, D. C. Beer, R. N. Grimes*, J. Am. Chem. Soc. *96*, 3090 (1974); b) *L. G. Sneddon, D. C. Beer, R. N. Grimes, ibid. 95*, 6623 (1973).

[83] *E. D. Jemmis, P. von R. Schleyer*, J. Am. Chem. Soc., in press.

# Physical Methods for the Microanalysis of Solids—General Significance, Recent Developments, and Limitations

By Manfred Grasserbauer[*]

The characterization of solid systems by physical methods ("physical analysis") is one of the most important future-orientated areas of analytical chemistry. Important developments are the increase of the informational content of analytical signals by application of mathematical methods, the investigation of extremely small amounts (microanalysis), as well as concentrations (trace analysis). New developments in analytical methodology and strategy in micro and surface analysis permit, for example, the direct identification of compounds in individual phases in the solid state, the quantitative elemental analysis of aerosol particles in the submicrometer region (identification of asbestos fibers), and highly sensitive distribution analysis of trace elements in semiconductors. Important technological-scientific problems can be explained in this way.

## 1. Definition, Significance and General Characteristics of Physical Methods of Microanalysis

On the basis of *Malissa*'s[1] division of analytical chemistry into chemical, physical, and biological sectors and of the definition of analytical chemistry recommended by a group of the Working Party on Analytical Chemistry (WPAC) of the Federation of European Chemical Societies (FECS)[2], it can be said that "Physical analysis is the science of extracting and evaluating chemical information on material systems with the aid of physical reagents".

The prefix "micro" in front of "physical analysis" indicates either that only very small quantities of the sample are used and determined (as in the general concept of microanalysis), or that microregions of nanometer to micrometer dimensions are characterized.

The "reagents" currently used in the realm of physical microanalysis are photons, electrons, protons, neutrons, and free ions.

To permit a general description of the part played by physical microanalysis in the characterization of solids the very term "characterization" must be more rigorously defined. A very good definition has been produced by the US National Academy of Sciences[3]:

"Characterization describes *those features* of the *composition* and *structure* of a material that are *significant* for a *particular preparation, study of properties* or *use* and *suffice* for *reproduction of the material*".

This means that the characterization of a solid includes information on
its average chemical composition,
the distribution of elements and phases,
the geometric structure, and
the electronic structure.

Figure 1 gives a synopsis of the most important and the most commonly used methods for obtaining this information. These are predominantly physical micromethods.

This is not to say chemical analysis has become obsolete. It still has a major role to play, especially for bulk analyses. Chemical methods, often being more accurate, are used for calibration, and when applied to the separation and concentration of trace elements significantly broaden the scope of physical methods; finally they are significant for a wide range of elements and substance groups for which only chemical techniques are applicable. Whereas in the last few decades chemical have rather tended to be eclipsed by physical methods, a renaissance of chemical analytical techniques now seems to be underway. This can be ascribed largely to a combination of chemical preparation steps with physical methods of determination, as impressively demonstrated by *Tölg*[4].

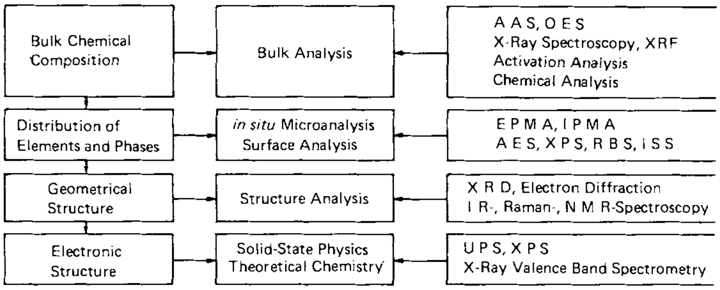


Fig. 1. Analytical characterization of solids. Abbreviations:

AAS = Atomic Absorption Spectrometry
OES = Optical Emission Spectrometry
XRF = X-Ray Fluorescence Analysis
EPMA = Electron Probe Microanalysis
IPMA = Ion Probe Microanalysis (also denoted by SIMS—Secondary Ion Mass Spectrometry)
AES = Auger Electron Spectrometry
XPS = X-Ray Photoelectron Spectrometry
RBS = Rutherford-Backscattering Spectrometry
ISS = Ion Scattering Spectrometry
XRD = X-Ray Diffraction Analysis
UPS = UV Photoelectron Spectrometry

In spite of these important new developments, in general it can be said that the advances in the analysis of solids achieved in recent decades can be traced to the application of physical micromethods.

---

[*] Prof. Dr. M. Grasserbauer
Institut für Analytische Chemie der Technischen Universität
Getreidemarkt 9, A-1060 Wien (Austria)

0570-0833/81/1212-1004 $ 02.50/0

The most important characteristics of physical methods are as follows:

1. High information content: suitable methods are available for bulk analyses, for studies of distributions, and for structural analyses. The information is directly concerned with elementary particles, whose nature, number, and arrangement determine the properties of a given substance (valence electrons, core electrons, atomic nuclei).
2. High absolute detection power: typical absolute detection limits are, for example, $10^{-6}$ to $10^{-12}$ g. In extreme cases the absolute detection limit can be as low as $10^{-20}$ g (microanalysis).
3. High relative detection power: typical relative detection limits are in the range mg/g to ng/g. In individual cases pg/g can be directly detected, or fg/g after concentration (trace analysis).
4. High selectivity, and generally even specificity of the analytical signal: this permits direct, unambiguous qualitative and quantitative analyses of complex systems of substances, usually without preliminary separation.
5. Small dimensions of the analytical volumes: by the selection of suitable (focusable) "reagents", signals, and conditions of excitation, regions from nm to µm can be selectively investigated and analyzed in solids (*in situ* micro- and surface-analysis).
6. Automazation: this enables the rapidly increasing number of analyses with tolerable expenditure of time, costs, and personnel to be coped with for the first time.

## 2. Trends in Development of Methods for Physical Microanalysis

Starting out from the characteristics of physical microanalysis, the targets of the most important development studies and trends, can be summarized thus:

1. Increase of the informational content of the analysis to obtain further-reaching (more detailed) information (*e.g.* compound-specific analysis of microregions in a solid with X-ray valence band spectroscopy or laser-Raman microdomain analysis[5]).
2. Elevation of the absolute detection power (reduction of absolute detection limits) of methods to enable the characterization of still smaller samples or smaller regions in the solid samples (*e.g.* phase analysis in the submicrometer range, characterization of surface layers in the nm range, and *in situ* micro-surface analysis with scanning Auger electron spectroscopy[6]).
3. Elevation of the relative detection power by the development of more sensitive trace-analysis techniques, by combination with chemical concentration methods (*e.g.* Hg in water or air[7]) or by the application of *in situ* trace methods such as ion-beam microanalysis (*e.g.: in situ* micro-trace analysis, trace analysis of surfaces, or thin layers).
4. Enhancement of the specificity of the analytical signals by mathematical signal processing (*e.g.* peak deconvolution, factor analysis, clustering techniques, general; incorporation of chemometrics[8]).
5. Increasing degree of automation of analytical systems by further development of computerized multielement techniques (*e.g.* ICP-Optimal Emission Spectrometry in process analysis[9]).

## 3. New Developments in *in situ* Micro- and Surface-Analysis

A substantial part of the present-day development of the analysis of solids, and also of analytical chemistry, falls into the sphere of *in situ* micro- and surface-analysis, two areas that are becoming increasingly important.

Since it would be impossible even to approximately describe all the important advances of the last few years in detail, three examples of the further development of microdomain and surface analysis have been selected. These examples are intended to illustrate the strategy and systematics that can be applied in analytical research in this field, but also to reflect the present state of the individual subareas.

On the basis of specific results, the selected themes will concentrate on the fundamental problems relating to
direct compound-specific *in situ* micro-analysis of solids by X-ray valence band spectroscopy;
quantitative X-ray microanalysis in the submicrometer range, and
quantitative characterization of trace element distributions.

### 3.1. Compound-Specific Analysis by X-ray Valence Band Spectrometry

The direct compound-specific analysis of microdomains (phases) of solids is of fundamental interest for clarifying the question of the maximum obtainable informational content of an X-ray spectrum, but also of practical significance for the identification of inclusions containing light elements that are difficult to quantify (*e.g.* B, N, C, O), or which are smaller than the analytical volume of the electron microprobe (a few micrometers in diameter).

The principle of this analytical method consists of an evaluation of the fine structure of the X-ray valence band spectrum excited in a microdomain of the sample with an electron microprobe. The spectrum reproduces in its intrinsic form the density of states of valence-band electrons taking part in the transition and thus, because of the dependence of the density of states on the type and arrangement of the atoms, constitutes a clear fingerprint of the excited compound. The intrinsic X-ray signal therefore contains not only clear information on the excited atom but also on its chemical bonding and hence on the compound in question[10].

In comparison with the intrinsic X-ray valence band spectrum, the measured spectrum is distorted by convolution with the absorption function of the X-ray radiation in the sample and the spectrometer function (constant), and has a high noise level due to the low signal intensity with the conventional analog (spectrometer scanning plus analog intensity measurement) recording techniques.

This can be clearly seen in the example of the $O_K$ spectra of $Cu_2O$, CuO, $2CuCO_3 \cdot Cu(OH)_2$, and $CuCO_3 \cdot Cu(OH)_2$ (Fig. 2). Direct compound identification is limited to a restricted number of systems with large differences in the spectral structure. To increase the number of these systems it is necessary to achieve a more precise reproduction of the fine structure by further development of the measurement techniques and to look for mathematical procedures which allow characterization of very slight differences in the fine structure.

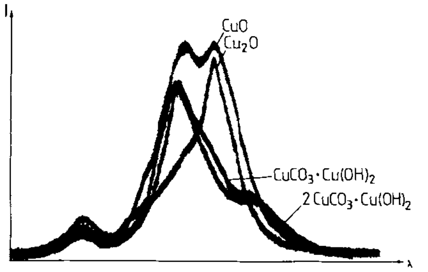


Fig. 2. X-Ray valence band spectra ($O_K$ bands) of various copper compounds and their characteristic structural parameters.

| Compound | $\lambda_{max}$ [Å] | Free-width at half maximum [Å] | Asymmetry factor |
|---|---|---|---|
| $Cu_2O$ | 23.662 | 0.14 | 1.1 |
| CuO | 23.658 | 0.25 | 0.8 |
| $2CuCO_3 \cdot Cu(OH)_2$ | 23.554 | 0.17 | 1.9 |
| $CuCO_3 \cdot Cu(OH)_2$ | 23.575 | 0.17 | 2.2 |

The improvement in the reproduction of the fine structure can be achieved by the application of digital recording with computer control of the spectrometer, and smoothing the spectra with the aid of a 5-point polynomial (after *Savitzky* and *Golay*[11]). The $Cu_{L\alpha}$ spectra of 14 copper compounds are shown in Figure 3[12]. Each spectrum was recorded in 512 measurement steps, each of 2 sec.The accuracy of the determination of the peak maximum wavelength (as a characterization parameter of the fine structure, *i.e.* the chemical shift) is 0.04 pm ($=4 \times 10^{-4}$ Å), but because of the small shift differences between similar compounds, an exact determination of this wavelength is insufficient for a definite identification of each individual compound on the basis of the $Cu_{L\alpha}$ spectrum: the different shapes of the bands should also be taken into account.

For this purpose it is necessary to quantify the differences in the spectral structure as accurately and objectively as possible, since mere optical distinction is insufficient and, moreover, a numerical description of the fine structure is necessary for storage in a spectrum data bank.

The principle of structure characterization of the X-ray valence band spectrum is that the form of the spectrum is represented by a nine-dimensional (band) vector (Fig. 4) which represents the signal width as a function of the intensity (signal height) at nine points and reproduces very clearly small differences in shape, as can be seen by comparing the Lα signals of Cu, $Cu_2O$, and CuO. Since according to this concept, the fine structure of a peak is represented as a point in (abstract) nine-dimensional space, it is sensible to transform the information, with least possi-

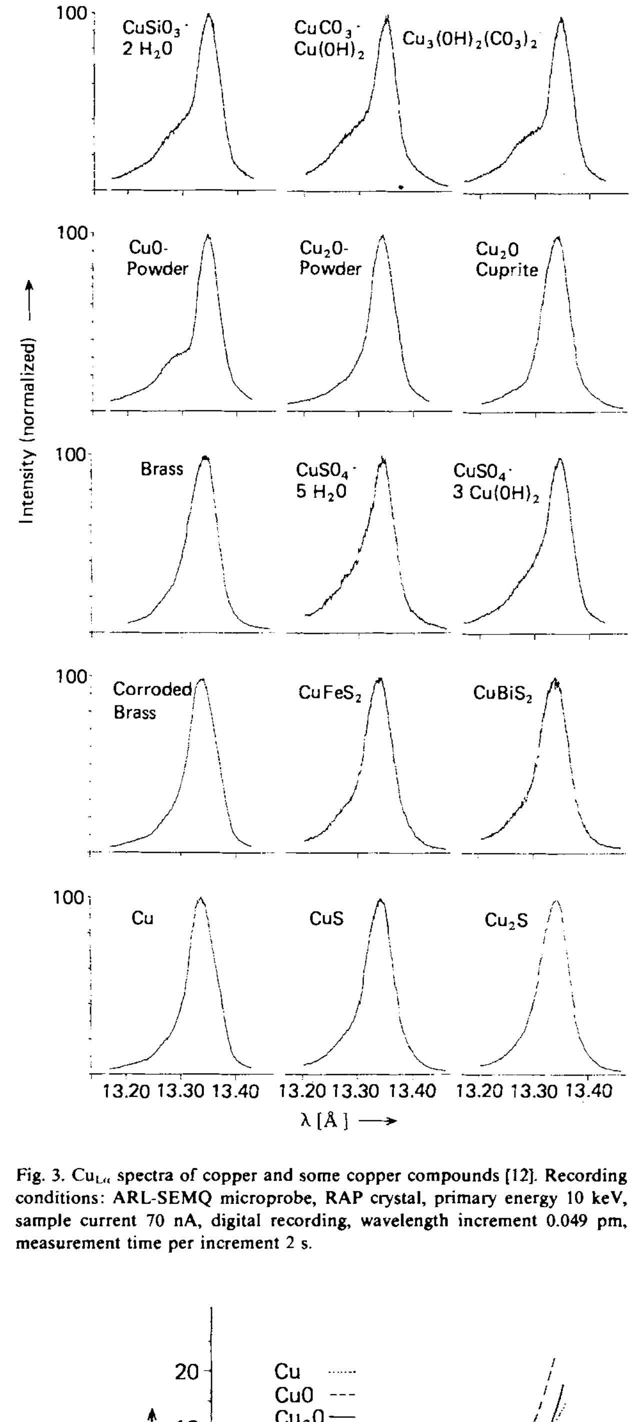


Fig. 3. $Cu_{L\alpha}$ spectra of copper and some copper compounds [12]. Recording conditions: ARL-SEMQ microprobe, RAP crystal, primary energy 10 keV, sample current 70 nA, digital recording, wavelength increment 0.049 pm, measurement time per increment 2 s.

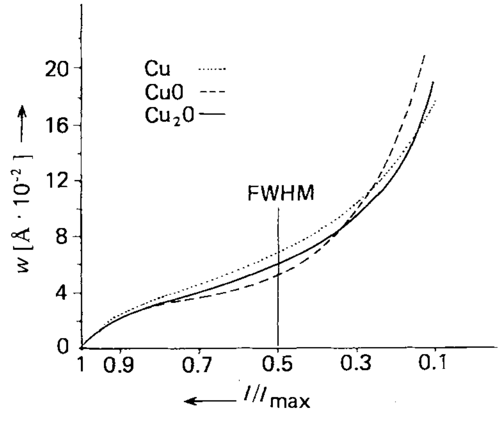


Fig. 4. Characteristic band lines of $Cu_{L\alpha}$ spectra of Cu, $Cu_2O$, and CuO [12]. $w$ = width, FWHM = free-width at half maximum.

ble information losses, into the easily pictured two-dimensional space. The representation space transformation method described by *Lin* and *Chen*[13] is suitable for this purpose. In this method, the distances of the points in nine-dimensional space from two suitably selected auxiliary functions (Gaussian functions) are determined in two directions and used as x, y-coordinates in a two-dimensional representation. These new coordinates $p_1^*$ and $p_2^*$ now give the shape of the signal in the two-dimensional representation (Fig. 5). The fine structure of a spectrum, and thus the identity of a given compound is represented as a point. The reproducibility of the fine structure measurement is shown by a circle (five measurements, 3 s value, 99% confidence interval). The distances between the circles correspond to differences in the spectral structure measured, and hence to the distinguishability of the compounds from other (similar) ones.

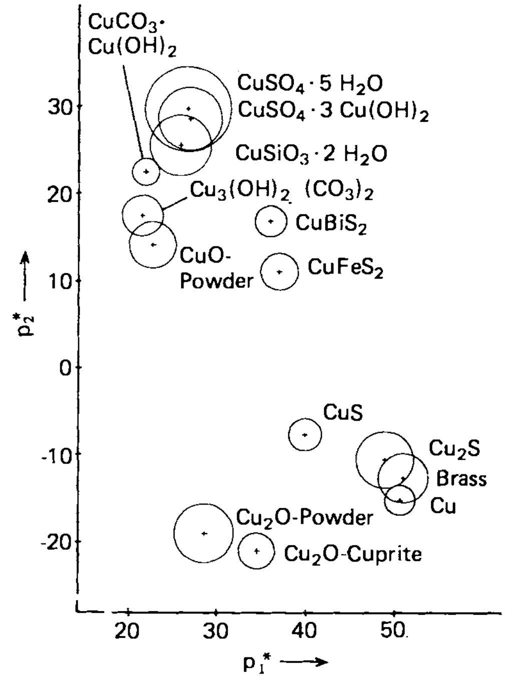


Fig. 5. Characterization of copper compounds on the basis of structure of the $Cu_{L\alpha}$ valence band spectrum in representation space. The circle diameters correspond to a confidence interval of 0.99 [12].

As the example shows, with the aid of this method even compounds with very slight differences in fine structure can be clearly identified simply from an evaluation of the X-ray valence band spectrum. Even compounds of very similar composition such as $CuCO_3 \cdot Cu(OH)_2$ and $2CuCO_3 \cdot Cu(OH)_2$ can be clearly distinguished. Differentiation with an electron microprobe on the basis of elementary analysis would be very difficult, because of the similar copper contents (55.1 and 57.2 wt-%).

The system described has also been used successfully for the characterization of iron compounds[14].

### 3.2. Quantitative X-ray Microanalysis in the Submicrometer Range

Quantitative X-ray microanalysis of inclusions and phases in solids can usually be carried out with an electron microprobe with an accuracy of a few relative percent[15], and has now joined the ranks of routine methods. The lateral resolution of the method is a few microns, because of scattering of the primary electrons in the bulk of the sample, and for many problems this limitation prevents the analysis of phases that, although smaller, still have a bearing on the properties, since when they are excited the matrix material is also determined. Quantitative analysis of submicrometer regions in bulk samples is virtually impossible. To identify such small particles it is necessary for them either to be isolated from the matrix as individual particles on an electron-transparent substrate, or at least to be available as thin-film samples. Both these preparation techniques are used with varying degrees of success.

The second basic limitation of this analysis is that, because of the small volume analyzed, extremely low X-ray intensities are produced.

The electron microprobe and the conventional scanning electron microscope are not suitable for quantitative analyses in the submicrometer range. It was only the introduction of the scanning transmission electron microscope, enabling highly sensitive generation and measurement of X-ray spectra because of high primary electron currents with very small beam diameters (nA at 10 nm, due to the special design of the objective lens) and large semiconductor detectors at very small distances from the sample (detector area 30 $mm^2$) that permitted the penetration of quantitative X-ray analysis into the submicrometer range[16].

Since some of the problems involved in analysis in the submicrometer range are completely different from those encountered in the microrange analysis of bulk samples, a careful analytical process development must be undertaken for each problem, and an appropriate strategy devised. This will be illustrated in greater detail using the example of a very difficult and complex analytical problem, namely the identification of asbestos fibers[17].

Asbestos fibers are found in dust fractions entering the lungs in cities (from brakes in motor vehicles, from the facades and roofs of buildings) in concentrations of a few $ng/m^3$, and in substantially higher concentrations in the asbestos-processing industry, in the vicinity of asbestos mines, and in certain cases in drinking water (Duluth, Lake Superior, taconite mining in Silver Bay)[18].

Although contradictory statements have been made about the influence exerted by such asbestos contents, it has been established that the prolonged effects of higher doses can give rise to lung cancer. It is agreed unanimously that suitable, highly sensitive analytical methods must be devised to allow chemical identification of fiber-like particles in water, air, and the soil and thus to show whether or not asbestos is present, and if so, what type and in what amount. The strategy of asbestos analysis is thus determined by the statement of the problem and by the boundary conditions (Fig. 6). The boundary conditions for the analyst are the normally very low concentrations of asbestos fibers in a sample, which rules out the application of a compound-specific averaging analysis such as X-ray diffractometry, and the small size of the fibers (thickness *ca.* 20—500 nm, length *ca.* 100 nm to 10 μm).

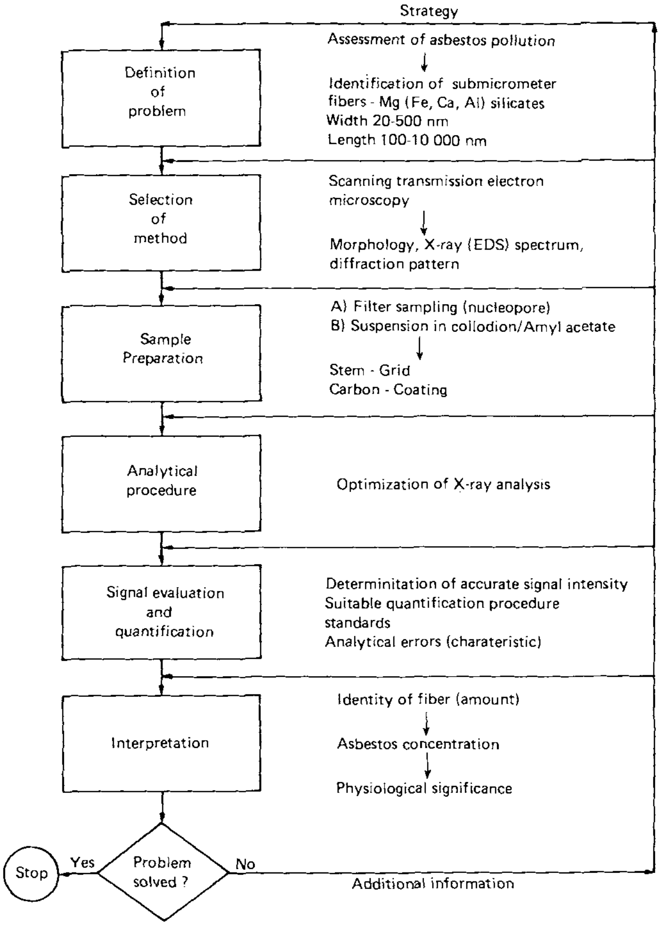


Fig. 6. Analytical strategy for the identification of asbestos fibers.

Thus, the only analytical method left is scanning transmission electron microscopy (STEM), which permits a detection of fibers in the particle conglomerate (Fig. 7), and an identification of the individual fibers by quantitative X-ray microanalysis and electron diffraction.

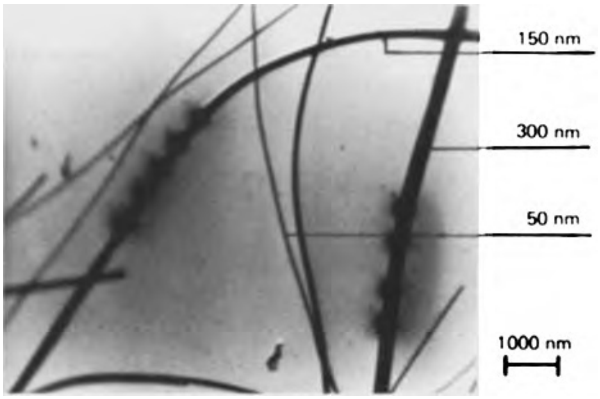


Fig. 7. STEM micrograph of asbestos fibers (chrysotile).

For the STEM investigation, the particles must be separated from one another on an electron-transparent substrate. Depending on the nature of the sample, various techniques of sample collection have been optimized for this purpose, such as extraction from air or water with Nuclepore® filters or transfer to carbon TEM grids from suspensions in collodion and amyl acetate.

The next step is optimization of the X-ray microanalysis—essentially in the direction of highest sensitivity and reproducibility of the results. The excitation energy ($E_0=40$ keV), the beam current ($i_s \approx$ nA), the angle of incidence of the primary beam ($\alpha=55°$), the recording angle ($\vartheta=24°$), and the distance of the detector from the fiber (20 mm) are all optimized.

Measurement of a fiber under the optimized conditions produces an X-ray spectrum characterized by a fairly high signal-to-background ratio (Fig. 8). From this X-ray spectrum the characteristic intensities must be picked out by suitable mathematical techniques with the highest possible accuracy. For this purpose, several steps are necessary—

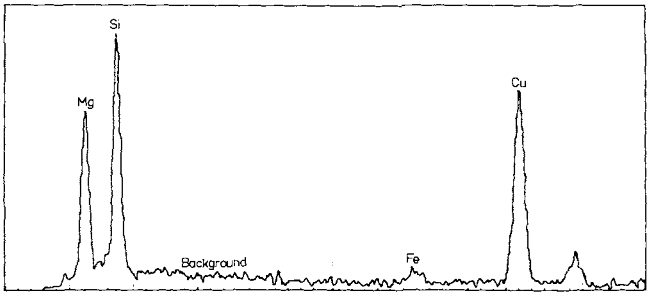


Fig. 8. X-Ray spectrum of an asbestos fiber (chrysotile), diameter 200 nm (Jeol 100C, excitation energy $E_0=40$ keV, measurement time t=200s).

1. Smoothing of the background
2. Subtraction of the background by linear interpolation
3. Signal integration.

In addition, the systematic and statistical errors must be calculated in the determination of the characteristic X-ray intensity. Systematic errors may arise from the following sources:

During excitation:

1. Excitation of the copper grid—not important for asbestos
2. Beam artefacts—loss of alkali or $H_2O$—low with asbestos
3. Contamination (Fig. 9)—radiation absorption, dependent on the fiber diameter; maximum 3%.

Fig. 9. Scanning transmission electron microscope photograph of olevine particle Contamination cone; for conditions see Fig. 8.

During evaluation:

1. Nonlinear background
2. Nonoptimized integration width

Statistical errors which must be considered are:

1. Statistical uncertainty of the X-ray intensity—especially in the case of elements present in low concentration
2. Statistical fluctuations of the background.

Evaluation of all these errors reveals that in the determination of the X-ray intensity of the principal elements occurring in asbestos fibers (Mg, Si, Ca, Al, Fe) the statistical errors are predominant (200 nm chrysotile fibers: Si 4 rel-%, Mg 10 rel-%, Fe 37 rel-%).

In the quantification it must be borne in mind that the X-ray intensities measured are dependent on the particle size, since the number of electrons penetrating the fiber, the energy they lose in the fiber, and the absorption of the generated X-ray intensity on exit under constant analytical conditions are all a direct function of the fiber diameter (Fig. 10).

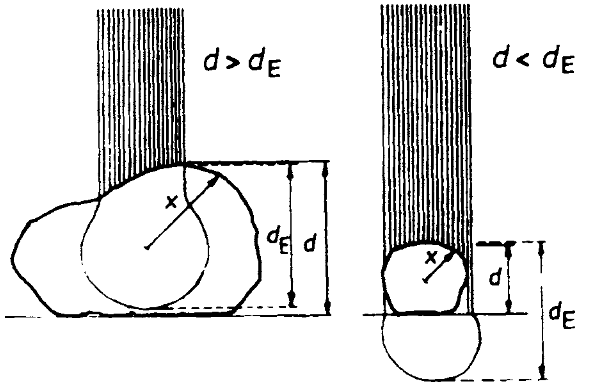


Fig. 10. Generation of the X-ray signal in submicrometer particles in comparison with large particles [16].
For large particles

$c_A \approx (I_A/I_A^*) c_A^*$ applies,

for submicro particles,

$I_A = f(d)$

$N_e$, transmission, and absorption are considered

$I_A = I_A^0 \cdot e^{-(\mu/\rho)\rho \cdot x}$

$I_A$, $I_A^*$ = (measured) characteristic X-ray intensities of element A in the sample and standard

$c_A$, $c_A^*$ = concentrations of element A in the sample and standard

$d$ = particle diameter

$d_E$ = depth of penetration of the primary electrons in a bulk sample (a few microns)

$N_e$ = number of electrons on the particle

$x$ = exit path length of the X-rays produced [cm]

$I_A^0$ = characteristic X-ray intensity of A excited within the particle

$\mu/\rho$ = mass absorption coefficient [cm$^2$ g$^{-1}$]

$\rho$ = density [g cm$^{-3}$].

Thus, the only method of quantification available is a ratio method in which the intensity ratios of the elements in the fiber are connected with their concentration ratios by a sensitivity factor ($k_{A/B}$)[19]:

$$\frac{c_A}{c_B} = k_{A/B} \cdot \frac{I_A}{I_B}$$

For a specific pair of elements (A and B) this sensitivity factor depends only on the fiber diameter and on the matrix, whereby the influence of the matrix on the main elements of asbestos fibers is slight in comparison with the dependence on the fiber diameter. Well-defined homogeneous standard substances (pure asbestos fibers) must be used for the determination of $k_{A/B}$ as a function of fiber diameter.

The values for a given fiber diameter are used for the analysis of the unknown fibers having the same diameter. The standard substances (chrysotile, crocidolite) are characterized by atomic absorption spectroscopy (AAS).

The accuracy of the analysis is determined above all by the statistical error of the determination of the X-ray intensities and by the accuracy of the reference analysis, *i.e.* by homogeneity of the calibration substances, since with the AAS *ca.* 100 mg of sample analyzed and with is STEM only *ca.* $10^{-12}$ mg.

When all the factors have been taken into account in accordance with the error propagation theorem, a relative analytical error of *ca.* ±25 rel-% is found for the quantitative analysis of the main elements in asbestos fibers *ca.* 200 nm thick. This is in sufficiently good agreement with the reference analyses (AAS) (Table 1).

Table 1. Comparison of the analytical values of asbestos fibers determined by the two methods.

| Methods | $c_{Mg}/c_{Si}$ | $c_{Fe}/c_{Si}$ |
|---|---|---|
| Atomic Absorption Spektrometry (AAS) | 1.040 | 0.096 |
| Scanning Transmission Electron Microscope (STEM) | 0.726 | 0.108 |
| Difference | −30.2% | +12.5% |

STEM analysis thus yields an often sufficiently accurate value for concentration ratios of measurable elements in the fiber and permits the determination of a stoichiometric empirical formula (oxygen is assigned in accordance with the oxidation state of the cations, $H_2O$ or OH are not determinable). This in turn determines (like the intensity ratios themselves) the type of the asbestos, in spite of a considerable mixing range (Table 2).

The identification of asbestos fibers in dust or water samples is supplemented by electron diffraction, which provides typical patterns (especially for chrysotile). This

Table 2. Current types of asbestos: empirical formulas, as well as characteristic concentration and X-ray intensity ratios of the main elements. Exitation energy $E_0 = 40$ keV, current $i_S = 10$ nA, fiber diameter $d = 200$ nm.

| Type of asbestos | Empirical formula | Conc. ratio | Int. ratio |
|---|---|---|---|
| Chrysotile | $Mg_3Si_2O_5(OH)_4$ | Mg : Si = 0.73 | 0.69 ± 0.06 |
| Crocidolite | $Na_2Fe_3^{II}Fe_2^{III}Si_8O_{22}(OH,F)_2$ | Fe : Si = 1.15 | 0.72 ± 0.08 |
| Amosite | $(Mg,Fe^{II})_7Si_8O_{22}(OH)_2$ | Mg : Si = 0.21 | 0.19 ± 0.03 |
| | | Fe : Si = 0.88 | 0.55 ± 0.05 |
| Tremolite | $Ca_2Mg_5Si_8O_{22}(OH,F)$ | Ca : Si = 0.22 | 0.26 ± 0.04 |
| | | Mg : Si = 0.27 | 0.25 ± 0.04 |
| Anthophyllite | $(Mg,Fe^{II})_7Si_8O_{22}(OH,F)_2$ | Mg : Si = 0.31 | 0.29 ± 0.04 |
| | | Fe : Si = 0.41 | 0.26 ± 0.03 |

$k_{Mg/Si} = 1.06 \pm 0.1$; $k_{Fe/Si} = 1.59 \pm 0.18$; $k_{Ca/Si} = 0.81 \pm 0.12$.

permits the construction of a scheme of identification based on a combination of data relating to the fiber's morphology (ratio of length to width), structure (electron diffraction), and elemental composition (Fig. 11).

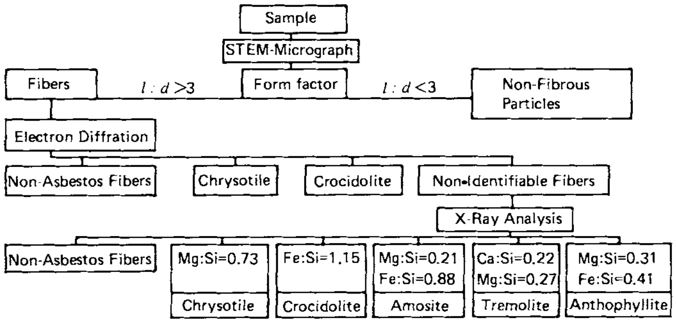


Fig. 11. Identification scheme for asbestos fibers in STEM (Concentration ratios were derived from X-ray-analytical data; l = length, d = diameter).

The quantity of the asbestos fibers, or their concentration, is determined from STEM pictures or stereometric processes. Although this analytical technique is very laborious, it constitutes the only method that yields results of sufficient accuracy for an evaluation of asbestos pollution.

### 3.3. Quantitative Distribution Analysis of Trace Elements

In many branches of materials science, characterization of the distribution of the trace elements (concentrations $\leq 0.01\%$) is one of the essential tasks of analytical chemistry, since trace amounts may exert a decisive influence on the properties of the material (*e.g.* in hard metals or steel), or may yield important information about the system under examination from their quantity and distribution (*e.g.* in the case of geological samples, information can be obtained on the rock-forming processes, age, and geochemical prospecting parameters).

If the trace elements are locally enriched to above *ca.* 0.1—1%, their distribution can be determined with the aid of electron probe microanalysis. Quantitative microdomain analysis gives the local concentration, while a stereometric evaluation, *e.g.* using the principle of X-ray micro-linear analysis or an automated area analysis[20,21] reveals their average content and distribution. In the event of an enrichment of the trace elements on the surfaces of the solid samples surface analysis methods, such as Auger electron spectrometry (AES), X-ray photoelectron spectrometry (XPS), and ion-scattering can be successfully applied. The characterization of the distribution of locally enriched trace elements has already become largely routine.

A distribution analysis of the trace elements when these are not locally enriched is substantially more difficult. The methods then used for the characterization must have, besides a high lateral resolution, a high detection capacity for microdomain analysis. At present, ion probe microanalysis (IPMA) is the most appropriate method for the *in situ* micro-trace analysis of solid samples[22]. This method has a lateral resolution of a few microns, a depth-resolution in the nanometer range, and (for many elements) detection limits of µg/g to ng/g.

In spite of these outstanding characteristics for *in situ* microtrace analysis, only a limited number of problems have so far been solved. This is essentially due to the fact that practical difficulties are encountered, caused primarily by interference between the analytical ions and the molecular ions, and only the present generation of instruments has offered some prospect of eliminating these problems (at least in part). In addition, full details of the interaction between primary ions and solids have not yet been adequately explained, and hence considerable quantification problems still remain for many elements and matrices. The greatest progress has undoubtedly been in the analysis of the distribution of dopants in semiconductors.

Knowledge of the total concentration and the distribution of the dopant elements is of major significance to semiconductor technology. In addition, the total dopant concentration must also be determined. Whereas the concentration of the electrically active fraction determines the maximal current, and the depth distribution of the active fraction determines the amplification factor of a transistor, the inactive fraction influences the diffusion behavior of the dopant elements during manufacture (*e.g.* by cluster formation). For the quite customary high dopant concentrations of more than $10^{21}$ atoms/cm$^3$ (*e.g.* for MOS transistors), the electrically inactive fraction is sometimes several times greater than the active fraction.

For this reason, the mathematical models used today to describe the diffusion behavior are really only accurate for concentrations below $5\times10^{19}$ atoms/cm$^3$[23]. At higher doping levels, the concentration dependence of the diffusion coefficients must first be exactly determined and incorporated into the model. The construction of a sufficiently accurate diffusion model is therefore of significance, because in this way it is also possible to control lateral (x,y-direction) diffusion processes occurring in the thermal treatment of semiconductor components during their manufacture. Because of the small size of the lateral structure ($\leq 1$ µm), analytical characterization of the lateral distribution is practically impossible; yet it is necessary to known this. At present, only the determination of the dopant distribution in planar semiconductors with relatively large surface areas has been determined analytically (*e.g.* implanted Si disks, with or without diffusion treatments).

Characterization of semiconductor components must include a quantitative (depth) distribution analysis of the total dopant concentration, and a separate distribution analysis of the electrically active fraction, since the inactive fraction can be determined only by difference. It is necessary to determine both profiles with a high degree of accuracy (regarding the scales of concentration and depth), and both should cover the widest possible range of concentration. Since the currently customary limits of (local) dopant element concentrations range from *ca.* $5\times10^{21}$ to *ca.* $10^{14}$ atoms/cm$^2$, an extremely wide dynamic range of $5\times10^7$ and very high sensitivity are required.

As an example of the possibilities and limitations of the distribution analysis of trace elements in semiconductors, only the situation with the most important dopants for silicon semiconductors—boron and arsenic—will be described. The analytical characteristics of the most common methods for the analysis of the electrically active fraction and for the total dopant concentration are summarized in Table 3.

Table 3. The most important methods used for the distribution analysis of dopants in semiconductors and their characteristics. NAA = Neutron Activation Analysis.

| Methods | Sensitivity limit [atoms/cm$^3$] | Depth resolution [nm] |
|---|---|---|
| 2-point resistance measurement | $10^{14}$ | 40 |
| 4-point resistance measurement | $10^{17}$-$10^{18}$ | 15 |
| NAA $^{10}B(n,\alpha)^7Li$ | $10^{14}$-$10^{15}$ | 20 |
| NAA $^{75}As(n,\gamma)^{76}As$ | $10^{17}$ | 20 |

The distribution of the electrically active fraction is determined by measuring the surface conductivity. The depth distribution is obtained either by measurements on tapered sections with an angle of inclination of 1° (2-point resistance measurement) or by repeated measurements on a planar sample after chemical dissolution of the topmost layer (*ca.* 10—50 nm) by specific anodic oxidation and with 30% hydrofluoric acid (4-point resistance measurement).

The advantage of 2-point resistance measurements is the high sensitivity ($10^{14}$ atoms/cm$^3$). The disadvantages are the considerable problems associated with the preparation of a polished section with a 1° angle of taper. The 4-point resistance measurement, on the other hand, while being very time-consuming is essentially easy to perform; however, its sensitivity is considerably lower (*ca.* $10^{17}$ atoms/cm$^3$).

Elemental analysis methods can be used to determine the distribution of the total dopant concentration. To date, neutron activation analysis of the dopant element in combination with repeated chemical removal of the topmost layer has been used most frequently for this purpose. Apart from the fact that the method is extremely lengthy, neutron activation analysis (with the usually readily available flux density) does not often have the sensitivity required and the necessary dynamic range of *ca.* $10^7$.

A second possibility is to record the depth profiles by an ion microprobe technique[24-29]. This method has *a priori* the great advantage that the depth profiles can be recorded directly within a short time. However, the depth profiles are given in the form of intensity of the measured secondary ion current *versus* time, and hence must be calibrated. This in turn requires the development of quantification processes characterized by a high degree of accuracy. The second disadvantage until recently was that the sensitivity was not sufficient for some dopant elements.

Progress in direct dopant-distribution analysis only came about as a result of the development of a new generation of instruments (*e.g.* CAMECA IMS-3F) with high primary-ion intensities (a few μA with a beam diameter of 50 μm), more sensitive secondary-ion measurements (focusing of the secondary ions emitted from the sample surface into the entrance slit of the mass spectrometer, and a low-noise detection system), and possibilities of separating the analytical ion (the dopant) from interfering molecular ions (silicon-oxides and -hybrides) by energy filtering or by high-resolution mass spectrometry[30].

Under optimized working conditions it is possible, for example, to measure the depth distribution of boron with the necessary depth resolution of 10 to 50 nm (in the case of profile depths of 500—1000 nm) down to a minimum concentration of $10^{14}$ atoms/cm$^3$ ($\triangleq$ 1 ng/g) (Fig. 12a).

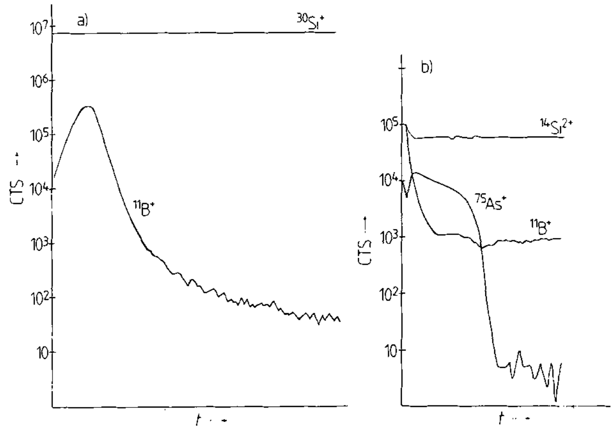


Fig. 12. a) Depth profile of boron in a silicon semiconductor, recorded with the ion microprobe. Primary ions $O_2^+$, primary ion current $i_P = 1000$ nA, excitation energy $E_0 = 10$ keV; $c_B = 5.8 \times 10^{19}$ atoms/cm$^3$, diameter $d = 1800$ nm; b) depth profile of arsenic in a silicon semiconductor, recorded with the ion microprobe. Primary ions $O_2^+$, primary ion current $i_P = 4000$ nA, excitation energy $E_0 = 13.0$ keV; $c_{As} = 4 \times 10^{19}$ atoms/cm$^3$, CTS signifies counts per unit time.

The distribution analysis of As is substantially more difficult, since this ion interferes with a silicon oxide ion ($^{75}As^+$ and $^{29}Si^{30}Si^{16}O^+$). This interference is eliminated by energy-filtering the atomic ion $^{75}As^+$ from the molecular ion, making use of the fact that atomic ions have a broader kinetic energy distribution than molecular ions. By selecting a carefully optimized energy threshold level, the molecular ions can be filtered out before entering the mass spectrometer. Thereby a fraction of the atomic ions (the fraction having energies lying in the range of kinetic energies of the molecule-ions) is also removed and is not measured. Loss of intensity by a factor of *ca.* 20 is, however, counterbalanced by an increase of the dynamic range by a factor of $10^4$.

Using energy filtering in a double-focusing mass spectrometer, a detection limit of *ca.* $10^{16}$ atoms/cm$^3$ ($\triangleq$0.5 μg/g) can be reached for the distribution analysis of As in Si (Fig. 12b). In comparison with the methods of elementaal analysis used up to now, this represents an improvement by a factor of 10-100.

Conversion of the time scale into a depth scale uses the sputter rates that can be calculated for the oxide layer and silicon using ellipsometry and interference microscopy.

In principle, quantification of the intensity axis can be carried out using measurements on an external standard. Sufficiently homogeneous standards of this kind are available for silicon samples, since doping can already be carried out during the manufacture of the single crystal. By normalizing the dopant intensity to a matrix ion ($^{28}Si^{2+}$) it is possible using this method, which corresponds to quantification with relative sensitivity factors, to determine maximum concentrations with an accuracy of *ca.* 5–10 rel-%.

For implanted semiconductor samples use can also be made of the integration method. The integrated intensity of a depth profile is directly proportional to the total dopant concentration. When the implantation dose (total concentration) is known, the proportionality factor can be determined after integration of the profile using a suitable polynomial. With this factor, the depth profile can be calibrated.

This method of integration yields highly accurate depth profiles (error 5—10 rel-%), as shown by comparative determinations with neutron activation analysis and electrical measurements (in this case with negligible cluster formation) (Fig. 13).

In principle, the use of ion beam microanalysis constitutes an essential improvement for characterizing dopants in semiconductors, and hence of *in situ* microtrace analysis in general.

In spite of this, the method still suffers from limitations, *e.g.* regarding the sensitivity towards As and the elimination of the chemical matrix effect. Despite the use of reactive oxygen primary ions, a sharp increase in the yield of secondary ions occurs in oxide layers, which can indicate spurious enrichment of the dopant element in the oxide layer (Fig. 13). One of the essential future tasks will be to improve the existing models for the quantitative determination of the matrix effects, or to develop new models. Since ion-beam microanalysis so far constitutes the only really feasible method for *in situ* trace analysis it is of considerable general significance.

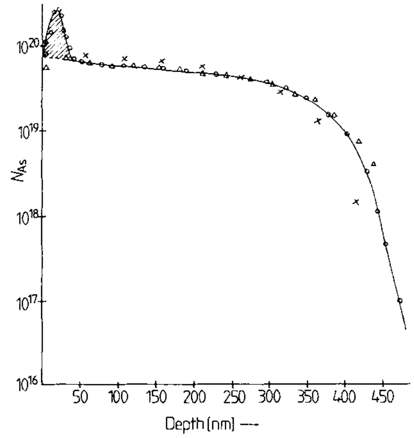


Fig. 13. Distribution of arsenic in a silicon semiconductor: comparison of the quantified IPMA profile (○) with results of electrical measurements and neutron activation analysis. (4 point resistence measurement) (△) and neutron activation analysis (×). The hatched area indicates the signal increase in the oxide layer. IPMA: Primary ions $O_2^+$, primary ion current $i_P = 1000$ nA, excitation energy $E_0 = 10$ keV.

## 4. Summary and Outlook

Advances in the field of physical microanalysis permit increasingly closer insight into the structure of matter. Most of the information necessary for the characterization of properties can be obtained, in the present state of the art, from "ideal" or simple substance systems, but there are still large gaps and problems in the characterization of "real", more complex systems, such as are encountered in most cases in technology. This applies, for example, to the sphere of (extreme) trace analysis of complex mixtures, such as airborne dusts, or to the surface characterization of industrial solids such as catalysts.

Reasons for this is that for many problems adequate methods do not exist and that not all the possibilities of deriving information by a combination of physical and chemical methods have yet been exhausted. The number of analytical laboratories equipped with the necessary instruments is small, even in the most highly industrialized countries.

Moreover, in many cases, the physical, mathematical, or information-theoretical foundations are still inadequately incorporated into the process of obtaining chemical analytical data. The integration of new concepts or of unifying principles, both in analytical chemistry as a whole[31,32] and for substances or partial regions such as surfaces[33], seems to be both sensible and potentially useful. The task of physical methods of analysis in the characterization of solids will further increase in future, above all in the wake of the burgeoning development of new technologies. Particularly important future fields of application will probably be energy research (*e.g.* characterization of photovoltaic solar cells and of materials for fusion reactors), the further development of semiconductor components (*e.g.* thin-film and surface analysis of optoelectronic elements), prospecting for raw materials (*e.g.* the application of "teleanalytical" methods for prospecting on seabeds), and, as ever, environmental questions (compound-specific analysis of physiologically active trace elements).

Received: April 15, 1981 [A 391 IE]
German version: Angew. Chem. *93*, 1059 (1981)

[1] *H. Malissa*, Z. Anal. Chem. *271*, 97 (1974).
[2] *R. Kellner:* Report on the FECHEM-Conference on Education in Analytical Chemistry in a Changing World, IUPAC International Newsletter on Chemical Education, in press.
[3] Report of Materials Advisory Board (MAB), no. 229 M, US National Academy of Sciences, Washington, D.C., 1967.
[4] *G. Tölg* in *H. Malissa, M. Grasserbauer, R. Belcher:* Nature, Aim and Methods of Microchemistry, Springer, Wien, in press.
[5] *M. Delhaye, P. Dhamelincourt*, J. Raman Spectrosc. *3*, 33 (1975).
[6] *H.-J. Dudek:* Auger-Elektronen-Mikroanalyse – eine neue Gerätegeneration für die Werkstoff-Forschung, Contribution from the Institut für Werkstoff-Forschung der Deutschen Forschungs- und Versuchsanstalt für Luft- und Raumfahrt, Köln 1977.
[7] *G. Tölg*, Pure Appl. Chem. *44*, 645 (1975).
[8] *B. R. Kowalski*, Anal. Chem. *52*, 112 R (1980).
[9] *K. Ohls*, Mikrochim. Acta, Suppl. *9*, 49 (1981).
[10] *M. Grasserbauer*, Z. Anal. Chem. *273*, 401 (1975).
[11] *A. Savitzky, M. J. E. Golay*, Anal. Chem. *36*, 1627 (1964).
[12] *H. Drack, S. Kosina, M. Grasserbauer*, Z. Anal. Chem. *295*, 30 (1979).
[13] *C.-H. Lin, H.-F. Chen*, Anal. Chem. *49*, 1357 (1977).
[14] *S. Kosina, M. Grasserbauer, H. Drack*, Talanta *26*, 765 (1979).
[15] *M. Grasserbauer* in *D. H. Carroll:* Proceedings of Euroanalysis III, Dublin 1978, Applied Science Publ., London 1979.
[16] *M. Grasserbauer*, Mikrochim. Acta *1978 I*, 320.
[17] *Ch. Malami, E. Hoke, M. Grasserbauer*, Mikrochim. Acta *1981 I*, 141.
[18] *C. C. Gravatt, Ph. D. La Fleur, K. F. J. Heinrich:* Proceedings of Workshop on Asbestos: Definitions and Measurement Methods, Gaithersburg 1977, NBS Spec. Publ. 506 (1978).
[19] *D. R. Beaman, H. J. Walker* in [18], p. 249.
[20] *H. Malissa, M. Grasserbauer, E. Hoke*, Mikrochim. Acta, Suppl. *6*, 205 (1975).
[21] *M. Pimminger, W. M. Terenyi, L. Kostelka, I. Cerny, M. Grasserbauer*, Mikrochim. Acta, in press.
[22] *A. Benninghoven, C. A. Evans, R. A. Powell, R. Shimizu, H. A. Storm:* Secondary Ion Mass Spectrometry II, Proceedings of the Stanford Conference 1979, Springer, Berlin 1979.
[23] *R. Tielert*, IEEE Trans. Electron Devices *ED-27*, 1497 (1980).

[24] *H. W. Werner*, Mikrochim. Acta, Suppl. *8*, 25 (1979).
[25] *T. W. Sigmon* in [22], p. 80.
[26] *C. W. Magee* in [22], p. 88.
[27] *A. M. Huber, G. Morillot, P. Merenda, N. T. Link* in [22], p. 91.
[28] *C. A. Evans, V. R. Deline, T. W. Sigmon* in [22], p. 95.
[29] *E. Zinner*, Scanning *3*, 57 (1980).
[30] *M. Grasserbauer, G. Stingeder, E. Guerrero, W. Fallmann*, Mikrochim. Acta, 1981 II, 469.
[31] *H. Malissa*, Z. Anal. Chem. *297*, 243 (1979).
[32] *H. Malissa*, Z. Anal. Chem., in press.
[33] *G. Resch, V. Gutmann*, Mitt. Braunschweigischen Wiss. Ges. *31*, 37 (1980).

# COMMUNICATIONS

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

## $Gd_5Cl_9C_2$: A Structure with Two Condensed Metal Octahedral and Interstitial $C_2$ Groups

By *Arndt Simon, Eberhard Warkentin*, and *René Masse*[*]

The structures of metal rich lanthanoid halides $LnX_y$ $(1 \leq y \leq 2)$ are characterized by the occurrence of isolated and condensed metal clusters[1]. In $Ln_7I_{12}$ $(=Ln_6I_{12}\cdot Ln)$ single octahedral $Ln_6$ clusters are found which are linked to infinite chains, double chains, or layers in the more metal rich compounds.

In the search for new compound types with condensed clusters we obtained the compound $Gd_5Cl_9C_2$. Its structure is surprising in two different ways. On the one hand a novel cluster consisting of two condensed metal octahedra occurs, and on the other an occupation of the octahedral centers of lanthanoid cluster compounds is shown for the first time.

The crystal structure consists of a close packed arrangement of quasimolecular $Gd_{10}Cl_{18}(C_2)_2$ clusters (Fig. 1). The cluster contains two $Gd_6$ octahedra ($d_{Gd-Gd}=321$ to 409 pm) which are connected *via* a common edge. Cl atoms lie in front of unconnected edges, as in the well-known $M_6X_{12}$ clusters ($d_{Gd-Cl}=261$ to 326 pm). The double octahedron is the first step in the condensation of $Ln_6X_{12}$ clusters *via* octahedral edges which—involving only *trans*-edges—leads to a series of general composition $Ln_{2+4n}X_{6+6n}$ (n is the number of $Ln_6$ octahedra involved). From this series only the first member $(n=1)$ and the last $(n=\infty)$ were previously known. The infinite $Ln_2X_3$ chain occurs as structural unit in the compounds $Tb_2Br_3$[2], $Er_4I_5$[3], and in the $Sc_5Cl_8$ type structures[4]. The *trans*-edge linked chain of $M_6X_{12}$ clusters also occurs in $NaMo_4O_6$[5]. Close relations to the clusters $Mo_9Y_{11}$ (Y = chalcogen[6]) exist which contain two face sharing octahedral clusters of the $Mo_6Y_8$ type.

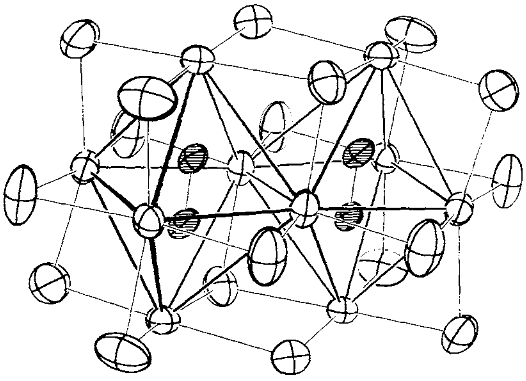


Fig. 1. "Dimeric" $Gd_{10}Cl_{18}C_4$ cluster. The metal atoms of the double octahedron are connected by bold lines; the C atoms are hatched.

Both octahedral centers in the $Gd_{10}Cl_{18}$ cluster are occupied by $C_2$ groups. The distance observed $d_{C-C}=146.5$ pm corresponds to a bond order of between 1 and 2. The distances $d_{Gd-C}$ are 221 pm to the apices and 248 or 266 pm to the atoms in the octahedral bases. A comparable $C_2$ group derived from ethane ($d_{C-C}=148$ pm) has already been found in the large low-symmetry cluster containing twelve metal atoms in the compound $Rh_{12}C_2(CO)_{25}$[7].

$Gd_5Cl_9C_2$ is formed by electrolysis of fused $GdCl_3$ in a graphite crucible (Gd anode, 1020 K, 700 mV) as black crystals which grind to a reddish powder[8]. The synthesis can also be prepared according to $2\,Gd_2Cl_3+GdCl_3+2\,C \rightarrow Gd_5Cl_9C_2$ in welded tantalum capsules at 970 K. The composition is proved by elemental analysis[9a], X-ray fluorescence and X-ray structure analyses[9b].

Received: July 13, 1981 [Z 931 IE]
German version: Angew. Chem. *93*, 1071 (1981)

---

[*] Prof. Dr. A. Simon, Dr. E. Warkentin
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)
Dr. R. Masse
Laboratoire de Cristallographie, C.N.R.S.
F-38042 Grenoble Cedex (France)

[1] *A. Simon*, Angew. Chem. *93*, 23 (1981); Angew. Chem. Int. Ed. Engl. *20*, 1 (1981).
[2] *H. Mattausch, A. Simon*, unpublished results.
[3] *K. Berroth, A. Simon*, J. Less-Common Metals *76*, 41 (1980).
[4] *K. R. Poeppelmeier, J. D. Corbett*, J. Am. Chem. Soc. *100*, 5039 (1978).
[5] *C. C. Torardi, R. E. McCarley*, J. Am. Chem. Soc. *101*, 3963 (1978).
[6] *A. Grüttner, K. Yvon, R. Chevrel, M. Potel, M. Sergent, B. Seeber*, Acta Crystallogr. *B 35*, 285 (1979).

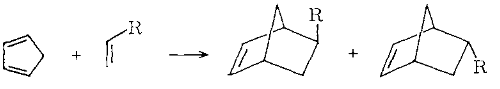
[7] *V. G. Albano, P. Chini, S. Martinengo, M. Sansoni, D. S. Strumolo,* J. Chem. Soc. Dalton Trans. *1978,* 459.
[8] *R. Masse, A. Simon,* Mat. Res. Bull. *16,* 1007 (1981).
[9] a) Dr. *A. Meyer,* Stuttgart is thanked for the elemental analyses; b) $Gd_5Cl_9C_2$ is monoclinic, space group $P2_1/c$ (No. 14), $a=918.2(3)$, $b=1612.0(5)$, $c=1288.6(4)$ pm, $\beta=119.86(2)°$; $Z=4$; $R=0.026$ with 3539 reflexions $I>2\sigma(I)$.

---

## Diels-Alder Reaction of Cyclopentadiene with Acrylic Acid Derivatives in Heterogeneous Phases

By *Harun Parlar* and *Rotraud Baumann*[*]

In the addition of the acrylic acid derivatives *(1a)*—*(1c)* to cyclopentadiene in homogeneous phases, the isomeric ratio of the products is hardly influenced by solvents or catalysts[1]; for the dienophiles acrolein *(1a)* and methyl acrylate *(1b)*, the ratio of *endo-* to *exo*-adducts is *ca.* 3 : 1, and, in contrast, *ca.* 3 : 2 for acrylonitrile *(1c)*.



*(1)* *(2)* *(3)*

*(a)*, R = CHO; *(b)*, R = $CO_2CH_3$; *(c)*, R = CN

Table 1. Percentage composition of the product mixtures of the Diels-Alder reaction of cyclopentadiene with acrylic acid derivatives absorbed on various activated surfaces. The values in brackets refer to reactions on non-activated surfaces [a].

| *(1)* | Silica gel | | Montigel [b] | | $Al_2O_3$ (neutral) | | Sea sand | | Cellulose | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *(2)* | *(3)* | *(2)* | *(3)* | *(2)* | *(3)* | *(2)* | *(3)* | *(2)* | *(3)* |
| *(a)* | 22.0 | 77.7 | 27.7 | 68.9 | 43.9 | 47.3 | 31.3 | 68.0 | 25.1 | 73.9 |
| | (19.2) | (80.1) | (20.4) | (79.6) | (48.8) | (51.2) | (22.6) | (76.5) | (26.7) | (72.8) |
| *(b)* | 10.5 | 87.5 | 6.6 | 90.7 | 2.9 | 93.7 | 23.5 | 71.1 | 24.3 | 71.4 |
| | (13.2) | (84.3) | (12.9) | (83.4) | (2.8) | (93.8) | (24.2) | (72.2) | (23.6) | (72.5) |
| *(c)* | 32.8 | 50.4 | 25.9 | 67.2 | 37.0 | 60.3 | 37.5 | 59.0 | 36.5 | 57.0 |
| | (35.8) | (60.1) | (32.0) | (65.0) | (38.3) | (58.1) | (38.0) | (57.5) | (36.7) | (58.4) |

[a] In homogeneous phases (2 h at 60 °C), cyclopentadiene and *(1a)*, *(1b)*, or *(1c)* give the following product ratios: *(2a)*:*(3a)* = 24.4 : 75.3; *(2b)*:*(3b)* = 24.2 : 71.5; *(2c)*:*(3c)* = 40.2 : 58.2. [b] Montigel is a natural montmorrillonite.

We have managed to achieve an isomer ratio of almost 1 : 1 in a purely heterogeneous reaction of cyclopentadiene with acrolein *(1a)* on non-activated neutral $Al_2O_3$. In the addition of acrylonitrile *(1c)* to cyclopentadiene on activated Montigel, considerably more *endo*-isomer *(3c)* is formed than in the same reaction under homogeneous conditions. Even more impressive is that the formation of the *exo*-isomer is almost completely blocked in the reaction of methyl acrylate *(1b)* with cyclopentadiene on non-activated $Al_2O_3$ (Table 1). The isomer ratios are almost independent of temperature (40—70 °C). Mutual condensation of the adducts can be excluded, since these are stable under the same reaction conditions.

Measurements of the absorption behavior of the starting materials at a maximal covering density of $10^{15}$ particles/$cm^2$ on a variety of surfaces, over different pressure and temperature ranges, indicate that the chemical composition of the absorbent only influences the covering density to a small extent (the bond strength is 25 kcal/mol); any special interaction of the educt with the surface, which could result in reduction in the intramolecular interactions, is therefore precluded[2]. Presumably, a small fraction of the molecules is strongly adsorbed on the surface. Under these conditions one of the two transition states is stabilized over the other by symmetry-controlled secondary orbital interactions[3].

*Procedure*

Solutions of cyclopentadiene (0.05 mol), prepared by thermolysis of dicyclopentadiene, and of the freshly distilled acrylic acid derivatives (0.05 mol), each in 50 mL of diethyl ether, are taken up successively on 30 mg of one of the carrier substances at 20 °C. After cautious evaporation of the solvent at 35 °C at atmospheric pressure, the heterogeneous mixture is warmed up to 50 °C for 4 h under constant stirring, and subsequently extracted (5 x 200 mL) with acetone in a Soxhlet apparatus over 6 h. After removal of the acetone under reduced pressure, the product mixture is purified by passage through a short silica gel column (silica gel 60, Merck, $l=15$ cm, $d=4$ cm, petroleum ether 60—90 °C). The product mixtures are analyzed by gas chromatography (glass column: 2 m, $d=0.4$ cm, 3% OV 17 on Chromosorb W-AW-DMCS 80—100 mesh, $T=60$ °C, carrier gas: $N_2$, 50 mL/min).

Received: April 15, 1981 [Z 933 IE]
German version: Angew. Chem. *93,* 1114 (1981)

CAS Registry numbers:
*(1a)*, 107-02-8; *(1b)*, 96-33-3; *(1c)*, 107-13-1; *(2a)*, 19926-88-6; *(2b)*, 769-85-7; *(2c)*, 2890-96-2; *(3a)*, 19926-90-0; *(3b)*, 2903-75-5; *(3c)*, 2888-90-6; cyclopentadiene, 542-92-7.

---

[1] *K. Alder, G. Stein, E. Rolland,* Justus Liebigs Ann. Chem. *525,* 247 (1936); *G. Calingaert, H. Soroos, H. Shapiro,* Ind. Eng. Chem. *36,* 1055 (1944); *C. D. Ver Nooy, C. S. Rondestvedt,* J. Am. Chem. Soc. *77,* 3583 (1955); *K. Alder, K. Heimbach, R. Reubke,* Chem. Ber. *91,* 1516 (1958); *W. R. Böhme, E. Schipper, W. G. Scharpf, J. Nichols,* J. Am. Chem. Soc. *80,* 5488 (1958); *A. C. Cope, E. Ciganek, N. A. Le Bel, ibid. 81,* 2799 (1959); *N. A. Belikova, V. G. Berezkin, A. F. Platé,* Zh. Obshch. Khim. *32,* 2942 (1962); J. Gen. Chem. (USSR) *32,* 2896 (1962); *F. Kasper,* Z. Chem. *5,* 153 (1965); *P. Wilder, D. B. Knight,* J. Org. Chem. *30,* 3078 (1965).
[2] *W. Roth,* Hoechst AG, Frankfurt, personal communication (1978).
[3] *R. B. Woodward, R. Hoffmann,* J. Am. Chem. Soc. *87,* 4388 (1965); Angew. Chem. *81,* 797 (1969); Angew. Chem. Int. Ed. Engl. *8,* 781 (1969).

---

[*] Dr. habil. H. Parlar, R. Baumann
Institut für Ökologische Chemie
der Gesellschaft für Strahlen- und Umweltforschung mbH München
D-8050 Freising-Attaching (Germany)

---

## Electrophilic Addition of a Sulfur, Selenium, and Tellurium Atom as well as of an $SO_2$ Molecule to a Metal-Metal Bond[**]

By *Werner Hofmann* and *Helmut Werner*[*]

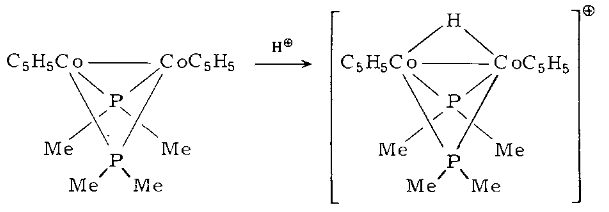
We have recently shown that the dinuclear complex *(1)* is nucleophilic[1a]. It reacts rapidly with $CF_3COOH$, even at room temperature, to give the cation *(2)* which has a symmetric, bent CoHCo bridge. The CoCo bond lengths in *(1)* and *(2)* (determined as $BPh_4$ salt) are closely similar [*(1)*: 2.544 Å; *(2)*: 2.517 Å][1b]. This indicates that the metal-metal interaction is little influenced by the protonation,

---

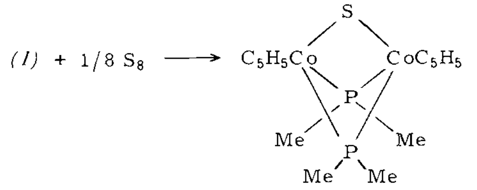
[*] Prof. Dr. H. Werner, Dr. W. Hofmann
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] Basic Metals, Part 26. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and, through a gift of chemicals, by BASF AG, Ludwigshafen. *E. Wittmann* is thanked for experimental work.—Part 25: *R. Feser, H. Werner,* Angew. Chem. *92,* 960 (1980); Angew. Chem. Int. Ed. Engl. *19,* 940 (1980).

and that the electronic interaction in the $Co_2H$ moiety can be described by a cyclic (3c,2e) bond.


(1) (2)

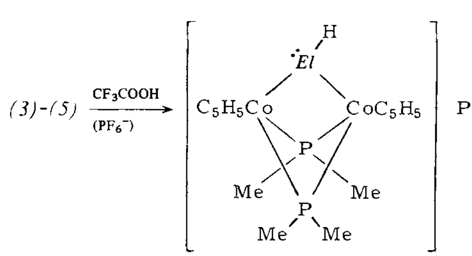
Rupture of the Co—Co bond should occur if the electrophile *El* added to *(1)* possesses free electrons available for bonding which can form two covalent M—*El* bonds with the electrons of the metal-metal bond. Atoms of main group VI satisfy this prerequisite. Thus, *(1)* reacts with cyclooctasulfur, under similar conditions as with $CF_3COOH$, to give the dinuclear complex *(3)*. The composition is confirmed by elemental analysis and mass spectra.


(3)

The selenium and tellurium compounds *(4)* and *(5)* are obtained analogously, but are formed considerably slower than *(3)* so that good yields are only obtained using a large excess of Se or Te, respectively. Gray selenium reacts more rapidly than the black allotrope with *(1)*.

$$(1) + 1/n\mathit{El}_n \rightarrow (C_5H_5Co)_2(\mu\text{-}PMe_2)_2(\mu\text{-}\mathit{El})$$
*(4)*, *El* = Se; *(5)*, *El* = Te

The bridge-forming chalcogen atoms in *(3)—(5)* are nucleophilic. In consequence, the dinuclear complexes react with $CF_3COOH$ upon addition of $NH_4PF_6$ to give the red-brown, air-stable salts *(6)—(8)* which show the conductivity of 1 : 1-electrolytes in nitromethane. To the best of our knowledge this is the first example of a dinuclear transition-metal compound with a bridging TeH ligand[2].

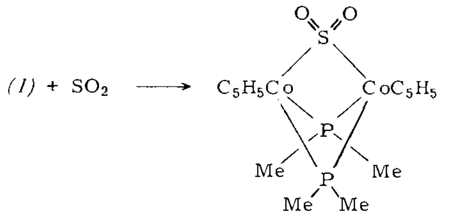

(6), *El* = S
(7), *El* = Se
(8), *El* = Te

Addition of a methyl cation to the chalcogen bridge is also possible. For example complex *(9)*, which forms from *(5)* and methyl iodide even at room temperature, was synthesized.

$$(5) + CH_3I \rightarrow [(C_5H_5Co)_2(\mu\text{-}PMe_2)_2(\mu\text{-}TeCH_3)]I$$
*(9)*

The ¹H-NMR spectra of the cations of *(8)* and *(9)* (Table 1) indicate that a lowering of the symmetry results from protonation or methylation, *i.e.* the chalcogen atom of the *El*H- or $\mathit{El}CH_3$-bridge is coordinated pyramidally and not in a trigonal planar fashion. In contrast to *(7)* and *(8)*, *(6)* shows only two NMR signals for the $PMe_2$ protons at room temperature, indicating a rapid inversion process at sulfur. The rate of this process decreases along the series S > Se > Te and follows the trend expected from the position of these elements in the periodic table.

The nucleophilicity of *(1)* is also demonstrated by its rapid reaction with $SO_2$ to give *(10)*. The black-brown, air-stable crystals are considerably less soluble than *(1)* in nonpolar solvents, which is in accord with the expected higher polar character of the (μ-$SO_2$) complex.


(10)

The reactivity of dinuclear transition-metal complexes having a metal-metal *double bond* with electrophiles, particularly with $CH_2$ and carbenes, has recently been investigated for the rhodium complex $[C_5Me_5Rh(\mu\text{-}CO)]_2$ by ***Hermann et al.***[3a], ***Shapley et al.***[3b], and ***Stone et al.***[3c]. Reactions of this compound with sulfur, selenium, tellurium, or $SO_2$ have not been studied. According to ***Balch et al.***[4a] and ***Brown et al.***[4b], the dinuclear complexes $[ClM(\mu\text{-}dpm)]_2$ (M = Pd, Pt; dpm = $Ph_2PCH_2PPh_2$), which contain an M—M *single bond*, are able to add a sulfur atom and $SO_2$. On the basis of our results obtained to date, we presume that *(1)*—and possibly also the analogous compounds $[C_5H_5Co(\mu\text{-}PPh_2)]_2$[5] and $[C_5H_5Co(\mu\text{-}SMe)]_2$[6]—have a similarly marked reactivity as the above mentioned palladium and platinum complexes towards electrophiles. The activation of small molecules by coordination to *two* metal centers is, above all, in catalysis[7]—particularly in model studies of the Fischer-Tropsch synthesis[8]—of current interest.

Table 1. ¹H-NMR data of complexes *(3)—(5)* and *(8)—(10)* (δ-values, TMS int.; *J* in Hz).

| Complex | Solvent | $C_5H_5$ | μ-$PMe_2$ δ | *J* (PH) | μ-*El*R |
|---|---|---|---|---|---|
| *(3)* | $C_6H_6$ | 4.40 s | 2.45 vt [a] | | |
| | | | 1.47 vt [b] | | |
| *(4)* | $C_6H_6$ | 4.37 s | 2.50 vt [a] | | |
| | | | 1.46 vt [b] | | |
| *(5)* | $C_6H_6$ | 4.37 s | 2.61 vt [a] | | |
| | | | 1.40 vt [b] | | |
| *(8)* | $CD_3NO_2$ | 4.94 s | 2.36 d (6 H) | 12.0 | [c] |
| | | | 1.94 d (12 H) | 11.0 | |
| | | | 1.83 d (6 H) | 11.0 | |
| *(9)* | $CD_3NO_2$ | 4.74 s | 1.88 d (6 H) | 12.0 | 1.70 [d] |
| | | | 1.85 d (12 H) | 12.0 | |
| | | | 1.64 d (6 H) | 12.0 | |
| *(10)* | $CD_3NO_2$ | 4.39 s | 2.50 vt [a] | | |
| | | | 1.85 vt [b] | | |

[a] *N* = 14.0 Hz. [b] *N* = 12.0 Hz. [c] Signal covered by $PMe_2$ signals. [d] Signal overlaps with the signals of the $PMe_2$ protons.

## *Procedure*

*(3)—(5)*: A solution of *(1)* (1.97 g, 5.3 mmol) and $S_8$ (172 mg, 0.67 mmol) in 25 mL of $C_6H_6$ is stirred for 1 h at room temperature. The solvent is completely removed *in vacuo*,

the residue extracted with tetrahydrofuran (THF), and the product precipitated with hexane. Purification occurs by column chromatography on silica gel using ether. *(3)*, red-brown crystals, decomp. = 116—118 °C, yield 1.19 g (53%).—For the preparation of *(4)* a five-fold excess of selenium, and for the preparation of *(5)* a 25-fold excess of tellurium, is used (both finely ground). The reaction times are 36 h (Se) and 48 h (Te), respectively. *(4)*, red-brown crystals, decomp. = 135 °C, yield 55%; *(5)*, red-brown crystals, decomp. = 170 °C, yield 50%.

*(10)*: A solution of *(1)* (432 mg, 1.17 mol) in 5 mL of $C_6H_6$ is stirred for 5 min in an atmosphere of $SO_2$. The solvent is completely removed *in vacuo* and the residue recrystallized from THF/hexane. *(10)*, black-brown crystals, m.p. = 176 °C—178 °C, yield 380 mg (75%).

Received: March 17, 1981 [Z 937 IE]
German version: Angew. Chem. *93*, 1088 (1981)

---

[1] a) *H. Werner, W. Hofmann*, Angew. Chem. *91*, 172 (1979); Angew. Chem. Int. Ed. Engl. *18*, 158 (1979); b) *H. Werner, W. Hofmann, J. Kocal, A. Kühn, L. F. Dahl*, unpublished results, see also [6b].

[2] *V. Küllmer, H. Vahrenkamp*, Chem. Ber. *110*, 228 (1977).

[3] a) *W. A. Herrmann, Ch. Bauer, J. Plank, W. Kalcher, D. Speth, M. L. Ziegler*, Angew. Chem. *93*, 212 (1981); Angew. Chem. Int. Ed. Engl. *20*, 193 (1981); *W. A. Herrmann, Ch. Bauer*, J. Organomet. Chem. *204*, C21 (1981); *W. A. Herrmann*, Adv. Organomet. Chem., in press; b) *A. D. Clauss, P. A. Dimas, J. R. Shapley*, J. Organomet. Chem. *201*, C31 (1980); c) *N. M. Boag, M. Green, R. M. Mills, G. N. Pain, F. G. A. Stone, P. Woodward*, J. Chem. Soc. Chem. Commun. *1980*, 1171.

[4] a) *A. L. Balch, L. S. Benner, M. M. Olmstead*, Inorg. Chem. *18*, 2966 (1979); b) *M. P. Brown, J. R. Fisher, R. J. Puddephatt, K. R. Seddon, ibid. 18*, 2808 (1979).

[5] *R. G. Hayter, L. F. Williams*, J. Inorg. Nucl. Chem. *26*, 1977 (1964).

[6] a) *R. B. King, P. M. Treichel, F. G. A. Stone*, J. Am. Chem. Soc. *83*, 3600 (1961); b) *W. Hofmann*, Dissertation, Universität Würzburg 1980.

[7] *E. L. Muetterties*, Bull. Soc. Chim. Belg. *84*, 959 (1975); *85*, 451 (1976).

[8] *E. L. Muetterties, J. Stein*, Chem. Rev. *79*, 479 (1979); *C. Masters*, Adv. Organomet. Chem. *17*, 61 (1979); *P. T. Wolczanski, J. E. Bercaw*, Acc. Chem. Res. *13*, 121 (1980).

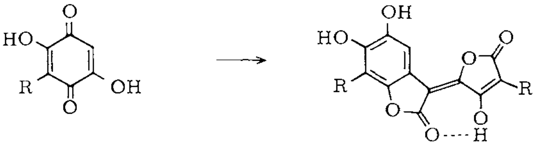
---

# Polyamide-Catalyzed Dimerization of 2,5-Dihydroxybenzoquinones to 4-Ylidenetetronic Acids; a Model for the Biosynthesis of Bovilactone-4,4[**]

By *Erhard Jägers* and *Wolfgang Steglich*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

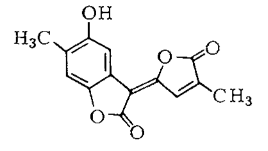
The fungal pigments bovilactone-4,4 *(2b)*[1a] and variegatorubin[1b] contain a 4-ylidenetetronic acid chromophore[2] (tetronic acid is 3-hydroxy-2-butene-4-olide). We found that the parent compound *(2a)* could be readily synthesized by heating 2,5-dihydroxybenzoquinone *(1a)* with acetylated polyamide-6 in inert solvents. The dilactone *(2a)*[3] was obtained in 68% yield after 2 d by performing the reaction in boiling ethyl acetate. Hereby, 17% unconverted *(1a)* could be reisolated, which in the more rapid dimerization with polyamide-6 powder [(10 h, 68% *(2a)*] is impossible because of irreversible bonding to the polymer[4]. Performing the reaction with acylated polyamide at room temperature resulted in the isolation of 8% *(2a)* after stirring for 14 d.



*(1a)*, R = H
*(1b)*, R = Geranylgeranyl

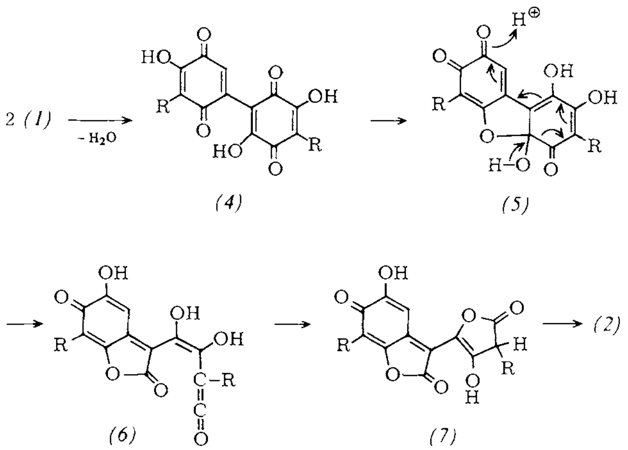
*(2a)*, R = H
*(2b)*, R = Geranylgeranyl

The absorption spectrum of *(2a)* is consistent with that of the dilactone *(3)*[3] prepared by *Posternak*[5]; careful analysis of the ¹³C-NMR spectrum confirms the given constitution[1a].



*(3)*

The initial step in the formation of *(2a)* is presumed to be condensation of *(1a)* to give the dibenzoquinone *(4)*, which then undergoes a Posternak rearrangement[5]. Thereby, the dienone *(5)*, the ketone *(6)*[6], and the tautomer *(7)* can be formulated as intermediates.



*(4)* *(5)*

*(6)* *(7)*

The nature of the polyamide catalysis is still unknown. Since the dimerization also proceeds with freshly reacetylated acetylated polyamide, the activity cannot only stem from basic centers. In this connection it is interesting to observe that *(2a)* is slowly formed when *(1a)* is heated in organic solvents with the difunctional catalyst 2-pyridone[7], but not upon addition of triethylamine, piperidine, or hydrochloric acid.

The mutual occurrence of *(2b)* and boviquinone-4 *(1b)*[8] in the sporophores of *Suillus bovinus* allows one to presume that the reaction course proposed is also of importance in the biosynthesis of *(2b)*. In fact, *(2b)* is obtained in a smooth reaction by boiling *(1b)* with polyamide-6 in ethyl acetate; a turnover of up to 28% requires 3 d[9].

## *Procedure*

A solution of *(1a)* (0.56 g) in 15 mL of ethyl acetate is refluxed for 2 d with acetylated polyamide-6 (MN-polyamide SC 6-AC, Macherey & Nagel, Düren). After evaporation of the solvent and extraction of the residue with ethyl acetate in a Soxhlet apparatus, 0.079 g of unreacted *(1a)* is reisolated together with 0.35 g of *(2a)* upon chromatography on acetylated polyamide using ethyl acetate.

Received: July 8, 1981 [Z 938 IE]
German version: Angew. Chem. *93*, 1105 (1981)

---

[*] Prof. Dr. W. Steglich, Dr. E. Jägers
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[**] Fungal Pigments, Part 39.—Part 38: *E. Jägers, B. Steffan, R. von Ardenne, W. Steglich*, Z. Naturforsch. *C36*, 488 (1981).

[1] a) *E. Jägers, W. Steglich,* Liebigs Ann. Chem., in press. b) *W. Steglich, W. Furtner, A. Prox,* Z. Naturforsch. *B25,* 557 (1970).

[2] *G. Pattenden,* Fortschr. Chem. Org. Naturst. *35,* 133 (1978).

[3] *(2a):* M.p. = 280 °C (decomp.); UV (MeOH): $\lambda_{max} = 272$ ($\lg\varepsilon = 4.10$), 290 (4.04), 360 (4.04), 450 nm (4.12); IR (KBr): 1785, 1745, 1650, 1629 $cm^{-1}$; $^1$H-NMR ([D$_6$]DMSO): $\delta = 5.85$, 6.65, 7.25 (each s, 3H), 10.25 (br., OH); MS: *m/z* 262 (75%, $M^+$, $C_{12}H_6O_7$), 192 (100, $C_9H_4O_5$); *(3):* $\lambda_{max} = 269$ ($\lg\varepsilon = 3.99$), 288 (4.02), 361 (4.15), 450 (3.73).

[4] Cf. *H. Endres,* Z. Anal. Chem. *181,* 331 (1961).

[5] *T. Posternak, R. G. Huguenin, W. Alcalay,* Helv. Chim. Acta *39,* 1564 (1956). Rearrangement of the dibenzoquinones was performed under conditions of acid catalysis.

[6] Cf. *e.g. H. W. Moore, R. J. Wickholm* in *S. Patai:* The Chemistry of Quinonoid Compounds, Part 1, Wiley, London 1974.

[7] *C. G. Swain, J. F. Brown, Jr.,* J. Am. Chem. Soc. *74,* 2538 (1952); *H. C. Beyerman, W. M. van den Brink,* Proc. Chem. Soc. *1963,* 266; *H. T. Openshaw, N. Whittaker,* J. Chem. Soc. *C 1969,* 89.

[8] *P. C. Beaumont, R. L. Edwards,* J. Chem. Soc. *C 1969,* 2398.

[9] Reaction time and yield apply to synthetic *(1b)* with a sterically nonuniform side chain. Interestingly, natural boviquinone-4 with an all-(*E*)-geranylgeranyl side chain is dimerized much more slowly by polyamide.

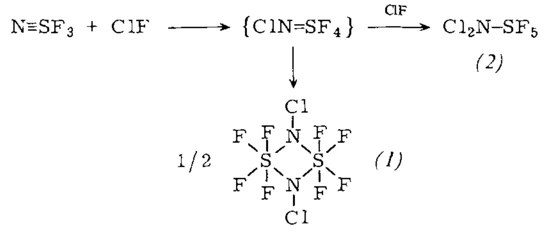
---

## Dimeric *N*-Chloroiminosulfur Tetrafluoride, a Cyclodiaza-λ$^6$-thiane with Hexacoordinated Sulfur[**]

By *Alfred Waterfeld* and *Rüdiger Mews*[*]

*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

The previously known cyclodiaza-λ$^6$-thianes[1] contain exclusively tetracoordinated sulfur atoms. However, by reacting $NSF_3$ and ClF we were able to isolate the novel cyclodiaza-λ$^6$-thiane *(1)* with hexacoordinated sulfur atoms, in addition to the previously described product of this reaction, *N,N*-dichloroaminosulfur pentafluoride *(2)*[2].



Whether the four-membered heterocycle is formed by direct dimerization of the *N*-chloroaminosulfur tetrafluoride or *via* ionic intermediates is still at present not clear. *N*-alkylaminosulfur tetrafluorides, such as *e.g.* $CH_3NSF_4$, do not dimerize[3].

The colorless compound *(1)* melts at 4 °C, and its vapor pressure at 20 °C is 7 torr. Whereas *(1)* decomposes in glass vessels at room temperature, it appears to be stable in passivated metal flasks.

*(1)* was characterized by elemental analysis and spectroscopic methods. Apart from the molecular ion at *m/z* 314 (36%), the EI mass spectrum (70 eV, cold source) shows peaks from the fragments $(M-ClF)^+$ 260 (20), $ClNSF_4^+$ 157 (85), $ClNSF_3^+$ 138 /34), $SF_5^+$ 127 (40), $NSF_3^+$ 103 (12), $SF_3^+$ 89 (100). In the FI mass spectrum, a peak for $(M-ClF)^+$ was found in addition to that of $M^+$. The IR and Raman spectra exhibit no coincidences[4], and hence the molecule is probably centrosymmetric with a *trans*-orientation of the two chlorine atoms. The NMR data can be interpreted using an $A_2B_2$ system as a simplification: $\delta(F_A) = 76.1$, $\delta(F_B) = 49.4$, $J(AB) = 140.8$ Hz.

### *Procedure*

ClF (22.9 g, 0.42 mol) and $NSF_3$ (21.8 g, 0.212 mol) are condensed into a Monel cylinder at −196 °C. The reaction mixture is slowly warmed up to −78 °C, and then to room temperature (Care! Warming too rapidly leads to violent explosions). Fractional condensation (−50, −95, −196 °C) using an oil-pump vacuum yields *(1)* (1.2 g, 3.6% yield) in the first cold trap and *(2)* (5.3 g, 11.8%)[2], together with small amounts of impurities[5], in the second.

Received: June 2, 1980 [Z 910 IE]
German version: Angew. Chem. *93,* 1075 (1981)

CAS Registry numbers:
*(1)*: 79593-52-5, *(2)*: 22650-46-0, ClF: 7790-89-8, $NSF_3$: 15930-75-3.

[1] *K. D. Schmidt, R. Mews, O. Glemser,* Angew. Chem. *88,* 646 (1976); Angew. Chem. Int. Ed. Engl. *15,* 614 (1976); *F. M. Tesky, R. Mews, B. Krebs, ibid. 91,* 231 (1979); *18,* 235 (1979); *H. W. Roesky, M. Aramaki, L. Schönfelder,* Z. Naturforsch. *B33,* 1072 (1978).

[2] *A. F. Clifford, G. R. Zeilenga,* Inorg. Chem. *8,* 979 (1969).

[3] *R. Mews,* Angew. Chem. *90,* 561 (1978); Angew. Chem. Int. Ed. Engl. *17,* 539 (1978).

[4] Spectra were recorded in various phases [IR (gas): 970 (s), 930 (vw), 889 (vs), 854 (vw), 811 (s), 777 (m), 617 (w), 578 (sh), 568 (m); Raman (liquid): 665 (m), 611 (w), 536 (w), 463 (w), 369 (vw), 350 (s), 293 (w), 207 (w), 182 (w)].

[5] $SF_5NSF_4$ and $(SF_5)_2NH$ are more readily accessible by other routes (*A. Waterfeld, R. Mews,* unpublished results).

---

[*] Prof. Dr. R. Mews, Dr. A. Waterfeld
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

---

## Cyanation of Tertiary Alkyl Chlorides: A Novel Method for the Geminal Dialkylation of Ketones[**]

By *Manfred T. Reetz* and *Ioannis Chatziiosifidis*[*]

The ambidentate cyanide ions[1] react with $S_N2$-active primary and secondary alkyl halides at the C atom to form nitriles[4] in accord with the Kornblum rule[2] and the HSAB principle[3]. In the case of tertiary alkyl halides only elimination of HX is observed[5]. Under $S_N1$ conditions, *N*-alkylation occurs *via* the Ritter reaction[6]. In order to solve the classic problem of the cyanation of tertiary alkyl halides [*(1)*→*(3)*], we reacted these with the readily accessible trimethylsilyl cyanide[7] *(2)* in the presence of catalytic amounts of $SnCl_4$.

$$\underset{(1)}{R_3C{-}Cl} + \underset{(2)}{(CH_3)_3SiCN} \xrightarrow{SnCl_4} \underset{(3)}{R_3C{-}CN} + \underset{(4)}{(CH_3)_3SiCl}$$

As shown in Table 1, the desired tertiary nitriles are readily obtained. Noteworthy is the CC coupling reaction of *exo*-2-chloro-2-methylnorbornane *(1j)*, which leads to the *exo*-nitrile *(3j)* with 100% stereoselectivity. Furthermore, the strict chemoselectivity in the reaction of *(5)* is notable: the tertiary nitrile *(6)* is formed exclusively.

The present CC coupling reaction is of synthetic interest, because the products can be variously modified *e.g.* by Grignard addition or reduction, leading to the otherwise

---

[*] Prof. Dr. M. T. Reetz, Dipl.-Chem. I. Chatziiosifidis
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

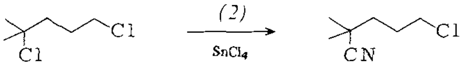
[**] This work was supported by the Fonds der Chemischen Industrie.

Table 1. Cyanation of *tert*-alkyl chlorides.

| *tert*-Alkyl chloride | Nitrile | Yield [a] [%] |
|---|---|---|
| 2-Chloro-2-methylpropane *(1a)* | 2-Methyl-2-propacarbonitrile *(3a)* | 75 (64) |
| 2-Chloro-2-methylbutane *(1b)* | 2-Methyl-2-butacarbonitrile *(3b)* | 80 (75) |
| 2-Chloro-2-methylheptane *(1c)* | 2-Methyl-2-heptacarbonitrile *(3c)* | 78 (70) |
| 5-Chloro-5-methylundecane *(1d)* | 5-Methyl-5-undecacarbonitrile *(3d)* | 80 (70) |
| 1-Chloro-1-methylcyclopentane *(1e)* | 1-Methylcyclopentacarbonitrile *(3e)* | 75 (67) |
| 1-Chloro-1-ethylcyclopentane *(1f)* | 1-Ethylcyclopentacarbonitrile *(3f)* | 87 (82) |
| 1-Chloro-1-methylcyclohexane *(1g)* | 1-Methylcyclohexacarbonitrile *(3g)* | 60 (38) |
| 1-Chloro-1-methylcycloheptane *(1h)* | 1-Methylcycloheptacarbonitrile *(3h)* | 85 (76) |
| 1-Chloro-1-methylcyclododecane *(1i)* | 1-Methylcyclododecacarbonitrile *(3i)* | 75 (60) |
| *exo*-2-Chloro-2-methylnorbornane *(1j)* | *exo*-2-Methyl-2-norbornacarbonitrile *(3j)* | 90 (84) |

[a] The values reflect the $^1$H-NMR spectroscopically estimated amounts; the data in brackets are the yields of isolated products. The structures of all products were confirmed analytically and spectroscopically.

not easily accessible neopentylamines. Since tertiary alkyl halides are *inter alia* conventionally accessible from ketones, the cyanation also provides a novel method for geminal dialkylation of ketones[8,9].



*(5)* *(6)*, 72%

### *Procedure*

$SnCl_4$ (25 mol%) is added slowly to a constantly stirred solution of the *tert*-alkyl chloride (10 mmol) and trimethylsilyl cyanide *(2)* (13 mmol) in 30 mL of anhydrous $CH_2Cl_2$ at room temperature under $N_2$. After 24—38 h the solution is poured onto ice-water and shaken vigorously. The organic phase is separated off, the aqueous phase washed twice with $CH_2Cl_2$, and the combined organic phases washed with a 10% solution of $NaHCO_3$. The solution is dried over $Na_2SO_4$, concentrated, and either distilled or recrystallized.

Received: January 12, 1981,
publication delayed at the authors' request [Z 912 IE]
German version: Angew. Chem. *93*, 1075 (1981)

---

[1] *R. Gompper*, Angew. Chem. *76*, 412 (1964); Angew. Chem. Int. Ed. Engl. *3*, 560 (1964).

[2] *N. Kornblum, R. A. Smiley, R. K. Blackwood, D. C. Iffland*, J. Am. Chem. Soc. *77*, 6269 (1955).

[3] *B. Saville*, Angew. Chem. *79*, 966 (1967); Angew. Chem. Int. Ed. Engl. *6*, 928 (1967); *T.-L. Ho:* Hard and Soft Acids and Bases Principle in Organic Chemistry, Academic Press, New York 1977.

[4] *K. Friedrich, K. Wallenfels* in *Z. Rappoport, S. Patai:* The Chemistry of the Cyano Group, Wiley-Interscience, New York 1970, p. 67.

[5] *L. Friedman, H. Shechter*, J. Org. Chem. *25*, 877 (1970).

[6] *L. I. Krimen, D. J. Cota*, Org. React. *17*, 213 (1969).

[7] *S. Hünig, G. Wehner*, Synthesis *1979*, 522; *J. K. Rasmussen, S. M. Heilman, ibid. 1979*, 523.

[8] *B. M. Trost*, Acc. Chem. Res. *7*, 85 (1074); *M. T. Reetz, W. F. Maier, I. Chatziiosifidis, A. Giannis, H. Heimbach, U. Löwe*, Chem. Ber. *113*, 3741 (1980). Review of methods for the preparation of compounds with quaternary C atoms: *S. F. Martin*, Tetrahedron *36*, 419 (1980).

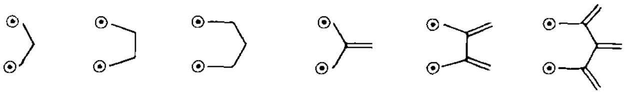
[9] Note added in proof: In the meantime, a procedure has been reported according to which certain tertiary alcohols can be converted into nitriles, *R. Davis, K. G. Untch*, J. Org. Chem. *46*, 2985 (1981).

---

## First Detection of a π-Coupled 1,5-Diradical *via* Cycloaddition[**]

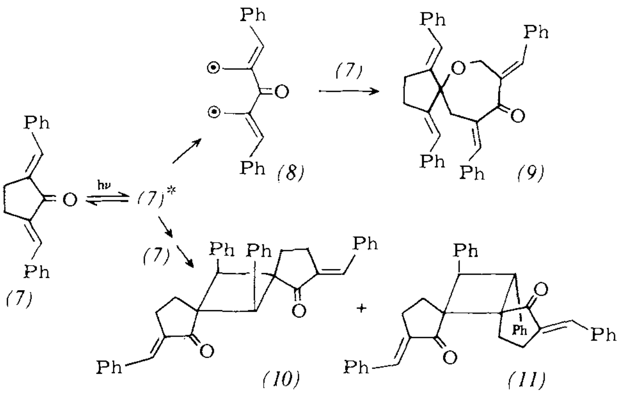
By *Gerd Kaupp* and *Inge Zimmermann*[*]

Diradicals such as *(1)*, *(2)*, *(3)*[1], *etc.* establish a homologous series. This has to be differentiated from a homologous series of π-coupled diradicals *(4)*[2], *(5)*[3], *(6)*, *etc.* We report on a cycloaddition of the first π-coupled 1,5-diradical. Thus, the formation and cycloaddition of *(8)* to a keto group competes favorably with [$2\pi+2\pi$]-dimerizations of electronically excited *(7)*.



*(1)* *(2)* *(3)* *(4)* *(5)* *(6)*

Irradiation of the crystalline dienone *(7)*, which is readily accessible from cyclopentanone and benzaldehyde, and which is used as a cosmetic light protection agent (UV-A range)[4], results in formation of the spiroheterocyclic compound *(9)* *via* cleavage of the five-membered ring and subsequent cycloaddition to the C=O-bond of a second molecule of *(7)*. Furthermore *(7)* dimerizes *via* the exocyclic double bonds to give the dispirocyclobutanes *(10)* and *(11)*. The product ratios *(9)*:*(10)*:*(11)*$=26:38:8$ do not change, whether or not *(7)* is crystallized slowly from methanol, or rapidly from dichloromethane, and whether or not air is excluded during irradiation. However, neither *(9)* nor *(10)*, but almost exclusively the head to head dimer *(11)* is formed in solution (dichloromethane; $\lambda > 380$ nm)[5] upon irradiation of *(7)*.



The structures and compositions of the dimers *(9)*, *(10)* (with mirror symmetry), and *(11)* (with rotational symmetry) were established by elemental analyses as well as by IR-, UV-, and $^1$H-NMR spectra (see Table 1). *(10)* and *(11)* are characteristically different from their centrosymmetric stereoisomer[6].

It is unusual that several products are stereoselectively formed with comparable yields upon irradiation of crystalline *(7)* (cf. *e.g.*[6]; further products which appeared in yields of <4% were not investigated). The formation of *(9)*,

---

[*] Prof. Dr. G. Kaupp, I. Zimmermann
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and the Wissenschaftliche Gesellschaft Freiburg i. Br. We thank Dr. *D. Hunkler* for recording the NMR spectra.

Table 1. Melting points, IR-, UV- and 250 MHz-$^1$H-NMR data of the compounds *(9)*, *(10)*, and *(11)*.

| Cpd. | M.p. [°C] | $^1$H-NMR (CDCl$_3$, δ-value, *J* [Hz]) | UV (CH$_2$Cl$_2$) $\lambda_{max}$ [nm] (log ε) | IR (KBr) [cm$^{-1}$] $\nu_{C=O}$ | $\nu_{C=C}$ |
|---|---|---|---|---|---|
| *(9)* | 284—285 | 7.42—7.26 (10H, m); 7.17—6.91 (14H, m); 4.18 (2H, s); 2.39 (4H, s); 1.84 (2H, s) | 308 (4.51), 314 (sh) | 1720, 1700 | 1625 |
| *(10)*<br>[a] | 256—257 | 7.58 (2H, t, *J* = 2.5); 7.55—7.49 (4H, m); 7.44—7.34 (6H, m); 7.33—7.19 (6H, m); 7.09—7.03 (4H, m); 4.43 (2H, s); 2.74—2.65 (4H, dAA'BB', *J* = 2.5); 2.43—2.35 (4H, BB'AA') | 314 (4.74), 320 (sh) | 1690 | 1610 |
| *(11)*<br>[a] | 156—157 | 7.53 (2H, t, *J* = 2.5); 7.45—7.14 (20H, m); 4.62 (2H, s); 2.81—2.67 (2H, m); 2.58—2.47 (2H, m); 2.45—2.26 (2H, m); 1.65—1.36 (2H, m) | 303 (4.66), 315 (sh), 322 (sh) | 1695 | 1625 |

[a] Centrosymmetric stereoisomer of *(10)* and *(11)*: M.p. = 250.5—251.5°C; δ = 7.34 (22H, m); 4.50 (2H, s); 3.1—2.6 (6H, m); 2.0—1.5 (2H, m) [6].

which gives preparatively good yields, is the first example of addition of a π-bond to a σ-bond of a five-membered ring. Usually such $[2\sigma+2\pi]$-additions proceed only if cyclopropane derivatives are involved, *via* intermediates of type *(1)* or *(4)*[2,7]. Therefore, it should be pointed out that upon light absorption the short-lived diradical *(8)* is formed in proximity to trapping molecules *(7)*, which are apparently favorably oriented. There is no interfering solvation envelope which has to be penetrated prior to the trapping by *(7)* to produce *(9)*. This, and the fact that no solid-state *E*/*Z*-isomerizations are observed suggest that further (also homologous) intermolecular additions of diradicals to double bonds upon irradiation of suitable crystals should be investigated. These should include intermolecular $[2\sigma+2\pi]$-additions of alkenes to non-additionally strained cyclopropane derivatives[1d,2], or to cyclopropane itself, which failed in solution.

### *Procedure*

*(7)* (1.04 g, 2.0 mmol) is evenly spread on the inner wall of a mirrored Dewar vessel (diameter 14 cm, height 20 cm) with some dichloromethane. After heating to 80°C for 1 h the crystalline film is irradiated from within for 3.5 h at 30-35°C using a mercury high-pressure lamp (Hanovia, 450 W) through a 5% solution of benzophenone in benzene (5 mm; λ > 380 nm). From the $^1$H-NMR-analysis are formed 400 mg (38%) *(10)*, 275 mg (26%) *(9)*, and 85 mg (8%) *(11)*. By preparative TLC (200g SiO$_2$, dichloromethane) and by crystallization (1,2-dichloroethane, toluene, and methanol, resp.) these products are isolated, purified, and separated from 190 mg (18%) of unreacted *(7)* and by-products.

Received: April 28, 1981 [Z 914 IE]
German version: Angew. Chem. *93*, 1107 (1981)

---

[1] a) *S. L. Buchwalter, G. L. Closs*, J. Am. Chem. Soc. *97*, 3857 (1975); b) *G. Kaupp, H.-W. Grüter*, Angew. Chem. *92*, 735 (1980); Angew. Chem. Int. Ed. Engl. *19*, 714 (1980); *G. Kaupp, E. Teufel, H. Hopf, ibid. 91*, 232 (1979) and *18*, 215 (1979), and references cited therein; *M. V. Encinas, J. C. Scaiano*, J. Chem. Soc. Perkin Trans. II *1980*, 56; c) *K. W. Ho, P. de Mayo*, J. Am. Chem. Soc. *101*, 5725 (1979); d) *P. G. Gassman*, Acc. Chem. Res. *4*, 128 (1971); e) *T. Martini, J. A. Kampmeier*, Angew. Chem. *82*, 216 (1970); Angew. Chem. Int. Ed. Engl. *9*, 236 (1970).

[2] *R. K. Siemionko, J. A. Berson*, J. Am. Chem. Soc. *102*, 3870 (1980); *P. Dowd, G. Senqupta, K. Sachdev, ibid. 92*, 5726 (1970).

[3] *W. R. Roth, M. Biermann, G. Erker, K. Jelich, W. Gerhartz, H. Görner*, Chem. Ber. *113*, 586 (1980).

[4] *D. Vorländer, K. Hobohm*, Ber. Dtsch. Chem. Ges. *29*, 1836 (1896); *R. Mayer*, Chem. Ber. *88*, 1853 (1955); *G. Konrad, H. Moeller*, DOS 2728241 (1979), K. Henkel G.a.A.; Chem. Abstr. *90*, P142073h (1979).

[5] 78% yield at 80% conversion. In tetrahydrofuran only (*E,Z*)-*(7)* seems to be formed: *H. George, H. J. Roth*, Tetrahedron Lett. *1971*, 4057.

[6] *G. C. Forward, D. A. Whiting*, J. Chem. Soc. C *1969*, 1868.

[7] a) *H. Prinzbach, D. Hunkler*, Chem. Ber. *106*, 1804 (1973); b) *D. Kaufmann, A. de Meijere*, Tetrahedron Lett. *1974*, 3831, and references cited therein; four-membered ring addition: *M. Šindler-Kulyk, W. H. Laarhoven*, J. Am. Chem. Soc. *98*, 1052 (1976); additions of oxiranes (aziridines) *via* carbonyl ylides or azomethine ylides: *K. Maruyama, A. Osuka*, Chem. Lett. *1979*, 77; *R. Huisgen*, Angew. Chem. *89*, 589 (1977); Angew. Chem. Int. Ed. Engl. *16*, 572 (1977).

---

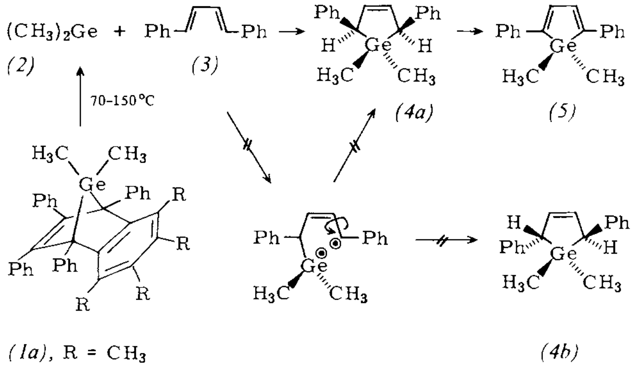
# Carbene-Analogous Germylenes (Germandiyls): Singlets or Triplets?— The First Stereospecific Cycloadditions of $R_2Ge$ to Conjugated Dienes[**]

By *Michael Schriewer* and *Wilhelm P. Neumann*[*]

Singlet carbenes add stereospecifically, triplet carbenes non-stereospecifically to olefins. Much less is known about silylenes $R_2Si$ in this respect, discussions are still continuing[2]. No experiments, however, have been reported concerning the singlet-triplet problem of germylenes $R_2Ge$ until now.

The smooth thermal generation of 7-germanorbornadienes, *e.g.* *(1)*, enables germylenes to be obtained at 70—150°C[3]. We now examined whether germylenes obtained in this way *e.g.* dimethylgermylene *(2)* reacts as a singlet or triplet in 1,4-additions to conjugated dienes[4].

Reaction of *(2)* with (*E,E*)-1,4-diphenylbutadiene *(3)* gave exclusively the *cis*-adduct *(4a)* (Table 1), whose dehydrogenation leads to *(5)*. The *trans*-isomer *(4b)* is not formed. The isomerization *(4a)* ⇌̸ *(4b)* is observed only upon UV irradiation of pure *(4a)*.



Similarly, pure (*E,E*)-3,4-diphenyl-2,4-hexadiene *(6)* and *(2)*, generated from *(1a)*, give only the *cis*-product *(7a)* (Table 1) and no detectable amounts of the *trans*-isomer *(7b)*.

The stereospecific preparation of *(4b)* or *(7b)*, respectively, starting from the corresponding (*Z,E*) isomers *(3)* or *(6)* was unsuccessful. The use of (*E,Z*)-1-phenyl-1,3-pentadiene also gave no reaction.

---

[*] Prof. Dr. W. P. Neumann, Dipl.-Chem. M. Schriewer
Lehrstuhl für Organische Chemie I der Universität Dortmund
Otto-Hahn-Str., D-4600 Dortmund 50 (Germany)

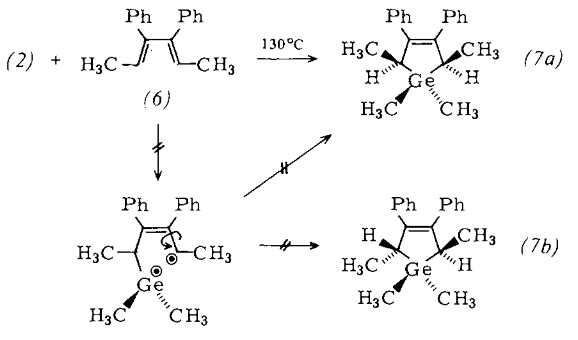
[**] *M. Schriewer*, Dissertation, Universität Dortmund, in preparation.— This work was supported by the Deutsche Forschungsgemeinschaft.

Table 1. Some $^1$H-NMR-data of the adducts *(4a)*, *(7a)*, *(9a)*, *(9b)* and *(9c)* (in $CCl_4$, $\delta$ values; singlets, if not otherwise stated).

| | Ge—$CH_3$ | C—$CH_3$ | C=C—CH | C=CH | $C_6H_5$ |
|---|---|---|---|---|---|
| *(4a)* | −0.59 | | 3.32 | 6.10 | 6.7–7.4 m |
| | 0.55 | | | | |
| *(7a)* | 0.32 | 1.15 d | 2.10 q | | 7 m |
| | 0.42 | | | | |
| *(9a)* | −0.23 | 2.20 | | 6.73 | 7.12 |
| *(9b)* | 0.66 | 2.23 | | 6.30 | 7.15 |
| *(9c)* | 0.23 | 2.16 | | 6.53 [a] | 7.20 |
| | | 2.21 | | 6.56 [a] | 7.23 |

[a] Somewhat broadened.

Unequivocal proof was made with the isomer-free *meso*-diallene *(8a)*[5]. Under mild conditions it reacts to give only the *(Z,Z)/(E,E)*-pair of isomers *(9a/9b)* (Table 1) as expected for a thermal [2+4]-cheletropic reaction of the germylene. The addition is disrotatory and is not influenced by steric hindrance of the phenyl groups since approach from both sides (routes *a* and *b*) is almost equally favored. The isomer *(9c)*, which should also be found in a stepwise addition *via* an intermediate biradical, was not found.



In this case a cross-check was successful: We prepared the previously unknown D,L form of the diallene *(8b)*, which gave exclusively the *(Z,E)* isomer *(9c)* (isomeric purity ≥98%, Table 1).

We therefore concluded that the dimethylgermylene *(2)*, generated thermally, reacts as a singlet species $^s(CH_3)_2Ge$: that is with paired electrons.

This conclusion is in accordance with the results of quantum chemical calculations, from which the singlet states for $H_2Ge$ and $(CH_3)_2Ge$ are lower in energy than the triplet states by 19 and 14 kcal/mol, respectively[6,7]. $H_2Sn$[6] and $H_2Si$[8] are also found to be more stable in the singlet state, whereas for the carbenes $H_2C$ and $(CH_3)_2C$ the ground state is the triplet state[1].

### *Procedure*

All experiments are carried out under argon. All reaction mixtures were checked ($^1$H-NMR) whether the corresponding isomers are present or not.

*(4a)*: *(1a)* (2.75 g, 4.6 mol) and *(3)* (2.30 g, 10 mmol) are heated for 1.5 h at 150 °C. After cooling, the mixture is pulverized and stirred for 0.5 h with 25 mL of EtOH. The filtrate is evaporated to half its volume *in vacuo* and residual *(3)* precipitates out, followed by 0.50 g (30%) of pure *(4a)* as colorless crystals (m.p. = 52 °C) upon cooling in a $CO_2$ bath. A further 50% (still impure) was obtained.

*(5a)*: A sample of *(4a)* is stirred in benzene with an equimolar amount of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone for 15 min at 25 °C, yielding *(5)* which is precipitated from $CH_2Cl_2$ with EtOH; m.p. = 128 °C[9].

*(7a)*: Prepared by analogy to *(4a)* from *(1a)* (2.0 g, 3.4 mmol) and *(6)* (2.3 g, 10 mmol) for 3 h at 130 °C. After evaporation of the EtOH filtrate, the residue is dissolved in a little $CH_2Cl_2$, and residual *(6)* is trapped as its adduct by adding tetracyanoethylene (NMR). Chromatography on a silica gel layer (pentane/$Et_2O$ 19 : 1) gives *(7a)* (from MeOH), m.p. = 65 °C; yield 100 mg (pure product).

*(9a)+(9b)*: *(1b)* (1.5 g, 2.8 mmol) and *(8a)* (1.1 g, 4.3 mmol) are heated for 3 h at 70 °C in 10 mL of anhydrous benzene and then almost evaporated to dryness *in vacuo*. The residue is taken up in 10 mL of pentane, filtered through 10 cm silica gel, evaporated to two thirds, and mixed with the same volume of EtOH. Upon cooling, *ca.* 300 mg *(9a)+(9b)* precipitates out (58% : 42%) in 3 fractions, the first being almost pure *(9a)*.

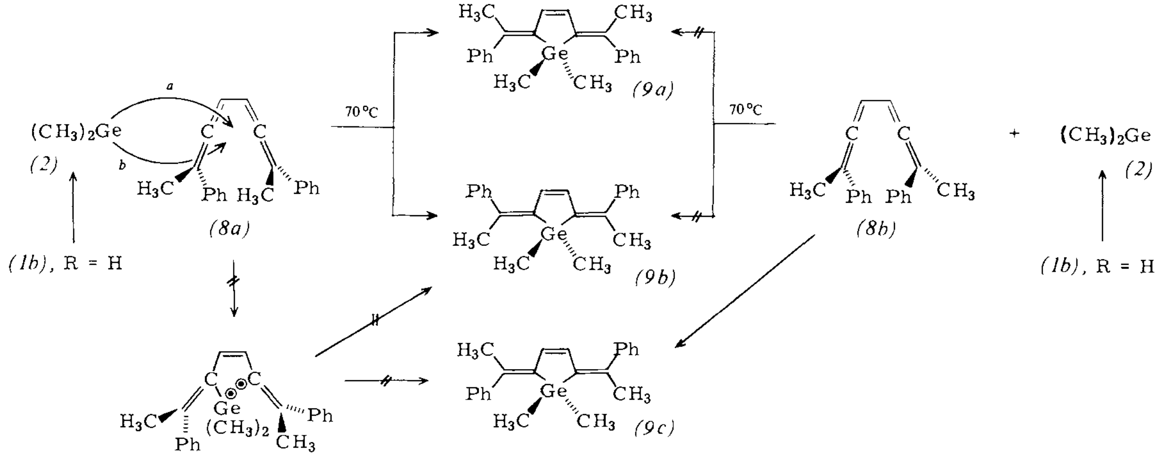
*(9c)* is synthesized analogously to *(9a)+(9b)* from *(1b)* and *(8b)*. *(8b)* is prepared analogously to *(8a)*[5] from *(Z,E)*-2,5-diphenyl-2,4-hexadiene and characterized by the $^1$H-NMR of its $SO_2$ adduct.

Received: May 20, 1981 [Z 917 IE]
German version: Angew. Chem. 93, 1089 (1981)

---

[1] Review: *M. Jones Jr., R. A. Moss*: Carbenes, Vol. I and II, Wiley, New York 1973/75.

[2] *P. P. Gaspar*: Reactive Intermediates *1*, 229 (1978).

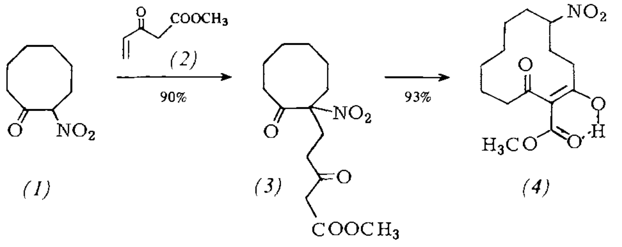


[3] *W. P. Neumann, M. Schriewer*, Tetrahedron Lett. *1980*, 3273.
[4] We have demonstrated[3] that this is possible and proceeds smoothly.
[5] *L. Skattebøl, K. Kleveland*, Acta Chem. Scand. *29*, 827 (1975).
[6] *G. Olbrich*, Chem. Phys. Lett. *73*, 110 (1980), and personal communication.
[7] *J.-C. Barthelat, B. S. Roch, G. Trinquier, J. Satgé*, J. Am. Chem. Soc. *102*, 4080 (1980).
[8] *J. A. Meadows, H. F. Schaefer III*, J. Am. Chem. Soc. *98*, 4383 (1976).
[9] *T. J. Barton, A. J. Nelson, J. Clardy*, J. Org. Chem. *37*, 895 (1972).

## The Carbon Zip Reaction: A Method for Expanding Carbocycles[**]

By *Yoshihiko Nakashita* and *Manfred Hesse*[*]

We have previously reported the ring expansion of *N*-alkylated lactams *via* the Zip reaction[1]. Using this reaction we have now also been able to expand carbocycles. The reaction principle, which has already been demonstrated in open-chain systems[2], is also applicable to cyclic systems for use in ring expansions, as exemplified here by an eight-membered ring: cyclooctanone was reacted with amyl nitrate, in the presence of K-*tert*-butoxide, to give 2-nitrocyclooctanone *(1)*[3].



Reaction of *(1)* with methyl 3-oxo-4-pentenoate *(2)*[4] in the presence of tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) yielded the Michael condensation product *(3)*, which in $CDCl_3$ is present mainly as the keto form[5]. Treatment of *(3)* with TBAF in THF (30 min, 0 °C/7 h, 20 °C) produced methyl 2-hydroxy-5-nitro-12-oxo-1-cyclododecenecarboxylate *(4)* (colorless needles from ethyl acetate/hexane) [m.p. = 81.1-81.8 °C; IR (KBr): 1678, 1652, 1580, and 1548 $cm^{-1}$]. The $^1H$-NMR spectrum indicates that four conformers are present [$\delta = 13.34 + 13.32$ (*ca.* 0.5 H) + 13.28 + 13.26 (*ca.* 0.2 H) dd-like, enol H; 4.97-4.50 (*ca.* 0.6 H) and 4.40-3.97 (*ca.* 0.4 H), 2 m, H-5; 3.9-3.7 (1 main signal at $\delta = 3.83$ and 4 smaller signals), $CH_3$]. The EI mass spectrum of *(4)*, like those of analogous compounds (cf. [2]), is not highly informative [$M^{+\cdot}$: $m/z$ 299 ($\ll 1$ rel%)]. The structure *(4)* was confirmed by X-ray structure analysis (Fig. 1).

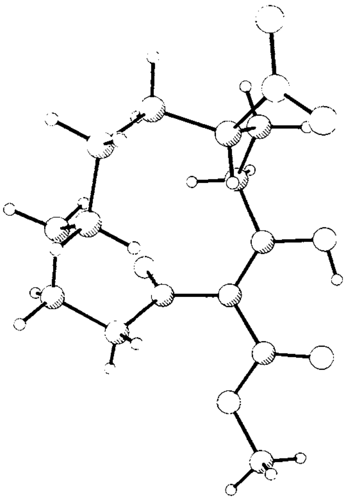


Fig. 1. Structure of *(4)* in the crystal [6].

The method described here is generally suitable for the synthesis of ring compounds by expansion[7].

Received: June 4, 1981 [Z 916 IE]
German version: Angew. Chem. *92*, 1077 (1981)

CAS-Registry numbers:
*(1)*, 13154-28-4; *(2)*, 37734-05-7; *(3)*, 79745-52-1; *(4)*, 79745-53-2.

---

[*] Prof. Dr. M. Hesse, Dr. Y. Nakashita
Organisch-chemisches Institut der Universität
Winterthurer-Strasse 190, CH-8057 Zürich (Switzerland)

[**] This work was supported by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung.

[1] *U. Kramer, A. Guggisberg, M. Hesse, H. Schmid*, Angew. Chem. *90*, 210 (1978); Angew. Chem. Int. Ed. Engl. *17*, 200 (1978); *U. Kramer, A. Guggisberg, M. Hesse*, Helv. Chim. Acta *62*, 2317 (1979), and references cited therein.

[2] *A. Lorenzi-Riatsch, Y. Nakashita, M. Hesse*, Helv. Chim. Acta *64*, 1854 (1981).

[3] *H. Feuer, P. M. Pivawer*, J. Org. Chem. *31*, 3152 (1966).

[4] *B. M. Trost, R. A. Kurz*, J. Org. Chem. *39*, 2648 (1974).

[5] *(3)*, 90 MHz-$^1H$-NMR: $\delta = 12.03$ (s, ≈0.1 enol. H), 4.99 (s, ≈0.1 olefin. H), 3.70 (s, $COOCH_3$), 3.42 (s, ≈1.8 H), 2.9-1.3 (16-H multiplet); IR ($CHCl_3$): 1747, 1724, 1659, 1632, 1544 $cm^{-1}$.

[6] The X-ray structure analysis of *(4)* was performed by Dr. *J. Bieri* and Dipl.-Chem. *R. Prewo* (Universität Zürich). Structures of ring compounds analogous to *(4)*: *J. Bieri, Y. Nakashita, R. Prewo, M. Hesse*, Helv. Chim. Acta, in preparation.

[7] *Y. Nakashita, M. Hesse et al.*, unpublished results of the syntheses of macrocyclic carbocycles, lactones, and lactams.

---

## Isobenzofulvene[**]

By *Gerhard Gross, Reinhard Schulz, Armin Schweig*, and *Curt Wentrup*[*]

In spite of several attempts[1] to prepare the parent isobenzofulvene (2-methylene-2*H*-indene) *(4)*, the molecule has never been directly observed. We now report the preparation and characterization of this long-sought compound[2].

2-1*H*-Indenylmethyl acetate *(2)* was obtained by flow pyrolysis of the diacetate *(1)*[3] through a 30 × 2 cm quartz tube at 550 °C using $N_2$ as carrier gas (1.8 torr). Flash vacuum pyrolysis of either *(1)* or *(2)* at 650 °C ($10^{-4}$ torr) resulted in a blue compound collected on a cold finger (−196 °C). The blue color disappeared on warming to *ca.* −100 °C, and after opening the apparatus, acetic acid and a mixture of $C_{20}H_{16}$ dimers could be isolated. The major dimer[4a] was purified by preparative layer chromatography and identified as the *endo*-dimer *(3)* from its $^1H$-NMR spectrum[1e].

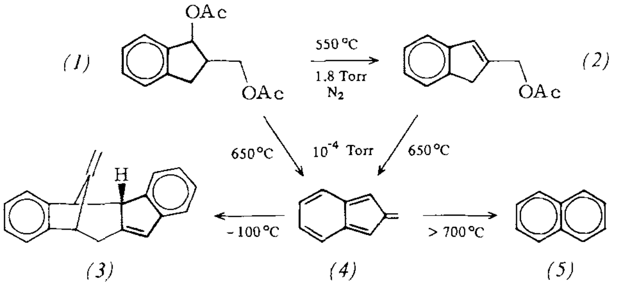
When the flash pyrolysis of either *(1)* or *(2)* was carried out at temperatures above 700 °C, naphthalene *(5)* was obtained together with the blue compound and its dimers. At 800 °C the product was almost exclusively naphthalene.

---

[*] Prof. Dr. C. Wentrup, G. Gross
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)
Prof. Dr. A. Schweig, Dipl.-Chem. R. Schulz
Fachbereich Physikalische Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)

[**] Part 94 of "Theory and Application of Photoelectron Spectroscopy". This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 93: *J. Kreile, A. Schweig, W. Thiel*, Chem. Phys. Lett. *79*, 547 (1981).

The same result was obtained when at 650 °C the pressure was increased using $N_2$ as carrier gas (*i.e.* increased contact time). These results indicate that the blue compound is isobenzofulvene *(4)* which isomerizes to naphthalene at elevated temperatures in the gas-phase, and dimerizes to *(3)* at low temperatures in the condensed state. When the products of the 650 °C flash pyrolysis were led directly into the source of a mass spectrometer, the spectrum of a compound $C_{10}H_8$ ($m/z$ 128 base peak) was obtained[4b].



Direct identification of the blue $C_{10}H_8$ compound as isobenzofulvene was achieved using variable temperature photoelectron spectroscopy (VTPES)[5a]. In this case *(2)* was pyrolyzed immediately above the ionization region of a photoelectron spectrometer (*ca.* $5\times10^{-2}$ torr, contact time *ca.* 0.1 s[5b]) and the spectra recorded as a function of temperature. Figure 1a shows the spectrum of the starting material *(2)* at 25 °C with prominent $^2A''(\pi)$ bands at 8.18 and 8.95 eV (vertical IP's) characteristic of indenes. Figure 1b gives the spectrum of the 590 °C pyrolyzate which, apart from bands due to *(2)*, shows a new low-energy band at 7.32 eV. Attempts to remove the starting material *(2)* by further temperature increase (> 650 °C) resulted in formation of *(5)* as indicated by the appearance of a sharp band at 8.15 eV. The spectrum of the pure new compound *(4)* between 7 and 10.5 eV was obtained by spectral subtraction[6] and is shown in Figure 1c (the spectrum beyond 10.5 eV is inaccessible due to the presence of acetic acid). On the basis of LNDO/S-PERTCI spectral calculations[7a,b,c] using a molecular geometry optimized with MNDO[7d] (Fig. 2), and comparison with the photoelectron spectra of 2*H*-indene derivatives *(6)*[8] and *(7)*[6], the new experimental bands at 7.32, 9.10 and 9.90 eV (Fig. 1c) can be unambiguously assigned to isobenzofulvene *(4)*.

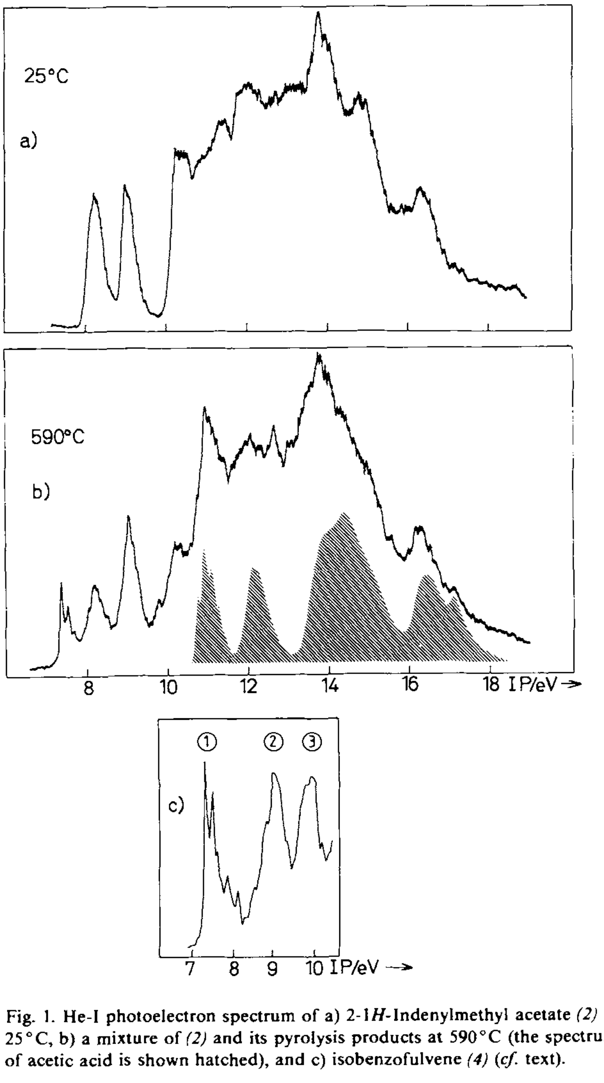


Fig. 1. He-I photoelectron spectrum of a) 2-1*H*-Indenylmethyl acetate *(2)* at 25 °C, b) a mixture of *(2)* and its pyrolysis products at 590 °C (the spectrum of acetic acid is shown hatched), and c) isobenzofulvene *(4)* (*cf.* text).

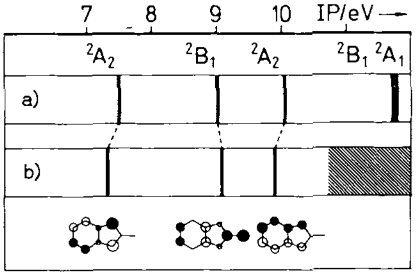
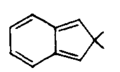
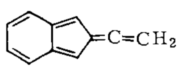


Fig. 2. a) Calculated (LNDO/S-PERTCI) and b) measured vertical ionization potentials (IP) for isobenzofulvene *(4)*.

*(6)*





*(7)*

Table 1. Excitation energies [eV] and oscillator strengths (in parenthesis) for isobenzofulvene *(4)*.

| | LNDO/S-PERTCI | CNDO/S-SECI | PPP-SECI |
|---|---|---|---|
| $^1B_2(\pi\rightarrow\pi^*)$ | 2.63 (0.03) | 2.42 (0.16) | 2.27 (0.03) |
| $^1A_1(\pi\rightarrow\pi^*)$ | 4.20 (0.35) | 4.17 (0.29) | 4.21 (0.10) |
| $^1B_1(\pi\rightarrow\sigma^*)$ | 4.35 (0) | 5.08 (0) | — |
| $^1B_2(\pi\rightarrow\pi^*)$ | 4.66 (0.09) | 4.36 (0.11) | 4.27 (0.06) |
| $^1A_2(\pi\rightarrow\sigma^*)$ | 4.83 (0) | 5.31 (0) | — |

The UV/VIS absorption data of *(4)*, calculated using the LNDO/S-PERTCI[7a,b], CNDO/S-SECI[9a], INDO/S-SECI[9b], and PPP-SECI[9c] methods (Table 1), are in accord with an azulene-like spectrum. The calculated absorption spectra are strongly dependent on geometry. In particular, a small reduction in bond alternation causes a significant long-wave shift of the first $^1B_2(\pi\rightarrow\pi^*)$ absorption; the ionization energies are hardly influenced, however.

Received: July 7, 1981 [Z 918 IE]
German version: Angew. Chem. 93, 1078 (1981)

---

[1] a) *H. Tanida, T. Irie, K. Tori,* Bull. Chem. Soc. Jpn. *45,* 1999 (1972); b) *P. L. Watson, R. N. Warrener,* Aust. J. Chem. *26,* 1725 (1973); c) *R. N. Warrener, G. J. Collin, G. I. Hutchison, M. N. Paddon-Row,* J. Chem. Soc. Chem. Commun. *1976,* 373; d) *R. N. Warrener, K. I. Gell, M. N. Paddon-Row,* Tetrahedron Lett. *1977,* 53; e) *R. N. Warrener, R. A. Russell, G. J. Collin, ibid. 1978,* 4447; f) Stable isobenzofulvenes see *K. Hafner, W. Bauer,* Angew. Chem. *80,* 312; Angew. Chem. Int. Ed. Engl. *7,* 297 (1968).

[2] *T. Koenig et al.*, University of Oregon, Eugene, USA have independently observed *(4)* by VTPE spectroscopy using a precursor different from the ones reported here; personal communication. A. S. thanks Prof. *Koenig* for his hospitality during a visit to Eugene (April, 1981).

[3] *V. N. Dashunin, A. V. Kozlova, M. S. Tovbina,* Probl. Poluch. Poluprod. Prom. Org. Sin., Akad. Nauk SSSR, Otd. Obshch. Tekh. Khim. *1967*, 209; Chem. Abstr. *68*, 114270 (1968).

[4] a) Molecular mass of the dimer, found 256.1249, calc. 256.1246; b) a detailed study of the mass spectra of *(4)* and *(5)* using CID/MIKE (collisionally induced dissociation/mass analyzed ion kinetic energy) spectroscopy is in progress: *G. Gross, A. Maquestiau, R. Flammang, C. Wentrup,* unpublished results.

[5] a) *A. Schweig, H. Vermeer, U. Weidner,* Chem. Phys. Lett. *26*, 299 (1974); *W. Schäfer, A. Schweig,* Z. Naturforsch. *A 30*, 1785 (1975); *G. Märkl, D. Rudnick, R. Schulz, A. Schweig,* unpublished results; b) the contact time is based on a value measured for argon in the same pyrolysis reactor.

[6] Cf. *R. Schulz, A. Schweig, C. Wentrup, H.-W. Winter,* Angew. Chem. *92*, 846 (1980); Angew. Chem. Int. Ed. Engl. *19*, 821 (1980).

[7] a) *G. Lauer, K.-W. Schulte, A. Schweig,* J. Am. Chem. Soc. *100*, 4925 (1978); b) *H.-L. Hase, G. Lauer, K.-W. Schulte, A. Schweig,* Theor. Chim. Acta *48*, 47 (1978); c) These calculations are for Koopmans ion states. Calculations for non-Koopmans states (shake-up states): *R. Schulz, A. Schweig,* unpublished results; d) *M. J. S. Dewar, W. Thiel,* J. Am. Chem. Soc. *99*, 4899 (1977).

[8] *P. Forster, R. Gschwind, E. Haselbach, U. Klemm, J. Wirz,* Nouv. J. Chim. *4*, 365 (1980).

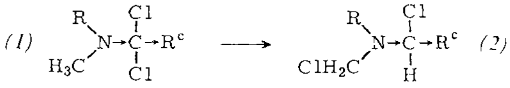
[9] a) *K.-W. Schulte, A. Schweig,* Theor. Chim. Acta *33*, 19 (1974); b) *G. Buemi, F. Zuccarello, A. Raudino,* J. Mol. Struct. *76*, 137 (1981); c) *R. G. Parr:* Quantum Theory of Molecular Electronic Structure, W. A. Benjamin, New York 1963; *N. Thon A. Schweig,* unpublished results.

## Intramolecular 1,3-Cl/H Exchange in $F_3CCCl_2N(CH_3)_2$ and $Cl_3CCCl_2N(CH_3)_2$[**]

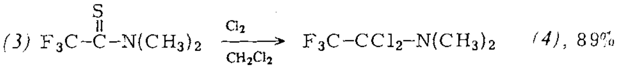
By *Monique Rover-Kevers, Luc Vertommen, Fabienne Huys, Robert Merényi, Zdenek Janousek,* and *Heinz Günther Viehe*[*]

*Dedicated to Professor Werner Reif on the occasion of his 60th birthday*

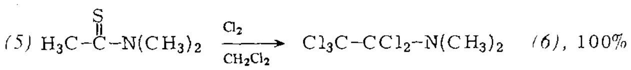
Compounds where the central $—CCl_2—$ moiety is flanked by an electron donor (amino group) and an electron acceptor (capto-dative, cd-substitution) undergo a 1,3-Cl/H exchange[1,2]. The rate of this rearrangement is very sensitive to the extent of the simultaneous electron-donation and -withdrawal properties of the substituents.



Thus, *(1a)* ($R=CH_3$, $R^c=ClC{=}\overset{\oplus}{N}(CH_3)_2$ can only be trapped at −60°[2]; *(1b)* ($R=CH_3$, $R^c=CO_2Et$, rearranges



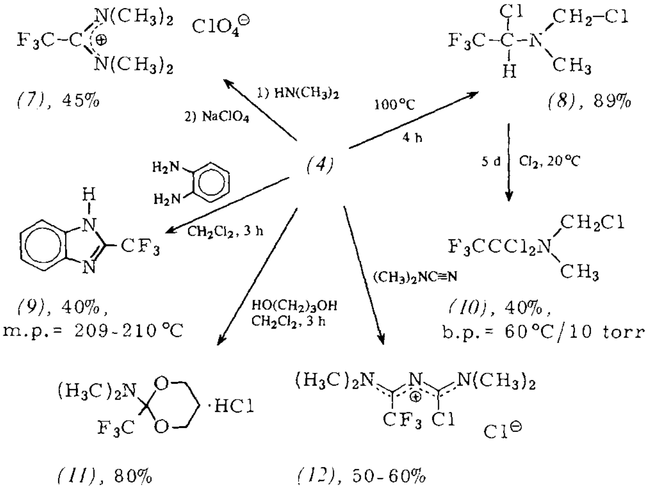
$$(3)\ F_3C-\overset{\overset{\displaystyle S}{\|}}{C}-N(CH_3)_2 \xrightarrow[CH_2Cl_2]{Cl_2} F_3C-CCl_2-N(CH_3)_2 \quad (4),\ 89\%$$



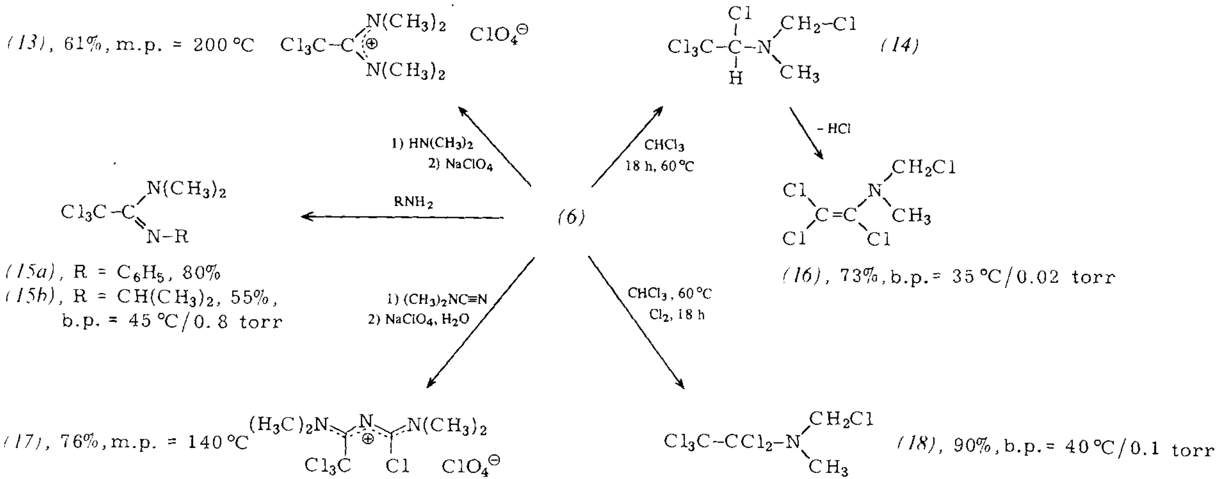
$$(5)\ H_3C-\overset{\overset{\displaystyle S}{\|}}{C}-N(CH_3)_2 \xrightarrow[CH_2Cl_2]{Cl_2} Cl_3C-CCl_2-N(CH_3)_2 \quad (6),\ 100\%$$

completely after 1 h at 20°[3]; with *(1c)* ($R=C_6H_5$, $R^c=CO_2C_2H_5$) the process takes 5 d at 20°[3]. This reflects the fact that the N-methylanilino group is significantly less electron donating than the dialkylamino group. We now report the reaction of dimethylamino compounds *(4)* and *(6)*, the amide chlorides of trifluoro and trichloroacetic acid; here the electron attracting substituents are $CF_3$ and $CCl_3$, respectively. *(4)* and *(6)* were prepared by chlorination of the thioamides *(3)*[4] and *(5)*.

The amide chlorides *(4)* and *(6)* are, for all pratical purposes, stable at room temperature, but rearrange quantita-



Scheme 1.



Scheme 2.

---

[*] Prof. Dr. H. G. Viehe, Dr. M. Rover-Kevers, Dr. L. Vertommen, Dr. F. Huys, Dipl.-Ing. R. Merényi, Dr. Z. Janousek
Université de Louvain, Laboratoire de Chimie Organique
Place Louis Pasteur 1, B-1348 Louvain-La-Neuve (Belgium)

[**] Capto-dative Substitution. Part 10. This work was supported by the Fonds National de la Recherche Scientifique and the Service de Programmation de la Politique Scientifique.—Part 9: *L. Stella, F. Pochat, R. Merényi,* Nouv. J. Chim. *5*, 55 (1981).

tively upon heating to give the new compounds *(8)* and *(16)*, respectively. Moreover, since *(4)* and *(6)* are very reactive towards C, N, O, and S nucleophiles, they constitute valuable synthons for introducing. —$CF_3$ and —$CCl_3$ groups, respectively, into various substrates as shown in the synthesis of compounds *(9)*, *(11)* and *(12)* as well as of *(15)*, *(17)* and *(18)*[5] (Schemes 1 and 2).

The rearrangement product *(14)* cannot be isolated since it eliminates HCl to give trichloroenamine *(16)*.

In order to gain some insight into the mechanism, we measured the kinetics of rearrangement of *(4)* in benzene, dioxane, and nitrobenzene at different temperatures. The plots show that the process is unimolecular and does not depend upon the polarity of the solvent. This precludes polar pathways and confirms that the process is intramolecular. Although no radicals have been detected to date by ESR spectroscopy, we consider a homolysis leading to a tight radical pair $[CF_3\underset{\odot}{C}ClN(CH_3)_2Cl]$ as very likely; a concerted process cannot, however, be excluded.

Table 1. Kinetics of the 1,3-Cl/H exchange *(4)*→*(8)*.

| Solvent | $T$ [°C] | $k \times 10^5$ [$s^{-1}$] | $A \times 10^{-13}$ [$s^{-1}$] | $E_a$ [kcal/mol] |
|---|---|---|---|---|
| Benzene | 72.5 | 1.14 | | |
| | 81 | 3.57 | 7.9 | 29.76 |
| | 91 | 10.40 | | |
| Dioxane | 72.5 | 1.74 | | |
| | 81.5 | 4.98 | 6.02 | 29.32 |
| | 92.5 | 17.50 | | |
| | 98.5 | 34.30 | | |
| Nitrobenzene | 74 | 2.64 | | |
| | 82.5 | 6.88 | 3.82 | 28.9 |
| | 91.5 | 19.60 | | |

### *Experimental*

*(4)* and *(6)*: Solutions of *(3)*[4] and *(5)* in $CH_2Cl_2$ are chlorinated by passing a rapid stream of chlorine through the solutions until the exothermic reaction has subsided. *(4)* is a colorless liquid b.p. = 25 °C/12 torr; $^1$H-NMR ($CDCl_3$): $\delta = 2.66$ ppm; $^{19}$F-NMR ($CDCl_3$): $\delta = -73.5$ ppm.—Solid *(6)* is obtained by evaporation of the $CH_2Cl_2$ and is purified by sublimation at 65 °C/0.02 torr. $^1$H-NMR ($CDCl_3$): $\delta = 2.83$.

*(8)*: *(4)* is heated to 100 °C over 4 h and distilled at 55 °C/10 torr. $^1$H-NMR ($CDCl_3$): $\delta = 2.66$ (s, 3 H), 5.03 (s, 2 H) and 5.36 (q, 1 H).

*(16)*: A solution of *(6)* in $CHCl_3$ is refluxed for 18 h. Crude *(16)* is purified by Kugelrohr distillation 35 °C/0.2 torr. $^1$H-NMR ($CDCl_3$): $\delta = 2.76$ (s, 3 H) and 5.15 (s, 2 H). When the transformation is performed in the presence of $Cl_2$, *(18)* is obtained.

### *Kinetic Measurements*

A solution of 0.1 g of *(4)* in 0.5 mL of the solvent was prepared in a NMR tube, which is then heated in a thermostated bath for a definite time. The rate constants were determined at various temperatures by $^1$H-NMR spectroscopy. An Arrhenius plot gives the values for the $A$ factor and the activation energy $E_a$, in each solvent.

Received: June 16, 1981 [Z 919 IE]
German version: Angew. Chem. 93, 1091 (1981)

CAS-Registry numbers:
*(3)*, 79770-08-4; *(4)*, 79770-09-5; *(5)*, 631-67-4; *(6)*, 79770-10-8; *(7)*, 79770-12-0; *(8)*, 79770-13-1; *(9)*, 312-73-2; *(10)*, 79770-14-2; *(11)*, 79770-15-3; *(12)*, 79770-16-4; *(13)*, 79770-17-5; *(15a)*, 79770-18-6; *(15b)*, 79770-19-7; *(16)*, 79770-20-0; *(17)*, 79770-22-2; *(18)*, 79770-23-3.

---

[1] *F. Huys, R. Merényi, Z. Janousek, L. Stella, H. G. Viehe*, Angew. Chem. *91*, 650 (1979); Angew. Chem. Int. Ed. Engl. *18*, 615 (1979).

[2] *Z. Janousek, F. Huys, L. René, M. Masquelier, L. Stella, R. Merényi, H. G. Viehe*, Angew. Chem. *91*, 651 (1979); Angew. Chem. Int. Ed. Engl. *18*, 616 (1979).

[3] *F. Huys*, Dissertation, Université Louvain-la-Neuve 1979.

[4] *Y. L. Yagupolskij, B. K. Kerzhner, L. M. Yagupolskij*, Zh. Org. Khim. *12*, 2213 (1976); J. Org. Chem. USSR *12*, 2148 (1976).

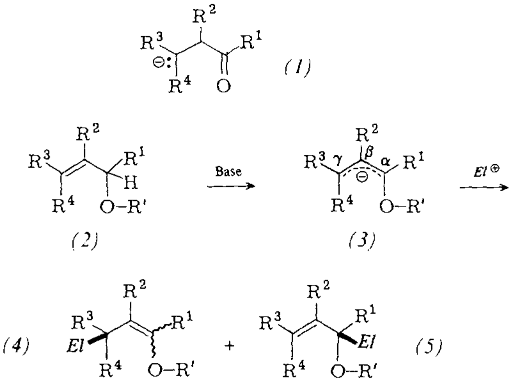
[5] All the new compounds were characterized by MS, $^1$H- and $^{13}$C-NMR.

## Highly Alkylated 1-Oxyallyl Anions from *N,N*-Dialkylcarbamic Acid Allyl Esters: γ-Hydroxyalkylation (Homoaldol Reaction)[**]

By *Dieter Hoppe, Rudolf Hanko, Alfons Brönneke*, and *Florian Lichtenberg*[*]

*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

1-Oxyallyl anions *(3)*, R' = alkyl[1], aryl[1] or trialkylsilyl[2,3] are synthetic equivalents of the unknown aldehyde- and ketone-homoenolates *(1)*; their scope of application, however, is very limited: 1) Anions of type *(3)* are indeed selectively γ-alkylated to enol ethers *(4)*; however, on addition of carbonyl compounds the α-adducts *(5)* predominate[1,2,4]. 2) Because of inadequate acidity only those allyl ethers *(2)* which bear at most one alkyl group can be deprotonated (in the absence of stabilizing M-substituents)[1,2]. 3) Wittig rearrangements and related reactions often take place, even at low temperatures[3,5].

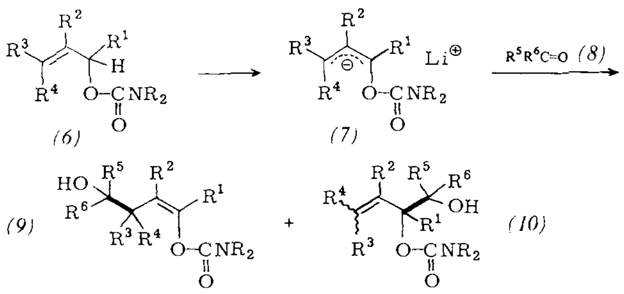


We report here on a novel type of 1-oxyallyl anions[6] which does not suffer these limitations: *N,N*-dialkylcar-

---

[*] Priv.-Doz. Dr. D. Hoppe, Dipl.-Chem. R. Hanko, Dipl.-Chem. A. Brönneke, Dipl.-Chem. F. Lichtenberg
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] Metalated Nitrogen Derivatives of Carbonic Acid in Organic Synthesis, Part 20. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Delivered in part at the Chemiedozenten-Tagung in Tübingen, March 25, 1981.—Part 19: *R. Hanko, D. Hoppe*, Angew. Chem. *93*, 115 (1981); Angew. Chem. Int. Ed. Engl. *20*, 127 (1981).



bamic acid allyl esters (6)—prepared from allyl alcohols and *N,N*-dialkylcarbamoyl chlorides[7]—are rapidly deprotonated to the lithium compounds (7) with *n*-butyllithium in diethyl ether/*N,N,N',N'*-tetramethylethylenediamine (TMEDA) at −78 °C (Table 1). The carbamoyl group of (6) is not attacked by butyllithium, even in the case of the 1,2,3-trialkylated allyl ester (6f). Solutions of (7) are stable up to *ca.* −50 °C. Hence, highly substituted 1-oxyallyl anions with a large variety of structural features are now accessible for the first time.

Unlike (3) the lithium compounds (7) take up aldehydes and ketones (8) predominantly at the γ-position to give the δ-hydroxyenolcarbamates (9); small amounts of the less polar allyl isomers (10) are easily separated by chromatography (Table 1). With exception of *E*-(9e) ($^1$H-NMR ($CCl_4$): $^3J_{1,2}=13$ Hz) and (9g), *Z*-enol esters are obtained [(9a), (9d) and *Z*-(9e): $^3J_{1,2}=6$ Hz; (9b) and (9c): $^4J_{1',2}=1.1$ Hz[5a]]. Thus, whenever it is sterically suitable the reacting species (7) prefers the 1-*Z*-configuration[1,2].

We presume that (7) is present as tight ion pair, in which the lithium cation is held at the α-C atom by the complexing carbamoyl oxygen (Fig. 1a): as a result the carbonyl compound (8) reacts with (7), *via* a six-membered transition state[8,9] (Fig. 1b), in the γ-position.

Solvolysis of (9) with $TiCl_4/H_2O$ or $CH_3OH$ affords the δ-hydroxycarbonyl compounds (homoaldols) (11) as lac-

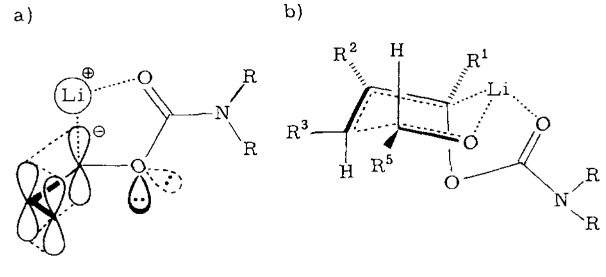
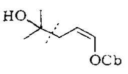
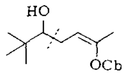
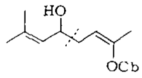
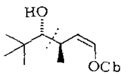
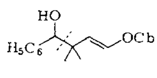
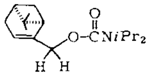
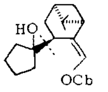
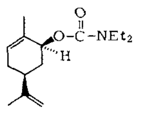
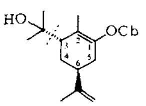


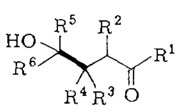
Fig. 1. a) (7) as tight ion pair. b) Transition state of the addition of carbonyl compounds to (7).

Table 1. Addition of aldehydes and ketones (8) to 1-oxyallyl anions (7) generated from (6). R = *i*Pr.

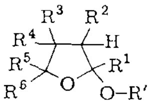
| | (6) | | | | (8) | | (9) [a] | | Yield [b] | (9):(10) [c] | *t* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | | | [%] | (γ:α) | [h] |
| (6a) | H | H | H | H | $CH_3$ | $CH_3$ |  | (9a) | 79 | 93:7 | 0.25 |
| (6b) | $CH_3$ | H | H | H | $(CH_3)_3C$ | H |  | (9b) | 93 | 97:<3 | 1 |
| (6b) | $CH_3$ | H | H | H | $(CH_3)_2C{=}CH$ | H |  | (9c) | 60 | 83:17 | 1 |
| (6c) | H | H | $CH_3$ | H | $(CH_3)_3C$ | H |  | (9d) [d] | 77 | 97:<3 | 1 |
| (6d) | H | H | $CH_3$ | $CH_3$ | $C_6H_5$ | H |  | (9e) [e] | 75 | 95:<5 | 1 |
| (6e) [f] |  | | | | $-(CH_2)_4-$ | |  | (9f) | 42 | 95:<5 | 1.5 |
| (6f) |  | | | | $CH_3$ | $CH_3$ |  | (9g) [g] | 65 | 95:<5 | 5 |

[a] Structure secured by $^1$H-NMR and IR spectra and by CH analysis; Cb = C(=O)N(*i*Pr)$_2$. [b] Pure (9) after chromatography. [c] Determined by isolation of the compounds or $^1$H-NMR spectroscopically. [d] *threo*-(9d):*erythro*-(9d) = 85:15, cf. [9].,[e] Contains *ca.* 5% *Z*-(9e) ($^1$H-NMR: $^3J_{1,2}=6$ Hz). [f] Prepared from (−)-myrtenol. [g] Cb = C(=O)NEt$_2$; (3*S*,5*S*)-(9g):(3*R*,5*S*)-(9g) = 92:8, determined by $^{13}$C-NMR spectroscopy.

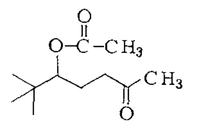
tols *(12)* or as lactol ethers *(13)*. After protection of the hydroxy group in *(9)*, deblocking leads to preparatively useful homoaldol derivatives with free carbonyl groups. Thus, the acetate of *(9b)* gives the γ-acetoxyketone *(14)* in 94% yield.



*(11)*



*(12)*, R′ = H
*(13)*, R′ = CH$_3$



*(14)*

*Procedure*

*(9)*: All operations must be carried out under N$_2$ with rigorous exclusion of moisture. A 1.60 N solution of butyllithium (3.40 mL, 5.50 mmol) in hexane is transferred within 15 min at −78 °C through a syringe cooled with dry-ice into a solution of *(6)*[7] (5.00 mmol) and TMEDA (0.83 mL, 5.50 mmol) in diethyl ether (15 mL). After 0.25—5 h (Table 1), a solution of *(8)* (5.30 mmol, 1.06 equiv.) in a few mL of ether is added to the mixture at −78 to −70 °C; after 2 hours stirring at this temperature the mixture is neutralized with glacial acetic acid (0.90 g, 15 mmol), allowed to warm, and worked-up in the usual way with ether/water. Chromatography on *ca.* 60 g silica gel with ether/petroleum ether (1 : 1) furnishes pure *(9)*, $R_f = 0.1-0.3$ [*(10)*: $R_f = 0.3-0.5$].

Received: July 31, 1981 [Z 920 IE]
German version: Angew. Chem. *93*, 1106 (1981)

CAS Registry numbers:

*(6a)*, 74562-19-9; *(6b)*, 79792-70-4; *(6c)*, 79792-71-5; *(6d)*, 79792-72-6; *(6e)*, 79792-73-7; *(6f)*, 79792-74-8; *(8)* (R$^5$, R$^6$ = CH$_3$), 67-64-1; *(8)* (R$^5$ = (CH$_3$)$_3$C, R$^6$ = H), 630-19-3; *(8)* (R$^5$ = (CH$_3$)$_2$C = CH, R$^6$ = H), 107-86-8; *(8)* (R$^5$ = C$_6$H$_5$, R$^6$ = H), 100-52-7; *(8)* (R$^5$, R$^6$ = (CH$_2$)$_4$), 120-92-3; (*Z*)-*(9a)*, 79792-75-9; (*Z*)-*(9b)*, 79792-76-0; (*Z*)-*(9b)* acetate, 79792-77-1; (*Z*)-*(9c)*, 79792-78-2; (*Z*)-*threo*-*(9d)*, 79792-79-3; (*Z*)-*erythro*-*(9d)*, 79792-80-6; (*E*)-*(9e)*, 79792-81-7; (*Z*)-*(9e)*, 79792-82-8; (*Z*)-*(9f)*, 79792-83-9; *(3S, 5S)*-*(9g)*, 79792-84-0; (3*R*, 5*S*)-*(9g)*, 79814-95-2; *(10a)*, 79792-85-1; *(10c)*, 79792-86-2; *(14)*, 79792-87-3

---

[1] a) *D. A. Evans, G. C. Andrews, B. Buckwalter*, J. Am. Chem. Soc. *96*, 5560 (1974); b) *D. A. Evans, D. J. Baillargeon, J. V. Nelson, ibid. 100*, 2242 (1978); c) *W. Oppolzer, P. H. Briner, R. L. Snowden*, Helv. Chim. Acta *63*, 967 (1980); d) *J. Hartmann, R. Muthukrishnan, M. Schlosser, ibid. 57*, 2261 (1974).

[2] By deprotonation: a) *W. C. Still, T. L. Macdonald*, J. Am. Chem. Soc. *96*, 5561 (1974); b) J. Org. Chem. *41*, 3620 (1976).

[3] From acylsilanes: *A. Hosomi, H. Hashimoto, H. Sakurai*, J. Org. Chem. *43*, 2551 (1978); b) *I. Kuwajima, M. Kato*, J. Chem. Soc. Chem. Commun. *1979*, 708; c) *H. J. Reich, R. E. Olson, M. C. Clark*, J. Am. Chem. Soc. *102*, 1423 (1980).

[4] For an exception cf. *M. Yamaguchi, T. Mukaiyama*, Chem. Lett. *1979*, 1279.

[5] a) Wittig rearrangement: *V. Rautenstrauch, G. Büchi, H. Wüst*, J. Am. Chem. Soc. *96*, 2576 (1974), and references cited therein; b) Brook rearrangement: Ref. [3] and *A. G. Brook*, Acc. Chem. Res. *7*, 77 (1974); b) rearrangement of (aroyloxy)allyl anions: *P. Beak, L. G. Carter*, J. Org. Chem. *46*, 2363 (1981).

[6] Detection and use of anions *(7)* generated *in situ*: *D. Hoppe, R. Hanko, A. Brönneke*, Angew. Chem. *92*, 637 (1980); Angew. Chem. Int. Ed. Engl. *19*, 625 (1980).

[7] With 1.5 equiv. pyridine (without solvent, 5—12 h, 80—100 °C) or [*(6f)*] from the lithium alkoxide according to: *L. E. Overman, C. B. Campbell, F. M. Knoll*, J. Am. Chem. Soc. *100*, 4822 (1978).

[8] Analogous to the aldol reaction of lithium *E*- and *Z*-enolates, cf. *W. A. Kleschick, C. T. Buse, C. H. Heathcock*, J. Am. Chem. Soc. *99*, 247 (1977).

[9] For the *threo*-selective homoaldol reaction with dialkylaluminum compounds see: *D. Hoppe, F. Lichtenberg*, Angew. Chem., in press.

---

# Total Synthesis of Zizyphin A and *N*-Acetylzizyphin B[**]

By *Ulrich Schmidt, Albrecht Lieberknecht, Hilmar Bökens*, and *Helmut Griesser*[*]

Until now, attempts to synthesize ansapeptides have only been partially successful[1]. Over the last ten years *ca.* 80 of these "peptide alkaloids", which complex with alkali earth metal ions and function as ionophores in plants, have been isolated and characterized[2]. Most peptide alkaloids show activity against gram-positive bacteria and lower funghi. Some inhibit energy transfer processes in chloroplasts.—We report here the first total synthesis of two peptide alkaloids—zizyphin A *(1)* and *N*-acetylzizyphin B *(2)* from *Zizyphus oenoplia*[3]—with a 13-membered ring having a 10-membered "handle", using a cyclization method previously developed by us[4].

By means of the route worked out for the preparation of *trans*-3-phenoxyproline[5], the methyl ester of 3-bromodehydroproline was reacted with sodium 3-*tert*-butoxycarbonyl-4-methoxyphenolate[6], the methoxycarbonyl group was saponified, and the dehydroproline derivative was reduced with dimethylaminoborane. The resulting mixture of *cis*- and *trans*-phenoxyproline derivatives could be separated by recrystallization. The *trans*-compound *(3)* was acylated at the proline nitrogen and finally converted into the methyl ester *(4)* by diazomethane. After cleavage of both *tert*-butyl groups and acylation of the proline nitrogen to give *(5)* [yield 21% relative to the methyl ester of bromodehydroproline], we synthesized the aminoacetyl group from the aromatic carboxy group.

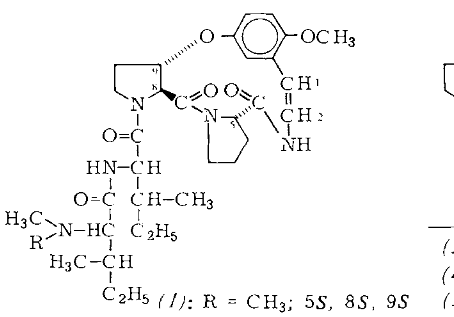
Reaction[7] of the imidazolide of *(5)* with the magnesium salt of monobenzyl malonate led to the benzyl acetylacetate *(6)* [yield 97% from *(5)*]; oximation of *(6)* to *(7)* [yield 91%], followed by catalytic hydrogenation of the oxime group, simultaneous catalytic debenzylation of the ester and decarboxylation of the keto acid formed the amino ketone *(8)*, which upon treatment with *N*-benzyloxycarbonylproline hydroxysuccinimide produced the diastereomeric amides *(9a)* and *(9b)* [yield 56% from *(7)*]. Reduction of the carbonyl group on C-1 with NaB(CN)H$_3$ to give *(10)*[8] [100 % yield], saponification of the methyl ester [yield 95%] and formation of a mixture of the four diastereomeric pentafluorophenyl esters *(11a—d)* [pentafluorophenol/dicyclohexylcarbodiimide; yield 83%] yielded the starting material for the ring-closure step which, after 5 h catalytic hydrogenation on palladium/charcoal using dilution techniques[4], produced the four diastereomeric alcohols *(12a—d)* in 80% yield.

It should be possible to form the double bond between C-1 and C-2 from the corresponding bromides *via* an elimination step. To preserve the acid-sensitive Boc protecting group, we reacted the mixture of alcohols *(12a—d)* with 1-bromo-*N*,*N*-2-trimethylpropenylamine[9] to produce a mixture of the diastereomeric bromides *(13a—d)*. Even this re-

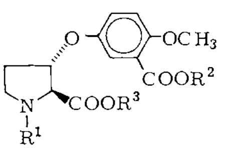
---

[*] Prof. Dr. U. Schmidt, Dr. A. Lieberknecht, Dipl.-Chem. H. Bökens, H. Griesser
*Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität*
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

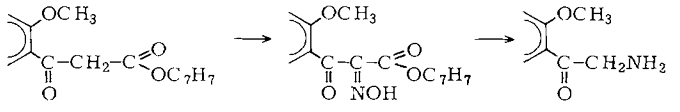
[**] Synthesis of Peptide Alkaloids, Part 4; Amino Acids and Peptides, Part 33. This work was supported by the Fonds der Chemischen Industrie, by BASF AG, and by the Deutsche Forschungsgemeinschaft. We thank Dr. *J. M. Muller* (Ciba-Geigy) and Dr. *G. Eckhardt* for providing samples of zizyphin A, Dr. *W. Rozdzinski* for recording numerous mass spectra, and Dr. *K.-D. Jany* for determining *allo*-isoleucine.—Parts 3 and 32, respectively: Tetrahedron Lett., *1981*, 4949.



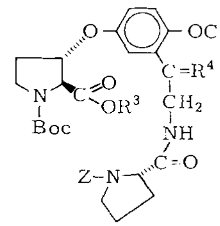
(1): R = $CH_3$; 5S, 8S, 9S
(2): R = $CH_3CO$; 5S, 8S, 9S



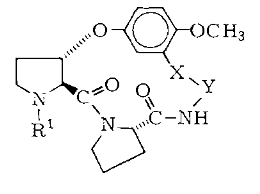
| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| (3) | H | *t*Bu | H |
| (4) | Boc | *t*Bu | $CH_3$ |
| (5) | Boc | H | $CH_3$ |



(6) (7) (8)



*a*: 1S, 5S, 8S, 9S
*b*: 1R, 5S, 8R, 9R
*c*: 1S, 5S, 8R, 9R
*d*: 1R, 5S, 8S, 9S



| | $R^3$ | $R^4$ |
|---|---|---|
| (9) | $CH_3$ | =O |
| (10) | $CH_3$ | H, OH |
| (11) | $C_6F_5$ | H, OH |

| | $R^1$ | X | Y |
|---|---|---|---|
| (12) | Boc | –CHOH– | –$CH_2$– |
| (13) | Boc | –CHBr– | –$CH_2$– |
| (14) | Boc | –CH= | =CH– |
| (15) | H | –CH= | =CH– |

sulted in the formation of small amounts of olefin. Reaction of the bromides with 1,5-diazabicyclo[5.4.0]undec-5-ene at 80 °C in acetonitrile led to a mixture of the diastereomeric olefins *(14a)* and *(14b)* in only 5% yield; accordingly only two of the four bromides *(13)* readily underwent hydrohalide elimination. Using 2,4,6-collidine and lithium bromide in diglyme at 100 °C, we obtained 50% yields, relative to *(12a–d)*. Thereby, the higher reaction temperature and lower reaction rate led to a greater population of conformers capable of elimination. Additionally, lithium bromide converts the sluggish diastereomers into more reactive species by reversing their configurations.

It is more advantageous to convert the mixture of alcohols into the mixture of selenides (tributylphosphine/p-nitrophenylselenocyanate) and to form the olefins by oxidation-elimination. By this means we obtained the mixture of the two pure olefins in 70% yield.

Both of the diastereomeric cyclopeptides *(14a)* and *(14b)* can be readily separated by chromatography on silica gel. In this case the ring compound with the "correct" (*SSS*)-configuration [*(14a)*]—as in all the natural products having this structure—has a large negative optical-rotation value (Table 1). After cleavage of the Boc group with trifluoroacetic acid (TFA), amine *(15a)* is firstly reacted with Boc-isoleucine hydroxysuccinimide ester, and after cleavage of the protecting group (TFA) is treated with activated dimethylisoleucine to give *(1)*. The synthetic product [38% from *(15a)*] is identical in every respect with zizyphin A *(1)*.—For the synthesis of *N*-acetylzizyphin B *(2)*, the amine *(15a)* was coupled with Boc-isoleucine as described above and after cleavage of the Boc group, reacted with the hydroxysuccinimide ester of *N*-methyl-*N*-acetyl isoleucine to give *(2)* [45% yield from *(15a)*].

Table 1. Physical data of some of the compounds.

| | M.p. [°C] | $[\alpha]^D_{20}$ (c) | (c) $CHCl_3$ | m/z |
|---|---|---|---|---|
| (1) | | −430 | (0.10) | 611 ($M^+$, 2%), 114 (100%) (20 eV) |
| (2) | | | | 639 ($M^+$, 100%), 170 (90%) (20 eV) |
| (4) | 101–102 | | | |
| (5) | 136 | | | 395 ($M^+$, 61%), 236 (100%) (70 eV) |
| (14a) | | −500 | (0.93) | 457 ($M^+$, 67%), 357 ($M^+$ − Boc, 21%), 70 (100%) (70 eV) |
| (15a) | | −480 | (0.26) | |

Received: September 1, 1981 [Z 922 IE]
German version: Angew. Chem. *93*, 1121 (1981)

---

[1] *U. Schmidt, A. Lieberknecht, H. Griesser, J. Häusler*, Angew. Chem. *93*, 273 (1981); Angew. Chem. Int. Ed. Engl. *20*, 281 (1981); *F. Rocchiccioli, F. X. Jarreau, M. Pais*, Tetrahedron *34*, 2917 (1978); *H. Rapoport et al.*, J. Am. Chem. Soc. *100*, 8202 (1978); J. Org. Chem. *45*, 4813 (1980).

[2] Review: *R. Tschesche, E. K. Kaussmann* in *R. H. Manske:* The Alkaloids, Vol. 15, Academic Press, New York 1975.

[3] *E. Zbiral, E. L. Ménard, J. M. Muller*, Helv. Chim. Acta *48*, 1801 (1963); *M. Pailer, E. Haslinger, E. Zbiral*, Monatsh. Chem. *100*, 1608 (1969); revised structure: *R. Tschesche, E. Kaussmann, G. Eckhardt*, Tetrahedron Lett. *1973*, 2577.

[4] *U. Schmidt, H. Griesser, A. Lieberknecht, J. Talbiersky*, Angew. Chem. *93*, 271 (1981); Angew. Chem. Int. Ed. Engl. *20*, 280 (1981).

[5] *J. Häusler, U. Schmidt*, Liebigs Ann. Chem. *1979*, 1881.

[6] Synthesized *via:* gentisic acid, 5-benzyloxy-2-hydroxybenzoic acid, 5-benzyloxy-2-methoxybenzoic acid, its *tert*-butyl ester, and catalytic debenzylation.

[7] *D. W. Brooks, L. D. L. Lu, S. Masamune*, Angew. Chem. *91*, 76 (1979); Angew. Chem. Int. Ed. Engl. *18*, 72 (1979).

[8] Ring closure using the ketone *(9)*, $R^3 = C_6F_5$ only proceeds with poor yield and with partial reduction of the keto-to-hydroxy group. The hydroxy group required for the later elimination was therefore prepared *before* the ring closure step.—The introduction of a hydroxy group, which is eliminated at the final stage of the synthesis, increases the number of diastereomers to four due to the non-stereoselective formation of a new asymmetric center, and hence leads to difficultly purifiable mixtures; the yields of subsequent steps, particularly in the ring closure are, however, so high that this disadvantage is more than balanced out.

[9] *L. Ghosez, J. Marchand-Brynaert* in *H. Böhme, H. G. Viehe:* Iminium Salts in Organic Chemistry, Part 1, Wiley, New York 1976, p. 421.

## [3 + 2]-Cycloadditions of Allyl Cations – Synthesis of Permethylcyclopentene and Other Highly Substituted Cyclopentenes[**]

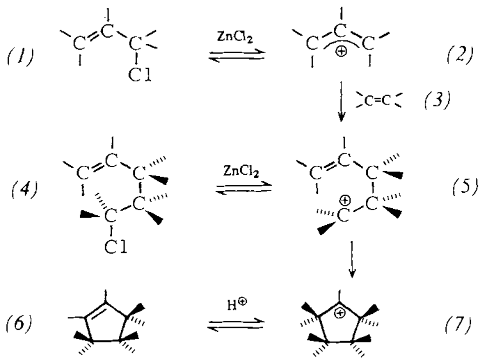
By *Herbert Klein* and *Herbert Mayr*[*]

Whereas [3 + 4]-cycloadditions of allyl cations to 1,3-dienes represent one of the most widely used synthetic approaches to seven-membered carbocycles[1a], only little attention has been paid to [3 + 2]-cycloadditions of allyl cations. Concerted [$3^+_s + 2_s$]-cycloadditions are thermally forbidden by orbital symmetry rules[1b] and a stepwise process involves a cyclization step *(5)*→*(7)* (Scheme 1), which is predicted to be unfavorable by the Baldwin rules[1c].

---

[*] Priv.-Doz. Dr. H. Mayr, Dipl.-Chem. H. Klein
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and, by gifts of chemicals, by Hoechst AG and BASF AG. Dr. *E. Wilhelm* is thanked for the NMR-spectra.

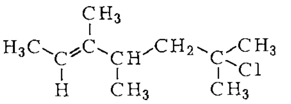


Scheme 1.

Apart from cyclopentanone syntheses with 2-siloxy[2d] or carbonyliron stabilized 2-oxyallyl cations[2a], [3+2]-cycloadditions of allyl cations to CC double bonds have previously only been observed in the gas phase[2b] or as minor reaction from 2-oxyallyl cations and 1,3-dienes[2c]. *Miller* and *Moore* obtained linear and cyclic products from the $ZnCl_2$ catalyzed reaction of prenyl chloride (1-chloro-3-methyl-2-butene) with alkynes[3a]. In contrast, the corresponding reaction with alkenes gives acyclic products exclusively[3b].

We have now found the reactions of 2-alkyl-substituted allyl cations of type *(2)* with alkenes *(3)* to present an easy access to highly substituted cyclopentenes. Isobutene *(3a)* and allyl chloride *(1a)* react at −78 °C in dichloromethane under $ZnCl_2$—$Et_2O$ catalysis[4a] to give the linear addition product (*E*)-6-chloro-3,4,6-trimethyl-2-heptene *(4a)*[5] in 81% yield.

In spite of the three-fold molar excess of isobutene used for this reaction, the 1:1-addition product *(4a)* is formed selectively, since *(1a)* dissociates faster than *(4a)*[3b,4b]. At room temperature, *(4a)* cyclizes in the presence of Lewis acids to yield the pentamethylcyclopentenes *(6a)* and *(6b)* (Scheme 1, Table 1). Additional methyl groups in *(4)* accelerate the cyclization reactions (*gem*-dialkyl effect[6]) and the reaction of *(1a)* with tetramethylethylene gives cyclopentene *(6d)* even at −78 °C. In many cases, mixtures of cyclopentenes and chlorocyclopentanes or acyclic products are obtained at −78 °C, which give the cyclopentenes shown in Table 1 when treated with Lewis acid at 0−25 °C. Sometimes, the cyclopentene yields can be increased if a slow stream of hydrogen chloride is bubbled through the reaction mixture during cyclization; this procedure probably prevents hydrogen chloride elimination from *(4)*.

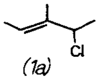
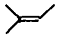
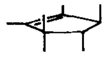
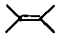
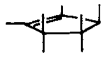
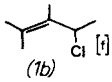
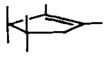
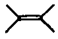
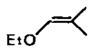
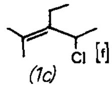
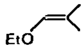
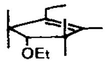
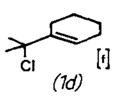
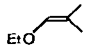

$$H_3C{-}CH{=}C(CH_3){-}CH(CH_3){-}CH_2{-}C(CH_3)_2Cl$$

(4a)

Ethyl vinyl ether polymerizes when reacted with allyl chloride *(1a)* and $ZnCl_2$, since the initially formed α-chloro ether *(4)* reacts faster with vinyl ether than allyl chloride *(1a)*[3b,4b]. In contrast, high yields of 1:1 products are obtained from 1-ethoxy-2-methyl-1-propene *(3d)* and these allyl chlorides. Now, the cyclization *(5)*→*(7)* is accelerated by the *gem*-dialkyl effect and the intramolecular reaction becomes faster than polymerization.

These results are in accord with the stepwise addition mechanism depicted in Scheme 1. From the cyclopentene substitution pattern it can be deduced that unsymmetrical allyl cations are primarily attacked at the less substituted terminus[8]. Unsymmetrical olefins react in the Markovni-

Table 1. Zinc chloride catalyzed reaction of allyl chlorides *(1)* with olefins *(3)*.

| Educts | | | $T$ [°C]/ | Products *(6)* | Yield | B.p. [°C/Torr] | $^{13}C$-NMR ($CDCl_3$) |
|---|---|---|---|---|---|---|---|
| *(1)* | *(3)* | *(1)/(3)* | $t$ [h] | | [%] [a] | [b] | δ-values |
|  *(1a)* |  *(3a)* | 1:4 | −78/8<br>20/0.5 [c] |  *(6a,b)* [d] | 61 | 48—54/20 | *(6a):* 45.5, 133.3, 138.1 (s), 40.6 (d), 48.4 (t), 9.6, 12.1, 20.0, 26.3, 28.3 (q); *(6b):* 39.2, 128.5, 133.9 (s), 53.4 (d), 52.4 (t), 13.4, 14.0, 24.1, 29.7 (q), 2-$CH_3$ covered |
| |  *(3b)* | 1:3 | −78/15<br>25/2 [c] |  *(6c)* | 70 | 55—60/12 | 47.0, 132.6, 138.6 (s), 47.5, 51.9 (d), 9.8, 11.9, 12.1, 17.3, 19.7, 26.3 (q) |
| |  *(3c)* | 1:3 | −78/15 |  *(6d)* | 86 | 49—50/2.5 [e] | 44.7, 49.5, 131.1, 136.6 (s), 50.5 (d), 10.0, 12.1, 12.6, 19.5, 21.4, 21.9, 22.9 (q) |
|  [f] *(1b)* |  *(3a)* | 1:5 | −78/15<br>25/0.5 [c] |  *(6e)* [g] | 42 | 59—65/15 | 42.1, 49.8, 127.7, 137.2 (s), 51.2 (t), 9.9, 14.2, 21.3, 24.6 (q) |
| |  *(3c)* | 1:3 | −78/7.5<br>25/0.5 [c] |  *(6f)* | 70 | 62—71/3 | 45.7, 49.8, 135.0 (s), 10.0, 21.7, 24.2 (q) |
| |  *(3d)* | 1:1 [h] | −78/15 |  *(6g)* | 73 | 70—80/5 | 47.5, 134.7 (s), 95.8 (d), 67.6 (t), 9.7, 16.0, 21.3, 28.3 (q) |
|  [f] *(1c)* |  *(3d)* | 1:1 [h] | −78/15<br>0/0.2 |  *(6h)* | 76 | 65—75/2 | 47.2, 47.9, 135.5, 140.8 (s), 95.8 (d), 18.2, 67.7 (t), 9.6, 14.8, 16.0, 21.3, 22.3, 28.3, 28.7 (q) |
|  [f] *(1d)* |  *(3d)* | 1:1 [h] | −78/15<br>0/0.2 |  *(6i)* | 81 | 53—58/1 | 46.8, 137.6 (s), 96.3 (d), 21.1, 23.2, 67.6 (t), 16.0, 21.4, 28.0 (q) |

[a] Based on *(1)*. [b] Bath temperature. [c] Cyclization after introduction of HCl. [d] *(6a)* and *(6b)* in the ratio 3:1. [e] Actual b.p. [f] Mixture of allyl isomers. [g] Apart from 15% 1,2,3,3,5,5-hexamethylcyclopentene; $^{13}C$-NMR ($COCl_3$) $\delta = 44.7$, 136.4 (s), 54.9 (t), 9.9, 28.8 (q). [h] *(1)* and *(3)* added simultaneously dropwise to the catalyst.

kov sense. In spite of contrary predictions[1c] cyclization *(5)→(7)* readily takes place, if a tertiary carbenium ion is formed[9]. The deprotonation of cyclopentyl cations *(7)* is reversible so that only the thermodynamically most stable elimination products *(6)* are isolated.

### *Procedure*

$ZnCl_2$ (2.2 g) was dissolved in ether (2.6 mL), diluted with 45 mL of $CH_2Cl_2$ and cooled to −78 °C. Successively, solutions of *(3c)* (5.30 g, 63.0 mmol) and *(1b)* (2.64 g, 19.9 mmol) each in 10 mL of $CH_2Cl_2$ were added dropwise. After 7.5 h at −78 °C the catalyst was extracted with conc. aqueous $NH_3$ and the organic phase was dried over $CaCl_2$. The crude product, obtained after evaporation of the solvent and excess alkene, was added to a solution of $ZnCl_2$ (4.4 g) in ether (5.2 mL) and $CH_2Cl_2$ (90 mL) at 25 °C. A stream of dry HCl was bubbled through the solution for *ca.* 1 min. After 35 min at 25 °C, the mixture was worked-up with aqueous ammonia as described above. Distillation yielded 2.50 g (70%) of pure octamethylcyclopentene *(6f)*.

Received: July 22, 1981 [Z 923 IE]
German version: Angew. Chem. *93*, 1069 (1981)

---

[1] a) *H. M. R. Hoffmann*, Angew. Chem. *85*, 877 (1973); Angew. Chem. Int. Ed. Engl. *12*, 819 (1973); b) *R. B. Woodward, R. Hoffmann, ibid. 81*, 797 (1969) and *8*, 781 (1969); c) *J. E. Baldwin*, J. Chem. Soc. Chem. Commun. *1976*, 734.

[2] a) *Y. Hayakawa, K. Yokoyama, R. Noyori*, J. Am. Chem. Soc. *100*, 1791 (1978); b) *M. W. E. M. van Tilborg, R. van Doorn, N. M. M. Nibbering*, Org. Mass Spectrom. *15*, 152 (1980); c) *H. M. R. Hoffmann, R. Chidgey*, Tetrahedron Lett. *1978*, 85; d) *H. Sakurai, A. Shirahata, A. Hosomi*, Angew. Chem. *91*, 178 (1979); Angew. Chem. Int. Ed. Engl. *18*, 163 (1979).

[3] a) *A. Miller, M. Moore*, Tetrahedron Lett. *1980*, 577; b) *H. Klein, A. Erbe, H. Mayr*, Angew. Chem., in press.

[4] a) Catalyst system: *H. Mayr, I. K. Halberstadt*, Angew. Chem. *92*, 840 (1980); Angew. Chem. Int. Ed. Engl. *19*, 814 (1980); b) Rules for selective formation of 1 : 1-addition products: *H. Mayr, ibid. 93*, 202 (1981), *20*, 184 (1981).

[5] *(4a)*: B.p. = 55—65 °C (bath)/2 torr; $^{13}$C-NMR ($CDCl_3$): $\delta$ = 11.92, 13.20, 22.02, 31.85, 33.4 (5 q), 40.19 (d), 50.30 (t), 71.20 (s), 118.43 (d), 140.00 (s).

[6] *C. K. Ingold*, J. Chem. Soc. *119*, 305 (1921); *G. S. Hammond* in *M. S. Newman*: Steric Effects in Organic Chemistry, Wiley, New York 1956, p. 460 pp; *B. Capon, S. P. McManus*: Neighboring Group Participation, Plenum Press, New York 1976, Vol. *1*, p. 58 pp.

[7] *(3d)* gives a complex mixture of 1 : 1-products with *(1a)*.

[8] The 1,1,2,3-tetramethylallyl cation is, however, attacked by isobutene to an extent of 15% at the more highly substituted end (Table 1, footnote [g]).

[9] Analogous cyclizations of the prenyl chloride-olefin-addition products must proceed *via* secondary cyclopentyl cations and were not observed [3b].

---

## Dodecamethyl-1λ$^3$,4λ$^3$-diphospha-2,3,5,6,7,8-hexastannabicyclo[2.2.2]octane, a Highly Symmetrical Cage Molecule[**]

By *Martin Dräger* and *Bernd Mathiasch*[*]

*Dedicated to Professor Leopold Horner on the occasion of his 70th birthday*

The reaction of white phosphorus with tin hydrides can be used to form SnP bonds[1]. In addition to the phosphane, we obtained the title compound *(1)* by reacting 1,1,2,2-tetramethyldistannane[2] with phosphorus *in the dark*.

$$3\,(CH_3)_4Sn_2H_2 + P_4 \xrightarrow[0\,°C,\ darkness]{Et_2O} \underset{(1)}{[(CH_3)_2Sn]_6P_2} + 2\,PH_3$$

Under the *action of light (1)* disproportionates to the norbornane-analogous *(2)*[1] and dimethylstannanediyl, which can be trapped as iodotrimethylstannane by reaction with $CH_3I$.

$$\underset{(1)}{[(CH_3)_2Sn]_6P_2} \xrightarrow{h\nu} \underset{(2)}{[(CH_3)_2Sn]_5P_2} + (CH_3)_2Sn:$$

The novel compound *(1)* forms as bright yellow crystals from benzene. The X-ray structure analysis[3] indicates, within the standard deviations, a chiral molecule with $D_3$ symmetry (six equivalent Sn atoms, two equivalent P atoms and six equivalent C atoms; cf. Fig. 1). The bicycle $Sn_6P_2$ is constructed from three $Sn_4P_2$ six-membered rings which share three bonds with each other and adopt the conformation of a boat, twisted by 26°.

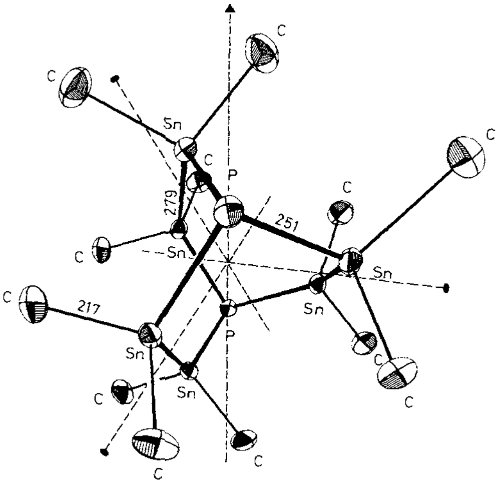


Fig. 1. Molecular structure of *(1)* in the crystal with average bond lengths [pm] (P···P distances; intramolecular 518, intermolecular 371 pm) and symmetry elements. Average bond- and torsion-angles [°]: Sn—P—Sn 98, P—Sn—Sn 117, C—Sn—C 107, Sn—Sn—C 109, P—Sn—C 107; PSn—SnP +26, SnSn—PSn −62, SnSn—PSn′ +37.

In solution at room temperature *(1)* has, on average, $D_{3h}$ symmetry: The NMR signals of all the methyl groups show a joint doublet arising from $^{31}$P-coupling[4]. The coupling constants $^3J$(PSnCH) and $^2J$(PSnC) confirm the previously found dependence on the torsion angle of the phosphorus lone pair of electrons and the coupling nuclei in *(2)*[1].

### *Procedure*

All operations are performed under argon, using solvents saturated with Ar: $Me_4Sn_2Cl_2$ (4 g, 10.9 mmol) is reduced to $Me_4Sn_2H_2$ at room temperature by $LiAlH_4$ in 70 mL of $Et_2O$. The solution is cooled to 0 °C and ice-water added under stirring. The ether layer is separated off, dried over $MgSO_4$, and poured onto white phosphorus (0.3 g, 9.7 mmol, less than the stoichiometric amount). The reaction vessel is kept dark and immediately cooled (0 °C). After 48 h the phosphorus is consumed, and the crystals formed are separated from the $Et_2O$ solution by suction and re-

---

[*] Prof. Dr. M. Dräger, Dr. B. Mathiasch
Institut für Anorganische Chemie und Analytische Chemie der Universität
Johann-Joachim-Becher-Weg 24, D-6500 Mainz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.

crystallized from benzene: yield 0.5 g (22%, relative to P), bright yellow, highly refractive crystals, m. p. = 220 °C (decomp.), readily soluble in $CH_2Cl_2$.

Received: February 1, 1980;
publication delayed at the authors' request [Z 929 IE]
German version: Angew. Chem. *93*, 1079 (1981)

---

[1] *B. Mathiasch, M. Dräger*, Angew. Chem. *90*, 814 (1978); Angew. Chem. Int. Ed. Engl. *17*, 767 (1978); *B. Mathiasch*, J. Organomet. Chem. *165*, 295 (1979).

[2] *B. Mathiasch*, Inorg. Nucl. Chem. Lett. *13*, 13 (1977); J. Organomet. Chem. *141*, 295 (1977).

[3] Cell data: $a = 1742.7(2)$, $b = 1026.5(2)$, $c = 1627.2(2)$ pm, $\beta = 104.74(2)°$, $V = 2815 \cdot 10^6$ pm$^3$, space group C2/c, $Z = 4$, $\rho_{X\text{-ray}} = 2.25$, $\rho_{exp} = 2.22$ g cm$^{-3}$; 3227 reflections ($\lambda = 71.069$ pm) of which 512 were unobserved ($< 2\sigma$), CAD4-diffractometer, $R = 0.022$, H atoms not considered.

[4] NMR data (in $CD_2Cl_2$, rel. TMS or $H_3PO_4$ ext.): $^1$H: $\delta = 0.55$, $^3J$(PSnCH) = 2.6, $^2J(^{117}$SnCH) = 43.4, $^2J(^{119}$SnCH) = 45.4, $^3J$(SnSnCH) = 15.6 Hz; $^{13}$C: $\delta = -4.28$, $^1J$(SnC) = 218, $^2J$(PSnC) = 11.0 Hz; $^{31}$P: $\delta = -299$, $^1J(^{117}$SnP) = 714, $^1J(^{119}$SnP) = 749, $^2J$(SnSnP) = 93 Hz.

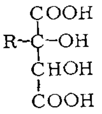
---

## Direct Diastereoselective Alkylation of Tartaric Acid Through an Enolate

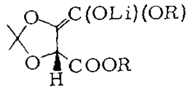
By *Reto Naef* and *Dieter Seebach*[*]

The usefulness of (+)- and (−)-tartaric acid as chiral starting materials (pool of chiral building blocks[1]) for syntheses would be greatly enhanced, if direct alkylation to give *(1)* could be achieved. Depending upon the stereochemical course of such a process, natural products with *erythro-(1)* structures[2], such as piscidic acid, fukiic acid, or loroglossine, which have hitherto been synthesized only as (±)-mixtures by elaborate routes, might become readily accessible in enantiomerically pure form.

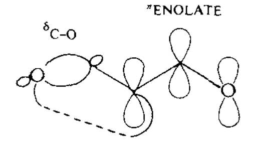
We have now succeeded in finding conditions for generating lithium enolates *(2a)* and *(2b)* from (*R*,*R*)-tartrate acetonides[3]. Alkylation with highly reactive electrophiles leads to pentasubstituted *trans/cis*-dioxolanes *(3)/(4)* in yields ranging from 40 to 80% (Table 1); the diastereomeric ratios of *ca.* 80 : 20 can be determined from the $^1$H-NMR spectra. The stability of the enolates *(2a)* and *(2b)*, sufficient for allylations and benzylations but not for *n*-alkylations, can be rationalized by assuming, that the rigid acetonide skeleton holds the enolate π-system and the C—O σ bond at an "aldol distance", perpendicular to each other [*(2c)*[4]], thus preventing β-elimination.



*(1)*

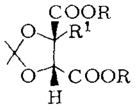


*(2a)*, R = $CH_3$
*(2b)*, R = $CH(CH_3)_2$

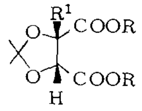


*(2c)*

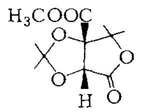
The enolate *(2a)* also adds to the carbonyl group of acetone: A 4 : 1-mixture of a diester of *(4f)* and of the lactone ester *(5)* (M. p. = 96—97 °C, $[\alpha]_D^{20} = -11.0$ ($c = 0.95$, $CHCl_3$)), which spontaneously crystallizes, is isolated in 60% yield. The minor component *(5)* must be a *cis*-bicyclo[3.3.0] system formed from an adduct of type *(3)* with *trans*-configuration. Thus, acetone has approached the enolate *(2a)* from the *Re*-face preferentially [see *(4f)* in Table 1]. In contrast, the *p*-methoxy-benzylation of *(2a)* must have occurred from the *Si*-face: the diastereomeric mixture *(3e)/(4e)* was hydrolyzed with 0.1 N HCl (methanol/water 1 : 1) to give the dihydroxyester, the major isomer of which was obtained by crystallization. According to the $^1$H- and $^{13}$C-NMR spectra, supported by measurements in the presence of a chiral shift reagent, and comparison with an authentic sample[2a, 5], the major product is the 97% enantiomerically pure *threo*-isomer *(6)* (m. p. = 107.0—107.5, $[\alpha]_D^{20} = -26.3$ ($c = 0.57$, $CHCl_3$)), while natural piscidic acid is *erythro-(7)*. By analogy, we assume that all main products of allylation and benzylation of *(2)* have the *trans*-configuration (Table 1), *i. e.* that the substitution of the α-proton of tartaric acid occurs with *retention* of configuration.



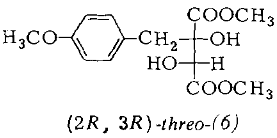
*(3)* *(a)*, $R^1 = CH_3$
*(b)*, $R^1 = CH(CH_3)_2$



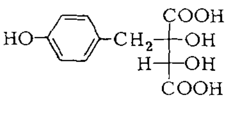
*(4)*



*(5)*



(2*R*, 3*R*)-*threo-(6)*



(2*R*, 3*S*)-*erythro-(7)*
(+)-piscidic acid

Table 1. Ratios of diastereomers, yields, and specific rotations of the products obtained from alkylations of *(2)*. The yields refer to distilled samples *(3)* + *(4)*, the rotations of which are given without diastereomer enrichments.

| Educt | | | | Products *(3)/(4)* | | |
|---|---|---|---|---|---|---|
| *(2)* | *El* | | $R^1$ | Yield [%] | *(3)* : *(4)* | $[\alpha]_D^{20}$ (*c* in $CHCl_3$) |
| *(2a)* | Allyl bromide | *(a)* | $CH_2CH{=}CH_2$ | 65 | 87 : 13 | −19.1° (1.52) |
| *(2b)* | Crotyl bromide | *(b)* | $CH_2CH{=}CHCH_3$ | 46 | 78 : 22 | −16.7° (1.08) |
| *(2c)* | 1-Bromo-3-methyl-2-butene | *(c)* | $CH_2CH{=}C(CH_3)_2$ | 75 | 82 : 18 | −28.8° (0.58) |
| *(2a)* | Benzyl bromide | *(d)* | $CH_2C_6H_5$ | 54 | 84 : 16 | −37.8° (1.00) |
| *(2a)* | *p*-Methoxybenzyl bromide | *(e)* | *p*-$C_6H_4OCH_3$ | 77 | 82 : 18 | −38.8° (5.58) |
| *(2a)* | Acetone | *(f)* | $C(OH)(CH_3)_2$ | 60[a] | | +15.2° (2.57) [b] |

[a] Total yield of *(4f)* and *(5)*, ratio 4 : 1. [b] Rotation value of pure *(4f)*.

### *Procedure*

*(3d)/(4d)*: To a solution of dimethyl (*R*,*R*)-tartrate acetonide (3.27 g, 15 mmol)[3] and benzyl bromide (3.06 g, 18 mmol) in 50 mL of tetrahydrofuran (THF)/10 mL of hexamethylphosphoric triamide, stirred under argon at −78 °C, is added within 30 min a solution of lithium diisopropylamide (16 mmol) in 50 mL of THF cooled at −70 °C. The temperature is allowed to rise to −10 °C over 6 h, the reaction mixture poured into 300 mL of diethyl ether, the resulting solution washed with water (5 × 200 ml), dried over magnesium sulfate, and the solvent removed by evaporation. Kugelrohr distillation (165 °C/0.005 torr) gives 2.5 g (54%) of the mixture *(3d)/(4d)* (84 : 16) as a yellow resin.

Received: July 6, 1981 [Z 939 IE]
German version: Angew. Chem. *93*, 1113 (1981)

---

[*] Prof. Dr. D. Seebach, Dipl.-Chem. R. Naef
Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

[1] *D. Seebach, E. Hungerbühler* in *R. Scheffold:* Modern Synthetic Methods, Vol. 2, Salle und Sauerländer, Aarau 1980, p. 91.

[2] a) *A. Nordal, G. Haustreit, J. Grether,* Medd. Nor. Farm. Selsk. *28,* 225 (1966); b) *S. Sakamura, T. Yoshihara, K. Toyoda,* Agric. Biol. Chem. *37,* 1915 (1973); *33,* 1795 (1969); c) *R. W. Gray, A. Guggisberg, K. P. Segebarth, M. Hesse, H. Schmid,* Helv. Chim. Acta *59,* 645 (1976).

[3] Precursor of *(2a): M. Carmack, C. J. Kelley,* J. Org. Chem. *33,* 2171 (1968); *D. Seebach, H.-O. Kalinowski, B. Bastani, G. Crass, H. Daum, H. Dörr, N. P. Du Preez, V. Ehrig, W. Langer, C. Nüssler, H.-A. Oei, M. Schmitt,* Helv. Chim. Acta *60,* 301 (1977); *J. A. Musich, H. Rapoport,* J. Am. Chem. Soc. *100,* 4865 (1978);—Precursor of *(2b)* by titanate catalyzed transesterification of the methyl ester: *D. Seebach, E. Hungerbühler, R. Naef, P. Schnurrenberger, B. Weidmann, M. Züger,* Synthesis, in press.

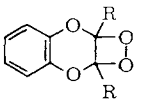
[4] Cf.: *A. B. Smith, III, P. J. Jerris,* Synth. Commun. *8,* 421 (1978); *J. Mulzer, T. Kerkmann,* Angew. Chem. *92,* 470 (1980); Angew. Chem. Int. Ed. Engl. *19,* 466 (1980); *J. E. Baldwin,* J. Chem. Soc. Chem. Commun. *1976,* 734, 736, 738.

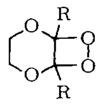
[5] *W. Heller, Ch. Tamm,* Helv. Chim. Acta *57,* 1766 (1974). We thank Prof. *Ch. Tamm,* Universität Basel, for an authentic sample of dimethyl (2*R*,3*S*)-(+)-4′-*O*-methylpiscidate.

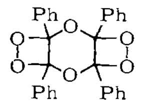
## Dihydrodioxetobenzodioxins: Synthesis and Chemiluminescence[**]

By *Waldemar Adam, Omar Cueto, Ernst Schmidt,* and *Kiyoshige Takayama*[*]

In our search for novel "high-energy" molecules for the thermal generation of electronically excited products, we undertook the preparation of the dioxetanes *(1)* derived from 1,4-benzodioxins *(4).* By analogy to the perhydrodioxetodioxins *(2)* and the bisdioxetane *(3),* which on thermolysis afford electronically excited ethylene glycol diester[1] and benzoic anhydride[2], respectively, in high yield, it was expected that electronically excited pyrocatechol diesters should be formed in high yields from 2a,8a-dihydro-1,2-dioxeto[3,4-*a*][1,4]benzodioxin *(1)*[3]. Herewith we report the preparation, characterization, and chemiluminescence of the novel dioxetanes *(1).*

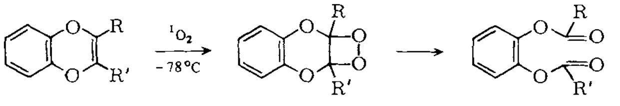

*(1)*


*(2)*


*(3)*

Photosensitized singlet oxygenation of a 0.03 M $CH_2Cl_2$ solution of the 1,4-benzodioxins *(4)*[4] at −78 °C, using polymer-bound Rose Bengal as sensitizer and a 400 W sodium street lamp as radiation source[5], led to complete consumption of the dioxins within 2 h, as evidenced by NMR monitoring. For example, with *(4a)* the olefinic proton at $\delta = 6.41$ disappeared with simultaneous appearance of the dioxetanyl proton at $\delta = 6.33$. On heating to 20 °C this signal also disappeared; in its place an aldehydic proton—as expected for *(5a)*—appeared.

The dioxetane *(1a),* was isolated by column chromatography (Florisil, −60 °C, $CH_2Cl_2$) and characterized spectroscopically[6]. On heating, pure *(1a)* quantitatively gave the pyrocatechol diester *(5a)*[7] with concomitant light emission.



*(4)* *(1)* *(5)*

*(a),* R = Ph, R′ = H; *(b),* R = Ph, R′ = Me; *(c),* R = R′ = Me

Photooxygenation of 2-methyl-3-phenyl and 2,3-dimethyl-1,4-benzodioxins, *(4b)* and *(4c),* respectively, afforded the corresponding dioxetanes *(1b)*[8] and *(1c)*[9] which upon heating were quantitatively transformed into the pyrocatechol derivatives *(5b)*[10] and *(5c)*[11], respectively, with light emission.

On thermal decomposition, the dioxetanes *(1)* chemiluminesce; however, the emission intensity was too weak to be useful for quantitative determination of the singlet quantum yields ($\Phi^{S}$). We therefore used the energy-transfer chemiluminescence to assess the quantum yields[3]. The activation parameters $\Delta H^{+}$ and $\Delta S^{+}$, and the singlet ($\Phi^{S}_{DPA}$) and triplet ($\Phi^{T}_{DBA}$) quantum yields, respectively, are collected in Table 1.

Table 1. Activation parameters and quantum yields for thermolysis of the dioxetanes *(1).*

| | *(1a)* | *(1b)* | *(1c)* |
|---|---|---|---|
| $\Delta H^{+}$ [kcal/mol] [a] | 23.8 ± 1.0 | 25.1 ± 1 | 26.2 ± 1 |
| $\Delta S^{+}$ [cal/mol/K] [a] | −5.1 ± 2 | −5.7 ± 2 | −3.7 ± 2 |
| $\Delta G^{+}$[kcal/mol] [b] | 25.7 ± 1 | 26.9 ± 1 | 27.3 ± 1 |
| $10^3\ \Phi^{S}_{DPA}$ [%] | 1.1 ± 0.3 | 1.6 ± 0.2 | 0.09 ± 0.02 |
| $\Phi^{T}_{DBA}$ [%] | 0.6 ± 0.06 | 3.5 ± 1.3 | 0.02 ± 0.01 |
| $\Phi^{T+S}$ [%] | 0.6 ± 0.06 | 3.5 ± 1.3 | 0.02 ± 0.01 |
| $\Phi^{T}/\Phi^{S}$ | 500 ± 300 | 2200 ± 700 | 200 ± 100 |

[a] Determined by isothermal kinetics using DBA-enhanced chemiluminescence. [b] At 293.2 K.

The activation parameters show that the dioxetanes *(1)* are of comparable stability to that of tetramethyl-1,2-dioxetane (TMD)[3]. As expected, the disubstituted dioxetanes *(1b)* and *(1c)* are more stable than the monosubstituted derivative *(1a),* but there is no difference in stability due to phenyl *versus* methyl substitution. From the quantum yields it is seen that, as with TMD, n,π* triplet states can be selectively generated from the dioxetanes *(1), i. e.* all derivatives *(1a)*—*(1c)* give very low yields of n,π* singlet states. Surprising is the very low total quantum yield of dioxetane *(1c).* The possibility of introducing substituents into the benzene ring and at the 2,3-positions should make derivatives assessible which exhibit high singlet excitation yields through intramolecular electron exchange[1].

Received: February 12, 1980,
in altered form July 5, 1981 [Z 924 IE]
German version: Angew. Chem. *93,* 1100 (1981)

CAS-Registry numbers:
*(1a),* 79792-88-4; *(1b),* 79792-89-5; *(1c),* 79792-90-8; *(4a),* 5770-58-1; *(4b),* 79792-91-9; *(4c),* 79792-92-0; *(5a),* 79792-93-1; *(5b),* 79792-94-2; *(5c),* 635-67-6.

---

[*] Prof. Dr. W. Adam, Dr. O. Cuerto, Dipl.-Chem. E. Schmidt, Dr. K. Takayama
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany) (address to which correspondence should be sent)
Department of Chemistry, University of Puerto Rico
Rio Piedras, Puerto Rico (USA)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the National Science Foundation, the National Institutes of Health, as well as by the Petroleum Research Fund.

[1] *K. A. Zaklika, A. L. Thayer, A. P. Schaap,* J. Am. Chem. Soc. *100,* 4916 (1978).

[2] *W. Adam, C.-C. Cheng, O. Cueto, I. Erden, K. Zinner,* J. Am. Chem. Soc. *101,* 4735 (1979).

[3] *W. Adam,* Adv. Heterocycl. Chem. *21,* 437 (1977).

[4] For the synthesis of 1,4-benzodioxins cf. *E. Schmidt*, Diplomarbeit, University of Würzburg 1981.

[5] *W. Adam, H. J. Eggelte*, J. Org. Chem. *42*, 3987 (1977).

[6] *(1a)*, 41% yield, yellow crystalline solid, m.p. = 70—72 °C ($n$-$C_5H_{12}/CH_2Cl_2$), >98% peroxide content by iodometric titration, satisfactory elemental analysis; $^1$H-NMR ($CCl_4$, TMS): $\delta = 6.33$ (1 H, s, =C—H), 7.16 (4 H, s, arom. protons), 7.45—7.61 and 7.83—7.97 (5 H, m, phenyl); IR ($CCl_4$): $\nu = 3080$, 2960, 1620, 1500, 1470, 1460 cm$^{-1}$.

[7] *(5a)*, 82% yield, b.p. = 110 °C/0.15 torr, $n_D^{20} = 1.5701$; satisfactory elemental analysis; $^1$H-NMR ($CCl_4$, TMS): $\delta = 7.00$—7.50 and 7.90—8.09 (5 H, m, phenyl), 7.12 (4 H, s, arom. protons), 7.95 (1 H, s, $H$—$CO_2$); IR ($CCl_4$): $\nu = 3080$ (aromatic CH), 1750 (C=O) cm$^{-1}$.

[8] *(1b)*, 35% yield, yellow crystalline solid, m.p. = 72—76 °C ($n$-$C_5H_{12}/CH_2Cl_2$), >98% peroxide content by iodometric titration, satisfactory elemental analysis; $^1$H-NMR ($CCl_4$, TMS): $\delta = 1.41$ (3 H, s, $CH_3$), 7.06 (4 H, s, arom. protons), 7.40—7.57 and 7.73—7.88 (5 H, m, phenyl); IR ($CCl_4$): 3080, 2950, 1615, 1495, 1455, 1395 cm$^{-1}$.

[9] *(1c)*, 33% yield, yellow crystalline solid, m.p. = 118—122 °C (dec.) ($n$-$C_5H_{12}/CH_2Cl_2$), satisfactory elemental analysis; $^1$H-NMR ($CCl_4$, TMS): $\delta = 1.81$ (6 H, s, $CH_3$) and 6.99 (4 H, s, arom. protons); IR ($CCl_4$): 3040, 3000, 1612, 1495, and 1264 cm$^{-1}$.

[10] *(5b)*, 83% yield, b.p. = 150 °C/0.10 torr, $n_D^{20} = 1.5631$, satisfactory elemental analysis; $^1$H-NMR ($CCl_4$, TMS): $\delta = 2.15$ (3 H, s, $CH_3$), 7.45 (4 H, s, arom. protons), 7.65—7.87 and 8.30—8.35 (5 H, m, phenyl); IR ($CCl_4$): 3080, 2960, 1775, 1755 cm$^{-1}$.

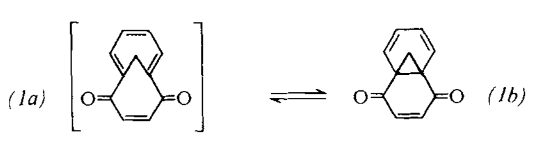
[11] *(5c)* formed quantitatively and IR and $^1$H-NMR identical with literature data, *H. Nimz, K. Das, N. M. Minemura*, Chem. Ber. *104*, 1871 (1971).

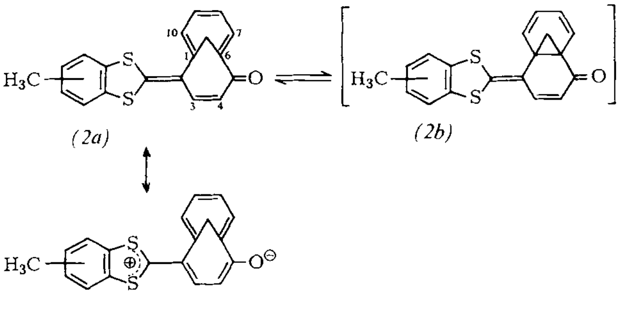
## Donor-Acceptor-Stabilized 1,6-Methano[10]annulene Derivatives[**]

By *Richard Neidlein* and *Hartmut Zeiner*[*]

*Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday*

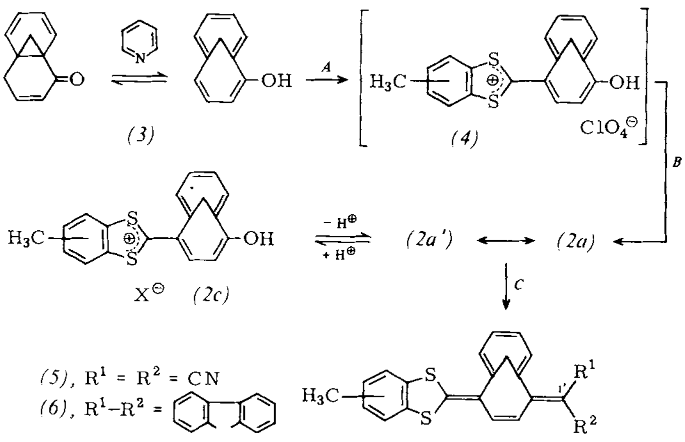
The diketo derivative *(1a)* of 1,6-methano[10]annulene, a homologue of 1,4-naphthoquinone, cannot be synthesized[1] since it is thermodynamically less stable than its valence isomer *(1b)*.





In contrast, however, the bicyclic quinoid structure is considerably more stable than the tricyclic structure if it is incorporated into an integral part of a "push-pull" system as in *(2a)*. No evidence that the valence isomer *(2b)* exists has been obtained to date[2]. To the best of our knowledge, *(2a)* is the first "push-pull"-stabilized quinomethide whose quinoid partial structure is not derived from a benzoid aromatic system.

The synthetic route to *(2a)* starting from the tautomeric/valence isomeric mixture *(3)*[3] is outlined in Scheme 1.



Scheme 1. *A:* 5-methyl-1,3-benzodithiolylium perchlorate [4], anhydrous $CH_3CN$, $N_2$, 20 °C, 12 h; *B:* $NEt_3$, $CH_2Cl_2$, 20 °C; *C:* Reaction to give *(5)* or *(6)*: dicyanoketene [5] or 9-carbonylfluorene [6], anhydrous toluene, $N_2$, 1.5—2 h.

The bicyclic cycloheptatriene structure of *(2a)* is based on spectroscopic evidence: in the $^1$H-NMR spectrum, the $CH_2$-bridge protons form an AX system with geminal coupling $^2J_{AX} = 10.7$ Hz; in contrast, 4—5 Hz would be expected for a tricyclic norcaradiene structure such as in *(2b)*[7]. A further index for *(2a)* is provided by the absorption of H-7 to H-10[8] (ABCD system at relatively low field strength ≥ 6.7). The "push-pull" effect in *(2a)* produces a carbonyl absorption at conspicuously low wavenumber, as well as a relatively high basicity; the negative solvatochromism of the longest wavelength UV bands indicates a marked contribution of the polar mesomeric structure *(2a')* to the ground state.

Conversion of the basic *(2a)* into the conjugated red-violet acid *(2c)* (Scheme 1) shifts the absorption of the $CH_2$-bridge protons (AB signal) 1.18 ppm upfield. With

Table 1. Selected physical data for compounds *(2a)*, *(5)*, and *(6)*.

*(2a)*: M.p. = 70—71 °C; yield 82%; $M^+ = 322.0485$ (calc. 322.0484); $^1$H-NMR (90 MHz, $CDCl_3$, TMS): $\delta = 0.65$ (d, AX signal, $^2J_{AX} = 10.7$ Hz, 1 H, $CH_2$), 3.29 (d, AX-signal, $^2J_{AX} = 10.7$ Hz, 1 H, $CH_2$), 2.37 (s, $CH_3$), 5.85 (d, AB signal, $^3J_{3,4} = 11.8$ Hz, H-4), 7.29 (d, AB-signal, $^3J_{3,4} = 11.8$ Hz, H-3), 6.86—7.34 (m, H-7 to H-10 and 3 arom. H) [8]; UV ($CH_3CN$): $\lambda_{max} = 244$ nm ($\varepsilon = 10094$), 316 (3154, sh), 445 (8306); UV ($CH_2Cl_2$): $\lambda_{max} = 245$ (11478, sh), 254 (10655, sh), 295 (4364, sh), 316 (3540, sh), 458 (9253); IR (KBr): 1610 cm$^{-1}$ (CO), 1535 (C=C); MS (100 eV, 170 °C): $m/z$ 322 (100%, $M^+$)

*(2c)* ≙ *(2a)* in $CF_3COOD$: $^1$H-NMR (90 MHz, TMS): $\delta = 0.21$ (d, AB-signal, $^2J_{AB} = 10.8$ Hz, 1 H, $CH_2$), 1.37 (d, AB-signal, $^2J_{AB} = 10.8$ Hz, 1 H, $CH_2$), 2.63 (s, $CH_3$), 6.63 ($\delta_{Ac}$, $^3J_{3,4} = 10.2$ Hz, H-4), 7.34—8.19 (m, H-3, H-7 to H-10 and 3 arom. H)

*(5)*: yield 52%; $M^+ = 370.0597$ (calc. 370.0597); $^1$H-NMR (90 MHz, $CD_2Cl_2$, TMS): $\delta = 0.80$ (d, AX signal, $^2J_{AX} = 10.9$ Hz, 1 H, $CH_2$), 2.75 (d, AX signal, $^2J_{AX} = 10.9$ Hz, 1 H, $CH_2$), 2.39 (s, $CH_3$), 6.49 (d, AB signal, $^3J_{3,4} = 11.1$ Hz, H-4), 6.98 (d, AB signal, $^3J_{3,4} = 11.1$ Hz, H-3), 7.05—7.46 (m, H-7 to H-10 and 3 arom. H)

*(6)*: M.p. = 128 °C; yield 46%; $^1$H-NMR (90 MHz, $CDCl_3$, TMS): $\delta = 0.89$ (d, AX system, $^2J_{AX} = 10.6$ Hz, 1 H, $CH_2$), 3.22 (d, AX signal, $^2J_{AX} = 10.6$ Hz, 1 H, $CH_2$), 2.32 (s, $CH_3$), 6.50 ($\delta_{Ac}$, $^3J_{3,4} = 11.6$ Hz, H-4), 6.86—7.86 (m, H-3, H-7 to H-10 and 11 arom. H); UV ($CH_3CN$): $\lambda_{max} = 204$ nm ($\varepsilon = 74976$), 230 (72179), 252 (43083), 264 (34131, sh), 318 (3917, sh), 340 (3357, sh), 522 (16226); UV ($CH_2Cl_2$): $\lambda_{max} = 305$ nm ($\varepsilon = 13885$, sh), 322 (7295, sh), 342 (5648, sh), 540 (17415); MS (100 eV, 250 °C): $m/z$ 470 (62%, $M^+$)

---

[*] Prof. Dr. R. Neidlein, Dr. H. Zeiner
Pharmazeutisch-chemisches Institut der Universität
Im Neuenheimer Feld 364, D-6900 Heidelberg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and by the Deutsche Forschungsgemeinschaft.

$\delta_{ABc}=0.79$ ($CF_3COOD$) they lie close to the characteristic high-field region of disubstituted 1,6-methano[10]annulenes ($\delta=-0.5$ to $+0.5$). Furthermore, aromatization of the $C_{11}$ bicycle in *(2c)* is also indicated by the paramagnetic shift of the low-field multiplet by 0.67 ppm, as well as the reduction of $^3J_{3,4}$ by ca. 1.6 Hz, suggesting a decrease of the bond order between C-3 and C-4.

Similar results are obtained with the "push-pull" stabilized quinodimethanes *(5)* and *(6)*, which are readily accessible from *(2a)* (Scheme 1); however, only *(6)* can be protonated at the exocyclic double bond (C5—C1′).

Received: June 3, 1980,
in altered form: July 8, 1981 [Z 927 IE]
German version: Angew. Chem. *93*, 1117 (1981)

CAS-Registry numbers:
*(2a)*, 79839-35-3; *(2c)*, 79855-11-1; *(3)* isomer I, 10474-50-7; *(3)* isomer II, 79839-36-4; *(5)*, 79855-12-2; *(6)*, 10474-55-2; 5-methyl-1,3-benzodithiolylium perchlorate, 72939-27-6; dicyancarbene, 4361-47-1; 9-carbonylfluorene, 486-25-9.

---

[1] *E. Vogel, E. Lohmar, W. A. Böll, B. Söhngen, K. Müllen, H. Günther*, Angew. Chem. *83*, 401 (1971); Angew. Chem. Int. Ed. Engl. *10*, 397 (1971).
[2] Temperature-dependent $^1H$-, and above all, $^{13}C$-NMR measurements are planned.
[3] *E. Vogel, W. Schröck, W. A. Böll*, Angew. Chem. *78*, 753 (1966); Angew. Chem. Int. Ed. Engl. *5*, 732 (1966).
[4] *L. Soder, R. Wizinger*, Helv. Chim. Acta *42*, 1733 (1959).
[5] *R. Neidlein, E. Bernhard*, Angew. Chem. *90*, 395 (1978); Angew. Chem. Int. Ed. Engl. *17*, 369 (1978).
[6] *H. Staudinger*, Ber. Dtsch. Chem. Ges. *39*, 3062 (1906).
[7] *D. J. Patel, M. E. H. Howden, J. D. Roberts*, J. Am. Chem. Soc. *85*, 3218 (1963).
[8] H-7 to H-10 absorb, together with the benzoid aromatic protons, in a complex non-analyzable multiplet.

---

## Potassium Metal Dispersed on Silica: A Versatile Reagent in Organic Chemistry[**]

By *Jaacov Levy, Dov Tamarkin, Henry Selig,* and *Mordecai Rabinovitz*[*]

In recent years there has been much interest in reagents supported on silica gel[1,2], on graphite[3], and on alumina[4]. We report here the preparation and some reactions of a new reagent in this class—potassium metal dispersed on silica gel.

Silica gel (1.500 g, BDH, 70—100 mesh, dried for 3 weeks at 100—120 °C) was heated to 170 °C and stirred under argon with metallic potassium (0.780 g, 0.02 mol, BDH, washed with petroleum ether, and 1-butanol in petroleum ether) for 20 min, and cooled to room temperature. A gray free flowing, relatively air stable powder *(1)* was obtained. X-ray powder diffraction studies show the material to be amorphous. Quenching *(1)* with water released hydrogen gas from whose volume it was determined that 85—90% of the potassium is in elemental form.

Several investigations were carried out in order to study the reactivity of *(1)*. Addition of benzophenone (1.82 g, 0.01 mol) in petroleum ether to *(1)*, prepared as above from 0.02 mol potassium under argon at room temperature, produced a strong blue coloration after 5 min. After 8 h at room temperature the mixture was quenched with water: isolation of the organic products afforded benzopinacol (1,1,2,2-tetraphenyl-1,2-ethanediol) (m.p. 179—180 °C, 72% yield, 1.3176 g, 0.0036 mol); and benzhydrol (m.p. 65—68 °C, 8% yield, 0.1450 g, 0.0008 mol). In contrast, no reaction was observed at room temperature with potassium metal; when heated to reflux a reaction took place which yielded a 1 : 1 mixture of benzopinacol and benzophenone in 60—80% total yield.

*(1)*, prepared from 0.02 mol potassium was reacted with bromobenzene (1.490 g, 0.0095 mol) in diethyl ether and petroleum ether to afford biphenyl (m.p. 65 °C, 82% yield, 0.603 g, 0.00389 mol); no polyphenylenes were observed. Similarly, iodobenzene afforded 81% biphenyl. The Fittig reaction of aryl halides with metallic potassium takes place at higher temperatures, and yields only 20—30% biaryls[5].

These examples show that the dispersion of potassium on silica *(1)* has greater reactivity and different selectivity than metallic potassium. The tendency of *(1)* to facilitate formation of "dimers" (benzopinacol, biphenyl) as exemplified by its reactions with benzophenone, bromobenzene and iodobenzene, may originate from the proximity of two reaction centers on the surface of the silica; on average 4.5—5 active sites per 100 Å$^2$ are found[6].

Received: May 29, 1981 [Z 926 IE]
German version: Angew. Chem. *93*, 1123 (1981)

CAS-Registry numbers:
Silica, 7631-86-9; potassium, 7440-09-7; benzophenone, 119-61-9; benzopinacol, 464-72-2; benzhydrol, 91-01-0; bromobenzene, 108-86-1; iodobenzene, 591-50-4; biphenyl, 92-52-4.

---

[1] For general review: *A. McKillop, D. W. Young*, Synthesis *1979*, 401.
[2] *K. M. Gitis, V. N. Medvedev, O. D. Sterlisov, M. I. Rozensart, V. I. Barishnikova*, Izv. Akad. Nauk SSSR, Ser. Khim. *1976*, 570. *K. G. Allum, R. D. Hancock, I. V. Howell, T. E. Lester, S. McKenzie, R. C. Pitkethly, P. J. Robinson*, J. Catal. *43*, 331 (1976); *K. J. A. Clarke, L. Manninger, T. Baird, ibid. 54*, 230 (1978); *J. T. Richardson, R. J. Dubus, ibid. 54*, 207 (1978); *B. N. Kusnetsov, I. A. Ovgyannikova, Y. A. Ryndin, S. B. Erenburg, A. B. Gil'var, Y. I. Ermakov*, Kinet. Katal. *19*, 749 (1978).
[3] *H. Selig, M. Rabinovitz, I. Agranat, C. H. Lin, L. Ebert*, J. Am. Chem. Soc. *98*, 1601 (1976); *M. Rabinovitz, I. Agranat, H. Selig, C. H. Lin, L. Ebert*, J. Chem. Res. (S) *1977*, 216, (M) *1977*, 2353; *I. Agranat, M. Rabinovitz, M. Selig, C. H. Lin*, Chem. Lett. *1975*, 1271; *H. Selig, L. Ebert*, Adv. Inorg. Radiochem. *23*, 281 (1980).
[4] *E. Czaran, J. Finster, K. H. Schnabel*, Z. Anorg. Allg. Chem. *443*, 175 (1978); *J. Rebek, R. McCready*, Tetrahedron Lett. *1979*, 4437.
[5] *O. Blum-Bergmann*, J. Am. Chem. Soc. *60*, 1999 (1938).
[6] *M. Zamora*, J. Chem. Phys. *82*, 588 (1978).

---

[*] Prof. Dr. M. Rabinovitz, J. Levy, D. Tamarkin, H. Selig
Department of Organic Chemistry
and Department of Inorganic and Analytical Chemistry
The Hebrew University of Jerusalem
Jerusalem 91904 (Israel)

[**] This work was supported by the Israel Commission for Basic Research.

---

## $[Fe_3S(S_2C_{10}H_{12})_3]^{2-}$: The First Synthetic Trinuclear Iron-Sulfur Cluster Compound

By *Gerald Henkel, Wolfgang Tremel,* and *Bernt Krebs*[*]

Preliminary results of an X-ray structure analysis by *Stout et al.*[1] as well as Mössbauer spectroscopic investigations by *Emptage et al.*[2] on a ferredoxin-like iron-sulfur protein ("iron-sulfur protein III") from *A. vinelandii*, first described by *Shethna*[3] and *Yoch* and *Arnon*[4] about 10 years ago, would suggest that the center with the low redox potential of −420 mV represents a novel type of trinuclear cluster.

*Stout et al.*[1] interpret this cluster as a 3Fe—3S center, whose structure can be derived from the dimeric $Fe_2S_2$ unit of the 2Fe—2S ferredoxins by insertion of a distorted planar $FeS_4$ group.

---

[*] Prof. Dr. B. Krebs, Dr. G. Henkel, Dipl.-Chem. W. Tremel
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

We report here on a novel trinuclear iron-sulfur cluster with tetrahedral coordination of the Fe atoms, which could be isolated for the first time as the $Fe_3S(SRS)_3^{2-}$ anion in the compound $[(C_2H_5)_4N]_2[Fe_3S_7C_{30}H_{36}]\cdot CH_3OH$ *(1)* and corresponds to the previously unknown central member in the series of tetrahedrally coordinated Fe—S cluster compounds $(Fe_nS_{4+n})^{z-}$ ($n=2$, 3, 4) with cubane-analogous structure of the terminal member.

The compound *(1)* is obtained as blackish-brown crystals on reaction of 1,2-bis(mercaptomethyl)-4,5-dimethylbenzene and sodium methoxide with iron(III) chloride and *p*-thiocresol in anhydrous methanol and subsequent precipitation with $N(C_2H_5)_4Cl$.

The structure of *(1)* was determined from single crystal diffractometer data (Syntex $P2_1$, $Mo_{K\alpha}$ radiation, graphite monochromator, scintillation counter, $2\theta$-$\theta$ scan, 4016 symmetry-independent reflections, $2\theta_{max}=44°$, $T=-133\,°C$) and refined to $R=0.068$ (Fig. 1). *(1)* crystallizes in space group $P\bar{1}$ of the triclinic system with two formula units per unit cell, the lattice constants, determined at $-133\,°C$, being $a=10.226(3)$, $b=16.505(4)$, $c=16.777(5)$ Å, $\alpha=81.97(3)$, $\beta=73.69(3)$, $\gamma=86.59(3)°$.

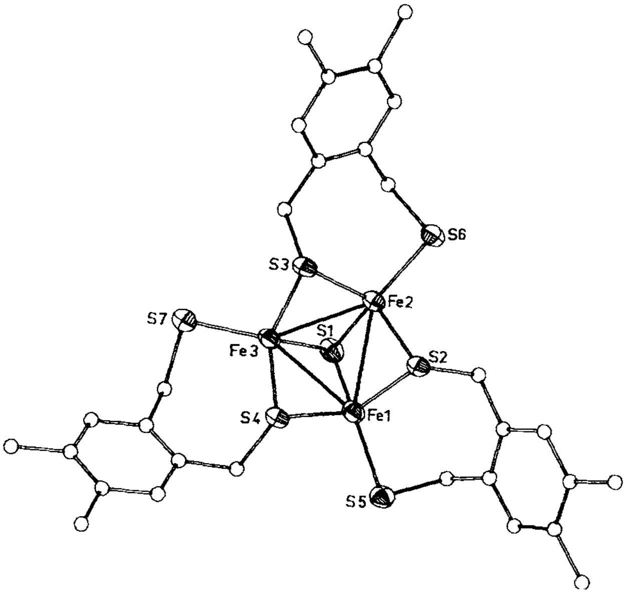


Fig. 1. Structure of the $[Fe_3S(S_2C_{10}H_{12})_3]^{2-}$ ion in crystals of *(1)* with vibration ellipsoids of the central $Fe_3S_7$ skeleton (50% probability level).

The structure of the Fe—S center derives from the $Fe_4S_4(SR)_4$ cubane structure, with one of the four tetrahedral iron positions not being occupied. The Fe atoms form a completely bonded triangle and are each surrounded by a tetrahedron of S atoms which is somewhat distorted from idealized symmetry. This tetrahedron consists of an inorganic S atom above the center of the metal triangle and three mercapto S atoms, two of which form slightly asymmetric bridges to neighboring Fe atoms.

The average lengths of equivalent Fe—S bonds are 2.303 Å (Fe1—S1, Fe2—S1, Fe3—S1), 2.345 Å (Fe1—S2, Fe2—S3, Fe3—S4), 2.350 Å (Fe1—S4, Fe2—S2, Fe3—S3) and 2.293 Å (Fe1—S5, Fe2—S6, Fe3—S7) with standard deviations of the individual values of 0.004 Å. The average distance between the Fe atoms of the cluster is 2.799 Å and thus lies in the upper range of Fe distances, as have been observed in the centers of the 4Fe—4S and 2Fe—2S ferredoxins[5] and their synthetic analogues—*e.g.*, 2.746 Å in $(Et_4N)_2[Fe_4S_4(SC_7H_7)_4]$ *(2)*[6] and 2.698 Å in $(Et_4N)_2[Fe_2S_2(S_2C_8H_8)_2]$ *(3)*[7]. The significance of the metal-metal interactions has already been pointed out, both in the case of the dinuclear as well as of the tetranuclear clusters[6,7]. Considering the formal oxidation states of iron (+2 in *(1)*, +2.5 in *(2)*, and +3 in *(3)*) a nearly linear correlation between oxidation states and metal-metal distances becomes clearly evident.

The IR spectrum of *(1)* shows three poorly resolved Fe—S vibration bands at 355, 320, and 298 $cm^{-1}$ (KBr disk). Preliminary results from Mössbauer spectroscopic investigations ($IS=0.58$ mm $s^{-1}$, $EQ=3.08$ mm $s^{-1}$, $T=293$ K) show good agreement with the values found for *tetrahedrally* coordinated iron(II)-sulfur complexes[5].

The central $Fe_3S_7$ unit of *(1)* with the six potential coupling sites is the first model for trinuclear iron-sulfur centers in proteins, whose existence could only recently be demonstrated[1,2]. The assumption of a more general significance of trinuclear iron-sulfur centers in biological processes is supported by results of investigations on aconitase[2,8] and ferredoxin from *Desulfovibrio gigas*[2].

Received: April 30, 1981 [Z 935 IE]
German version: Angew. Chem. *93*, 1072 (1981)

---

[1] *C. D. Stout, D. Ghosh, V. Pattabhi, A. H. Robbins*, J. Biol. Chem. *255*, 1797 (1980).

[2] *M. H. Emptage, T. A. Kent, B. H. Huynh, J. Rawlings, W. H. Orme-Johnson, E. Muenck*, J. Biol. Chem. *255*, 1793 (1980).

[3] *Y. I. Shethna*, Biochim. Biophys. Acta *205*, 58 (1970).

[4] *D. C. Yoch, D. I. Arnon*, J. Biol. Chem. *247*, 4514 (1972).

[5] *W. Lovenberg:* Iron Sulfur Proteins, Vols. 1 and 3, Academic Press, New York 1973 and 1976, respectively.

[6] *B. A. Averill, T. Herskovitz, R. H. Holm, J. A. Ibers*, J. Am. Chem. Soc. *95*, 3523 (1973).

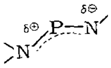
[7] *J. J. Mayerle, S. E. Denmark, B. V. DePamphilis, J. A. Ibers, R. H. Holm*, J. Am. Chem. Soc. *97*, 1032 (1975).

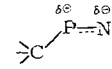
[8] *D. M. Kurtz, R. H. Holm, F. J. Ruzicka, H. Beinert, C. J. Coles, T. P. Singer*, J. Biol. Chem. *254*, 4967 (1979).

## *tert*-Butylimino-*tert*-butylphosphane: An Inorganic Carbene Analogue[**]

By *Edgar Niecke, Reinhold Rüger*, and
*Wolfgang W. Schoeller*[*]

Unlike resonance-stabilized amino(imino)phosphanes of the allyl-anion type *(A)*[1] a highly polar $p_\pi$ bonding system is to be expected in *P*-alkylated iminophosphanes *(B)*, whose existence we have now demonstrated by synthesis of *tert*-butylimino-*tert*-butylphosphane *(4)*.

(*A*)




(*B*)

The lithium salt *(3)*, obtainable from *(1)* by chlorine/fluorine exchange and subsequent metalation, gave the desired product *(4)* on vacuum pyrolysis.

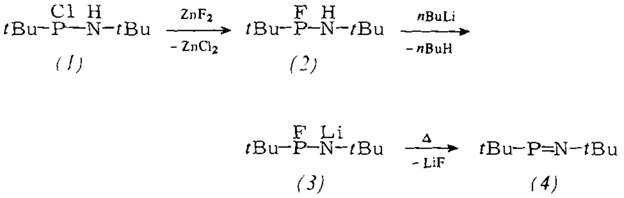
*(4)* is an intense yellow liquid, which is extremely sensitive to oxidation and hydrolysis, but stable for at least a

---

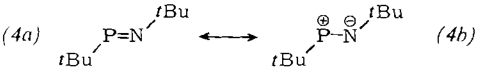
[*] Prof. Dr. E. Niecke, Dr. R. Rüger, Priv.-Doz. Dr. W. W. Schoeller
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld 1 (Germany)

[**] Phosphazenes with Coordination Numbers 2 and 3, Part 23. Delivered in part in a lecture at the 3rd Symp. Inorg. Ring Systems, Graz, August 1981. This work was supported by the Fonds der Chemischen Industrie.—Part 22: *E. Niecke, K. Schwichtenhövel, H. G. Schäfer, B. Krebs*, Angew. Chem. *93*, 1033 (1981); Angew. Chem. Int. Ed. Engl. *20*, 963 (1981).

few days at −40 °C. The monomeric structure of *(4)* follows from the doublet-splitting of the $^{1}$H- and $^{13}$C{$^{1}$H}-NMR signals of the two *tert*-butyl groups. The magnitude



of $J_{CNP}$ (13.4 Hz) indicates the energetically more favorable *trans*-form[2]. The $^{31}$P-NMR signal of *(4)* ($\delta = 472$) shows a drastic deshielding of the phosphorus compared with iminophosphanes of type *(A)* ($\delta = 290-330$[1,3]), which can be ascribed to considerable contribution of *(4b)* to the ground state of *(4)*[4].

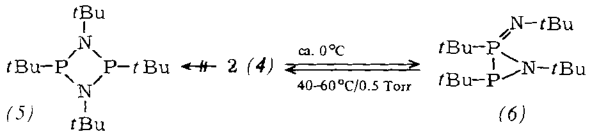


When *(4)* is warmed to above 0 °C, it dimerizes within a few minutes (within a few hours in solution) by [2 + 1]-cycloaddition to give the 1,2$\lambda^3$,3$\lambda^5$-azadiphosphiridine *(6)*—a pale-yellow, viscous liquid (only *one* diastereomer). The thermodynamically favored [2 + 2]-cycloaddition[5] to the 1,3,2$\lambda^3$,4$\lambda^3$-diazadiphosphetidine *(5)* does not take place. Also remarkable is the chelotropic fragmentation of *(6)* under mild conditions, which makes this heterocycle an ideal source of iminophosphane *(4)*.

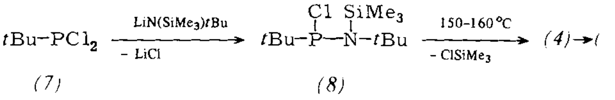
Table 1. Some spectroscopic data of compounds *(2)*, *(4)*, *(6)* and *(8)* [a]. In the case of *(2)*, *(4)* and *(8)* *m/z* 57 ($t$Bu$^+$) is the base line.

| | *(2)* [b] | | *(4)* | | ⩾P: *(6)* | | ⩾P= | | *(8)* [c] | |
|---|---|---|---|---|---|---|---|---|---|---|
| $\delta^{31}$P ($J_{PP}$ [Hz]) | 113.8 | | 472.2 | | −43.2 | (226) | 28.2 | | 147.0 | |
| $\delta^{1}$H ($J_{HP}$ [Hz]) [d] | | | | | | | | | | |
| PNH/PNSiMe$_3$ | 2.0 | (23) | | | | | | | 0.21 | (4.0) |
| PCMe$_3$ | 0.87 | (12.6) | 1.12 | (10.2) | 1.40 | (19.8) | 1.05 | (12.8) | 1.03 | (16.0) |
| PNCMe$_3$ | 1.15 | (0.8) | 1.42 | (1.6) | 1.33 | (1.5) | 1.30 | (0.9) | 1.20 | (<0.2) |
| $\delta^{13}$C ($J_{CP}$ [Hz]) [e] | | | | | | | | | | |
| PCC$_3$ | 24.1 | (16.7) | 23.6 | (11.8) | 29.6 | (23.5) | 31.3 | (8.0) | | |
| PC | 32.2 | (12.5) | 38.7 | (39.7) | 38.0 | (124.5) | 34.1 | (45.0) | | |
| PNCC$_3$ | 32.6 | (8.9) | 30.8 | (13.4) | 29.9 | (1.2) | 34.6 | (18.4) | | |
| PNC | 50.1 | (12.4) | 60.4 | (4.7) | 54.4 | (18.6) | 51.4 | (11.4) | | |
| MS (70 eV) *m/z* | 179 ($M^+$, 8%) | | 159 ($M^+$, 7%)<br>102 (($M-t$Bu)$^+$, 30%) | | | | | | 267 ($M^+$, 3%) | |

[a] 30% solution in CD$_2$Cl$_2$ [*(2)*, *(6)*, *(8)*] or [D$_8$]toluene [*(4)*] with H$_3$PO$_4$ as external ($^{31}$P) or TMS as internal standard ($^{1}$H, $^{13}$C); 300 K [*(2)*, *(6)*, *(8)*] or 237 K [*(4)*]. [b] $J_{PF} = 965$, $J_{HNPF} = 1$, $J_{HCNPF} = 1.2$, $J_{CCPF} = 1.8$, $J_{CPF} = 12.0$, $J_{CCNPF} = 2.0$, $J_{CNPF} = 3.4$ Hz. [c] Data for the preferred rotamer with the SiMe$_3$ group arranged elliptically to the "free" electron pair of the P atom. [d] For *(6)*: $|J_{HP} + J_{HP'}|$. [e] For *(6)*: $|J_{CP} + J_{CP'}|$.



A more direct route to *(6)* has proven to be the thermally-induced elimination of chlorosilane from [*tert*-butyl(trimethylsilyl)amino]-*tert*-butyl(chloro)phosphane *(8)*, which is obtainable from *tert*-butyldichlorophosphane *(7)* and lithium *tert*-butyl(trimethylsilyl)amide.



The difference in reaction behavior of iminophosphane *(A)* and *(B)* is consistent with results of MNDO calculations[6], according to which both systems have two high level σ(P)- and π-orbitals with energy differences o $E_\sigma - E_\pi = 0.3$ eV in *(A)* and −1.1 eV in *(B)*, respectively giving the frontier orbitals π,π*, for *(A)* and σπ* for *(B* The latter corresponds to the orbital sequence characteristic for carbenes and, together with the high electrophilicity of the phosphorus, explains the carbene-analogous behavior of *(4)*.

The composition and constitution of *(6)*, as well as of the precursors *(2)* and *(8)*, are confirmed by elemental analysis, mass spectra [*(2)*, *(8)*], cryoscopic molecular weight determination [*(6)*] and NMR-data (Table 1).

## *Experimental*

All experiments were carried out under inert gas and with rigorous exclusion of moisture. The solvents were purified and dried by column chromatography on Al$_2$O$_3$ (Super I, basic).

*(2)*: A mixture of *(1)*[7] (39.1 g, 0.2 mol) and anhydrous ZnF$_2$ (41.3 g, 0.2 mol) is stirred for 10 min at 140 °C. The resulting crude product is separated from any ZnCl$_2$ and is then distilled from a 10 cm Vigreux column, yield 27 g (76%) as water-clear, mobile liquid, b.p. 48–50 °C/12 torr.

*(8)*: A mixture of LiN(SiMe$_3$)$t$Bu (15.1 g, 0.1 mol) in THF (100 mL) is added dropwise at 40 °C to a stirred solution of *(7)*[8] (19.6 g, 0.1 mol) in 20 mL of THF. After stirring for 2h at 50 °C, filtration, and removal of solvent, the residue is fractionally distilled; yield 16 g (59%) as pale yellow liquid, b.p. 58—60 °C/0.2 torr.

*(4)* from *(2)*: A solution of *n*-butyllithium (2.3 mL, 0.05 mol; 23% in *n*-hexane) is slowly added dropwise at −78 °C to a stirred solution of *(2)* (9 g, 0.05 mol) in pentane (50 mL) and diethyl ether (20 mL). After stirring for 1h at −78 °C the solvent is removed by slowly warming to −10 °C. The residue (mainly *(3)* and the by-product $t$Bu($n$Bu)P—NH$t$Bu[9]) is pyrolyzed at 50—60 °C/0.5 torr; the volatile products are collected in two cold traps (0 °C/−78 °C) mounted in series. After 4 h, 3.6 g of *(4)* together

with *ca.* 10% of the by-product are collected in the −78 °C trap; double re-condensation leads to 2.4 g (32%) of pure *(4)*.

*(6)* from *(8)*: 13.4 g (0.05 mol) of *(8)* is pyrolyzed in a 10-cm Vigreux column at 40 torr and 160—170 °C, the temperature of the column not being allowed to exceed 40 °C; yield: 4.7 g (60%) (oil).

*(4)* from *(6)*: 3.1 g (0.01 mol) of *(6)* is heated to 60—70 °C at 0.1 torr. The volatile *(4)* thus formed is collected in a micro-trap cooled to −196 °C; yield: >90%.

Received: September 22, 1981 [Z 945 IE]
revised: October 19, 1981
German version: Angew. Chem. *93*, 1110 (1981)

CAS Registry numbers:
*(1)*, 24411-61-8; *(2)*, 79933-14-5; *(3)*, 79933-15-6; *(4)*, 79933-16-7; *(6)*, 79933-17-8; *(7)*, 25979-07-1; *(8)*, 79933-18-9.

---

[1] Review: *E. Niecke, O. J. Scherer*, Nachr. Chem. Tech. *23*, 395 (1975); *E. Fluck*, Top. Phosphorus Chem. *10*, 193 (1980).

[2] The *trans*-form could be established in the case of amino(imino)phosphanes: *S. Pohl*, Angew. Chem. *88*, 723 (1976); Angew. Chem. Int. Ed. Engl. *15*, 687 (1976); Z. Naturforsch. *B32*, 1342 (1977).

[3] *J. Neemann, U. Klingebiel*, Chem. Ber. *114*, 527 (1981); *O. J. Scherer, H. Conrad*, Z. Naturforsch. *B36*, 515 (1981).

[4] A larger deshielding of doubly coordinated phosphorus could be observed only in the case of the corresponding phosphonium ion $[t\mathrm{Bu{-}P{\equiv}NMe_2}]^+$ ($\delta = 512$); *A. H. Cowley, M. Lattmann, J. C. Wilburn*, Inorg. Chem. *20*, 2916 (1981).

[5] Review: *O. J. Scherer*, Nachr. Chem. Tech. Lab. *28*, 392 (1980).

[6] a) Energy-optimized MNDO calculations on the model systems $H_2N{-}P{=}N{-}CH_3$ for *(A)* and $H_3C{-}P{=}N{-}CH_3$ for *(B)*; b) for a general discussion of the electronic properties of phosphorus-element (p-p)π bond systems see: *W. W. Schoeller, E. Niecke*, unpublished.

[7] *M. Fild, O. Stelzer*, Inorg. Synth. *14*, 4 (1973).

[8] *O. J. Scherer, P. Klusmann*, Angew. Chem. *81*, 743 (1969); Angew. Chem. Int. Ed. Engl. *8*, 752 (1969).

[9] $t$Bu($n$Bu)P—NH$t$Bu: MS (70 eV): $m/z$ 217 (11%, $M^+$), 104 (100%, $t\mathrm{BuPNH_2^+}$); $^{31}$P-NMR: $\delta = 35.9$, b.p. 70—73 °C/0.5 torr.

## *gem*-Bis(halooxy) Compounds from *cis*- and *trans*-Tetrafluordioxotellurium(VI) Acid, $(HO)_2TeF_4$[**]

By *Brigitte Pötter, Dieter Lentz, Hans Pritzkow,* and *Konrad Seppelt*[*]

*Dedicated to Professor Oskar Glemser on the occasion of his 70th birthday*

In octahedral compounds of the nonmetals, *cis-/trans*-isomers are only rarely observed[1]; often only one isomeric form occurs. Until now $(HO)_2TeF_4$ could be detected only spectroscopically along with $(HO)_xTeF_{6-x}$ derivatives[2]. $Na_2TeO_2F_4$, a salt of the *cis*-acid, forms as a thermodynamically stable product in the pyrolysis of $NaTeOF_5$[3].

Fusing a mixture of $HOTeF_5$ and $Te(OH)_6$ in an autoclave gives a mixture of $(HO)_xTeF_{6-x}$ from which *cis*- and *trans*-$(HO)_2TeF_4$ can be sublimed out at room temperature as major products [yield 76.5%] as colorless, difficultly volatile crystals; *cis*:*trans* ≈ 2.25 : 1 (from statistical theory 4 : 1). The isomers can readily be separated *via* the silyl esters whose melting and boiling points differ significantly.

$$cis/trans\text{-}(HO)_2TeF_4 + 2\,Me_3SiCl \xrightarrow{60\,^\circ C} cis/trans\text{-}(Me_3SiO)_2TeF_4 + 2\,HCl$$

*cis*-$(Me_3SiO)_2TeF_4$ is a clear, stable liquid; M.p. = −10 °C, b.p. = 79 °C/20 mbar and the $^{19}$F-NMR spectrum shows a typical $A_2B_2$ pattern ($\delta_A = 28.59$, $\delta_B = 35.51$, $J_{AB} = 161.4$ Hz). *trans*-$(Me_3SiO)_2TeF_4$ is a colorless solid, m.p. = 47.0 °C, b.p. = 77.5 °C/20 mbar and only one sharp line occurs in the $^{19}$F-NMR spectrum ($\delta = 32.56$). Its structure was confirmed by X-ray diffraction analysis (Fig. 1).

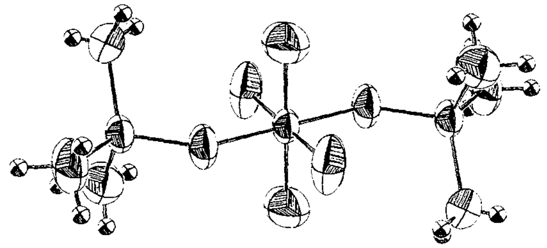


Fig. 1. Molecular structure of *trans*-$(CH_3)_3SiO_2TeF_4$ in the crystal. $P2_1/n$, $a = 1035.0(3)$, $b = 1127.0(3)$, $c = 636.0(2)$ pm, $\beta = 90.132°$; 2222 reflections. All atoms except H were refined anisotropically. $R_w = 0.025$; ∢ TeOSi = 137.4°.

Interestingly, pure *cis*-$(Me_3SiO)_2TeF_4$ can be prepared from $Me_3SiOTeF_5$ by reaction with disiloxane.

$$Me_3SiOTeF_5 + Me_3SiOSiMe_3 \xrightarrow{100\,^\circ C} cis\text{-}(Me_3SiO)_2TeF_4 + Me_3SiF$$

Its formation is obviously kinetically controlled (NMR limit of detection for the *trans*-isomer < 1%).

From the isomerically pure silyl ester, the isomerically pure acids are obtained by reaction with HF.

$$(Me_3SiO)_2TeF_4 + 2\,HF \rightarrow (HO)_2TeF_4 + 2\,Me_3SiF$$

*cis*-$(HO)_2TeF_4$ is a colorless, sublimable solid, m.p. = 106 °C; $^{19}$F-NMR: $A_2B_2$ spectrum ($\delta_A = 34.33$, $\delta_B = 42.37$, $J_{AB} = 149.47$ Hz). Likewise, *trans*-$(HO)_2TeF_4$ is a colorless, sublimable solid, m.p. = 116 °C; $^{19}$F-NMR: sharp singlet ($\delta = 39.65$). Both acids are thermally stable well above 100 °C, they do not interconvert, and are soluble in water without decomposition.

The structure also remains intact in simple chemical reactions:

$$cis\text{-}(HO)_2TeF_4 + 2\,ClF \xrightarrow{-78\,^\circ C,\ CFCl_3} 2\,HF + cis\text{-}(ClO)_2TeF_4$$

$$cis\text{-}(ClO)_2TeF_4 + Br_2 \xrightarrow{-78\,^\circ C} Cl_2 + cis\text{-}(BrO)_2TeF_4$$

$$trans\text{-}(HO)_2TeF_4 + 2\,ClF \xrightarrow{0\,^\circ C,\ CFCl_3} 2\,HF + trans\text{-}(ClO)_2TeF_4$$

$$trans\text{-}(ClO)_2TeF_4 + Br_2 \xrightarrow{-78\,^\circ C} Cl_2 + trans\text{-}(BrO)_2TeF_4$$

Compounds with vicinal bis(halogenoxy) groups were, to our knowledge, unknown. Both bis(chloroxy)tellurium tetrafluorides are yellow liquids: *cis*-$(ClO)_2TeF_4$, m.p. = −77.8 °C, b.p. < 20 °C/$10^{-2}$ mbar, $^{19}$F-NMR: $A_2B_2$ spectrum ($\delta_A = 51.71$, $\delta_B = 57.37$, $J_{AB} = 159.7$ Hz);

---

[*] Prof. Dr. K. Seppelt, Dipl.-Chem. B. Pötter, Dr. D. Lentz
Institut für Anorganische und Analytische Chemie
der Freien Universität
Fabeckstrasse 34—36, D-1000 Berlin 33 (Germany)
Dr. H. Pritzkow
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

*trans*-$(ClO)_2TeF_4$, m.p. = −66.7 °C, b.p. <20 °C/$10^{-2}$ bar, $^{19}F$-NMR: singlet ($\delta = 54.65$). They are moisture and light sensitive. *cis*-$(BrO)_2TeF_4$, a red liquid, is thermally highly unstable and decomposes at *ca.* 0 °C (m.p. = −31.5 °C); the *trans*-isomer is more stable, (m.p. = 23 °C, $^{19}F$-NMR: singlet at $\delta = 51.60$).

Starting from *cis*-$(HO)_2TeF_4$, a polymeric xenon compound is obtainable:

$$cis\text{-}(HO)_2TeF_4 + XeF_2 \xrightarrow[20\,^\circ C]{C_4F_9SO_2F} 2\,HF + (\text{—}Xe\text{—}OTeF_4O\text{—})_n$$

This faintly yellow solid is insoluble in all common solvents and decomposes above 80 °C vigorously with evolution of xenon.

All new compounds were identified by elemental analyses as well as by IR spectroscopy.

Received: September 8, 1980 [Z 936a IE]
German version: Angew. Chem. *93*, 1095 (1981)

---

[1] *R. Höfer, O. Glemser*, Angew. Chem. *85*, 1105 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1000 (1973); *D. Lentz, H. Pritzkow, K. Seppelt*, Inorg. Chem. *17*, 1926 (1978); *K. Seppelt*, Angew. Chem. *91*, 199 (1979); Angew. Chem. Int. Ed. Engl. *18*, 186 (1979).

[2] *L. Kolditz, I. Fitz*, Z. Anorg. Allg. Chem. *349*, 175 (1967); *G. W. Fraser, G. D. Meikle*, J. Chem. Soc. Chem. Commun. *1974*, 624; *U. Elgad, H. Selig*, Inorg. Chem. *14*, 140 (1975); *Note added in proof: cis-* and *trans-*$(HO)_2TeF_4$ have also recently been described by *W. Trötsch, F. Sladky*, Chem. Commun. *1980*, 927. The physical data of *trans*-$(HO)_2TeF_4$ are comparable, the melting point of *cis*-$(HO)_2TeF_4$ is found to be 59° higher (hydrate formation?).

[3] *K. Seppelt*, Z. Anorg. Allg. Chem. *406*, 287 (1974).

---

# $CH_3\text{—}SF_4^+SbF_6^-$, a "Sulfuranonium" Salt[**]

By *Gert Kleemann* and *Konrad Seppelt*[*]

The kinetic stability of sulfur hexafluoride against all chemical attack is widely known and can be explained by the almost perfect shielding of the sulfur atom by the six fluorine ligands. The alkyl derivatives $CH_3\text{—}SF_5$ and $C_2H_5\text{—}SF_5$, likewise, are inert towards concentrated bases or lithium alkyls even at higher temperatures. When attacked by Lewis acids, however, the abstraction of a fluoride ion in the primary step is readily possible.

Methyl- and ethylsulfur pentafluoride were prepared according to:

$$CH_2{=}SF_4 \xrightarrow[-78\,^\circ C]{HF} CH_3\text{—}SF_5{}^{[1]}, \qquad \text{B.p.} = 26\,^\circ C$$

$$ClCO\text{—}CH_2\text{—}SF_5{}^{[2]} \xrightarrow[\text{1. ether 2. } H_2O]{LiAlH_4} HOCH_2CH_2\text{—}SF_5 \xrightarrow[CH_2Cl_2,\ \text{pyridine}]{TosCl}$$

$$Tos\text{—}OCH_2CH_2\text{—}SF_5{}^{[3b]} \xrightarrow[(nC_4H_9)_2O]{LiAlH_4} C_2H_5\text{—}SF_5, \qquad \text{B.p.} = 61\,^\circ C$$

Both react readily at low temperatures with $AsF_5$ or $SbF_5$, forming colorless solids that decompose irreversibly at room temperature.

$$RSF_5 + EF_5 \xrightarrow{-70\,^\circ C} RSF_4^+EF_6^- \xrightarrow{20\,^\circ C} SF_3^+EF_6^- + RF$$

The intermediate products and their decomposition reactions were investigated by NMR spectroscopy in the $CH_3SF_5/SbF_5$ system with $SO_2$ as solvent (cf. Fig. 1).

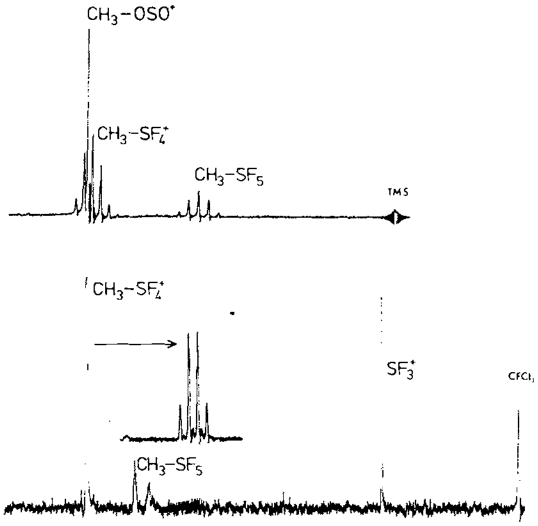


Fig. 1. $^1H$- and $^{19}F$-NMR spectra (below) of a $CH_3SF_5$ and $SbF_5$ solution in $SO_2$ at −80 °C.
$CH_3SF_5$: $\delta_H = 3.4$, $\delta_{FA} = -84.0$, $\delta_{FB_4} = -70.5$, $J_{HF} = 10.25$ Hz, $J_{AB_4} = 150$ Hz; $CH_3SF_4^+$: $\delta_H = 5.28$, $\delta_F = -80.7$, $J_{HF} = 8.6$ Hz; $CH_3OSO^+$: $\delta_H = 5.35$ (cf. [4]); $SF_3^+$: $\delta_F = -25.5$.
In the $^{19}F$-NMR spectrum several broad peaks for the Sb—F atoms are additionally observed at $\delta = +100$ to $+150$.

Besides the known peaks of the starting compound $CH_3\text{—}SF_5$[2], a quintet appears in the $^1H$-NMR spectrum and a quartet in the $^{19}F$-NMR spectrum, which are assigned to the $CH_3\text{—}SF_4^+$ cation. This interpretation presumes the magnetic equivalence of the fluorine atoms through rapid intramolecular exchange. Further peaks indicate the decomposition ot the "sulfuranonium" ion, thus

$$CH_3\text{—}SF_4^+ \xrightarrow{SO_2} CH_3\text{—}OSO^{+[3]} + SF_4 \xrightarrow{SbF_5} SF_3^+SbF_6^-$$

whereby $CH_3^+$ could be formed as intermediate.

Our results indicate that:

- either the displacement of a fluorine atom in $SF_6$ by the sterically similar methyl or ethyl group leads to a drastic change in the electronic properties of the molecule, in particular it causes an increase in the basicity of the remaining fluorine atoms,
- or the reactivity of $SF_6$ in the presence of the strongest Lewis acids has not been sufficiently explored to date.

Received: April 6, 1981 [Z 936b IE]
German version: Angew. Chem. *93*, 1096 (1981)

CAS Registry numbers:
$CH_3SF_4{}^+SbF_6{}^-$, 79899-72-2; $CH_3SF_6$, 753-79-7; $C_2H_5SF_5$, 65227-32-9; $CH_2{=}SF_4$, 66793-25-7; $ClCOCH_2SF_5$, 2353-88-0; $CH_3OSO^+$, 59970-36-4; $CH_3SF_4{}^+$, 79898-82-1; $SF_3{}^+$, 30313-36-1; $C_2H_5SF_4{}^+SbF_6{}^-$, 79899-74-4

---

[*] Prof. Dr. K. Seppelt, Dipl.-Chem. G. Kleemann
Institut für Anorganische und Analytische Chemie
der Freien Universität
Fabeckstrasse 34—36, D-1000 Berlin 33 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *H. Bock, J. E. Boggs, G. Kleemann, D. Lentz, H. Oberhammer, E. M. Peters, K. Seppelt, A. Simon, B. Solouki*, Angew. Chem. *91*, 1008 (1979); Angew. Chem. Int. Ed. Engl. *18*, 944 (1979).

[2] *G. Kleemann, K. Seppelt*, Chem. Ber. *112*, 1140 (1979).

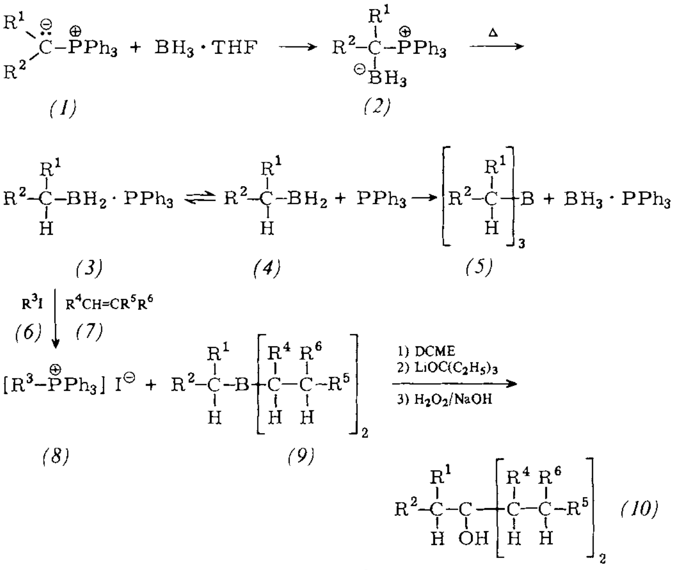
[3] The ion $CH_3OSO^+$ is formed also from $CH_3F/SbF_5$ in $SO_2$ or $SO_2ClF$: cf. *G. A. Olah, D. J. Donovan, H. C. Lin*, J. Am. Chem. Soc. *98*, 2661 (1976).

# Monoalkylboranes from Alkylidene(triphenyl)phosphoranes and Borane; Combination of Ylide Reactions and Hydroboration[**]

By *Hans Jürgen Bestmann, Kurt Sühs,* and *Thomas Röder*[*]

*Dedicated to Professor Leopold Horner on the occasion of his 70th birthday*

Alkylidenetriphenylphosphoranes *(1)* add $BH_3$ (as adduct with ether, tetrahydrofuran or amines) to give the stable phosphonioborates *(2)*[1]. *Köster* and *Rickborn*[2] found that when *(2a)* and *(2e)* (Table 1) are heated in boiling chlorobenzene a clear solution is formed which on treatment with acids liberates two moles of hydrogen per mole of *(2)*; on the strength of this they concluded that *(3)* is formed. Consistent with this conclusion, trialkylboranes *(5)* and triphenylphosphane–borane are formed on heating *(2)* in boiling decalin.



*(6a), (8a)*: $R^3 = CH_3$; *(6b), (8b)*: $R^3 = C_6H_5CH_2$
DCME = $Cl_2HCOCH_3$

We have now been able to confirm the rearrangement of *(2)* to *(3)* with numerous examples. The reaction (in chlorobenzene) was followed $^{31}$P-NMR spectroscopically. The adducts *(3)*, which can be isolated in a crystalline or an oily state, do not disproportionate; on acid hydrolysis they evolve two moles of hydrogen per mole of *(3)*. The reactions carried out by us are listed in Table 1.

In solution an equilibrium exists between the adducts *(3)* on the one hand, and the monoalkylboranes *(4)* and triphenylphosphane on the other; this equilibrium lies predominantly on the side of *(3)* at room temperature. If a solution of *(3)* in tetrahydrofuran is treated with methyl iodide *(6a)* or, better, benzyl iodide *(6b)*, then triphenylphosphane is removed as the sparingly soluble phosphonium salt *(8)*, and the free monoalkylboranes *(4)* remain in solution. We have thus found a simple entry[4] to the preparatively very useful[5] compounds *(4)*; monoalkylboranes *(4b–d)* with unbranched chains, as well as monomethyl- *(4a)*, monobenzyl- *(4e)* and monoisopropylborane *(4f)*, can be prepared without difficulty. If the monoalkylboranes *(4)* obtained from *(3)* are liberated by reaction with *(6)* in the presence of an olefin *(7)* at room temperature, a hydroboration takes place, leading to the "mixed" trialkylboranes *(9)*, which can be converted by known methods[6a], *e.g.* into the tertiary alcohols *(10)*. We usually employed the dichloromethyl methyl ether–$LiOC(C_2H_5)_3$–$H_2O_2$ (DCME) method[6b]. Table 2 lists some examples.

Table 2. Tertiary alcohols *(10)* obtained by reaction of the adducts *(3)* with methyl iodide *(6a)* in the presence of an olefin *(7)* in tetrahydrofuran at room temperature and subsequent conversion, by the DCME method, of the borane *(9)* formed. The reaction times *(t)* can be shortened by use of benzyl iodide *(6b)* instead of *(6a)*.

| $R^1$ | $R^2$ | $R^4$ | $R^5$ | $R^6$ | *t* [h] | B.p. [°C/torr] [8] | Yield [%] [7] |
|---|---|---|---|---|---|---|---|
| H | H | —$(CH_2)_4$— | | H | 70 | 79–82/0.15 | 30 |
| $CH_3$ | H | H | $n$-$C_3H_7$ | $CH_3$ | 88 | 85–88/0.12 | 41 |
| $n$-$C_9H_{19}$ | H | H | $n$-$C_3H_7$ | $CH_3$ | 60 | 128–131/0.05 | 40 |
| $C_6H_5$ | H | H | $n$-$C_5H_{11}$ | H | 87 | 128–132/0.05 | 52 |
| $CH_3$ | $CH_3$ | H | $n$-$C_5H_{11}$ | H | 41 | 114–117/0.15 | 50 |

Ring closure takes place on reaction of diolefins with monoalkylboranes, as has already been demonstrated in the case of monotectylborane[6a,c]. Reaction of the adducts *(3)* with *(6)* in the presence of 1,5-cyclooctadiene leads to formation of the bridged boranes *(11)*, which can be converted by the DCME-method[6b] into the corresponding tertiary alcohols *(12)* [*(12a)* from *(3b)* on using *(6b)*; *(12b)* from *(3c)* on using *(6a)*; reaction times 24 h and 78 h, b.p. 80–85 °C/0.01 torr and 96–100 °C/0.05 torr[8], yield 41% and 50%, respectively[7]].

Table 1. Phosphonioborates *(2)* from phosphorus ylides *(1)* and borane, and triphenylphosphane—monoalkylboranes *(3)* by rearrangement of *(2)*.

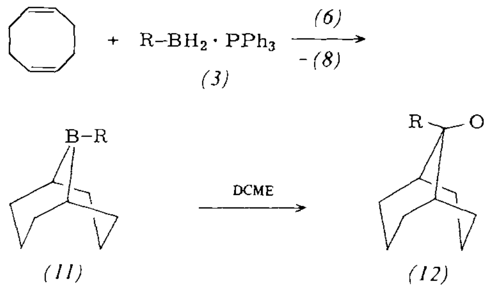
| | $R^1$ | $R^2$ | *(2)* Yield [%] | M.p. [°C] | $^{31}$P-NMR [3] | IR (B—H) [cm$^{-1}$] | Rearrangement time/temp. *(2)*→*(3)* | *(3)* Yield [%] | $^{31}$P-NMR [3] | IR (B—H) [cm$^{-1}$] |
|---|---|---|---|---|---|---|---|---|---|---|
| *a* | H | H | 94 | 190 | +31.81 | 2250 | 7 h/131 °C | 95 | +17.37 | 2330 |
| *b* | $CH_3$ | H | 93 | 171 | +34.15 | 2240 | 30 min/131 °C | 93 | +15.64 | 2310 |
| *c* | $n$-$C_5H_{11}$ | H | 89 | 138 | +33.28 | 2240 | 25 min/131 °C | 94 | +17.53 | 2310 |
| *d* | $n$-$C_9H_{19}$ | H | 57 | 109 | +33.40 | 2260 | 25 min/131 °C | 88 | +17.34 | 2350 |
| *e* | $C_6H_5$ | H | 92 | 141 | +27.78 | 2270 | 20 min/100 °C | 93 | +16.20 | 2310 |
| *f* | $CH_3$ | $CH_3$ | 97 | 112 | +38.82 | 2240 | 12 min/100 °C | 94 | +15.00 | 2130 |

The adduct *(3c)* reacts with 2,3-dimethylbutadiene in the presence of *(6b)* to give the boracyclopentane derivative

---

[*] Prof. Dr. H. J. Bestmann, Dipl.-Chem. K. Sühs, Dipl.-Chem. Th. Röder
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

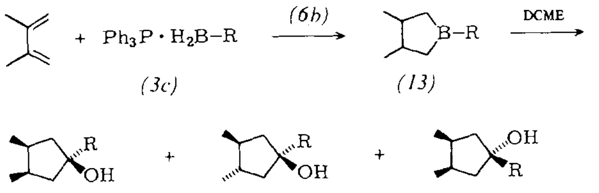
[**] Delivered in part in a lecture at the International Symposium "Metallo-Organics in Organic Synthesis", July 14—17, 1980 in Swansea (Wales).—We thank Prof. *G. Wilke*, Mülheim-Ruhr (Germany) for supplying (*Z*)-1,2-divinylcyclobutane.



(11) (12)

(12a): R = $C_2H_5$; (12b): R = $n$-$C_6H_{13}$

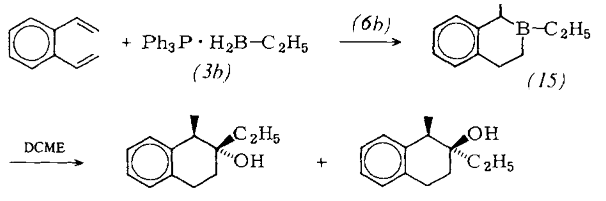
(13). Reaction of (13) according to the DCME method, followed by oxidation, furnishes a 55 : 43 : 2 mixture of three alcohols (b.p. 69–73 °C/0.02 torr, yield 43%[7]), which, according to GC/MS and NMR spectra, are the isomeric cyclopentanols (14). The product formed in least yield is assigned the all-*cis* structure (14c).



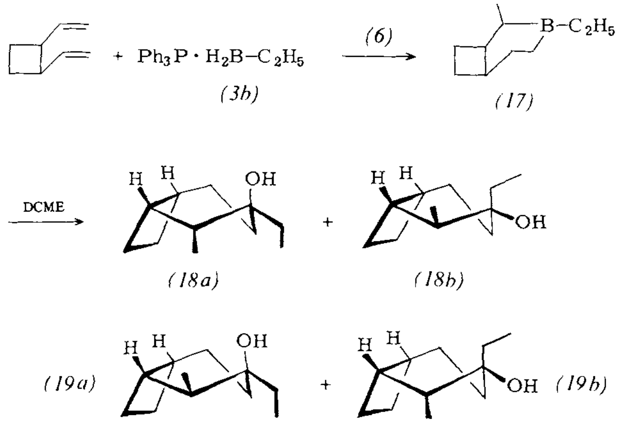
(14a) (14b) (14c)

R = $n$-$C_6H_{13}$

*o*-Divinylbenzene[9], which is readily accessible from phthalaldehyde and methylenetriphenylphosphorane, reacts with (3b) in the presence of (6b) to give a cyclic product, which on treatment by the DCME method gives three isomers (GC/MS) in the ratio 52 : 44 : 4 by weight (b.p. 79–83 °C/0.01 torr, yield 46%[7]). The $^{13}$C-NMR spectrum of the two main compounds is reconcilable only with a mixture of the dialkyltetrahydronaphthols (16a) and (16b). (The constitution of the third isomer is still unclear.) This means that the cyclizing hydroboration of *o*-divinylbenzene with (3b) proceeds largely regiospecifically with formation of a six-membered ring to give (15).



(16a) (16b)



With the same regioselectivity, reaction of (3b) with (*Z*)-1,2-divinylcyclobutane should afford the borabicyclooctane derivative (17) whose conversion by the DCME method would lead to four isomers. We found four alcohols and a still unidentified compound (38 : 22 : 19 : 17 : 4). On GC/MS analysis, the alcohols (proportion 96%, b.p. 69–73 °C/0.01 torr, yield 40%[7]) gave the same mass spectrum. A gas chromatographic separation of the isomers (14a) and (14b), (16a) and (16b), as well as (18a, b) and (19a, b) on the preparative scale, which would enable an unambiguous assignment of the isomers to the GC peaks, has so far met without success.

The Wittig reaction enables the synthesis of olefins from carbonyl compounds and phosphorus ylides. The general method described here for the conversion of ylides into monoalkylboranes and their subsequent reaction with olefins provides a combination of ylide reactions and hydroboration, whose scope of application still remains to be investigated in detail.

Received: June 24, 1981 [Z 925 IE]
supplemented: August 3, 1981
German version: Angew. Chem. 93, 1098 (1981)

---

[1] *M. F. Hawthorne*, J. Am. Chem. Soc. *80*, 3480 (1958); *83*, 367 (1961); *D. Seyferth*, Angew. Chem. *72*, 36 (1960); *D. Seyferth, S. D. Grim*, J. Am. Chem. Soc. *83*, 1613 (1961); cf. also *H. Schmidbaur, G. Müller, G. Blaschke*, Chem. Ber. *113*, 1480 (1980).

[2] *R. Köster, B. Rickborn*, J. Am. Chem. Soc. *89*, 2782 (1967).

[3] In chlorobenzene, $H_3PO_4$ as external standard, $\delta$-values.

[4] For other methods for the synthesis of monoalkylboranes (as pyridine or amine complex) cf. *M. F. Hawthorne*, J. Am. Chem. Soc. *81*, 5836 (1959) and [5a, b].

[5] a) *H. C. Brown, S. K. Gupta*, J. Am. Chem. Soc. *93*, 4062 (1971); b) *H. C. Brown, E. Negishi, J. J. Katz, ibid. 94*, 5893 (1972); c) *E. Negishi, H. C. Brown*, Synthesis *1974*, 77.

[6] a) *H. C. Brown*: Organic Synthesis via Boranes, Wiley, New York 1975; b) *H. C. Brown, B. A. Carlson*, J. Org. Chem. *38*, 2422 (1973); c) *H. C. Brown, C. D. Pfaffenberger*, J. Am. Chem. Soc. *89*, 5475 (1967); *H. C. Brown, E. Negishi, ibid. 89*, 5477 (1967).

[7] Yields based on reacted (2) (not optimized).

[8] Bath temperature on Kugelrohr-distillation.

[9] *G. Wittig, H. Eggers, P. Duffner*, Justus Liebigs Ann. Chem. *619*, 10 (1958).

---

## Alcoholate Clusters ("Aggregates") and Their Role in Alkyne-Forming Elimination Reactions[**]

By *Manfred Schlosser* and *Tran Dinh An*[*]

Consistent with an earlier prediction[1], unusual reaction orders have been found for potassium *tert*-butoxide when used as a dehydrohalogenating reagent in solvents of low polarity. The values for the indices *n* in the rate equation, which reflect the influence of the base concentration on the reaction rate, lie between 0.5 and 0.75 in the case of *syn*-eliminations (*cis*-1,2-dichlorocyclodecane in toluene: 0.5[2a]; *meso*-3,4-dichloro-2,2,5,5-tetramethylhexane in tetrahydrofuran or *tert*-butyl alcohol: 0.5 and 0.7, respectively[2b]), and between 0.75 and 1.2 in the case of *anti*-eliminations (*cis*-1,2-dichlorocyclodecane in toluene: 0.75[2a];

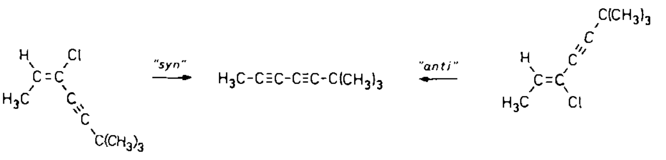
---

[*] Prof. Dr. M. Schlosser, Dipl.-Chem. Tran Dinh An
Institut de Chimie Organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne (Switzerland)

[**] This work was supported by the Schweizerischen Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project 2.128.0-78). Special thanks are due to Prof. *J. F. Bunnett*, Santa Cruz (Calif.) for his hospitality and numerous valuable discussions; the greater part of this work was carried out in his laboratory.

*meso*-3,4-dibromo-2,5-dimethylhexane in toluene: 1.0[2a]; *meso*- or *dl*-4,5-dichlorooctane in benzene 0.75[2a]; *meso*-3,4-dichloro-2,2,5,5-tetramethylhexane in tetrahydrofuran or *tert*-butyl alcohol: 0.8 and 1.2, respectively[2b]). Making the sound[3], but not strictly proven assumption, that potassium *tert*-butoxide exists predominantly as a tetrameric "aggregate" in solvents of low polarity, these reactions are mainly induced by dimeric and trimeric and, occasionally, by tetrameric base associates.

We decided to extend our investigations to *acetylene*-forming eliminations, since these differ in several respects from the *olefin*-forming ones. (*Z*)- and (*E*)-3-chloro-6,6-dimethyl-2-hepten-4-ynes *(1)* were chosen as model substrates, because interfering side-reactions like *E2cb* processes[7] or allene formation[8] may then be ruled out. Indeed, on reaction with base, 6,6-dimethyl-2,4-heptadiyne *(2)* was formed as sole product.



*E-(1)*   *(2)*   *Z-(1)*

The reaction orders (see Fig. 1 and Table 1) are approximate by 0.6 for the *syn*-elimination in three different solvents and about 0.8 (in tetrahydrofuran and toluene) or 1.1 (in *tert*-butyl alcohol) for the *anti*-elimination. According to the "variable transition state model"[9] the mechanisms of acetylene-forming eliminations are much more like *E1cb* processes than those of olefin-forming eliminations. Nevertheless, here also, dimeric, trimeric or—more rarely—tetrameric alcoholate aggregates participate in the rate-determining step. They exert a push-pull action on the reacting halide and initiate a closed cyclic electron- and particle-*motion* ("conveyor belt mechanism"), as indicated, *e.g.* in *syn-(3)* and *anti-(3)*.

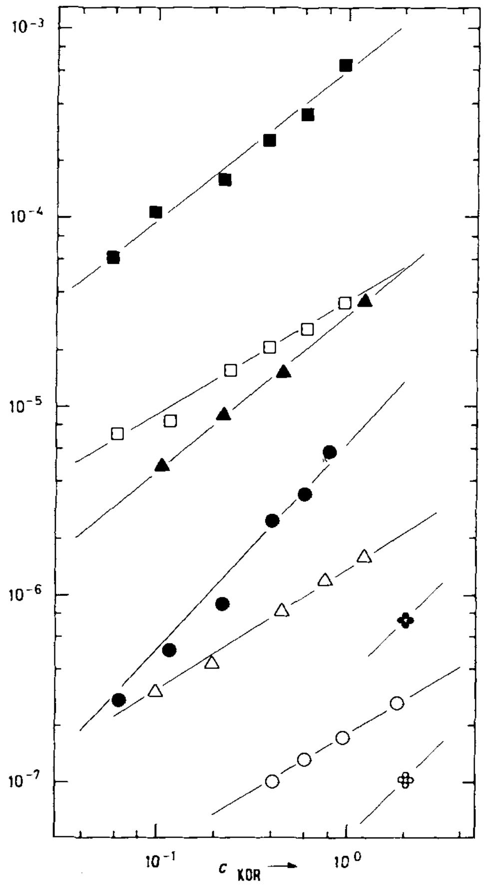
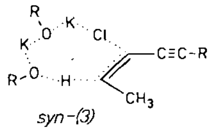


Fig. 1. Double logarithmic plot of the pseudoconstants $k_1^{\psi}$ $s^{-1}$ against the "formal" alcoholate concentration [mol/L]. Light and dark symbols designate *syn*- and *anti*-eliminations, respectively; squares, triangles, and circles: with potassium *tert*-butylalcoholate in tetrahydrofuran, toluene, and *tert*-butyl alcohol, respectively; rosettes: with potassium ethoxide in ethanol.

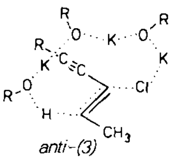
Table 1. Rate of the *syn*- and *anti*-periplanar cleavage of hydrogen chloride from (*E*)- and (*Z*)-3-chloro-6,6-dimethyl-2-hepten-4-yne with potassium *tert*-butylalcoholate or potassium ethoxide: Effect of solvent and base concentration.

| Solvent (Temperature) | *syn*-Elimination [a] $c_{KOR}$ | $k_1^{\psi}\cdot10^6$ | tan | *anti*-Elimination [a] $c_{KOR}$ | $k_1^{\psi}\cdot10^6$ | tan |
|---|---|---|---|---|---|---|
| $C_4H_8O$ (60 °C) | 0.063 | 7.1 | | 0.060 | 60 | |
| | 0.12 | 8.3 | | 0.10 | 104 | |
| | 0.25 | 15.1 | | 0.23 | 156 | |
| | 0.40 | 20.3 | | 0.40 | 252 | |
| | 0.63 | 25.6 | | 0.63 | 352 | |
| | 1.00 | 34.7 | 0.60 | 1.00 | 526 | 0.80 |
| $C_6H_5CH_3$ (80 °C) | 0.10 | 0.30 | | 0.11 | 4.8 | |
| | 0.20 | 0.42 | | 0.23 | 8.8 | |
| | 0.46 | 0.80 | | 0.46 | 14.4 | |
| | 0.79 | 1.18 | | 0.47 | 14.8 | |
| | 0.80 | 0.72 [b] | | 0.79 | 23.4 | |
| | 1.26 | 1.55 | 0.63 | 1.26 | 35.5 | 0.83 |
| $(CH_3)_3COH$ (80 °C) | — | — | | 0.065 | 0.27 | |
| | — | — | | 0.12 | 0.50 | |
| | 0.42 | 0.10 | | 0.23 | 0.88 | |
| | 0.61 | 0.13 | | 0.42 | 2.46 | |
| | 0.97 | 0.17 | | 0.61 | 3.40 | |
| | 1.90 | 0.26 | 0.60 | 0.83 | 5.70 | 1.1 |
| $C_2H_5OH$ (70 °C) | 2.13 | 0.1 [c] | (1.0) [d] | 2.13 | 7.1 [c] | (1.0) [d] |

[a] In the first column $c_{KOR}$ denotes the "formal" or "titratable" concentration of the alcoholate; it is found by titrimetric determination of the hydroxide concentration (mol/L) after hydrolysis. The second column contains pseudoconstants $k_1^{\psi}$ for a 1st order reaction (dimension: $s^{-1}$), which are obtained on plotting the chlorodimethylheptenyne concentration as a function of the reaction time; in order to obtain true reaction rate constants the pseudoconstants must be divided by the—unknown—concentration of "active base". In the third column the tangent (tan) is given, which defines the slope of the straight line through the points on plotting the pseudoconstants $k_1^{\psi}$ against the respective formal concentrations $c_{KOR}$ (Fig. 1). This data multiplied by the degree of aggregation of the potassium *tert*-butoxide in the ground state gives the number of the base molecules which are jointly active in promoting the reaction.—[b] This measurement, obviously erroneous is not taken into account in Fig. 1.—[c] The *syn/anti* reactivity ratio for the elimination of HCl from *trans*- and *cis*-propenyl chloride, instead of being around 70, as here, approaches 800 [*S. I. Miller*, J. Org. Chem *26*, 2619 (1961)].—[d] Since, at least in this concentration range, potassium ethoxide exists to a very large extent as dissociated free ions (and also reacts as such) a reaction order of 1.0 with respect to the base is to be expected, unless salt effects (cf. [2b]) intervene.



*syn-(3)*



*anti-(3)*

There is no point in comparing stereo- or regiochemically different routes which are accessible to a given elimination reaction as long as it is unknown whether the same reagents (such as monomeric, dimeric or oligomeric potassium *tert*-butoxide) are always involved. Therefore, before listing *syn/anti* or Hofmann/Saytzeff ratios, one should first measure each reaction order with respect to the base.

Received: June 10, 1981 [Z 934a IE]
German version: Angew. Chem. *93*, 1114 (1981)

CAS Registry numbers:
*(E)-(1)*, 79816-81-8; *(Z)-(1)*, 79816-88-9; *(2)*, 821-73-8.

[1] *M. Schlosser* in Houben-Weyl: Methoden der organischen Chemie, Vol. *V/1b*, p. 40, Thieme Verlag, Stuttgart 1972.

[2] a) *M. Schlosser, G. Jan, E. Byrne, J. Sicher*, Helv. Chim. Acta *56*, 1630 (1973); b) *M. Schlosser, Tran Dinh An, ibid. 62*, 1194 (1979).

[3] *V. A. Bessonov, P. P. Alikhanov, E. N. Guryanova, A. P. Simonov, I. O. Schapiro, E. A. Yakovleva, A. I. Schatenstein*, Zh. Obshch. Khim. *37*, 109 (1967); Chem. Abstr. *66*, 115041u (1967); *V. Halaška, L. Lochmann, D. Lím*, Collect. Czech. Chem. Commun. *33*, 3245 (1968).

[4] *M. Schlosser, V. Ladenberger*, Chem. Ber. *104*, 2873 (1971).

[5] Prepared by addition of 3,3-dimethyl-1-butynyllithium to propanal, oxidation with chromium oxide, and treatment with phosphorus pentachloride; separation of isomers by gas chromatography (6 m, 15% silicone rubber UCW-98, 120 °C).

[6] All the new compounds were identified by elemental analysis and by IR, NMR, and mass spectra.

[7] *M. Schlosser, V. Ladenberger*, Chem. Ber. *100*, 3877, 3893, 3901 (1967).

[8] Cf. *e.g. D. R. Taylor*, Chem. Rev. *67*, 317 (1967); *F. Naso, L. Ronzini*, J. Chem. Soc. Perkin Trans. I *1974*, 340.

[9] *J. F. Bunnett*, Angew. Chem. *74*, 731 (1962); Angew. Chem. Int. Ed. Engl. *1*, 225 (1962); Surv. Prog. Chem. *5*, 53 (1969).

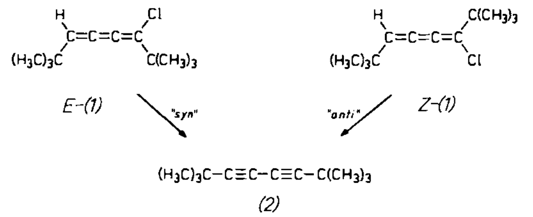
# Base-Promoted 1,4-Elimination Reactions: On the Origin of an Eventual *syn*-Stereoselectivity[**]

By *Manfred Schlosser, Claudio Tarchini, Tran Dinh An, Renzo Ruzziconi*, and *Paul J. Bauer*[*]

The mechanism of base-promoted elimination reactions remains an ever fascinating problem[1]. A currently intriguing question is how concertedness and stereoselectivity are affected on going from 1,2- to 1,3- or 1,4-elimination processes[2], thus separating the two reaction centers by insertion of one or two carbon units. So far, investigations of 1,4-conjugate eliminations have been confined to cyclic models which may be expected to favor a boat-shaped transition state facilitating a *syn*-, and discriminating against an *anti*-mode of cleavage[3]. We have now devised and prepared a linear model system, which has allowed us to study the fundamental features of a 1,4-conjugate elimination mechanism in what we had hoped to be a more unambiguous way.

Starting with 2,2,7,7-tetramethyl-4-octyn-3,6-diol[4] (*meso/dl*-mixture), 3,6-dichloro-2,2,7,7-tetramethyl-4-octyne (*meso/dl*-mixture, b.p. 58—60 °C/0.2 torr)[5] was obtained by treatment with triphenylphosphane and tetrachloromethane. The dichloro derivative was stirred with potassium *tert*-butoxide in pentane at −50 °C and converted into a 3 : 1 mixture of (*Z*)- and (*E*)-3-chloro-2,2,7,7-tetramethyl-3,4,5-octatriene *(1)* (30%, b.p. 63—64 °C/2 torr)[5,6], separable by gas chromatography[7]. When heated with alcoholates both isomers underwent 1,4-dehydrochlorination affording 2,2,7,7-tetramethyl-3,5-octadiyne *(2)*[5] in quantitative yield.

The decrease in concentration of *(1)* as a function of time was monitored by UV measurements (*Z*- and *E-(1)*: $\lambda_{max} = 248$ nm, ε 48000), NMR spectroscopy (using the



*tert*-butyl signals as an internal standard) or gas chromatography (45 m C-20M "SCOT" glass-capillary column, 80 °C). In addition, the relative rates $k_{syn}/k_{anti}$ ($=k_E/k_Z$) were measured in competition experiments using substoichiometric amounts of base. In the polar solvents methanol and dimethyl sulfoxide, or in the presence of the macrocyclic polyether 1,4,7,10,13,16-hexaoxacyclooctadecane ([18]crown-6) the reactivity of both isomers was virtually the same. On the other hand, in *tert*-butyl alcohol, tetrahydrofuran, or benzene *(E)-(1)*, was converted, with *syn*-elimination, into the diacetylene *(2)* at least 35 times faster than the (*Z*)-isomer (see Table 1).

Table 1. Dehydrohalogenation of (*E*)- and (*Z*)-3-chloro-2,2,7,7-tetramethyl-3,4,5-octatriene *(1)*: relative rates of *syn*- and *anti*-elimination ($k_{syn}/k_{anti}$).

| Base/Solvent system [a] | In the presence of [18]crown-6 | In the absence of [18]crown-6 |
|---|---|---|
| $KOCH_3/CH_3OH$ | — | 3.2 |
| $KOC(CH_3)_3/(CH_3)_2SO$ | 0.95 | 0.96 |
| $KOC(CH_3)_3/(CH_3)_3COH$ | 1.8 | 35 |
| $KOC(CH_3)_3/C_4H_8O$ | 2.0 | >35 |
| $KOC(CH_3)_3/C_6H_6$ | 2.4 | >35 |

[a] Alkoxide and substrate *(1)* concentrations roughly 0.6 and 1.2 M, respectively. The reaction was run in methanol at 50 °C and in all other cases at 25 °C.

In $CH_3OD$, $(CH_3)_3COD$ or $(CD_3)_2SO$, the chlorocumulenes did not incorporate any deuterium. Moreover, no (*Z/E*)-isomerization[8] of *(1)* was detected under the reaction conditions. Thus, in methanol and dimethyl sulfoxide either an irreversible E1cb process or a concerted, although still E1cb-like mechanism should be operative[9]. We favor the second hypothesis since the rate constants of (*Z*)- and (*E*)-*(1)* in methanol, when compared to related substrates[10], are fairly high. The low stereoselectivity may then be explained by the increasing distance between the reaction centers when going from acetylene-forming 1,2- to 1,4-eliminations. In this way, the differences in orbital interactions and hence the discrimination between the *syn*- and *anti*-mode vanish.

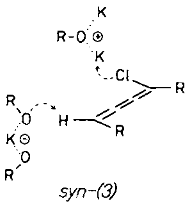
The reappearance of stereoselectivity in solvents of low polarity must be attributed to special factors. As demonstrated already in several other cases[11] oligomeric alcoholate species, so-called "aggregates" or fragments thereof, are now the effective reagents. Indeed, in the reaction between (*Z*)- or (*E*)-*(1)* and potassium *tert*-butoxide in *tert*-butyl alcohol, the "formal" base concentration was also found to enter the rate equation with an exponent of 0.8. This points at the action of a trimeric entity on both isomers (see [11]). Two complex ions[12] $[(H_3C)_3COK_2]^{\oplus}$ and $[(H_3C)_3COKOC(CH_3)_3]^{\ominus}$, cooperatively effecting the elimination through transition states *syn*- and *anti-(3)* would be in perfect agreement with this conclusion. The observed *syn*-stereoselectivity should then be a consequence of enhanced concertedness due to the pull-effect of the cation[13]. This, however, would be inconflict with the common belief that replacement of methoxide by *tert*-butoxide, a stronger base, will inevitably render the elimination

---

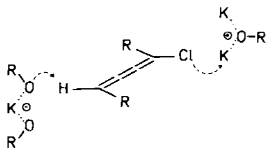
[*] Prof. Dr. M. Schlosser, Dr. C. Tarchini, Dipl.-Chem. Tran Dinh An, Dr. R. Ruzziconi
Institut de Chimie Organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne (Switzerland)
Dr. P. J. Bauer
Institut für Neurobiologie der Kernforschungsanlage
Postfach 1913, D-5170 Jülich (Germany)

[**] This work was supported by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung (Projects 2.293-0-74, 2.467-0-75, 2.693-0-76, 2.128-0-78).

mechanism more, not less, E1cb-like. Therefore, we prefer to postulate again a "conveyer belt" process[11] as defined by transition states *syn*- and *anti-(4)*. The *syn*-mode would then be privileged for obvious and trivial geometrical reasons.

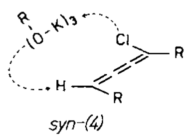


*syn-(3)*

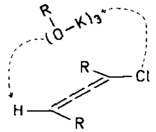


*anti-(3)*

R = C(CH$_3$)$_3$



*syn-(4)*



*anti-(4)*

Perhaps also the stereoselectivity of vinylogous substitutions ($S_N2'$ reactions), electronically related to 1,4-conjugate eliminations, depends more on external factors than on inherent orbital-control. This would explain why sometimes the *syn*- and sometimes the *anti*-mode are dominant[14].

Received: July 2, 1981 [Z 934b IE]
German version: Angew. Chem. *93*, 1116 (1981)

CAS Registry numbers:
*(E)-(1)*, 79898-95-6; *(Z)-(1)*, 79898-96-7; 6130-98-9; 2,2,7,7-tetramethyl-4-octyne-3,6-diol, 79898-97-8 3,6-dichloro-2,2,7,7-tetramethyl-4-octyne, 79898-98-9

---

[1] *J. F. Bunnett*, Angew. Chem. *74*, 731 (1962); Angew. Chem. Int. Ed. Engl. *1*, 225 (1962); *J. Sicher, ibid. 84*, 177 (1972) and *11*, 200 (1972), respectively; *F. G. Bordwell*, Acc. Chem. Res. *5*, 374 (1972); *M. Schlosser* in Houben-Weyl: Methoden der organischen Chemie, Vol. *V/1b*, Thieme Verlag, Stuttgart, 1972, pp. 9—44; *W. H. Saunders*, Acc. Chem. Res. *9*, 19 (1976); *W. H. Saunders, A. F. Cockerill:* Mechanisms of Elimination Reactions, Wiley, New York 1973.

[2] a) 1,3-Cyclizations: *M. Schlosser, G. Fouquet*, Chem. Ber. *107*, 1162, 1171 (1974); *D. E. Applequist, W. F. Pfohl*, J. Org. Chem. *43*, 867 (1978);—b) 1,4-Fragmentations: *C. A. Grob, P. W. Schiess*, Angew. Chem. *79*, 1 (1967); Angew. Chem. Int. Ed. Engl. *6*, 1 (1967); *C. A. Grob, ibid. 81*, 543 (1969) and *8*, 535 (1969), respectively; *B. Spahić, M. Schlosser*, Helv. Chim. Acta *63*, 1242 (1980);—c) 1,4-Conjugate Eliminations: *S. J. Cristol*, Acc. Chem. Res. *4*, 393 (1971); *R. K. Hill, M. G. Bock*, J. Am. Chem. Soc. *100*, 637 (1978).

[3] Cf. [2c]: Dehydroanthracenes prefer a boat-conformation already in the ground-state; overlap between electrons of the incipient carbanion (E1cb-type mechanism!) and the neighboring aromatic rings should still enhance this tendency. The conformational requirements of the transition state of 2-cyclohexenol dichlorobenzoates are less safely predicted; since, however, a *bona fide* monomeric base in a non-dissociative solvent (toluene) was involved, a cyclic group transfer mechanism (privileging *syn*-elimination) appears highly probable.

[4] *W. B. Sudweeks, H. S. Broadbent*, J. Org. Chem. *40*, 1131 (1975).

[5] Correct NMR, UV, IR and mass spectra as well as combustion analytical data have been obtained for all new or otherwise important compounds.

[6] Dipole measurements alone allowed an unequivocal assignment of configurations (*P. J. Bauer*, unpublished work). *(Z)-(1)* ($\delta(^1H) = 5.47$, 1.18 and 1.01 in benzene) melts between −8 and −6 °C, whereas *(E)-(1)* ($\delta(^1H) = 5.36$, 1.19 and 0.98), which has a longer retention time on Carbowax columns, only becomes more and more viscous and finally glassy below −40 °C. Incidentally, the sterically related (*E*)- and (*Z*)-isomers ($\delta(^1H) = 5.50$ and 1.09 or 5.45 and 1.12, respectively, in CDCl$_3$) of the non-halogenated "di-*tert*-butylbutatriene" (prepared from *meso*- and *dl*-3,6-dichloro-2,2,7,7-tetramethyl-4-octyne by treatment with zinc and separated by gas chromatography) melt at 64—65 °C and 21—23 °C, respectively. These melting points have so far not been reported by other authors (*H. Yamazaki*, J. Chem. Soc. Chem. Commun. *1976*, 841; *M. Tigchelaar, H. Kleijn, C. J. Elsevier, J. Meijer, P. Vermeer*, Tetrahedron Lett. *1981*, 2237) who also claim the isolation of one or both of these isomers.

[7] 6 m glass column, 30% diethyleneglycol succinate on Chromosorb WAW 60/80, 10 min 120 °C, then 3 °C/min up to 200 °C, injector and detector temperature 150 °C.

[8] Allenyl and butatrienyl anions should rapidly invert or even be linear, as some of the isoelectronically related ketenimines are (cf. *J. J. Daly*, J. Chem. Soc. *1961*, 2801).

[9] The acidity of the methine group, occupying both an olefinic and allylic position, may just reach the threshold pK$_a$-value of 28 (*S. Andreades*, J. Am. Chem. Soc. *86*, 2003 (1964)) required for methoxide-mediated carbanion formation.

[10] *M. Schlosser, V. Ladenberger*, Chem. Ber. *104*, 2873 (1971).

[11] *M. Schlosser, G. Jan, E. Byrne, J. Sicher*, Helv. Chim. Acta *56*, 1630 (1973); *M. Schlosser, Tran Dinh An, ibid. 62*, 1194 (1979); Angew. Chem. *93*, 1114 (1981); Angew. Chem. Int. Ed. Engl. *20*, 1039 (1981).

[12] The same and related ions have been previously invoked for an α-deprotonation effected by potassium *tert*-butoxide (*J. G. Pritchard, A. A. Bothner-By*, J. Phys. Chem. *64*, 1271 (1960)). The kinetic data would also be compatible with the alternative assumption that neutral species—namely, a potassium *tert*-butoxide monomer and a dimer—cooperatively generate ionic fragments (*e.g.* $[K(HOC(CH_3)_3)]^{\oplus}$ and $[((H_3C)_3COK)_2Cl]^{\ominus}$ in the course of the elimination reaction.

[13] Cf. *D. H. Hunter, D. J. Shearing*, J. Am. Chem. Soc. *93*, 2348 (1971); *R. A. Bartsch*, Acc. Chem. Res. *8*, 239 (1975).

[14] *G. Stork, A. F. Kreft*, J. Am. Chem. Soc. *99*, 3850, 3851 (1977); *J. Staroscik, B. Rickborn, ibid. 93*, 3046 (1971); *D. M. Wieland, C. R. Johnson, ibid. 93*, 3047 (1971); *H. L. Goering, R. R. Josephson, ibid. 98*, 7854 (1976); *W. Kirmse, F. Scheidt, H. J. Vater, ibid. 100*, 3945 (1978); *A. Kreft*, Tetrahedron *1977*, 1035; *S. Godtfredsen, J. P. Obrecht, D. Arigoni*, Chimia *31*, 62 (1977).

## Molecular Structures of Tri-*O*-acetyl-D-glucal and Ethyl-4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-2-hexenopyranoside

By *Wolfgang Voelter, Wolfram Fuchs, John J. Stezowski,* and *Petra Schott-Kollat*[*]

*Dedicated to Professor Karl Folkers on the occasion of his 75th birthday*

2,3-Unsaturated pyranoses are intermediates frequently used for the synthesis of derivatives of rare natural carbohydrates, *e.g.* amicetose (2,3,6-trideoxy-*erythro*-hexose)[1]. Biologically important amino sugars, *e.g.* ossamine (4-dimethylamino-2,3,4,6-tetradeoxy-*threo*-hexose)[2], its *erythro*-isomer forosamine[3] and tolyposamine (4-amino-2,3,4,6-tetradeoxy-*erythro*-hexose)[3] can be obtained by $S_N$ reactions at C-4. The most elegant method for the preparation of 2,3-unsaturated pyranosides such as *(2)* is the boron trifluoride-ether catalyzed reaction of glycals such as *(1)* with alcohols[4]. To clarify the course of this reaction we carried out X-ray structural analyses on tri-*O*-acetyl-D-glucal *(1)* (obtained by reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide with zinc[5]) and the ethyl-4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-2-hexenopyranoside *(2)* prepared therefrom (Fig. 1, Table 1).

With exception of the C—O ester bond C3—O3 in *(1)* (1.454(2)) and C4—O4 in *(2)* (1.458(2)) adjacent to the double bond, the molecules exhibit normal atomic distances: the two ester bonds are about 0.01 Å longer than in analogous ester groups of the sugars. According to the dihedral angles[8] both unsaturated sugars exist in the half-chair form. All ester groups are *trans* oriented.

---

[*] Prof. Dr. W. Voelter, Dipl.-Chem. W. Fuchs
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)
Dr. J. J. Stezowski, P. Schott-Kollat
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

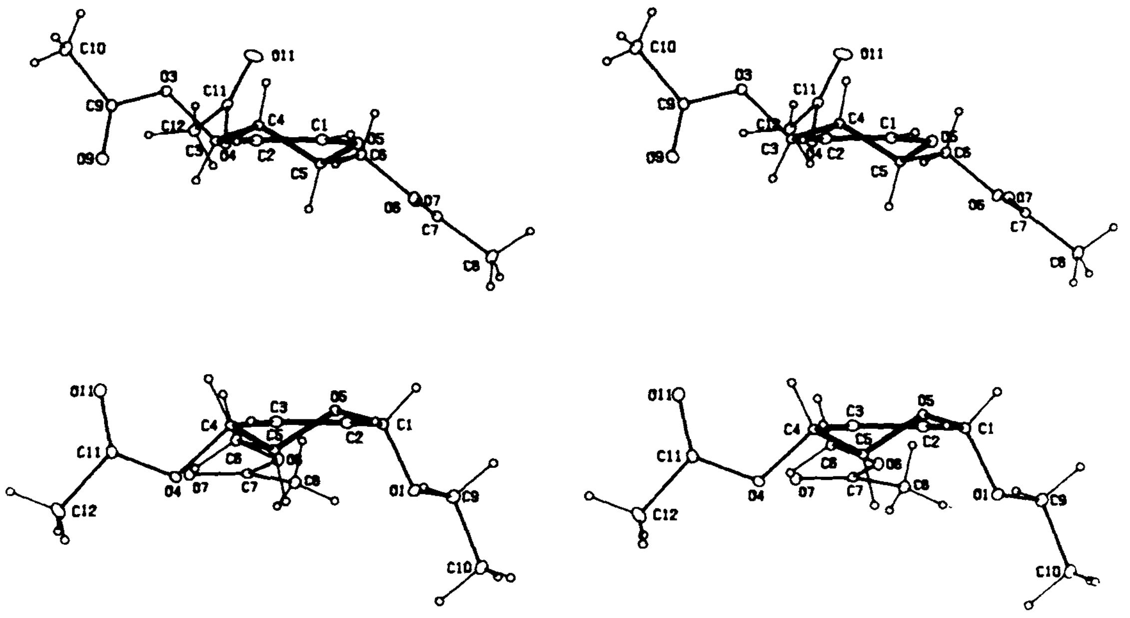
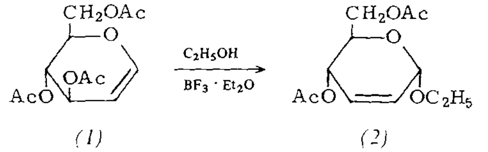


Fig. 1. Stereoscopic diagram of the half-chair conformation of the unsaturated sugars *(1)* and *(2)* in the crystal. Crystallographic data: *(1)*: space group $P2_12_12_1$; $Z=4$; cell constants at 120 K: $a=5.2210(7)$, $b=15.234(2)$, $c=16.307(1)$ Å; *(2)*: space group $P2_12_12_1$; $Z=4$; $a=5.3320(4)$, $b=14.571(1)$, $c=16.479(2)$ Å.—The sets of high-resolution data ($2\theta_{max}=75°$ for *(1)* and 80° for *(2)*, monochromatic $Mo_{K\alpha}$ radiation, $\lambda=0.71069$ Å) are corrected for Lorentz and polarization effects, and were recorded according to the "ω"-scan method. The original crystal structure models [6] were refined to $R=0.046$ and $R_w=0.052$ for *(1)* and to $R=0.041$ and $R_w=0.048$ for *(2)* (3220 and 3922 reflections, respectively) [7].



*(1)* *(2)*

Table 1. Bond lengths, bond angles and dihedral angles of *(1)* and *(2)*

| Bond lengths [Å] | | *(1)* | *(2)* | |
|---|---|---|---|---|
| C1—C2 | | 1.327(2) | 1.506(2) | |
| C1—O5 | | 1.369(2) | 1.427(2) | |
| C2—C3 | | 1.500(2) | 1.331(2) | |
| Bond angles [°] | | | | |
| C2—C1—O5 | | 125.0(1) | 111.9(1) | |
| C1—C2—C3 | | 121.9(1) | 121.9(1) | |
| Dihedral angles [°] | | | | |
| O5—C1—C2—C3 | | − 3.2(3) | 12.1(2) | |
| C1—C2—C3—C4 | | − 13.9(2) | 1.9(2) | |
| C2—C3—C4—C5 | | 45.8(2) | 17.3(2) | |
| C3—C4—C5—O5 | | − 65.0(2) | − 50.0(1) | |
| C4—C5—O5—C1 | | 48.4(2) | 68.1(1) | |
| C5—O5—C1—C2 | | − 15.1(2) | − 48.0(1) | |
| C2—CX—OX—C9 | X = 3 | − 78.5(2) | − 175.6(1) | X = 1 |
| CX—OX—C9—C10 | X = 3 | 174.6(1) | − 178.3(1) | X = 1 |
| C5—C4—O4—C11 | | − 104.7(1) | − 141.4(1) | |
| C4—O4—C11—C12 | | 178.1(1) | 176.1(1) | |
| C4—C5—C6—O6 | | − 173.9(1) | 177.1(1) | |
| C5—C6—O6—O7 | | 152.0(1) | 159.8(1) | |
| C6—O6—C7—C8 | | 177.7(1) | 171.7(1) | |

The numbers in brackets are estimated standard deviations to the last eignificant figure.

It is clear from this X-ray structure analysis that the $BF_3$-catalyzed reaction *(1)*→*(2)* essentially takes place in one plane and is stereospecific, since the C-atoms 1—3 are planar oriented, both in the educt as well as in the product.

Received: September 8, 1980 [Z 928 IE]
revised: April 24, 1981
German version: Angew. Chem. *93*, 1070 (1981)

CAS Registry numbers:
*(1)*, 2873-29-2; *(2)*, 3323-72-6

---

[1] *C. L. Stevens, K. Nagarajan, T. H. Haskell,* J. Org. Chem. *27,* 2991 (1962).
[2] *C. L. Stevens, G. E. Gutowski, C. P. Bryant, R. P. Glinski, O. E. Edwards, G. M. Sharma,* Tetrahedron Lett. *1969,* 1181.
[3] *J. S. Brimacombe, L. W. Doner, A. J. Rollins, A. K. A. Radhi,* J. Chem. Soc. Perkin Trans. I *1973,* 1295.
[4] *R. J. Ferrier, N. Prasad,* J. Chem. Soc. *C 1969,* 570.
[5] *W. Roth, W. Pigman:* Methods in Carbohydrate Chemistry, Vol. 2, Academic Press, New York 1974.
[6] *P. Main, L. Lessinger, M. M. Woolfson, G. Germain, J. P. Declerq:* Multan 77, A Program for the Automatic Solution of Crystal Structures from X-ray Diffraction data. University of York 1977.
[7] *J. M. Stewart, P. A. Machin, C. Dickinson, H. Ammon, H. Heck, H. Flack:* The X-ray System, Version of 1976. Tech. Rep. TR-446, Computer Science Center, Univ. of Maryland, College Park, MD.
[8] *W. L. Duax, D. A. Norton:* Atlas of Steroid Structures, Vol. 1, Plenum, New York 1975.

## Heterogeneous Hydrogenation of Organic Halogen Compounds by Carrier-Supported Organotin Hydrides[**]

By *Herbert Schumann* and *Bernd Pachaly*[*]

Organotin hydrides, especially tributylstannane, are indispensable as hydrogenating agents in organic synthesis[1]. Thus, for example, they convert alkyl halides into the corresponding hydrocarbons, the organotin hydride itself being converted into an organotin halide, which must be separated from the product of reduction. This separation can, however, be circumvented by using polymeric insoluble reagents, such as organotin hydrides supported on polysty-

---

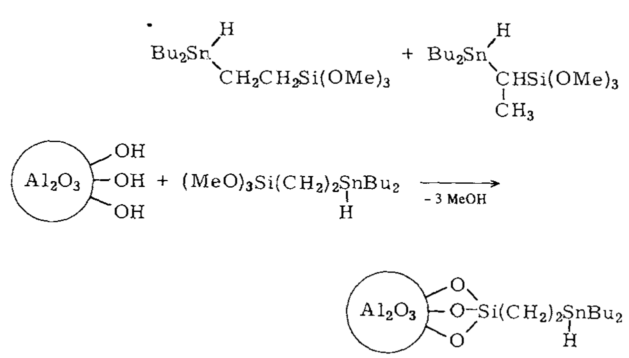
[*] Prof. Dr. H. Schumann, Dipl.-Chem. B. Pachaly
Institut für Anorganische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Paul Rauschert KG.

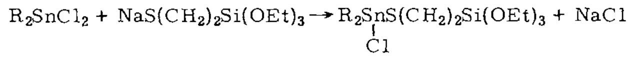
rene[2]. To improve the method—and particularly the stability and regeneratability of the reagent—we supported soluble organotin hydrides on solid *inorganic* carriers.

Hydrostannation of trimethoxy(vinyl)silane with dibutylstannane affords an isomeric mixture of dibutyl(1- and 2-trimethoxysilylethyl)tin hydride, which reacts with aluminum oxide or silica gel with cleavage of methanol:

$$Bu_2SnH_2 + CH_2{=}CHSi(OMe)_3 \xrightarrow{AIBN}$$

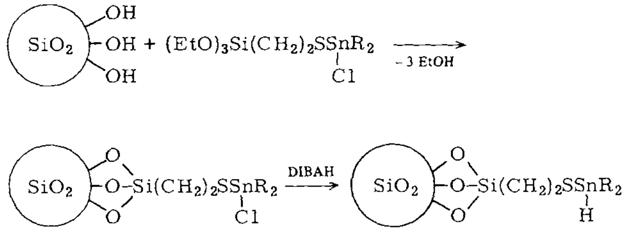


A second possibility is the incorporation of terminal triethoxysilylated organotin halides onto silica or alumina and subsequent hal/H exchange with diisobutylaluminum hydride (DIBAH):



$$R_2SnCl_2 + NaS(CH_2)_2Si(OEt)_3 \rightarrow R_2\underset{Cl}{Sn}S(CH_2)_2Si(OEt)_3 + NaCl$$

R = Bu, b.p. = 185-189°C/13 torr
R = Ph, b.p. = 190°C/10 torr



The amount of substance incorporated was found to average 1.3 molecules of organotin compound per nm$^2$ surface area of solid (gravimetric determination), *i.e.* within the range (0.5 to 1.5 molecules/(nm)$^2$ carrier) already quoted for such incorporation of reagents[3]. The reactive hydrogen was determined indirectly by reaction with CH$_3$I (measurement of amount of CH$_4$ liberated) and was found to average 48% of active organotin hydride referred to the amount of supported substance. Table 1 lists the yields of hydrocarbon that could be achieved on reduction of alkyl halides with the modified reagent at 40°C in cyclohexane after 2 h. 1,1-Dichloro-2,2-diphenylcyclopropane (DCDPCP) is completely reduced to 1,1-diphenylcyclopropane (DPCP) (NMR detection) within 24 h.

Table 1. Reduction of alkyl halides with carrier-supported organotin hydrides.

| Reducing agent (active amount in mmol) | Substrate g (mmol) | Product mL (% conv. ref. to t inhydride) |
|---|---|---|
| SiO$_2$—Si(CH$_2$)$_2$SSnBu$_2$H | CH$_3$I | CH$_4$ |
| (15.6) | 4.5 (32) | 140 (40) |
| SiO$_2$—Si(CH$_2$)$_2$SSnPh$_2$H | C$_4$H$_9$Br | C$_4$H$_{10}$ |
| (0.27) | 3.0 (22) | 2.4 (40) |
| Al$_2$O$_3$—Si(CH$_2$)$_2$SnBu$_2$H | CH$_3$I | CH$_4$ |
| (8) | 1.5 (11) | 85 (48) |
| Al$_2$O$_3$—Si(CH$_2$)$_2$SnBu$_2$H | DCDPCP | DPCP |
| (2) | 0.43 (2) | 100% |

*Procedure*

Di-*n*-butyltin dihydride (2.73 g, 13 mmol), trimethyl(vinyl)silane (1.93 g, 13 mmol) and azoisobutyl nitrile (AIBN) (100 mg) are stirred together for 24 h at 60°C. The reaction mixture ($\nu$SnH 1795 cm$^{-1}$) is dissolved in ether (200 mL) and heated under reflux with 29 g of dried Al$_2$O$_3$ for 24 h. Removal of the solution by filtration, washing with ether, and drying, furnishes 33.8 g of loaded Al$_2$O$_3$. A trial test with CH$_3$I showed the proportion of active organotin hydride to be 0.17 nmol/g carrier material.

The polymer-supported reducing agents (with 6 mL cyclohexane/g) were allowed to react with alkyl halides (Table 1). Evolution of gas was complete after 2 h at 40°C. The incorporated organotin halides can be reconverted into the organotin hydrides by reaction with diisobutylaluminum hydride in ether/toluene (loss of activity 57%).

Received: March 12, 1981 [Z 902 IE]
German version: Angew. Chem. 93, 1092 (1981)

CAS Registry numbers:
CH$_3$I, 74-88-4; C$_4$H$_9$Br, 109-65-9; DCDPCP, 3141-42-2; (EtO)$_3$Si(CH$_2$)$_2$SSn(Cl)Bu$_2$, 79593-37-6; (EtO)$_3$Si(CH$_2$)$_2$SSn(Cl)Ph$_2$, 79593-38-7; (MeO)$_3$Si(CH$_2$)$_2$Sn(H)Bu$_2$, 79593-39-8; (MeO)$_3$SiCH(CH$_3$)Sn(H)Bu$_2$, 79593-40-1; Al$_2$O$_3$, 1344-28-1; SiO$_2$, 7631-86-9.

---

[1] *H. G. Kuivila*, Synthesis *1970*, 499.
[2] *N. M. Weinshenker, G. A. Crosby, J. Y. Wong*, J. Org. Chem. *40*, 1966 (1975).
[3] *R. G. Bowman, R. L. Burwell Jr.*, J. Am. Chem. Soc. *101*, 2877 (1979).

## Di-*tert*-butylthia- and -selenadiphosphirane[**]

By *Marianne Baudler, Horst Suchomel,*
*Gabriele Fürstenberg,* and *Ulrike Schings*[*]

*Dedicated to Professor Leopold Horner on the occasion of his 70th birthday*

Cyclic compounds containing the P$_2$X moiety (X = C[1a], Si[1b], B[1c], As[1d], Ge[1e], Sn[1f]) have become preparatively accessible in the past few years. In all cases a considerable kinetic stabilization of the P$_2$X moiety was achieved by bulky substituents on the three ring atoms. We have now examined whether analogues with unsubstituted ring members, such as sulfur or selenium, are also capable of existence and can be isolated.

Small amounts of 2,3-di-*tert*-butyl-1,2,3-thiadiphosphirane *(1)* (about 1 mol-%) could be identified $^{31}$P-NMR spectroscopically for the first time in the reaction of tri-*tert*-butylcyclotriphosphane[2] with sulfur (1 : 3, boiling te-

---

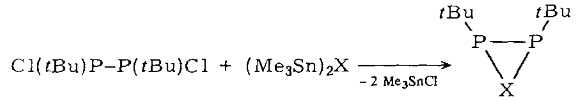
[*] Prof. Dr. M. Baudler, Dr. H. Suchomel, G. Fürstenberg, Dipl.-Chem. U. Schings
Institut für Anorganische Chemie der Universität
Greinstrasse 6, D-5000 Köln 41 (Germany)

[**] Contributions to the Chemistry of Phosphorus, Part 108. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 107; *M. Baudler, Y. Aktalay, K.-F. Tebbe, Th. Heinlein*, Angew. Chem. *93*, 1020 (1981); Angew. Chem. Int. Ed. Engl. *20*, 967 (1981).

trahydrofuran (THF)); an enrichment compared to the main products $(t\mathrm{BuPS})_3$[3a] and $[t\mathrm{BuP(S)S}]_2$[3b] could not be achieved, however, by varying the reaction parameters. All the more surprising was the finding that *(1)* is obtainable in 36% yield (99% purity) by high-vacuum distillation after removal of the solvent and thermolysis of the product mixture at 130 °C. The formation is apparently achieved by ring contraction of higher-membered phosphorus-sulfur heterocycles.

Larger amounts of *(1)* could be detected $^{31}$P-NMR spectroscopically in the reaction of sulfur dichloride with 1,2-di-*tert*-butyldiphosphane[4] (1 : 1, boiling toluene) or with the diphosphasilirane $(t\mathrm{BuP})_2\mathrm{SiPh}_2$[1b] (1 : 1 : 1, boiling dioxane).

A particularly suitable preparative approach is the [2+1]-cyclocondensation of 1,2-di-*tert*-butyl-1,2-dichlorodiphosphane[5] with bis(trimethylstannyl) sulfide[6] (1:1, boiling THF). With bis(trimethylstannyl) selenide[7], the 2,3-di-*tert*-butyl-1,2,3-selenadiphosphirane *(2)* is obtained. The four-membered ring compounds $(t\mathrm{BuP})_4$ and $(t\mathrm{BuP})_3\mathrm{X}$ as well as the five-membered heterocycle with an exocyclic chalcogen atom $(t\mathrm{BuPX})_3$ are formed as by-products; in the case of *(2)* the five-membered ring compound $(t\mathrm{BuP})_4\mathrm{Se}$ is also formed. The product pattern depends on the concentration of the reactants, the reaction time and the quantities used; under suitable conditions the proportion of *(1)* or *(2)* is about 60 mol-%. The compounds can be isolated by high-vacuum distillation, in the case of *(2)* with subsequent low-temperature crystallization.



*(1)*, X = S
*(2)*, X = Se

*(1)* and *(2)* are, respectively, pale and bright yellow, viscous, evil-smelling liquids which are stable for weeks at −30 °C when not exposed to air and light. They readily dissolve in organic solvents, but the solutions—above all, of *(2)*—are less stable. The composition of *(1)* and *(2)* is confirmed by correct elemental analyses (C, H, P, S, and Se, respectively) as well as mass spectra with high relative intensity of the $M^+$ ions [*(1)*: $m/z = 208$ (100%); *(2)*: 256 (88%)]. The constitution follows from the $^{31}\mathrm{P}\{^1\mathrm{H}\}$-NMR spectra, which in each case show a singlet in the characteristic high-field region for phosphorus three-membered ring compounds[8] [*(1)*: $\delta = -91.5$ (THF, 301 K); *(2)*: $\delta = -76.9$, $J(\mathrm{P}^{77}\mathrm{Se}) = 135.2$ Hz (pentane, 213 K)]. The downfield shift of *(2)* in comparison to *(1)* is ascribed to the larger P—Se bond length and the resultant widening of the P—P—Se angles. The high-field position of the respective singlets in the $^1\mathrm{H}\{^{31}\mathrm{P}\}$-NMR spectra is also typical for substituents on the three-membered ring [*(1)*: $\delta = 0.94$ (benzene, 298 K; *(2)*: 0.97 (benzene, 300 K)]. The configuration cannot be deduced from the NMR spectra; but *tert*-butyl groups should be *trans*-oriented as in other $\mathrm{P_2X}$ compounds[1b,c,e,9].

Compared to analogous phosphorus three-membered ring compounds, *(2)* and, in particular, *(1)* are astonishingly stable towards heat and towards polar solvents such as THF. This high kinetic stability is apparently caused by the steric shielding of the *tert*-butyl substituents and by the free electron pairs on the heteroatoms.

### *Procedure*

*(1)*: 1,2-Di-*tert*-butyl-1,2-dichlorodiphosphane (14.1 g, 57.1 mmol) and bis(trimethylstannyl) sulfide (20.6 g, 57.3 mmol) in 300 mL THF are allowed to react to completion at the boiling temperature with stirring (about 187 h, $^{31}$P-NMR monitoring). After removal of the solvent trimethyltin chloride is condensed at 0.45 torr and maximum bath-temperature of 35 °C over a 10 cm Vigreux column fitted with an air-cooled bridge into a receiver cooled with liquid nitrogen. Distillation of the residue over a Zincke apparatus at 0.15 torr and bath-temperature of 70—75 °C yields 5.1 g (43%) of *(1)*, b.p. 45—46 °C/0.15 torr, which solidifies to a colorless solid at −78 °C; purity >99% ($^{31}$P-NMR).

*(2)*: A mixture of 1,2-di-*tert*-butyl-1,2-dichlorodiphosphane (6.4 g, 25.9 mmol) and bis(trimethylstannyl) selenide (10.47 g, 25.8 mmol) in 120 mL THF is heated under reflux for about 36 h. Since the amount of *(2)* passes through a maximum, $^{31}$P-NMR control is frequently necessary. After removal of solvent and trimethyltin chloride as in *(1)* the orange-yellow, liquid residue is distilled at $5 \times 10^{-4}$ torr at a bath-temperature of 110 °C through a Zincke apparatus, fitted with a 5 cm extension, into a receiver cooled to −78 °C; yield 2.85 g (43%), b.p. 57—58 °C/$5 \times 10^{-4}$ torr, purity 97% (rest $(t\mathrm{BuP})_3\mathrm{S}$, $^{31}$P-NMR). Dissolution in *n*-pentane (5 mL) and cooling to −78 °C yields, after 3 d, 2.19 g (33%) of almost colorless crystals, which after removal of the mother liquor are washed with 2 mL of cold pentane; purity 100%.

Received: July 31, 1981 [Z 943 IE]
German version: Angew. Chem. *93*, 1087 (1981)

CAS Registry numbers:
*(1)*, 79898-83-2; *(2)*, 79898-84-2; bis(trimethylstannyl) sulfide, 1070-91-3; bis(trimethylstannyl) selenide, 7262-34-2; 1,2-di-*tert*-butyl-1,2-dichlordiphosphane, 79898-85-4

---

[1] a) *M. Baudler, F. Saykowski*, Z. Naturforsch. *B 33*, 1208 (1978); b) *M. Baudler, H. Jongebloed*, Z. Anorg. Allg. Chem. *458*, 9 (1979); c) *M. Baudler, A. Marx, J. Hahn*, Z. Naturforsch. *B 33*, 355 (1978); *M. Baudler, A. Marx*, Z. Anorg. Allg. Chem. *474*, 18 (1981); d) *M. Baudler, S. Klautke*, Z. Naturforsch. *B 36*, 527 (1981); e) *M. Baudler, H. Suchomel*, Z. Anorg. Allg. Chem., in press; f) *M. Baudler, H. Suchomel*, lecture, Int. Conf. Phosphorus Chem., Durham 1981; ACS Symp. Ser., in press.
[2] a) *M. Baudler, J. Hahn, H. Dietsch, G. Fürstenberg*, Z. Naturforsch. *B 31*, 1305 (1976); b) *M. Baudler, Ch. Gruner, ibid. B 31*, 1311 (1976); c) *M. Baudler, J. Hellmann*, Z. Anorg. Allg. Chem., in press.
[3] a) *M. Baudler, E. Därr, G. Fürstenberg*, unpublished; b) *M. Baudler, Ch. Gruner, G. Fürstenberg, B. Kloth, F. Saykowski, U. Özer*, Z. Anorg. Allg. Chem. *446*, 169 (1978).
[4] *M. Baudler, Ch. Gruner, H. Tschäbunin, J. Hahn*, Chem. Ber., in press.
[5] *M. Baudler, J. Hellmann*, Z. Anorg. Allg. Chem., in press.
[6] *H. Kriegsmann, H. Hoffmann*, Z. Chem. *3*, 268 (1963).
[7] Preparation analogous to the synthesis of $(\mathrm{Ph_3Sn})_2\mathrm{Se}$ according to *M. Schmidt, H. Ruf*, Chem. Ber. *96*, 784 (1963).
[8] *M. Baudler*, Pure Appl. Chem. *52*, 755 (1980), and references cited therein.
[9] a) *K.-F. Tebbe*, Z. Anorg. Allg. Chem. *468*, 202 (1980); b) *M. Fehér, R. Fröhlich, K.-F. Tebbe, ibid. 446*, 169 (1978); c) *B. Freckmann, R. Fröhlich, K.-F. Tebbe*, Abstr. 5th Europ. Cryst. Meet., Copenhagen, 90-P2-5a (1979).

---

## A Ternary Crown Ether "Supercomplex": X-Ray Structure Analysis of the 1 : 1 : 1 Adduct of Dibenzo-[18]-Crown-6, Potassium Iodide, and Thiourea[**]

By *Rolf Hilgenfeld* and *Wolfram Saenger*[*]

X-ray structural analyses have made a decisive contribution[1b] to the investigation of the complexing properties of

---

[*] Prof. Dr. W. Saenger, Dipl.-Chem. R. Hilgenfeld
Abteilung Chemie, Max-Planck-Institut für Experimentelle Medizin
Hermann-Rein-Str. 3, D-3400 Göttingen (Germany)

[**] Structures of Polyether Complexes, Part 18.—Part 17: *R. Hilgenfeld, W. Saenger*, Z. Naturforsch. *B 36*, 242 (1981).

cyclic crown ethers and their open-chain analogues towards metal ions[1a]. Oligoethers also form inclusion complexes with ionic or neutral guest molecules[2a], and are therefore considered, *inter alia*, as simple enzyme models[2b]. According to X-ray crystallographic findings the interactions between host and guest in such adducts can mainly be ascribed to N—H...O or C—H...O hydrogen bonding[3].

In 1971, *Pedersen* obtained crystalline ternary complexes between crown ether, metal salt, *and* thiourea in the molar ratio 1:1:1, 2:1:1, 1:1:4, and 1:1:6[4] on reaction of some metal-salt complexes of benzo-[15]-crown-5 and dibenzo-[18]-crown-6 with thiourea (in methanol). Such "super complexes" are potential models for transition states of reactions assisted by crown ethers, *e.g.* nucleophilic substitutions in which stereospecificity has been observed[5]. The existence of loose adducts, in which the crown ether cation complex as well as substrate and anion participate would afford an explanation for this effect. Since no information on the structures of the ternary adducts was available, we decided to determine the structure of the 1:1:1-complex of dibenzo-[18]-crown-6, potassium iodide and thiourea[6].

The crystal structure is found to be polymeric (Fig. 1). The potassium ion is situated at the center of the crown ether cavity and is in contact with all six ether oxygen atoms with $K^+$...O distances between 2.71 and 2.80 Å; the sevenfold coordination is completed by the iodide ion ($K^+$...$I^-$ 3.57 Å) to give a hexagonal pyramid. This part of the complex is similar to that in the 1:1 adduct of dibenzo-[18]-crown-6 with KI, the crystals of which are found to contain two independent complex molecules[7]: in one, the apical $K^+$ coordination site is occupied by a water molecule, in the second (as in the present case), it is occupied by the $I^-$ anion.

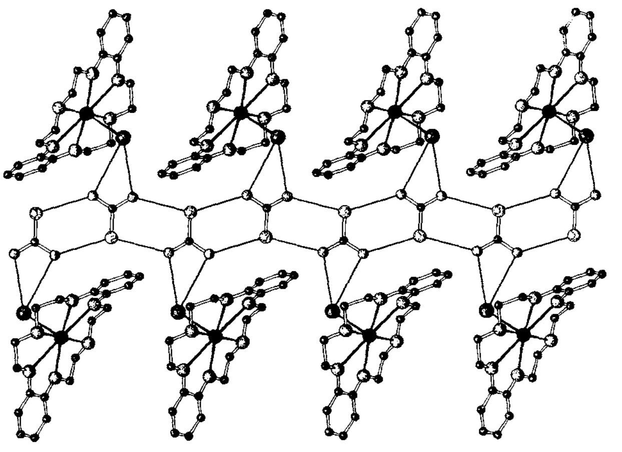


Fig. 1. Polymeric structure of the 1:1:1 complex of dibenzo-[18]-crown-6, potassium iodide, and thiourea (hydrogen atoms not shown). Hydrogen bonds are indicated by thin lines. Atomic spheres symbolize, with increasing radius, C, N, O, S, and I; the $K^+$ ions are shown in black. We thank Dr. *E. Keller*, Freiburg (Germany), for the computer plot programm SCHAKAL.

The thiourea neither participates in the complexation of the metal ion, nor has it any contact with the polyether ligand; instead, it forms polymeric chains coupled by hydrogen bonds which run through the crystal structure in the direction of the *c*-axis. One hydrogen atom of each amino group is in contact with the sulfur atom of the neighboring (symmetry generated) thiourea molecule (N...S 3.43(1) and 3.49(1) Å), while the other participates in N—H...$I^-$ hydrogen bonding. The two H-bonds of this latter type formed by each thiourea molecule are of different strength with lengths of 3.55(1) and 3.85(1) Å; the respective I—N—C angles are 110.3(8) and 95.7(7)°. The hydrogen atoms of the thiourea molecule could not be determined with certainty from the difference Fourier synthesis.

The anion plays an important role as hydrogen bond acceptor and as a link between crown-ether complex and thiourea chains. It is therefore of interest to investigate whether anions other than the readily polarizable $I^-$ ion form such complexes. *Pedersen* has also obtained ternary complexes with $SCN^-$[4], which is as soft as $I^-$. On the other hand, we were unable to prepare the corresponding adduct with the hard $F^-$ ion; this is also explainable in terms of the high KF lattice energy, which prevents formation of a crystalline crown-ether complex. Presumably the "supercomplexes" are formed only with sufficiently soft anions.

Received: May 4, 1981 [Z 930 IE]
German version: Angew. Chem. 98, 1082 (1981)

CAS Registry number:
1:1:1 adduct, 73839-92-2

---

[1] a) *C. J. Pedersen*, J. Am. Chem. Soc. *89*, 7017 (1967); *F. Vögtle, E. Weber*, Angew. Chem. *91*, 813 (1979); Angew. Chem. Int. Ed. Engl. *18*, 753 (1979); b) *R. Hilgenfeld, W. Saenger*, Top. Curr. Chem., *101*, 1 (1982) *W. Saenger, I.-H. Suh, G. Weber*, Isr. J. Chem. *18*, 253 (1979).

[2] a) *D. J. Cram, J. M. Cram*, Acc. Chem. Res. *11*, 8 (1978); *F. Vögtle, H. Sieger, W. M. Müller*, Top. Curr. Chem. *98*, 107 (1981); b) *W. D. Curtis, D. A. Laidler, J. F. Stoddart, G. H. Jones*, J. Chem. Soc. Perkin Trans. I *1977*, 1756; *Y. Chao, G. R. Weisman, G. D. Y. Sogah, D. J. Cram*, J. Am. Chem. Soc. *101*, 4948 (1979); *J. F. Stoddart* in *A. Braibanti*: Bioenergetics and Thermodynamics, D. Reidel, Dordrecht 1980, p. 43; c) *R. C. Helgeson, K. Koga, J. M. Timko, D. J. Cram*, J. Am. Chem. Soc. *95*, 3021 (1973); *M. Newcomb, J. P. Toner, R. C. Helgeson, D. J. Cram*, *ibid. 101*, 4941 (1979).

[3] *R. Hilgenfeld, W. Saenger*, Z. Naturforsch. *B 36*, 242 (1981); *I.-H. Suh, W. Saenger*, Angew. Chem. *90*, 565 (1978); Angew. Chem. Int. Ed. Engl. *17*, 534 (1978); *R. Kaufmann, A. Knöchel, J. Kopf, J. Oehler, G. Rudolph*, Chem. Ber. *110*, 2249 (1977).

[4] *C. J. Pedersen*, J. Org. Chem. *36*, 1690 (1971).

[5] *A. El Basyony, J. Klimes, A. Knöchel, J. Oehler, G. Rudolph*, Z. Naturforsch. *B 31*, 1192 (1976); *D. J. Sam, H. E. Simmons*, J. Am. Chem. Soc. *94*, 4024 (1972); *A. Knöchel, G. Rudolph, J. Thiem*, Tetrahedron Lett. *1974*, 551.

[6] We thank Prof. *F. Vögtle*, Bonn, for stimulating this investigation.—Thin plate-like crystals (from acetone), m.p. 211 °C; space group $P2_1/c$, $a = 892.9(3)$, $b = 3212.7(10)$, $c = 922.7(3)$ pm, $\beta = 104.02(5)°$, $Z = 4$, $\rho_{X\text{-ray}} = 1.557$ g cm$^{-3}$, $\mu = 124.8$ cm$^{-1}$; 2629 independent data were collected on a Stoe four-circle diffractometer and corrected for absorption effects; $R = 7.1\%$. Atomic coordinates are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW (UK).

[7] *M. G. Myskiv, T. Glowiak, B. Jezowska-Trzebiatowska, K. B. Yatsymirsky, E. I. Hladyshevsky, L. I. Budarin, A. I. Teliatnyk*, 12th Int. Congr. Crystallogr., Warszawa 1978.

---

## A New Route to 6a-Carbacyclins—Synthesis of a Stable, Biologically Potent Prostacyclin Analogue[**]

By *Werner Skuballa* and *Helmut Vorbrüggen*[*]

*Dedicated to Professor Ferdinand Bohlmann on the occasion of his 60th birthday*

The therapeutic use of prostacyclin ($PGI_2$) *(1)*, a potent vasodilator and inhibitor of blood-platelet aggregation, is

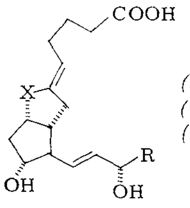
---

[*] Dr. W. Skuballa [+], Prof. Dr. H. Vorbrüggen
Forschungslaboratorium der Schering AG, Berlin/Bergkamen
Postfach 650311, D-1000 Berlin 65 (Germany)

[+] Author to whom correspondence should be addressed.

[**] Prostaglandin Analogues, Part 4.—Part 3: *W. Skuballa*, Tetrahedron Lett. *21*, 3261 (1980).

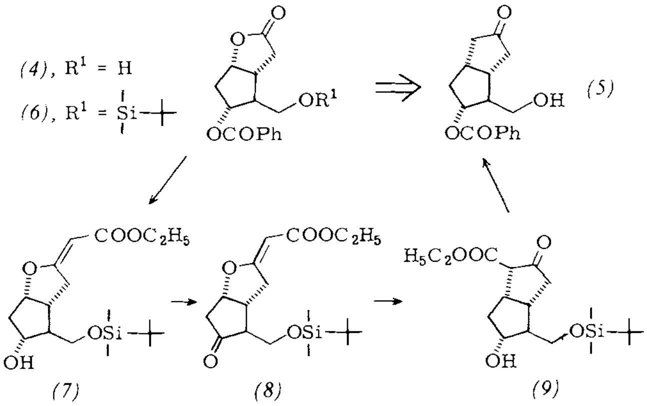
limited due to the extreme instability of the enol-ether function[1]. In the search for stable and biologically active analogues an essential target molecule was the 6a-carbacyclin *(2)*[2].



*(1)*, X = O, R = $n$-$C_5H_{11}$
*(2)*, X = $CH_2$, R = $n$-$C_5H_{11}$
*(3)*, X = $CH_2$, R = $CH(CH_3)$-$CH_2$-$C{\equiv}C$-$CH_3$

We describe here a novel and economic entry to this class of substances using as example the synthesis of the 6a-carbacyclin *(3)*, modified in the lower side-chain and selected for clinical testing.

Our aim, starting from the commercially available, optically active "Corey lactone" *(4)*[3], was to synthesize the versatile, optically active intermediate *(5)* by formal replacement of the ring oxygen atom by a methylene group.

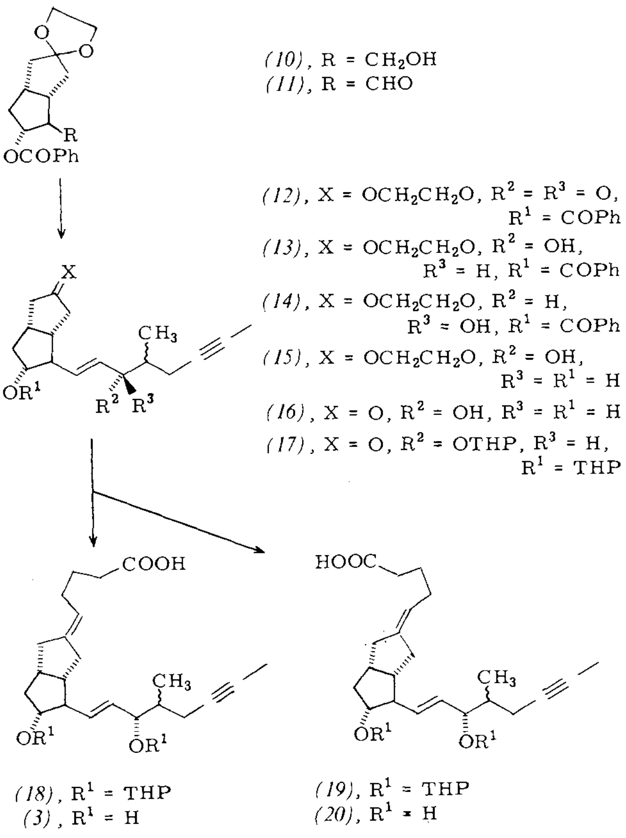


Scheme 1.

The ease of preparation and high stereoselectivity of the reaction pathway shown in Scheme 1 permits the general synthesis of bicyclo[3.3.0]octane derivatives.

After protection of the alcohol function in *(4)* ($ClSiMe_2tBu$, dimethylformamide, imidazole), reaction of the silyl ether *(6)* with lithiated ethyl acetate in tetrahydrofuran (THF) at −70 °C, acid-catalyzed dehydration (TsOH, toluene, 25 °C), and subsequent cleavage of the benzoate ($K_2CO_3$, methanol, 25 °C) afford the α,β-unsaturated ester *(7)* in 70% yield. After Collins- or Jones-oxidation of *(7)* to give the ketone *(8)*, a one-pot reaction with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) at 0 °C in THF[4] and subsequent addition of $NaBH_4$ and $CH_3OH$ furnishes regio- and stereoselectively the bicyclo[3.3.0]octane derivative *(9)* (yield 70%, starting from *(7)*). Decarbethoxylation of *(9)* with 1,4-diazabicyclo[2.2.2]octane (toluene, $H_2O$, 110 °C)[5], evaporation to dryness, benzoylation of the residue (PhCOCl, 0 °C, 10 min), and cleavage of the silyl ether ($AcOH/H_2O/THF$ 65 : 35 : 10, 25 °C) lead to the ketone *(5)* in 88% yield.

After ketalization of *(5)*, *(10)* is oxidized to the aldehyde *(11)* ($CrO_3 \cdot 2C_5H_5N$, $CH_2Cl_2$, 0 °C) and the crude product condensed with 3-methyl-2-oxo-5-heptynylphosphonic acid dimethyl ester[6] (NaH, dimethoxyethane, 0 °C) in a Wittig-Horner reaction to give the α,β-unsaturated ketone *(12)*. Reduction of *(12)* ($NaBH_4$, $CH_3OH$, −40 °C) yields a mixture of the alcohols *(13)* and *(14)*; chromatographic separation of the more polar β-alcohol *(14)* affords the allyl alcohol *(13)*, which is converted by transesterification ($K_2CO_3$, $CH_3OH$) into *(15)*. Cleavage of the ketal function to give *(16)*, followed by treatment with dihydropyran furnishes the tetrahydropyranyl (THP) derivative *(17)*. Wittig reaction of the ketone *(17)* with $Ph_3P{=}CH(CH_2)_3COONa$ (DMSO, 45 °C) affords, after chromatographic separation, the (*E*)-isomer *(18)* and the less polar (*Z*)-isomer *(19)*, which are converted after cleavage of the tetrahydropyranyl moiety into *(3)* and *(20)*, respectively[7].



*(10)*, R = $CH_2OH$
*(11)*, R = CHO

*(12)*, X = $OCH_2CH_2O$, $R^2$ = $R^3$ = O, $R^1$ = COPh
*(13)*, X = $OCH_2CH_2O$, $R^2$ = OH, $R^3$ = H, $R^1$ = COPh
*(14)*, X = $OCH_2CH_2O$, $R^2$ = H, $R^3$ = OH, $R^1$ = COPh
*(15)*, X = $OCH_2CH_2O$, $R^2$ = OH, $R^3$ = $R^1$ = H
*(16)*, X = O, $R^2$ = OH, $R^3$ = $R^1$ = H
*(17)*, X = O, $R^2$ = OTHP, $R^3$ = H, $R^1$ = THP

*(18)*, $R^1$ = THP
*(3)*, $R^1$ = H

*(19)*, $R^1$ = THP
*(20)*, $R^1$ = H

Table 1. Some physical data of the compounds *(3)*, *(5)*, *(7)*, *(9)*, and *(20)*. The elemental analyses of the new compounds are in good agreement with the calculated values [9].

| | |
|---|---|
| *(3)*: | IR (film): 3350, 1710, 970 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 0.94$ and 1.02 (3 H, d, $J = 6.5$ Hz, 16-$CH_3$—CH), 1.78 (3 H, m, $CH_3$—C≡C—), 3.50–4.09 (2 H, m, 15-H, 11-H), 5.18 (1 H, t, $J = 7$ Hz, 5-H), 5.38–5.56 (2 H, m, 13-H, 14-H) |
| *(5)*: | IR (film): 3450, 1735, 1715, 1280 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 3.77$ (2 H, t, $J = 5.5$ Hz, CH—$CH_2OH$), 5.38 (1 H, q, $J = 6.5$ Hz, 11-H), 7.36–7.71 (3 H, m, arom. H), 7.98–8.08 (2 H, m, arom. H) |
| *(7)*: | IR (KBr): 3460, 1700, 1635 $cm^{-1}$; $^1H$-NMR ([$D_6$]DMSO): $\delta = 0$ (6 H, s, $(CH_3)_2Si$), 0.83 (9 H, s, $SiC(CH_3)_3$), 1.12 (3 H, t, $J = 7$ Hz, $CH_3$—$CH_2$—), 3.58 (2 H, t, $J = 5.5$ Hz, CH—$CH_2OSi$), 3.71 (1 H, m, 11-H), 3.97 (2 H, q, $J = 7$ Hz, $CH_3$—$CH_2$—O—), 4.76 (1 H, dt, $J = 7 + 3$ Hz, 9-H), 5.06 (1 H, m, —CH=C) |
| *(9)*: | IR (film): 3440, 1755, 1725, 1660, 1620 $cm^{-1}$; $^1H$-NMR ([$D_6$]DMSO): $\delta = 0$ (6 H, s, $(CH_3)_2Si$), 0.83 (9 H, s, $SiC(CH_3)_3$), 1.03 and 1.14 (3 H, t, $J = 7$ Hz, $CH_3$—$CH_2$—), 3.78 (1 H, m, 11-H), 4.08 (2 H, q, $J = 7$ Hz, $CH_3$—$CH_2$—O), 4.62 and 4.73 (1 H, d, $J = 5$ Hz, OH) |
| *(20)*: | IR (film): 3380, 1710, 970 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): $\delta = 0.94$ and 1.02 (3 H, d, $J = 6.5$ Hz, 16-$CH_3$—CH—), 1.80 (3 H, m, $CH_3$—C≡C—), 3.53–4.13 (2 H, m, 15-H, 11-H), 5.24 (1 H, t, $J = 7$ Hz, 5-H), 5.47–5.62 (2 H, m, 13-H, 14-H) |

*(3)* is a potent vasodilator and inhibitor of blood-platelet aggregation and exhibits the same pharmacological activity profile and comparable efficacy as prostacyclin[8].

Received: April 8, 1981 [Z 913 IE]
German version: Angew. Chem. *93*, 1080 (1981)

CAS Registry numbers:
*(3)*, 73873-87-7; *(4)*, 39746-00-4; *(5)*, 74842-93-6; *(6)*, 64982-34-9; *(7)*, 79745-54-3; *(8)*, 79745-55-4; *(9)*, 79745-56-5; *(10)*, 74818-60-3; *(11)*, 74818-14-7; *(12)*, 79812-92-3; *(13)*, 79812-93-4; *(15)*, 79812-94-5; *(16)*, 79812-95-6; *(17)*, 79745-57-6; *(18)*, 79745-58-7; 3-methyl-2-oxo-5-heptynylphosphonic acid dimethyl ester, 79745-59-8

---

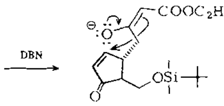
[1] *S. Moncada, R. Gryglewski, S. Bunting, J. R. Vane*, Nature *263*, 663 (1976); *K. C. Nicolaou, G. P. Gasic, W. E. Barnette*, Angew. Chem. *90*, 360 (1978); Angew. Chem. Int. Ed. Engl. *17*, 293 (1978).

[2] a) *D. R. Morton, F. C. Brokaw*, J. Org. Chem. *44*, 2880 (1979); b) *A. Barco, S. Benetti, P. Pollini, P. G. Baraldi, C. Gandolfi, ibid. 45*, 4776 (1980); c) *Y. Konishi, M. Kawamura, Y. Arai, M. Hayashi*, Chem. Lett. *1979*, 1437; d) *A. Sugie, H. Shimomura, J. Katsube, H. Yamamoto*, Tetrahedron Lett. *1979*, 2607; e) *M. Shibasaki, J. Ueda, S. Ikegami, ibid. 1979*, 433; f) *K. Kojima, K. Sakai, ibid. 1978*, 3743; g) *K. C. Nicolaou, W. J. Sipio, R. L. Magolda, S. Seitz, W. E. Barnette*, J. Chem. Soc. Chem. Commun. *1978*, 1067.

[3] *E. W. Yankee, U. Axen, G. L. Bundy*, J. Am. Chem. Soc. *96*, 5865 (1974), and references cited therein.

[4] Most likely ring opening takes place first to give the anion *(21)* followed by subsequent intramolecular Michael addition. Intermediate products could not be observed. A similar stereoselective annelation is known: *V. Osterthum, E. Winterfeldt*, Chem. Ber. *110*, 146 (1977); cf. also [2b].

*(8)*



*(21)*

[5] *B. S. Huang, E. I. Parish, D. H. Miles*, J. Org. Chem. *39*, 2647 (1974). Addition of some water improves the yields and enables the reaction to be carried out under milder conditions.

[6] The phosphonate is obtained from methylmalonic acid diethyl ester by alkylation with 1-bromo-2-butyne, decarbethoxylation with lithium chloride in dimethyl sulfoxide (DMSO), and subsequent reaction with the lithium salt of methylphosphonic acid dimethyl ester.

[7] The configuration of the trisubstituted $\Delta^5$-double bond is established by comparison of the biological activities of *(3)* and *(20)*; the unnaturally configurated (*Z*)-isomer *(20)* displays markedly lower biological activity.

[8] a) *J. Casals-Stenzel, M. Buse, O. Loge, P. Vischer, E. Wittkopf*, Therapiewoche *30*, 7853 (1980); b) *M. Haberey, B. Maass, G. Mannesmann, W. Skuballa, M.-H. Town, H. Vorbrüggen, ibid. 30*, 7860 (1980). *K. Schrör, H. Darius, R. Matzky, R. Ohlendorf*, Naunyn-Schmiedebergs Arch. Pharmacol. *316*, 252 (1981). Schering-Code for *(3)* is ZK 36374 (proposed generic name Ciloprost), for *(20)* ZK 36375.

[9] We thank Dr. *A. Seeger* for the interpretation of the spectra and Mr. *K. Cornelius* and Mr. *D. Schmidt* for valuable assistance with the preparations.

---

# 18,19-Didehydrocorrinoids—Possible Intermediates in the Biosynthesis of Vitamin $B_{12}$

By *Bernd Dresow, Ludger Ernst, Lutz Grotjahn*, and *Volker B. Koppenhagen*[*]

Under cobalt-deficient conditions nonsulfur purple bacteria release considerable amounts of metal-free corrinoids into the medium[1,2]. Thus, up to 3 mg/L of a mixture of isomer-free hydrogenobyrinic acid *c*-amide *(1)* and hydrogenobyrinic acid *a,c*-diamide can be isolated from the culture filtrate of *Rhodopseudomonas sphaeroides*. These compounds do not appear to be biogenetic precursors of the cobalt-containing corrinoids. Incorporation of the central $Co(CN)_2$-group into the crude product *(1)* yields cobyrinic acid *c*-amide *(2)* and a small amount (4%) of a blue cobalt-

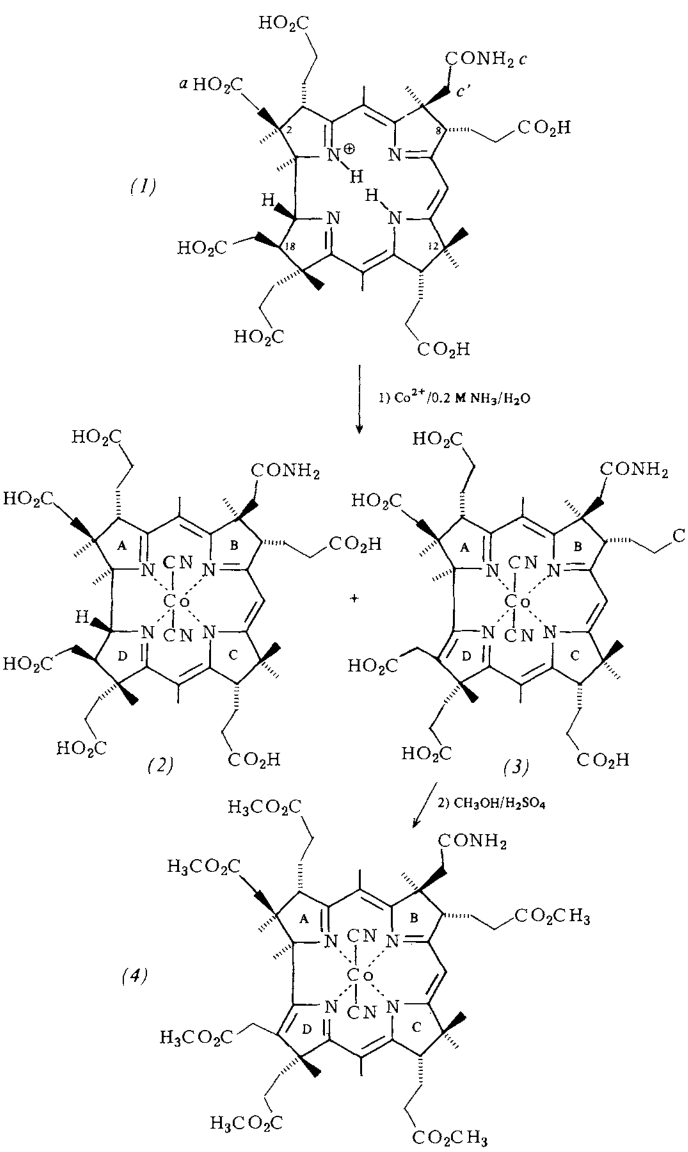


Table 1. NMR spectroscopic data of *(4)*.

| $^1$H-NMR (400 MHz, $CDCl_3$, TMS, $\delta$ values) | $^{13}$C-NMR [a] (101 MHz, $CDCl_3$, $\delta$ values) |
|---|---|
| 6.96, 5.23 (in each case 1 br. s, NH); 5.64 (10-H); 3.74, 3.72, 3.70, 3.67, 3.622, 3.616 (in each case one $OCH_3$); 3.47/3.38 ($J_{AB}$ = 16.7 Hz, 18-$CH_2$); 3.07 (*ca.* dd with $J$ = 6.9 and 3.4 Hz, 13-H); 2.38 (15-$CH_3$); 2.16 (5-$CH_3$); 1.80 (7-$CH_3$); 1.76, 1.53, 1.50, 1.40 (1-, 2-, 12α-, 17-$CH_3$); 1.22 (12β-$CH_3$) | 177.5 (2C), 174.7, 173.74, 173.67, 173.0, 172.7, 172.4, 172.03 (2C), 171.95, 169.6 (seven CO and C-4,9,11,14,16); 161.6 (C-6); 151.6 (C-19); 124.6 (C-18); 106.9 (C-5); 104.9 (C-15); 92.4 (C-10); 84.7 (C-1); 65.2 (C-17); 58.5 (C-8); 56.6 (C-3); 52.8 (C-13); 52.6, 51.9, 51.8 (in each case one $OCH_3$); 51.7 (three $OCH_3$); 47.9, 47.0 (C-2,12); 46.1 (C-*c'*); 41.1 (C-*d'*); 34.3, 32.7, 31.2, 31.0, 30.7, 29.8, 29.1, 28.7, 26.6, 25.8 (nine $CH_2$ and 12β-$CH_3$); 24.9 (1-$CH_3$); 20.4 (17-$CH_3$); 19.5, 19.2 (7-, 12α-$CH_3$); 16.2 (2-$CH_3$); 15.8 (5-$CH_3$); 15.4 (15-$CH_3$) |

[a] The resonances of the quaternary and the methoxy carbons could be identified on the basis of their low intensities. The relative intensities between $\delta$ = 178 — 170 could not be determined with absolute certainty because of the low signal-to-noise ratio. No signal was found for C-7; by analogy to the spectrum of cobester *c*-amide in $CDCl_3$ (unpublished) it is expected at $\delta$ = 51-52, presumably hidden under other resonances in this region. $CDCl_3$: $\delta$ = 77.05.

---

[*] Dr. V. B. Koppenhagen, Dr. B. Dresow, Dr. L. Ernst, Dr. L. Grotjahn
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

containing by-product, for which we have proposed the structure 18,19-didehydrocobyrinic acid *c*-amide *(3)*[2]. Such a compound is of interest in its metal-free, non-amidated form as the connecting link between metal-free and cobalt-containing corrinoids in the biosynthesis of vitamin $B_{12}$[2]. We have now unambiguously proved the structure of the hexamethyl ester of *(3)* as dicyano-18,19-didehydrocobyrinic acid hexamethyl ester *c*-amide *(4)*.

The absorption spectrum of *(4)* shows the typical α,β,γ-structure of cobalt-containing corrinoids. The substantial bathochromic shift of the main absorption bands (369→396 nm, 545→590 nm, and 584→626 nm) compared to those of the heptamethyl ester of dicyanocobyrinic acid ("cobester") indicates a lengthening of the corrin chromophore.

The presence of the same peripheral groups as in the hexamethyl ester of *(2)* follows from the $^1$H-NMR spectrum, which contains the signals of the protons of one amide group and of six methoxy- and eight angular methyl groups. An AB system ($J$ = 16.7 Hz) appears at $\delta$ = 3.47/3.38 which is assigned to the methylene group of a $CH_2CO_2Me$ moiety adjacent to a double bond. The position of this double bond and that of the amide function follows from the $^{13}$C-NMR spectrum, which was recorded despite the small amount of substance available (*ca.* 2 mg = *ca.* 2 μmol, recording time 64 h for 351000 accumulations). The deshielding of C-5, 7, and 8 and of C-*c'* by 3—5 ppm in *(4)* (relative to "cobester"[3]) and the shielding of C-6 by *ca.* 2 ppm are consistent with a *c*-amide group. In cobester[3] the signals of C-18 and C-19 appear at $\delta$ = 39.2 and 74.7, respectively; in *(4)* they are shifted into the olefinic region, presumably to $\delta$ = 124.6 and 151.5, respectively. The signals of C-17 ($\delta$ = 58.3→65.2), C-1 ($\delta$ = 82.5→84.7) and 17-$CH_3$ ($\delta$ = 18.3→20.4) are also clearly shifted downfield. The above data indicate that *(4)* is the $\Delta^{18}$-olefin.

The molecular ion in the FD mass spectrum ($M^+$ = 1071) is consistent with the empirical formula ($C_{53}H_{70}N_7O_{13}Co$). The base peak (1019) corresponds to $M^+ - 2CN$.

Received: April 15, 1981 [Z 915 IE]
German version: Angew. Chem. *93*, 1076 (1981)

---

[1] *B. Dresow, G. Schlingmann, W. S. Sheldrick, V. B. Koppenhagen*, Angew. Chem. *92*, 303 (1980); Angew. Chem. Int. Ed. Engl. *19*, 321 (1980).

[2] *B. Dresow, G. Schlingmann, L. Ernst, V. B. Koppenhagen*, J. Biol. Chem. *255*, 7637 (1980).

[3] *L. Ernst*, Liebigs Ann. Chem. *1981*, 376.

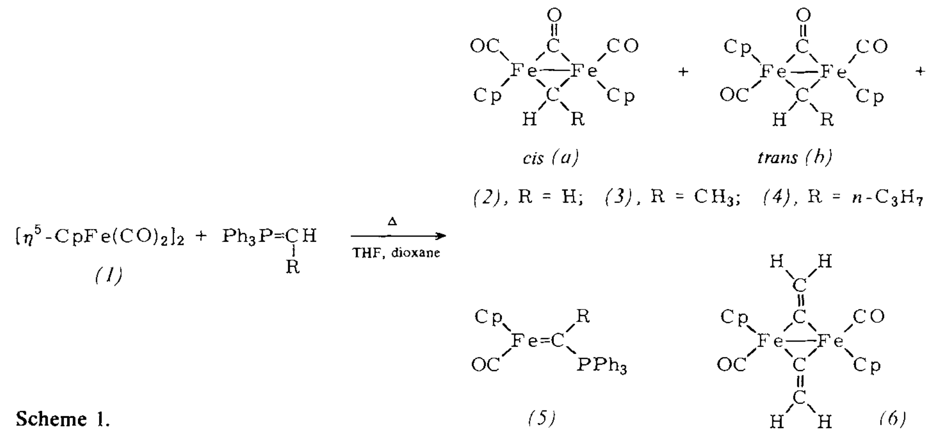
---

## Novel Reactions of Phosphorus Ylides with Carbonyl(cyclopentadienyl)metal Complexes: Preparative Access to μ-Alkylidene Complexes and Unexpected Acylations[**]

By *Richard Korswagen, Reinhold Alt, Dieter Speth,* and *Manfred L. Ziegler*[*]

Phosphorus ylides $R_3P{=}CR'R''$ prove to be astonishingly versatile in their reactions with metal complexes. Essentially three types of reaction have already been reported: 1) ligand exchange with formation of products in which the ylide carbon atom functions as σ-donor[1]; 2) ligand exchange and transylidation whereby a hydrogen atom attached to ylide carbon is replaced by an organometallic group[2]; 3) peripheral ligand reactions in which CO groups of the complex participate[3].

We have now discovered two further different types of reaction which take place between phosphorus ylides and organometallic substrates.



Scheme 1.

On reaction of the iron complex *(1)* with ylides $PH_3P{=}CHR$ (Scheme 1) we obtained μ-alkylidene complexes as major products (50—60%). The μ-methylene complex *(2)* is formed in both *cis*-form *(2a)* as well as the *trans*-form *(2b)*; both isomers can be isolated in the pure state by means of low-temperature chromatography. The same holds for the μ-ethylidene complex *(3)*. The *cis*- and *trans*-isomers differ slightly in their solubility in apolar solvents (as expected the *trans*-form is the more soluble). *(2a)* and *(2b)* are found to be in equilibrium (≈3 : 1) in solution at room temperature; at −80 °C the solutions of the pure isomers are stable. *(2a)* exists in two modifications in the solid state [*(2a)* and *(2a')*] whose $^1$H-NMR spectra are identical. The compounds *(2)*—*(4)* were characterized by elemental analysis and by their IR, $^1$H-NMR, $^{13}$C-NMR and mass spectra[4], and, in the case of the *cis*-isomer *(2a)*, also by X-ray structure analysis (Fig. 1)[5].

Besides the μ-alkylidene complexes we were able, in each case, to isolate organometal-substituted ylides *(5)*; the species *(6)* could be detected only by mass spectroscopy. The preparation of μ-alkylidene complexes *via* phosphorus ylides is new (syntheses with diazaalkanes[6] or dihaloalkanes[7] are known).

---

[*] Prof. Dr. M. L. Ziegler, Dipl.-Chem. R. Korswagen, R. Alt, D. Speth
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

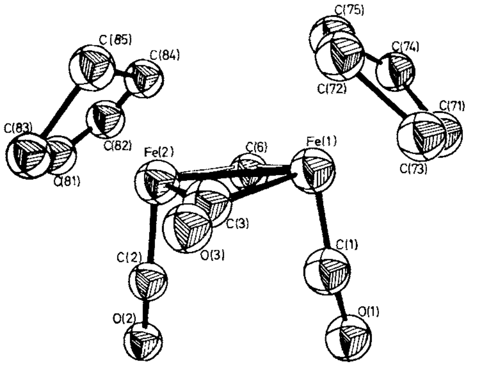
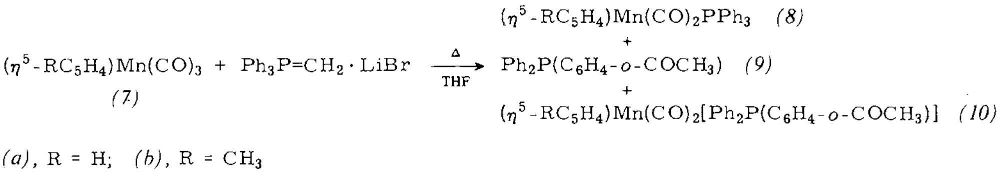


Fig. 1. ORTEP diagram of the μ-methylene complex *(2a)*: the thermal ellipsoids correspond to a probability of 50%.

The manganese complex *(7b)* reacts with methylene- or benzylidenephosphoranes in a ligand exchange reaction to give $(\eta^5\text{-CH}_3\text{C}_5\text{H}_4)\text{Mn(CO)}_2\text{—CHRPR}'_3$[1b] and with trimethyl(methylene)phosphorane, after photolysis of an intermediate formed by peripheral ligand substitution at a CO group, to give $(\eta^5\text{-CH}_3\text{C}_5\text{H}_4)\text{Mn(CO)}_2\text{—CH}_2\text{PMe}_3$[3b]. We have now reacted the complexes *(7)* under reflux in tetrahydrofuran (THF) with $\text{Ph}_3\text{P}{=}\text{CH}_2$ (Scheme 2).



$$(\eta^5\text{-RC}_5\text{H}_4)\text{Mn(CO)}_3 + \text{Ph}_3\text{P=CH}_2\cdot\text{LiBr} \xrightarrow[\text{THF}]{\Delta} \begin{array}{l} (\eta^5\text{-RC}_5\text{H}_4)\text{Mn(CO)}_2\text{PPh}_3 \quad (8)\\ \quad + \\ \text{Ph}_2\text{P(C}_6\text{H}_4\text{-}o\text{-COCH}_3) \quad (9)\\ \quad + \\ (\eta^5\text{-RC}_5\text{H}_4)\text{Mn(CO)}_2[\text{Ph}_2\text{P(C}_6\text{H}_4\text{-}o\text{-COCH}_3)] \quad (10)\end{array}$$

*(7)*

*(a)*, R = H; *(b)*, R = $\text{CH}_3$

Scheme 2.

The compounds *(9)* and *(10)* were characterized by elemental analysis and by IR, NMR and mass spectra[8]; in the case of complex *(10b)* also by an X-ray structure analysis[9]. In the course of their formation a phenyl ring of the $\text{Ph}_3\text{P}$ unit was acylated in the *ortho*-position; the acylation product *(9)* is present, both bonded as ligand in *(10)*, as well in the free state.

The phosphane-complexes *(8)* were identified on the basis of data in the literature. The mechanism of the reaction is still unclear. Participation not only of the ylide but also of a CO group is evident.

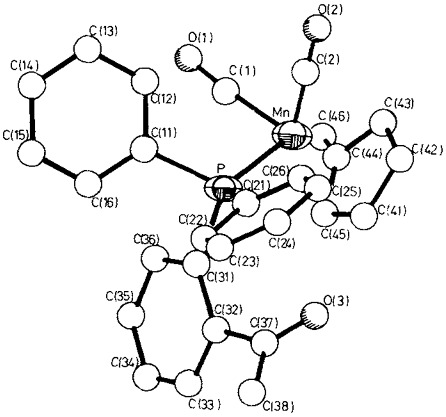


Fig. 2. ORTEP diagram of the peripherically acylated phosphane-complex *(10b)*; the thermal ellipsoids correspond to a probability of 50%.

*Procedure*

Preparation of *(2a)* and *(2b)*: A suspension of $[\text{Ph}_3\text{PCH}_3]\text{Br}$ (2 g, 5.65 mmol) in anhydrous THF (100 mL) under an atmosphere of $\text{N}_2$ is treated dropwise with a 15% solution of *n*-butyllithium in *n*-hexane until a clear orange solution is formed. After addition of 1 g (2.82 mmol) of *(1)* the mixture is heated under reflux for 24 h (10 h with dioxane as solvent). 10 g silica gel (0.05—0.2) is added to the solution, which is then evaporated down in a rotary evaporator. The brown residue is extracted with 200 ml of diethyl ether and the deep-red solution "prechromatographed" on a column ($\text{Al}_2\text{O}_3$ neutral, activity 1; 20 × 3.5 cm, ether). The first, yellow fraction contains $\text{Ph}_3\text{P}$ and a little ferrocene. The second, violet and third, orange-red zones are rechromatographed ($\text{Al}_2\text{O}_3$ neutral, activity 1, 25 × 2.5 cm, ether) together at −20 °C. Elution of a small amount of $\text{Ph}_3\text{P}$ is followed by a violet, second zone containing *(2b)*, whose eluate is collected under $\text{N}_2$ at −50 °C. The bright-orange, third zone contains *(5)*, R = H, the red-orange, fourth zone *(2a)*, which is eluted under the same conditions as *(2b)*. Each of the solutions is evaporated down to *ca.* 25 mL under high vacuum at −50 °C and treated with 25 mL *n*-pentane. After a few days over dry ice, red-violet and cherry-red crystals of *(2a)* and *(2a')*, respectively, and dark violet crystals of *(2b)* separate out. The complexes are air-stable at room temperature; the total yield of *(2a)* and *(2b)* [m.p. 168—170 °C (dec.)] is 600 mg (63%).

Preparation of *(10a)* [*(10b)* analogously]: *(7a)* is allowed to react with the ylide, as described for *(1)*. After prepurification on the column the filtrate still contains unreacted *(7a)* besides the products *(8a)*, *(9)* and *(10a)*. The ether solution is evaporated down to 50 mL and, after addition of 50 mL of *n*-pentane, cooled to −60 °C; besides *(10a)* mainly *(7a)* and *(9)* crystallize out (the mother liquor contains *(7a)* together with *(8a)* and $\text{PPh}_3$). The mixture of crystals is dissolved in ether (10 mL) and separated by preparative TLC (20 × 20 × 0.2 cm, silica gel 60, cyclohexane/diethyl ether ≈ 1 : 1). The yellow, first zone contains *(7a)* and *(8a)*, the yellow, second zone *(9)*, and the likewise yellow, third zone *(10a)*.—The air-stable crystals of *(10a)* and of *(10b)* melt at 168 and 170 °C, respectively, with decomposition; *(9)* melts at 143 °C. The yields of *(10a)* and *(10b)* are 2 and 6%, respectively.

Received: October 20, 1980 [Z 911 IE]
revised: March 24, 1981
German version: Angew. Chem. *93*, 1073 (1981)

CAS Registry numbers:
*(1)*, 12154-95-9; *(2a)*, 79838-80-8; *(2b)*, 79896-43-8; *(3a)*, 79897-17-9; *(3b)*, 75829-77-5; *(4)*, 79838-81-9; *(5)*, R = H, 79839-82-0; *(5)*, R = $\text{CH}_3$, 79839-83-1; *(5)*, R = *n*-$\text{C}_3\text{H}_7$, 79839-84-2; *(6)*, 79839-85-3; *(7a)*, 12079-69-5; *(7b)*, 12108-13-3; *(8a)*, 12100-41-3; *(8b)*, 12100-95-7; *(9)*, 50777-63-4; *(10a)*, 79839-86-4; *(10b)*, 79839-87-5; $[\text{Ph}_3\text{PCH}_3]\text{Br}$ 1779-49-3; $\text{Ph}_3\text{P}{=}\text{CH}_2$ 3487-44-3; $\text{Ph}_3\text{P}{=}\text{CHCH}_3$ 1754-88-7; $\text{Ph}_3\text{P}{=}\text{CH-}n\text{-C}_3\text{H}_7$, 3728-50-5

---

[1] a) *L. Knoll*, J. Organomet. Chem. *148*, C25 (1978); b) *193*, 47 (1980).
[2] *J. C. Baldwin, N. L. Keder, C. E. Strouse, W. C. Kaska*, Z. Naturforsch. *B 35*, 1289 (1980).
[3] a) *W. C. Kaska, D. K. Mitchell, R. F. Reichelderfer, W. D. Korte*, J. Am. Chem. Soc. *96*, 2847 (1974); b) *H. Blau, W. Malisch*, Angew. Chem. *92*, 1063 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1019 (1980).

[4] IR, $\nu_{CO}$ [$cm^{-1}$]: crystals (Nujol, KBr) of *(2a)* 1998 sh, 1962 vs, 1940 s, 1825 w, 1775 s, 1745 s; *(2a')* 1994 sh, 1973 vs, 1932 s, 1820 m, 1738 vs; *(2b)* 1998 m, 1952 vs, 1930 s, 1802 sh, 1780 s. In $CH_2Cl_2$ solution: 1985 vs, 1943 s, 1782 s (*cis/trans* 3 : 1).—$^1$H-NMR, $\delta$-values (300 MHz, $CDCl_3$ solution, int. TMS, room temperature): *(2a)* 10.29 (s, 1 H), 8.38 (s, 1 H), 4.74 (s, 10 H); *(2b)* 9.54 (s, 2 H), 4.77 (s, 10 H).—MS, *m/z*: *(2a)* 340 (molecular ion, 16.5%); *(2b)* 340 (molecular ion, 30%).

[5] Monoclinic crystals from ether/pentane, $C^5_{2h}$-$P2_1/n$, $a=900.0(12)$, $b=2277.2(22)$, $c=656.7(16)$ pm, $\beta=103.69(27)°$, $Z=4$, 752 reflections ($I>3\sigma(I)$), preliminary $R$ value 0.098.

[6] *W. A. Herrmann*, Angew. Chem. *90*, 855 (1978); Angew. Chem. Int. Ed. Engl. *17*, 800 (1978); *W. A. Herrmann, J. Planck, D. Riedel, M. L. Ziegler, K. Weidenhammer, E. Guggolz, B. Balbach*, J. Am. Chem. Soc. *103*, 63 (1981); *W. A. Herrmann, P. Planck*, Z. Naturforsch. *B85*, 680 (1980).

[7] *C. E. Sumner Jr., P. E. Reley, R. E. Davis, R. Pettit*, J. Am. Chem. Soc. *102*, 1752 (1980).

[8] IR [$cm^{-1}$]: *(10a)* $\nu_{CO}$ 1927 vs, 1867 vs, 1855 vs, 1830 sh, $\nu_{COCH_3}$ 1690 m; *(10b)* $\nu_{CO}$ 1922 vs, 1863 vs, 1852 vs, 1830 sh, $\nu_{COCH_3}$ 1690 s.—$^1$H-NMR (300 MHz, $\delta$-values, int. TMS, 20°C): *(10a)* 7.89 (m, 1 H), 7.46, 7.32 (m, 13 H), 4.34 (s, 5 H), 1.89 (s, 3 H); *(10b)* 7.89 (br, 1 H), 7.42, 7.30 (m, 13 H), 4.16 (d, 4 H), 1.96 (s, 3 H), 1.92 (s, 3 H).—$^{31}$P-NMR (90 MHz, $\delta$-values, $CDCl_3$, $H_3PO_4$ ext.): *(10b)* 95.92 (br).—MS, *m/z*: *(10b)* 494 (molecular ion, 3.5%); *(9)* 304 (molecular ion, 100%).

[9] Tetragonal crystals from ether/pentane, $C^2_4$-$P4_1$, $a=1003.5(4)$, $c=2392.2(9)$ pm, $Z=4$; 779 reflections ($I>2.5\sigma(I)$), $R_w=0.046$.

---

## Second Sphere Coordination of Cationic Platinum Complexes by Crown Ethers—

## The X-Ray Crystal Structure of $[Pt(bpy)(NH_3)_2\cdot Dibenzo[30]crown\text{-}10]^{2+}[PF_6]^-_2\cdot xH_2O$ ($x\approx 0.6$)[**]

By *Howard M. Colquhoun, J. Fraser Stoddart, David J. Williams, John B. Wolstenholme*, and *Ryszard Zarzycki*[*]

Since the possibility of second sphere coordination[2] of transition metal complexes was first alluded to by *Werner*[1] in 1913, it has become apparent[3] that the binding of an outer layer of ligands to transition metal (M) ammine complexes is usually a result of (N—H···X) hydrogen bonding between the $NH_3$ ligands and electron donor atoms (X) present in counterions, solvent molecules, or other ligands. The fact that [18]crown-6 (18C6) and dibenzo-[18]crown-6 (DB18C6)[4] form strong adducts with primary alkylammonium ($RNH_3^+$) ions through multiple hydrogen bonding suggested[5] to us that coordinated ammonia ($M—NH_3^{\delta+}$) should bind to crown ethers in a similar manner. Indeed, we have been able to isolate[6] the crystalline adducts, [*trans*-$PtCl_2(PMe_3)NH_3\cdot$DB18C6] and [{*trans*-$PtCl_2(PMe_3)(NH_3)$}$_2\cdot$18C6], and have demonstrated[6] that the macrocyclic polyethers serve as second sphere ligands *via* (N—H···O) hydrogen bonding to $NH_3$ ligands in the first sphere.

We now report on the ability of the $[Pt(bpy)(NH_3)_2]^{2+}$ ion to form 1 : 1-adducts with 18C6, DB18C6, DB24C8, DB30C10, and DB36C12[7]. In addition to the expected (N—H···O) hydrogen bond formation between the *cis*-$NH_3$ ligands on $Pt^{II}$ having a square planar environment and polyether components of these crown ethers, the benzene rings (π-donors) in DB24C8, DB30C10, and DB36C12 all enter into stabilizing charge-transfer (CT) interactions with the aromatic rings of the bipyridyl ligand (π-acceptor).

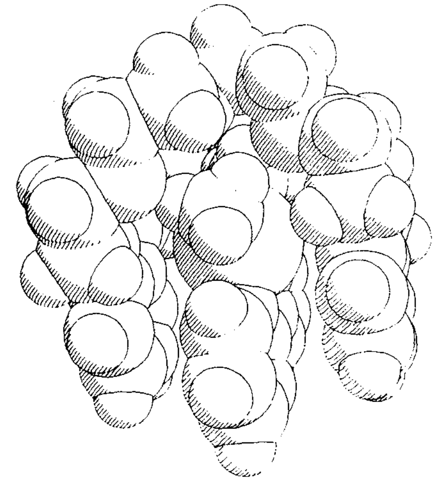


Fig. 1. Computer drawing of a space-filling molecular model based on the crystal structure of the 1 : 1-adduct formed between $[Pt(bpy)(NH_3)_2]^{2+}$ and DB30C10. Direct visual comparison with the representation of the structure shown in Figure 2 is necessary in order to appreciate the structural detail. Crystals of $[Pt(bpy)(NH_3)_2(DB30C10)]^{2+}[PF_6]^-_2\cdot$*ca.* $0.6\,H_2O$ are monoclinic; space group $P2_1/n$, $a=16.081(2)$, $b=15.912(2)$, $c=18.718(2)$ Å, $\beta=101.34(1)°$, $V=4696$ Å$^3$, $Z=4$, $\rho_c=1.74$ g cm$^{-3}$, $\mu(Cu_{K\alpha})=72$ cm$^{-1}$. Of the 5250 independent reflections ($\theta\leqslant 50°$, $Cu_{K\alpha}$ irradiation), 453 were classified as unobserved. The structure was solved by the heavy atom method and refined anisotropically with absorption corrected data to $R=0.053$.

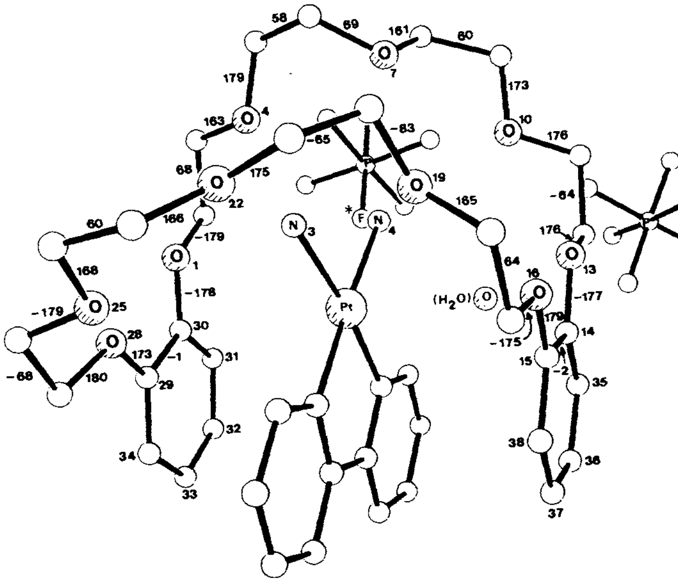


Fig. 2. Crystal structure of $[Pt(bpy)(NH_3)_2(DB30C10)]^{2+}[PF_6]^-_2\cdot$*ca.* $0.6\,H_2O$. Bond lengths [Å] in the host molecule: C—C (excluding $C_{Aryl}$—C), 1.39—1.45; $C_{Aryl}$—O, 1.35—1.37. Bond angles [°] in the host molecule: COC (excluding $C_{Aryl}$OC), 110—115; $C_{Aryl}$OC: 116—118. Torsion angles [°] (OCCO and CCOC) in the host are shown beside the relevant CC and CO bonds in the structure. Hydrogen bond distances, $R_{N\cdots X}$ Å; angles ($\theta_N$ and $\theta_H^0$) between COC planes and a) the NO vectors and b) the HO vectors: $R_{N4\cdots O4}=3.02$, a) 36, b) 37; $R_{N4\cdots O10}=2.90$, a) 0, b) 14; $R_{N3\cdots O19}=2.99$, a) 15, b) 24; $R_{N4\cdots F}=3.20$ (hydrogen atoms were located unambiguously). (In the case of N4, a rigid body refinement of the $NH_3$ ligand was possible. Since the thermal parameters were anisotropic for N3, rigid body refinement of the $NH_3$ ligand was not possible; however, the H atom involved in hydrogen bonding to O19 was identified from the difference map.) Separations [Å] between aromatic rings in the guest and host: bpy-benzene ring (14/38) = 3.45 (minimum), 3.47 (average); bpy-benzene ring (29/34) = 3.48 (minimum), 3.52 (average). Angles [°] between the planes of the aromatic rings: bpy-benzene ring (14/38) = 0.9; bpy-benzene ring (29/34) = 2.2; benzene ring (14/38)-benzene ring (29/34) = 1.4.

---

[*] Dr. H. M. Colquhoun
Corporate Laboratory, Imperial Chemical Industries Ltd.
P.O. Box 11, The Heath, Runcorn, Cheshire WA7 4QE (England)
Dr. J. F. Stoddart [+], J. B. Wolstenholme
Department of Chemistry, The University
Sheffield S3 7HF (England)
Dr. D. J. Williams, R. Zarzycki
Chemical Crystallography Laboratory
Department of Chemistry, Imperial College
London SW7 2AY (England)

[+] Author to whom correspondence should be addressed.

[**] The work was supported in part by the Science Research Council (United Kingdom).

Addition of diethyl ether to a dichloromethane solution containing equimolar amounts of $[Pt(bpy)(NH_3)_2]^{2+}[PF_6^-]_2$ *(1)*[8] and DB30C10 resulted in the formation of a crystalline 1 : 1-adduct which proved amenable to X-ray structural analysis (Fig. 1 and 2). Undoubtedly, the most fascinating features of this structure—apart from the hydrogen bonding between three of the ten O atoms in the crown ether and three of the six hydrogen atoms associated with the $NH_3$ ligands in the complex, are the π-π stabilizing interactions[9] between the two benzene rings in the host molecule and one of the two pyridine rings of the 2,2′-bipyridyl ligand in the guest complex. At first glance, the involvement of relatively few hydrogen bonds with respect to both host and guest is remarkable. However, the relative geometries essential for effective CT-interaction between these two species militate against the involvement of the four "phenolic" O atoms[10] in the hydrogen bonds. Also, one of the H atoms on one of the two $NH_3$ ligands forms a hydrogen bond to an F atom in one of the $PF_6^-$ counterions. Although the structure was found to incorporate *ca.* 0.6 $H_2O$, the water molecule does not enter into any hydrogen bonding interactions with the crown ether[11]. Notable features of the gross conformation of the crown are: 1) The absence of any molecular symmetry, and 2) the departure from a conformation where the sequence of torsion angles in the two polyether loops reads $ag^+a\ ag^-a$ (*a* signifies *anti* with *ca.* 180°, and *g gauche* with *ca.* ±65°); exceptions are provided by C5—C6—O7—C8 and C18—O19—C20—C21 which have values of +69° and −83°, respectively.

The manner in which the crown ether envelopes the transition metal complex is quite remarkable and the question arises: What is the structure and stability of the 1 : 1-adduct in solution? The UV spectrum of a solution of *(1)* in $CH_3CN$ (Fig. 3) is essentially unchanged upon addition of 1 equivalent molar amount of 18C6; however, in the presence of the same amount of DB30C10, the intensities of the $\pi \rightarrow \pi^*$ absorptions of the bipyridyl ligand[12] at $\lambda_{max} = 306$ and 318 nm are significantly reduced. A band at 275 nm, characteristic[4a] of the annelated benzene rings of DB30C10 is also evident, but more importantly, a broad absorption appears in the charge-transfer region ($\lambda_{max} \approx 350$ nm). Solutions of *(1)* become visibly more strongly colored on addition of DB30C10.

Comparison of the $^1H$-NMR spectra of 18C6, DB18C6, DB24C8, DB30C10, and DB36C12 recorded in $CD_2Cl_2$ with those of the corresponding 1 : 1 adducts with *(1)* (Table 1) reveals that the mutual influences of ring currents (associated with the benzene rings in the host molecules and the pyridine rings of the bpy ligand in the guest complex) on the chemical shifts of the aromatic protons manifest themselves most noticeably in the *(1)*·DB30C10 adduct. In particular, the appreciable upfield shift of 0.52 ppm for the protons on the benzene rings on 1 : 1-adduct formation is accompanied by equally dramatic upfield shifts of 0.38 and 0.68 ppm, respectively, for the 3,3′-H and 6,6′-H in the bpy ligand. Inspection of space-filling molecular models confirms that both hydrogen bonding and CT-interactions should be optimized in *(1)*·DB30C10 (Fig. 1).

Thus, appropriate crown ether derivatives can enter into second sphere coordination with suitable transition-metal

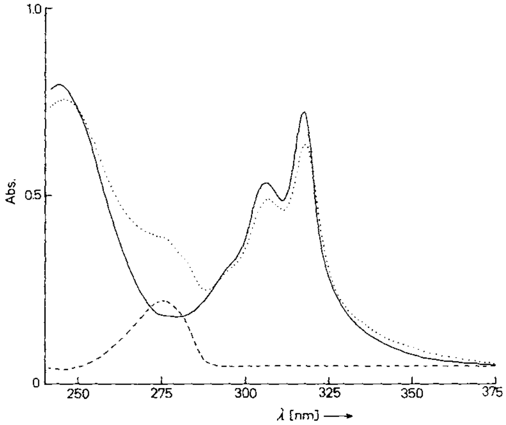


Fig. 3. UV spectra ($CH_3CN$, $4 \times 10^{-5}$ M, $d = 1$ cm) of a) DB30C10 (----) ($\lambda_{max} = 275$ nm; $\varepsilon = 4250$), b) *(1)* and *(1)*·18C6 (—) ($\lambda_{max} = 245$, 306, 318 nm; $\varepsilon = 18750$, 12000, 16750), and c) *(1)*·DB30C10+18C6 (······) ($\lambda_{max} = 246$, 275, 307, 318 nm; $\varepsilon = 17500$, 8500, 11000, 14750).

Table 1. $^1H$-NMR chemical shifts [a] for 18C6, DB18C6, DB24C8, DB30C10, and DB36C12, as well as the 1 : 1-adducts of these crown ethers with *(1)*.

| Crown Ether | Signals from *(1)* [b] | | | | | Signals from the crown ethers [c] | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| or Adduct | 3,3′-H | 4,4′-H | 5,5′-H | 6,6′-H | $NH_3$ | $C_6H_4$ | $OCH_2^\alpha$ | $OCH_2^\beta$ | $OCH_2^\gamma$ | $OCH_2^\delta$ | $OCH_2^\varepsilon$ |
| 18C6 | — | — | — | — | — | — | 3.58 (s) | — | — | — | — |
| *(1)*·18C6 | 8.77 (d) | 7.73 (t) | 8.36 (t) | 8.36 (d) | 4.77 (bs) | — | 3.72 (s)<br>(+0.14) | — | — | — | — |
| DB18C6 | — | — | — | — | — | 6.86 (s) | 4.13 (m) | 3.95 (m) | — | — | — |
| *(1)*·DB18C6 | 8.68 (d)<br>(−0.09) | 7.65 (t)<br>(−0.08) | 8.35 (t)<br>(−0.01) | 8.23 (d)<br>(−0.13) | 4.74 (bs)<br>(−0.03) | 6.85 (m)<br>(−0.01) | 4.14 (m)<br>(+0.01) | 3.94 (m)<br>(−0.01) | — | — | — |
| DB24C8 | — | — | — | — | — | 6.87 (s) | 4.11 (m) | 3.84 (m) | 3.75 (s) | — | — |
| *(1)*·DB24C8 | 8.48 (d)<br>(−0.29) | 7.63 (t)<br>(−0.10) | 8.23 (t)<br>(−0.13) | 7.92 (d)<br>(−0.44) | 4.38 (bs)<br>(−0.39) | 6.59 (s)<br>(−0.28) | 3.99 (m)<br>(−0.12) | 3.83 (m)<br>(−0.01) | 3.68 (s)<br>(−0.07) | — | — |
| DB30C10 | — | — | — | — | — | 6.88 (s) | 4.11 (m) | 3.83 (m) | 3.70 (m) | 3.64 (m) | — |
| *(1)*·DB30C10 | 8.39 (d)<br>(−0.38) | 7.68 (t)<br>(−0.05) | 8.20 (t)<br>(−0.16) | 7.74 (d)<br>(−0.62) | 4.62 (bs)<br>(−0.15) | 6.36 (s)<br>(−0.52) | 3.93 (m)<br>(−0.19) | 3.84 (m)<br>(+0.01) | 3.78 (s)<br>(+0.08) | 3.78 (s)<br>(+0.14) | — |
| DB36C12 | — | — | — | — | — | 6.88 (s) | 4.12 (m) | 3.83 (m) | 3.68 (m) | 3.63 (m) | 3.60 (s) |
| *(1)*·DB36C12 | 8.57 (d)<br>(−0.20) | 7.58 (t)<br>(−0.15) | 8.18 (t)<br>(−0.18) | 7.97 (d)<br>(−0.39) | 4.67 (bs)<br>(−0.10) | 6.69 (m)<br>(−0.19) | 4.00 (m)<br>(−0.12) | 3.77 (m)<br>(−0.06) | 3.68 (m)<br>(0.00) | 3.63 (m)<br>(0.00) | 3.62<br>(+0.02) |

[a] The spectra were recorded at room temperature ($CD_2Cl_2$, TMS) with a 220 MHz spectrometer (Perkin Elmer R 34). [b] The values in brackets indicate how strongly the respective signals are shifted relative to the corresponding signals in *(1)*·18C6. [c] The values in brackets indicate how strongly the signal is shifted in relation to the corresponding signal of the respective crown ethers.

complexes in solution and in the crystalline state *via* CT-interactions, as well as by hydrogen bonding.

## *Experimental*

*(1)*·18C6: *(1)* (330 mg, 0.43 mmol) and 18C6 (230 mg, 0.87 mmol) were dissolved in $CH_2Cl_2$ (30 mL) and $Et_2O$ added dropwise until the first trace of permanent cloudiness was evident. The solution was allowed to stand overnight and the resulting yellow crystals were filtered off, washed with $Et_2O$, and dried. Yield 270 mg (61%); m.p. = 231 °C; IR (Nujol): 3200 m (NH), 1620 m (NH), 1105 s (CO), 820 vs (PF) $cm^{-1}$.

*(1)*·DB30C10: The corresponding crystalline 1 : 1-adduct with DB30C10 was prepared similarly using equimolar proportions of complex and crown. Elemental analysis and IR spectroscopy indicated the presence of just under 1 molar equivalent of water (cf. X-ray crystal structure). Yield 30%; m.p. = 191°; IR (Nujol): 3660 m, 3590 m (OH), 3200 m (NH), 1630 m, 1610 m, 1595 m (OH and/or NH), 1100 s (CO), 820 vs (PF) $cm^{-1}$.

So far, attempts to isolate crystalline 1 : 1-adducts of *(1)* with DB18C6, DB24C8, and DB36C12 have not been successful.

Received: July 21, 1981 [Z 941 IE]
German version: Angew. Chem. *93*, 1093 (1981)

---

[1] *A. Werner*, Neuere Anschauungen auf dem Gebiete der anorganischen Chemie, 3rd Edition, Vieweg Braunschweig, 1913.

[2] *J. Bjerrum*, Adv. Chem. Ser. *62*, 178 (1967).

[3] *J. Chatt, L. A. Duncanson, L. M. Venanzi*, J. Chem. Soc. *1956*, 2713; *S. F. Mason, B. J. Norman*, Chem. Commun. *1965*, 335; *J. Chatt, G. J. Leigh, N. Thankarajan*, J. Chem. Soc. *A 1971*, 3168; *W. A. Freeman*, Inorg. Chem. *15*, 2235 (1976).

[4] a) *C. J. Pedersen*, J. Am. Chem. Soc. *89*, 7017 (1967); b) *D. J. Cram, J. M. Cram*, Acc. Chem. Res. *11*, 8 (1978); c) *J. F. Stoddart*, Chem. Soc. Rev. *8*, 85 (1979).

[5] *H. M. Colquhoun, J. F. Stoddart*, J. Chem. Soc. Chem. Commun. *1981*, 612.

[6] *H. M. Colquhoun, J. F. Stoddart, D. J. Williams*, J. Chem. Soc. Chem. Commun. *1981*, 847.

[7] [18]Crown-6, dibenzo-[18]crown-6, and dibenzo-[24]crown-8 were purchased from Aldrich. Dibenzo-[30]crown-10 and dibenzo-[36]crown-12 were synthesized in the following stepwise manner from the monobenzyl ether [*J. Druey*, Bull. Soc. Chim. Fr. *1935*, 1737] of 1,2-dihydroxybenzene: 1) condensation (NaH, tetrahydrofuran (THF), reflux) of this protected phenol in turn with the bistosylates derived from tetraethylene- and pentaethylene-glycols afforded, respectively, 1,11-bis(*o*-benzyloxyphenoxy)-3,6,9-trioxaundecane (75%, oil) and 1,14-bis-(*o*-benzyloxyphenoxy)-3,6,9,12-tetraoxatetradecane (74%, m.p. = 49–51 °C). 2) Hydrogenolysis ($H_2$, Pd/C, MeOH—$CH_2Cl_2$) of these dibenzyl ethers gave the corresponding non-crystalline diphenols in quantitative yields. 3) Condensations (NaH, THF, 45–55 °C) of these two diphenols with tetraethyleneglycol and pentaethyleneglycol bistosylates, respectively, led to dibenzo[30]crown-10 (25%, m.p. = 104–106 °C, lit. 106–107.5 °C, *C. J. Pedersen*, J. Am. Chem. Soc. *89*, 7017 (1967)), and dibenzo-[36]crown-12 (28%, M.p. = 73.5–74 °C).

[8] Prepared by addition of $NH_4^+PF_6^-$ to an aqueous solution of the dichloride (*G. T. Morgan, F. H. Burstall*, J. Chem. Soc. *1934*, 965).

[9] $CHCl_3$ solutions of complexes formed between 2,2′-binaphthyl-[20]crown-6 and arenediazonium ions are yellow to red (*G. W. Gokel, D. J. Cram*, J. Chem. Soc. Chem. Commun. *1973*, 481; *E. P. Kyba, R. C. Helgeson, K. Madan, G. W. Gokel, T. L. Tarnowski, S. S. Moore, D. J. Cram*, J. Am. Chem. Soc. *99*, 2564 (1977)); this is characteristic of CT-interactions between a π-acceptor (*e.g.* a *p*-nitrophenyl group) and a π-donor (*e.g.* a naphthalene ring).

[10] In fact, the magnitudes of the relevant torsion angles shown in Figure 2 reveal that an optimum p-π interaction is possible between one of the lone pairs on each of the "phenolic" O atoms and the π-systems of the benzene rings.

[11] The water molecule does form weak hydrogen bonds to the two $PF_6^-$ ions.

[12] *W. R. McWhinnie, J. D. Miller*, Adv. Inorg. Nucl. Chem. *12*, 162 (1969).

---

# Does a Molecule have the Same Conformation in the Crystalline State and in Solution? Comparison of NMR Results for the Solid State and Solution with those of the X-ray Structural Determination

By *Horst Kessler, Gottfried Zimmermann, Hans Förster, Jürgen Engel, Gerhard Oepen,* and *William S. Sheldrick*[*]

The exact conformation of compounds in the crystalline state may be relatively easily determined by means of X-ray structural analysis. Does this conformation also exist in solution or do the interactions of the molecule with its surroundings—lattice forces[1], on the one hand, and solvation on the other—lead to structural changes? Since it has recently become possible to obtain high resolution NMR spectra from solids as well, it is now feasible to compare structures in the crystal and in solution using *one* method alone.

We wish to report here two examples in which the most stable conformation in solution is not that which exists in the crystal structure, namely the *Z,E*-isomerism at a partial CN double bond and at a CC double bond. The second case is a configuration isomerism, which, however, displays a smooth transition to a conformation isomerism[2]. In the first example, two conformations exist in the crystal (as demonstrated by X-ray structural analysis and solid state NMR spectroscopy), whereas in solution only an average conformation is observed, which, however, equili-

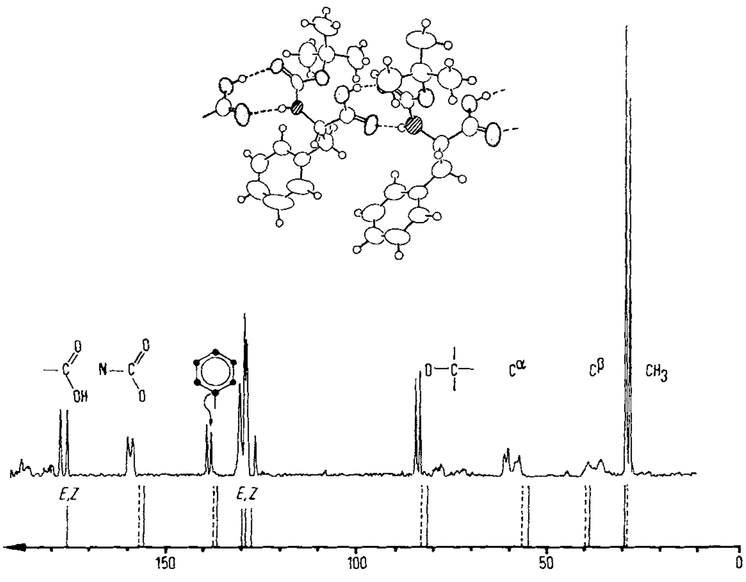


Fig. 1. Crystal structure and 75.46 MHz $^{13}C$-CP-MAS-NMR spectrum (δ-values, CP-MAS stands for "Cross Polarization-Magic Angle Spinning") of crystalline *(1)* [4]. $^{13}C$-signals for a $CDCl_3$ solution are given in the line spectrum below: solid lines: (*E*)-conformer; broken lines: (*Z*)-conformer.

---

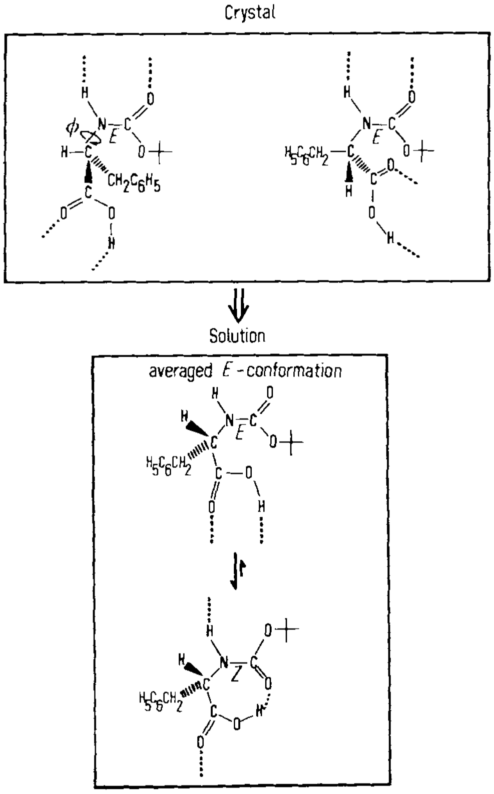
[*] Prof. Dr. H. Kessler, Dr. G. Zimmermann
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt 50 (Germany)
Dr. H. Förster
Bruker Analytische Meßtechnik GmbH
Silberstreifen, D-7512 Rheinstetten (Germany)
Dr. J. Engel, Dr. G. Oepen
Chemiewerk Homburg
Daimlerstrasse 25, D-6000 Frankfurt 1 (Germany)
Dr. W. S. Sheldrick
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

brates to another structure. In the second example, one crystal conformation is converted upon dissolving into several primary conformations, which are then transformed to a further stable solution conformation.

We were previously able to show that Boc-Phe-OH (*tert*-butoxycarbonyl phenylalanine) *(1)* exists as a rotamer with an *E*-configurated urethane bond in the crystal, which, however, contains two conformers in the unit cell, whose significant difference lies in the torsion angle $\phi$ (NH—C$^\alpha$H)[3].

The solid state $^{13}$C-NMR spectrum (Fig. 1) clearly shows a doubling of all signals in the ratio 1 : 1. If the crystals are dissolved at $\leqslant -50\,^\circ$C in $CD_2Cl_2$ and the NMR spectrum immediately recorded, only a single set of signals of the *E*-conformer is identified. The *E*-conformer is almost completely transformed within a few hours at $-50\,^\circ$C into the Z-conformer, which is more stable in solution (Scheme 1). The interpretation of the $^{13}$C chemical shifts of the crystalline compound is difficult. Nevertheless, it may be clearly recognized that the signals of C$^\alpha$ and those of the quaternary C atoms of the *tert*-butyl group and the urethane carbonyl group are shifted to low field, because the urethane group participates in two intermolecular hydrogen bonds. The associated reduction in the electron density of the urethane group is also observed for the *Z*-conformer in solution (formation of an intra- and an intermolecular hydrogen bond)[3,5]. As a result, the chemical shifts of the *Z*-conformer in solution are more similar to those of the *E*-conformer in the crystal, rather than those of the non-associated *E*-conformer in solution.



Scheme 1. Conformations of *tert*-butoxycarbonylphenylalanine *(1)* in the crystal and in solution.

On the basis of an X-ray structural analysis, the vinylogous amide $H_{11}C_6COCH{=}CHNHCH_3$ *(2)*[6] has an *E*-configuration at the CC double bond and a *Z*-configuration at the partial CO—C= and =C—N double bonds. The molecules of *(2)* form relatively weak NH...O hydrogen bonds of length 2.90 Å in the crystal lattice. The solid state $^{13}$C-NMR spectrum (Fig. 2) shows only a single set of signals. If the solid is dissolved in $CD_2Cl_2$ at low temperature ($\leqslant -80\,^\circ$C), the NMR spectra indicate the presence of two conformers (*ca.* 4 : 1); on the basis of the olefinic coupling constants of the protons, both have the *E*-configuration at the double bond ($^3J_{HH} = 13.3$ Hz). At higher temperatures

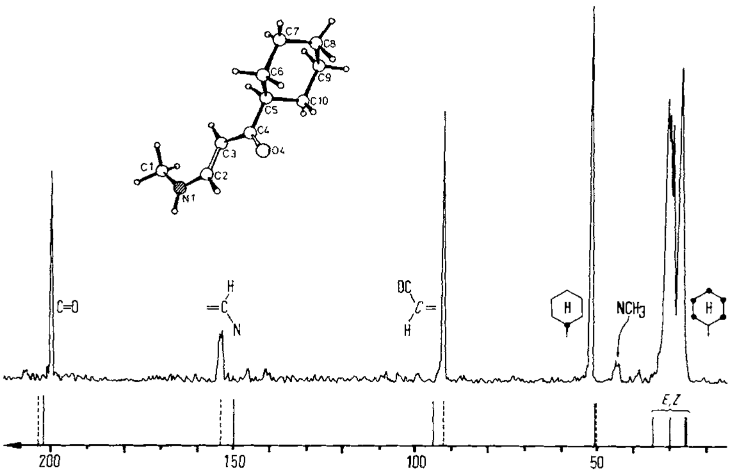
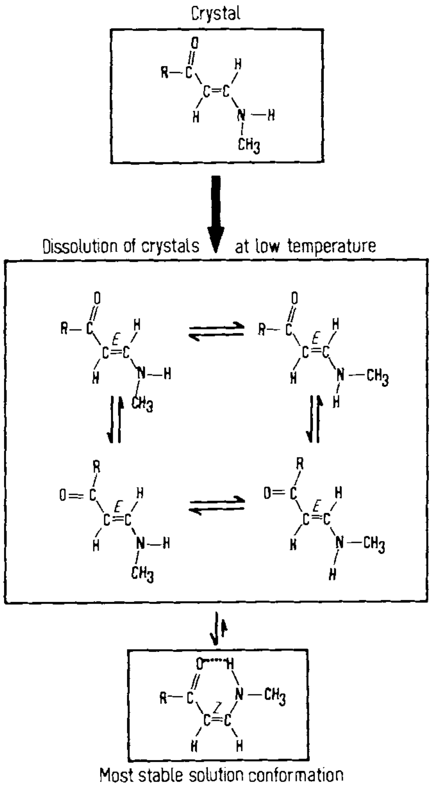


Fig. 2. Crystal structure and 75.46 MHz $^{13}$C-CP-MAS-NMR spectrum (δ-values) of crystalline *(2)* [4]. $^{13}$C-signals for a $CD_2Cl_2$ solution are given in the line spectrum below: solid lines: *E*-conformer; broken lines: *Z*-conformer.



Scheme 2. Conformations of 1-methylamino-1-nonen-3-one *(2)* ($R = C_6H_{11}$) in the crystal and in solution.

the line-shape changes allow the detection of two different dynamic processes, which may be assigned to inhibited rotations about the partial CC and CN double bonds of the *E*-isomers (Scheme 2).

Above *ca.* 0 °C conversion into the isomer with *Z*-configurated CC double bond, which contains an intramolecular hydrogen bond ($\delta_{NH}=9.7$ in $CD_2Cl_2$ at 0 °C), is observed within a few minutes; in comparison, $\delta_{NH}=4.9$ ppm for the *E*-isomer. Once again the chemical shifts for the *Z*-isomer in solution are similar to those of the *E*-isomer in the crystal. As was discussed for *(1)*, changes in the chemical shifts are essentially due to hydrogen bonding. After allowing the solution to stand at room temperature for several days the equilibrium lies at 7% *E*- and 93% *Z*-isomer. A vinylogous amide, in which the *N*-methyl group in *(2)* is replaced by an *N*-phenyl group, behaves in a completely analogous manner.

*(1)* and *(2)* represent clear examples in which the crystal structure is not consistent with the most stable conformation in solution. It could be argued that this state of affairs is only observed when intra- and/or intermolecular hydrogen bonds compete with one another. An example contrary to this assumption, which we have studied, is *cyclo*-($Pro_2$-Bzl-Gly), whose crown conformation in the crystal[7] equilibrates to 90% to a new boat conformation when dissolved in $CD_2Cl_2$[8]. The NMR spectroscopic demonstration of this inconsistency is only possible when the conversion of the crystal conformation into a different solution conformation is slow on the NMR time scale. Conformational differences between crystal and solution will more readily ensue the more polar a molecule is and the greater its tendency to form hydrogen bonds, by means of which interactions with the surroundings (crystal effects, solvation, association) may become stronger than intramolecular forces.

It therefore follows that conclusions on the conformations of polar molecules in solution, which are based on either molecular structure calculations ("isolated" molecules) or on X-ray structural analyses (molecule in a "rigid" crystal lattice), must be drawn with reservation.

Received: July 9, [Z 940 IE]
revised: October 6, 1981
German version: Angew. Chem. *93*, 1085 (1981)

CAS Registry Numbers:
*(1)*, 13734-34-4; *E-(2)*, 79898-80-9; *Z-(2)*, 79898-81-0.

---

[1] *P. Dauber, A. T. Hagler*, Acc. Chem. Res. *13*, 105 (1980).

[2] *H. O. Kalinowski, H. Kessler*, Top. Stereochem. *7*, 295 (1973).

[3] *J. W. Bats, H. Fuess, H. Kessler, R. Schuck*, Chem. Ber. *113*, 520 (1980).

[4] Decoupling field strength 18 G. The rotational side bands are suppressed; the resolution is mathematically enhanced. The unsymmetrical signal splitting of the C atom bonded to nitrogen is due to an interaction with the quadrupolar $^{14}N$ nucleus.

[5] *M. Branik, H. Kessler*, Chem. Ber. *108*, 2176 (1975).

[6] Vinylogous amides in solution have been intensively studied by NMR spectroscopy, *e.g. J. Dabrowski, K. Kamienska-Trela, C. Kozerski*, Org. Magn. Reson. *6*, 499 (1974); *H. Möhrle, H. W. Reinhardt*, Arch. Pharm. *314*, 767 (1981), and references cited therein.

[7] *H. Fuess*, unpublished results.

[8] *H. Kessler, P. Krämer, G. Krack*, Isr. J. Chem. *20*, 188 (1980).

---

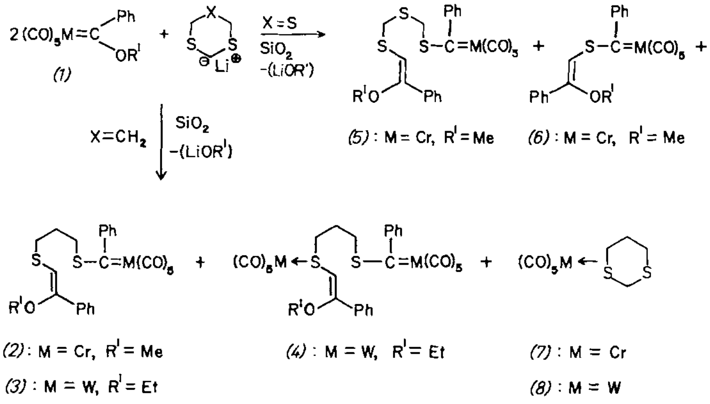
## Ring-Opening Reactions of 2-Lithio-1,3-dithiane and 2-Lithio-1,3,5-trithiane with Carbene Complexes of Chromium and Tungsten

By *Helgard G. Raubenheimer, Ernst Otto Fischer, Ulrich Schubert, Carl Krüger,* and *Yi-Hung Tsay*[*]

Reactions of lithiothioacetals with hexacarbonyl complexes of chromium and tungsten, involving CO insertion and affording heterometallocyclic carbenethioether chelates, are well established[1]. Alkoxycarbene(pentacarbonyl) complexes of the same metals are also highly susceptible to nucleophilic attack[2] and the carbene carbon atom has been shown to react, among others, with organolithium compounds[3] and phosphanes[4]. No reaction with diorgano sulphides is known. We have found that alkoxycarbene complexes such as *(1)* react with 2-lithio-1,3-dithiane or -1,3,5-trithiane and that carbene carbon atoms add to the negatively charged carbon atom and a neutral sulphur atom of the heterocycle. Subsequent removal of one alkoxy group leads to novel molecular rearrangements which involve two types of ring-opening in the parent sulphur-containing compounds.

The metalated thioacetals, $LiCH(SR)_2$ (R = Me, Ph), reacted with the complexes *(1)* (M = Cr, W) at −60 °C in ether to yield either extremely thermolabile dark yellow oils, or (with M = Cr, R = Ph) light yellow precipitates. All these compounds were insoluble in tetrahydrofuran (THF) and turned red again above −20 °C due to the re-formation of the complex *(1)*. The presumed formation of 1 : 1-adducts was substantiated for solid products by elemental analysis. These results indicated the possibile formation of sulphur ylide complexes in the reaction of carbene complexes with lithiothioacetals in which the Lewis basicity of the sulphur atoms is increased due to the negative charge on the adjacent carbon atom.

Reaction of the carbene complexes *(1)* with 2-lithio-1,3-dithiane or 2-lithio-1,3,5-trithiane in ether/THF at −60 °C produced salt-like compounds, which upon treatment with $SiO_2$[3b] afforded the thiocarbene compounds *(2)*—*(4)*, and *(5)* and *(6)*, respectively (Scheme 1).



Scheme 1.

---

[*] Prof. Dr. H. G. Raubenheimer [+], Prof. Dr. E. O. Fischer,
Priv.-Doz. Dr. U. Schubert
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)
Priv.-Doz. Dr. C. Krüger, Dr. Y.-H. Tsay
Max-Planck-Institut für Kohlenforschung
Lembkestr. 5, D-4330 Mülheim-Ruhr (Germany)

[+] Author to whom correspondence should be addressed and who greatfully acknowledges financial support by the Alexander von Humboldt Stiftung. Present address: Department of Chemistry, Rand Afrikaans University, P.O. Box 524, Johannesburg 2000 (South Africa).

The chromium analogue of *(4)* was detected, but not isolated in pure form, since it always contained small quantities of *(2)*. The sulphide complexes *(7)* and *(8)* had been described before[1]. The new phenyl(thiocarbene) complexes *(2)*—*(6)* were characterized by elemental analyses and spectroscopic measurements (Table 1); the molecular structures of *(5)* and *(6)* were defined by single crystal X-ray diffraction studies[5] (Fig. 1 and 2). Bond lengths and angles in corresponding parts of the molecules are the same in both complexes, as is also the arrangement of the substituents at the carbon-carbon double bond. With $(CO)_5CrC(Me)SPh$[6] there is good correspondence concerning the bonding parameters of the carbene carbon atom.

Table 1. Some physical data of the new thiocarbene complexes *(2)*—*(6)* [a].

| | Yield [%] | M.p. [°C] | IR ($\tilde{\nu}_{CO}$) [cm$^{-1}$], hexane | $^{13}$C-NMR [b] |
|---|---|---|---|---|
| *(2)* | 22 | oil | 2064 w, 1966 s, 1952 w | 362.0 |
| *(3)* | 28 | oil | 2066 w, 1955 s, 1948 w | 327.0 |
| *(4)* | 11 | oil | 2074 w, 1958 sh, 1941 s | 328.6 |
| *(5)* | 44 | 76 | 2061 w, 1965 s, 1950 sh | 345.7 |
| *(6)* | 17 | 82 | 2066 w, 1970 s, 1955 w | — |

[a] Satisfactory $^1$H-NMR spectra and elemental analyses were also obtained for all the new compounds. [b] C (carbene), $CDCl_3$, −30 °C, rel. int. TMS.

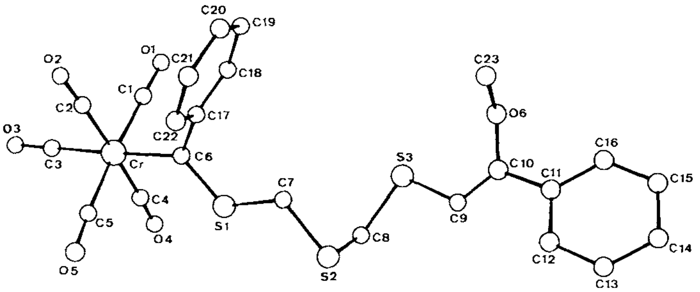


Fig. 1. Molecular structure of *(5)* in the crystal. Cr—C6 202.7(5), C6—S1 167.3(5), S1—C7 183.9(5), C7—S2 177.3(5), S2—C8 180.3(6), C8—S3 179.6(6), S3—C9 174.7(6), C9—C10 132.4(8), C10—O6 138.5(8) pm. Cr—C6—S1 120.6(3), Cr—C6—C17 123.7(3), C6—S1—C7 109.5(2), C7—S2—C8 100.1(2), C8—S3—C9 99.7(3)° [8].

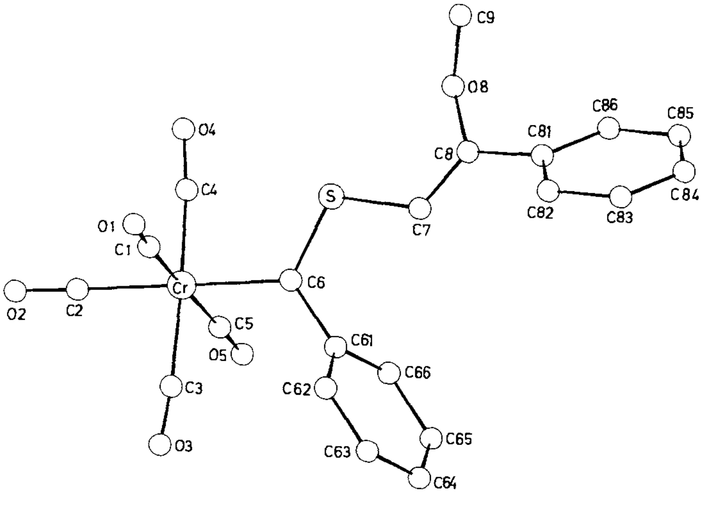
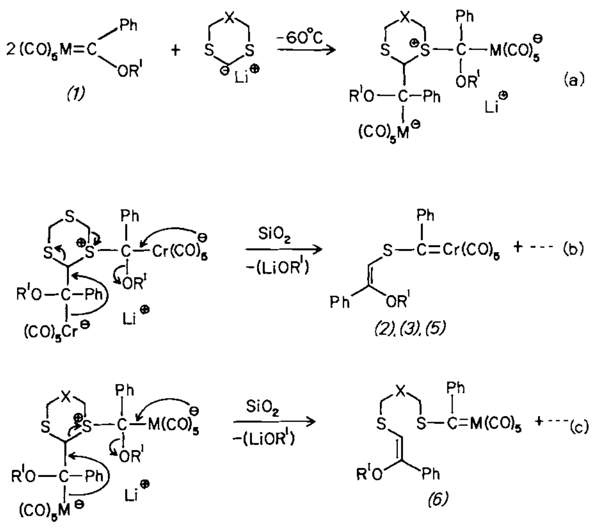


Fig. 2. Molecular structure of *(6)* in the crystal. Cr—C6 202.9(10), C6—S 167.1(10), S—C7 175.9(11), C7—C8 131(2), C8—O8 137(1) pm. Cr—C6—S 119.0(6), Cr—C6—C61 122.9(7), C6—S—C7 109.2(5)° [8].

The first step in the synthesis probably involves the formation of a 2:1-adduct which contains both a metal ylide carbon atom and a metal alkyl carbon atom (Scheme 2a). The formation of the main products can then be explained in terms of the rearrangements given in Schemes 2b and 2c. The latter is the most important route to trithianes, whereas β-elimination is the dominant mode of decomposition for the dithiane derivatives. In the case of dithiane it was found that the $(CO)_5M$-moieties then react with the uncoordinated sulphur atom of the product to form the complex *(4)*; the metal-sulphur bond in *(4)* is very labile.



Scheme 2.

The formation of all the new carbene complexes, which provide examples of the involvement of two metal centers in unusual ring-opening reactions, is also especially interesting in view of the current interest in thiovinyl derivatives[7]. In each case, the olefinic phenyl group is situated *trans* to the sulphur atom.

Received: June 2, 1981 [Z 942 IE]
German version: Angew. Chem. 93, 1103 (1981)

---

[1] *H. G. Raubenheimer, S. Lotz, H. W. Viljoen, A. A. Chalmers*, J. Organomet. Chem. *152*, 73 (1978).

[2] a) *E. O. Fischer, U. Schubert, H. Fischer*, Pure Appl. Chem. *50*, 857 (1978); b) *T. F. Block, R. F. Fenske, C. P. Casey*, J. Am. Chem. Soc. *98*, 441 (1976).

[3] a) *C. P. Casey, T. J. Burkhardt*, J. Am. Chem. Soc. *95*, 5833 (1973); b) *E. O. Fischer, W. Held, F. R. Kreissl*, Chem. Ber. *110*, 3842 (1977).

[4] *F. R. Kreissl, C. G. Kreiter, E. O. Fischer*, Angew. Chem. *84*, 679 (1972); Angew. Chem. Int. Ed. Engl. *11*, 643 (1972).

[5] *(5)*: $C_{23}H_{18}O_6S_3Cr$, space group $P\bar{1}$, $a = 666.8(1)$, $b = 1111.4(2)$, $c = 1848.3(2)$ pm, $\alpha = 103.48(1)$, $\beta = 95.96$, $\gamma = 96.60°$, $Z = 2$, $\rho(\text{calc.}) = 1.364$ g/cm$^3$. 4807 independent reflections; $R = 0.046$, $R_w = 0.059$ for 2915 reflections $I > 2\sigma(I)$. *(6)*: $C_{21}H_{14}O_6SCr$, space group $P2_1/c$, $a = 633.2(3)$, $b = 1615.6(9)$, $c = 2086.4(12)$, $\beta = 103.05°$ (−20 °C), $\rho(\text{calc}) = 1.426$ g/cm$^3$. 3660 independent reflections; $Z = 4$, $R = 0.087$, $R_w = 0.073$ for 1700 reflections $F_0 \gtrsim 3.9\sigma(F_0)$ [8].

[6] *R. J. Hoare, O. S. Mills*, J. Chem. Soc. Dalton *1972*, 653.

[7] a) *J. J. Fitt, H. W. Gschwend*, J. Organomet. Chem. *44*, 303 (1979); b) *F. Cooke, R. Moerck, J. Schwindeman, P. Magnus*, J. Org. Chem. *45*, 1046 (1980) and references cited therein; c) cf. *B.-T. Gröbel, D. Seebach*, Synthesis *1977*, 357.

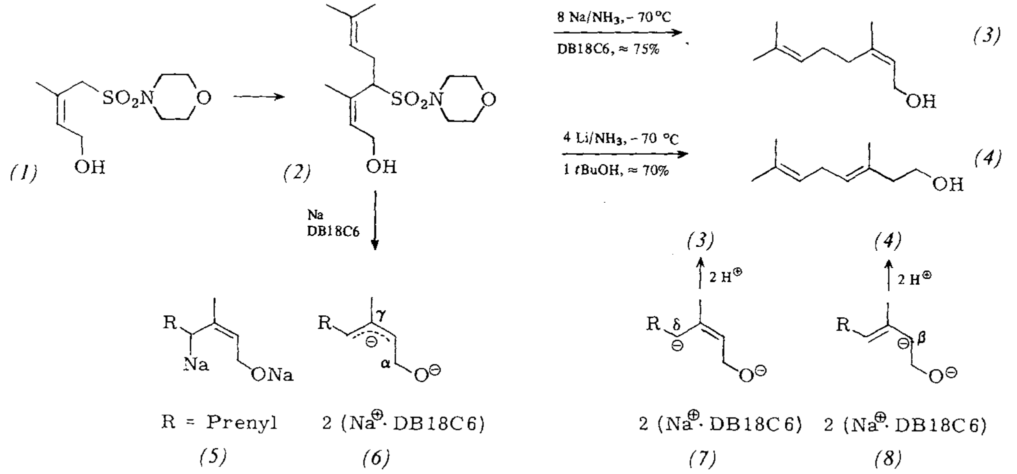
[8] Further details of the crystal structure investigations can be obtained from the Fachinformationszentrum Energie Physik Mathematik, D-7514 Eggenstein-Leopoldshafen by quoting the depository number CSD 50046, the authors and literature references.

# Crown Ether-Assisted Change of Regioselectivity in the Reductive Cleavage of Allylsulfonamides

By *Alexander M. Moiseenkov, Evgeni V. Polunin,* and *Alexei V. Semenovsky*[*]

The widely used two-step carbon chain elongation reaction in isoprenoids *via* alkylation of a sulfur-stabilized allyl anion has the main disadvantage that both during the alkylation[1] as well as during the subsequent reductive desulfurization[2,3] procedures formation of double bond isomers is possible. Although the regioselectivity of such alkylations (α *vs.* γ) has been frequently studied, little attention has been directed toward improving this step at the desulfurization stage.

We discuss here one of the possible approaches towards solving this problem, exemplified by the reductive desulfonylation of nerylsulfonamide *(2)*. The latter was found to be the only (α)-prenylation product derived from the hydroxysulfonamide *(1)* (as its dilithium salt) which we have recently proposed for the $C_5$-homologation of isoprenoids[4].



Reduction of *(2)* under a variety of conditions such as with amalgams, electrochemically, or with dissolving metals in amines, results in a mixture of nerol *(3)*, isogeraniol *(4)*[3,4], and $C_{10}$-hydrocarbons, the whole process being highly selective with respect to isogeraniol *(4)*. Hence, with Li in $NH_3$ in the presence of *t*BuOH (molar ratio 1 : 4 : 1) at −70 °C, the regioisomers *(3)* and *(4)* are formed in the ratio 7 : 93 in 70% yield. Reaction with Na in $NH_3$ at −70 °C under these conditions gives *(3)* : *(4)* ≈ 15 : 85. In order to avoid the unwanted hydrogenolysis process the known mode of conversion of the alcohol into its alcoholate[3,5] (with *n*BuLi in the molar ratio 1 : 2 in tetrahydrofuran (THF) at 0 °C) was tried. In this case, however, although the yield of the alcohols did not enhance markedly, the relative portion of isogeraniol *(4)* was found to be substantially diminished in favor of nerol *(3)*. Thus, reduction of the alcoholate of *(2)* with Li in $NH_3$ at −70 °C gave *(3)* and *(4)* in the ratio 30 : 70. Pretreatment of *(2)* with NaH (1 : 1) and subsequent reaction with Na in $NH_3$ at −70 °C led to a similar result.

In the second case, the observed effect can be explained by increased polarization of the O—Na bond in the probable key disodium intermediate *(5)* (or in the corresponding intimate ion pairs). It was, therefore, reasonable to expect that the yield of nerol *(3)* would increase due to the additional ionization of the polarized C—Na and O—Na σ-bonds in such an intermediate (or in the corresponding intimate ion pairs). This could arise by introducing into the reaction sphere a macrocyclic polyether capable of complexing $Na^\oplus$ ions[6]. As expected, reduction of *(2)* with Na in $NH_3$ at −70 °C in the presence of dibenzo-[18]crown-6 (DB18C6) (molar ratio 1 : 8 : 0.1) gives, with a reproducible yield of ~75%, nerol *(3)* containing no more than 4% of isogeraniol *(4)*.

The above result may be interpreted in terms of preferential δ-protonation of the free ion pairs *(6)* specifically solvated by participation of the polyether. Of the two mesomeric forms *(7)* and *(8)*, *(7)* is favored due to the better separation of the negative charge[7].

Thus, the crown ether-assisted regiospecific reductive desulfonylation opens up the possibility of employing the hydroxysulfonamide *(1)* as an effective cisoid isoprenoid synthon for the stereospecific construction of polyprenols. Using this procedure, we have recently successfully synthesized (2*Z*, 6*Z*, 10*Z*, 14*E*, 18*E*)-farnesylfarnesol.

## *Experimental*

To a solution of Na (370 mg, 16 mmol) in $NH_3$ (50 mL) containing DB18C7 (72 mg, 0.2 mmol) at −70 °C under Ar was added a solution of *(2)* (605 mg, 2 mmol) in THF over 5 min with constant stirring. After an additional 2 min, the excess Na was decomposed with $NH_4Cl$, $NH_3$ evaporated off, and the residue treated with water and extracted with hexane. The usual work-up gave 290 mg of product which was chromatographed on silica gel (30 g). Gradient elution, hexane→ether (up to 50 vol.% of ether) yielded 230 mg (75%) *(3)*, b.p. = 105 °C/10 torr, contaminated with 2—4% *(4)*.

Received: May 5, 1980 [Z 921 IE]
German version: Angew. Chem. *93*, 1122 (1981)

CAS Registry numbers:
*(2)*, 74323-42-5; *(3)*, 106-25-2; *(4)*, 16750-94-0; DB18C6, 14187-32-7.

---

[*] Prof. Dr. A. V. Semenovsky (deceased), Dr. A. M. Moiseenkov [+],
Dipl.-Chem. E. V. Polunin
N. D. Zelinsky Institute of Organic Chemistry,
USSR Academy of Sciences
Leninsky Prosp. 47, Moscow 117913 (USSR)

[+] Author to whom correspondence should be addressed.

[1] *J. F. Biellmann, J. B. Ducep,* Tetrahedron *27*, 5861 (1971); *P. M. Atlani, J. F. Biellmann, S. Dube, J. J. Vicens,* Tetrahedron Lett. *1974*, 2665; *J. Hartmann, R. Muthukrishnan, M. Schlosser,* Helv. Chim. Acta *57*, 2261 (1974); *T. Nakai, H. Shiono, M. Okawara,* Tetrahedron Lett. *1975*, 4027.

[2] *J. E. Baldwin, R. E. Hackler, D. P. Kelly,* J. Am. Chem. Soc. *90*, 4758 (1968); *E. E. van Tamelen, R. A. Holton, R. E. Hopla, W. E. Konz, ibid.*

94, 8228 (1972); *K. Narasaka, M. Hayashi, T. Mukajyama,* Chem. Lett. *1972,* 259; *P. A. Grieco, Y. Masaki,* J. Org. Chem. *39,* 2135 (1974); *M. Kodama, Y. Matsuki, S. Ito,* Tetrahedron Lett. *1975,* 3065; *1976,* 1121; *D. Savoia, C. Trombini, A. Umani-Ronchi,* J. Chem. Soc. Perkin Trans. I *1977,* 123; *M. Kodama, S. Yokoo, H. Yamada, S. Ito,* Tetrahedron Lett. *1978,* 3121.

[3] *M. Julia, D. Uguen, A. Callipolitis,* Bull. Soc. Chim. Fr. *1976,* 519.

[4] *A. M. Moiseenkov, E. V. Polunin, A. V. Semenovsky,* Tetrahedron Lett. *1979,* 4759.

[5] *K. Mori, M. Ohki, M. Matsui,* Tetrahedron *30,* 715 (1974); *T. Kato, H. Takayanagi, T. Uyehara, Y. Kitahara,* Chem. Lett. *1977,* 1009.

[6] *N. S. Poonia, A. V. Bajaj,* Chem. Rev. *79,* 389 (1979).

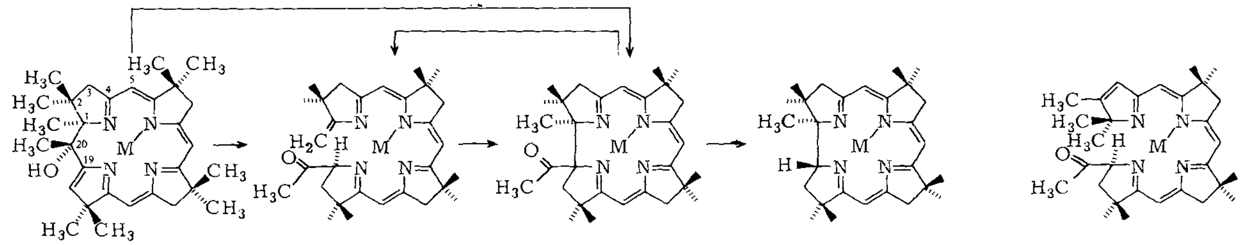
[7] *G. L. Olson, H.-C. Cheung, K. D. Morgan, C. Neukom, G. Saucy,* J. Org. Chem. *41,* 3287 (1976).

[8] *A. M. Moiseenkov, E. V. Polunin, A. V. Semenovsky,* Tetrahedron Lett. *1981,* 3309.

# The Dihydrocorphinol→Corrin Ring Contraction: A Potentially Biomimetic Mode of Formation of the Corrin Structure[**]

By *Vittorio Rasetti, Kurt Hilpert, Alexander Fässler, Andreas Pfaltz,* and *Albert Eschenmoser*[*]

Recently we reported[1] the synthesis of the octahydroporphinoid (dihydrocorphinoid) metal complexes *(1a)* and *(1b)*, their thermal rearrangements to the 19-acetylcorrin complexes *(3a)* and *(3b)*, respectively ("dihydrocorphinol[2] → corrin ring contraction"), and the deacylation of *(3a)* by hydroxide ions to give the nickel(II) nonamethylcorrinate *(4a)*. These transformations point to a possible mechanism for the formation of the characteristic corrinoid (A—D) ring connection in vitamin $B_{12}$ biosynthesis. The corphinoid structure *(1)* of the starting material for the ring contraction was inspired by the structure of "Factor III"[3]; the latter is the most advanced intermediate in corrin biosynthesis to be isolated to date. The ring contraction *(1)→(3)* is closely related, both structurally and mechanistically, to our 1-methylidene-1,19-secocorrin→corrin cycloisomerization[4], especially to the non-photochemical (A→D)-cyclization of a 1-methylidene-19-formyl-1,19-secocorrin reported in 1977[4c, 5]. The earlier conditions necessary for the conversions *(1a, b)→(3a, b)* (melting at 295° and 260°, respectively) were unsatisfactory with regard to the intended role of the reaction as a potentially[6] biomimetic model. We now describe further properties and variants of the reaction, among which are conditions that permit the ring contraction to proceed even at room temperature.



*(1a)*, M = $Ni^+(ClO_4^-)$
*(1b)*, M = $Co(CN)_2$
*(1c)*, M = $Zn^+(ClO_4^-)$
*(1d)*, M = $H(H^+/CF_3COO^-)$

*(2a)*, M = $Ni^+(ClO_4^-)$
*(2c)*, M = $Zn^+(ClO_4^-)$

*(3a)*, M = $Ni^+(ClO_4^-)$
*(3b)*, M = $Co(CN)_2$
*(3c)*, M = $ZnCl$
*(3d)*, M = $H(H^+/ClO_4^-)$

*(4a)*, M = $Ni^+(ClO_4^-)$

*(5a)*, M = $Ni^+(ClO_4^-)$

Scheme 1. Summary of the reaction conditions (RT = room temperature). All compounds were isolated crystalline and characterized spectroscopially (UV/VIS, IR, $^1H$- and $^{13}C$-NMR, MS). For experimental details: *K. Hilpert,* Dissertation, ETH Zürich (in preparation).

| Reactions | Reaction conditions and yields |
|---|---|
| *(1a)→(3a)* | cf. [1] |
| *(1b)→(3b)* | cf. [1] |
| *(3a)→(4a)* | cf. [1] |
| *(1c)→(2c)* | evacuated tube, in the dark, 220 °C (70 s), yield 33%, apart from 28% educt and 13% *(5a)*, isolated as Ni complex; or: visible hν (150 Watt) in $CH_2Cl_2 + CF_3COOH$ ($7 \cdot 10^{-4}$ M), 40 °C, yield 50% |
| *(2c)→(2a)* | $CF_3COOH$, $Ni(OAc)_2 \cdot 4H_2O$ in $CH_3CN$, RT, yield 88% |
| *(2a)→(3a)* | $CH_3COOH/(C_2H_5)_3N$ (4 : 1) in toluene, 100 °C, 2 h, evacuated tube, yield 90% [a] |
| *(2c)→(3c)* | hν visible (150 Watt) in benzene/$CH_2Cl_2$ (6 : 1) (degassed), 25 °C, yield 75% [b] |
| *(3c)→(3d)* [c] | $CF_3COOH/CH_3CN$ (1 : 100), 0 °C, 30 min, argon, in the dark, 62% *(3d)* + 20% educt |
| *(3c)→(2a)* | a) $CF_3COOH/CH_3CN$ (1 : 10), RT, 16 h in the dark; b) $Ni(OAc)_2 \cdot 4H_2O/NaOAc$, RT, 3 h, yield 81% |

[a] In the 19-formyl model series [4c], the analogous ring closure occurs within hours at room temperature (cf. *A. Pfaltz,* Dissertation ETH No. 6184, Juris-Verlag Zürich 1978, p. 167). [b] *(3c)* was isolated crystalline as the chlorozinc(II) complex (m. p. = 230 °C). [c] 19-Acetyl-1,2,2,7,7,12,12,17,17-nonamethylcorrinium perchlorate, orange crystals, M. p. = 139 °C. — UV/VIS ($C_2H_5OH$): $\lambda_{max} = 263$ ($\log\varepsilon = 4.47$), 292 sh (4.22), 307 sh (4.41), 321 (4.53), 371 (3.72), 392 sh (3.56), 458 sh (3.76), 488 sh (4.06), 512 (4.10) nm. — $^1H$-NMR ($CDCl_3$/300 MHz): 9 $CH_3$ singlets between $\delta = 1.02$ and 1.46, 1.99 ($CH_3CO$), 1.88/2.65 (AB/$J = 14$/2 H-18), 2.92/3.11 (AB/$J = 19$/2 H-3), 2.89/2.91 (ABX/$J_{AB} = 19$; $J_{BX} = 1.8$/2 H-13), 2.83/2.87 (AB/$J = 19$/2 H-8), 5.43 (t/$J = 1.8$/H-15), 5.63/5.64 (2 s/H-5 and H-10), 11.86/13.17 (2 s br., 2 NH) ($J$ in Hz). — $^{13}C$-NMR ($CDCl_3$, 75 MHz): $\delta = 19.5-29.2$ (8 q/10 $CH_3$), 42.6—52.0 (4 t/4 $CH_2$), 43.2—52.2 (4 s/C-2,7,12,17), 78.8 (s/C-1), 91.1 (s/C-19), 91.4—93.3 (3 d/3 CH), 155.8—193.5 (6 s/6 $>$C=N), 210.8 (s/$>$C=O).

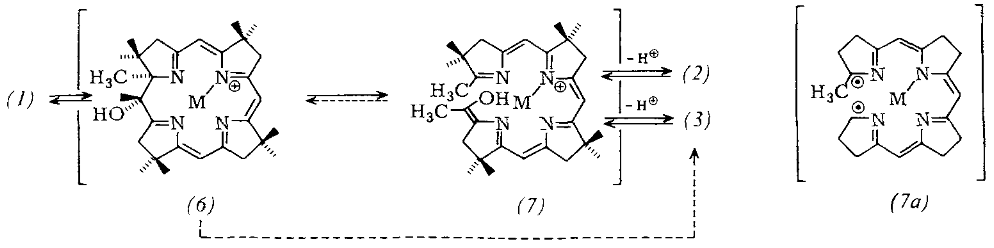
Melting the *metal-free* ligand *(1d)* (as the crystalline trifluoroacetate, m. p. = 194 °C) for one minute in an evacuated tube at 215 °C did not lead to ring-contraction. Instead, ring-opening occurred (evidently followed by skeletal rearrangement) to give the ligand system of *(5a)*, which was isolated as the crystalline nickel(II) complex. The same occurred with *(1d)* in pure trifluoroacetic acid (TFA) at 80 °C in 1 h (though the reaction was not observed even

---

[*] Prof. Dr. A. Eschenmoser, Dr. V. Rasetti,
dipl. Ing. Chem. ETH K. Hilpert, dipl. Naturwiss. ETH A. Fässler,
Dr. A. Pfaltz
Laboratorium für Organische Chemie
Eidgenössische Technische Hochschule, ETH-Zentrum
Universitätstrasse 16, CH-8092 Zürich (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung. Dr. *E. Zass* is thanked for assistance in completing the manuscript.

after days at room temperature)[7]. With the zinc(II) complex *(1c)*, careful control of the melting conditions (see Table 1) enabled the undesired skeletal rearrangement to be largely avoided in favor of formation of the zinc(II) 19-acetyl-1-methylidene-1,19-secocorrinate *(2c)*. The same dihydrocorphinol→secocorrin ring-opening occurred at room temperature upon irradiation of the zinc complex *(1c)* with visible light in dichloromethane under conditions of strict oxygen exclusion in the presence of traces of TFA. In the absence of TFA, but otherwise under the same conditions, *(1c)* was photostable; this supports the notion that protonation of the starting material to give the iminium derivative *(6)* is a prerequisite for the (electrocyclic) ring-opening step, *(1)→(2)* (cf. Scheme 2).



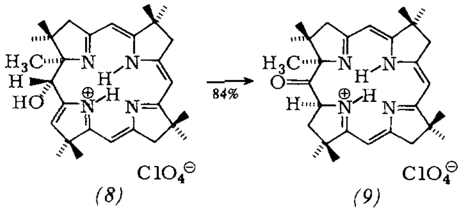
Scheme 2. Intermediates in the dihydrocorphinol → corrin ring contraction [8].

The nickel(II) 19-acetylsecocorrin complex *(2a)*, readily accessible from *(2c)* by metal exchange, cyclized in a manner closely analogous to the 1,19-secocorrin → corrin cycloisomerization in the 19-formyl model series[4c]. Cyclization of *(2a)* to the 19-acetylcorrin complex *(3a)* in acetic acid/triethylamine (4:1)/toluene was almost quantitative within 2 h at 100 °C. The reaction also occurred at room temperature, but required weeks (cf. Scheme 1).

The metal-free form of the 19-acetylcorrin *(3d)* could be obtained by photochemical (A→D) cycloisomerization of the zinc complex *(2c)*, followed by (very careful) decomplexation of the zinc(II) corrinate *(3c)* with TFA in acetonitrile at 0 °C (see Scheme 1). Decomplexation of *(3c)* at room temperature followed by recomplexation with Ni$^{II}$ led exclusively to the nickel(II) secocorrinate *(2a)*. *This is the first time we have encountered an (A→D) ring opening of a corrin to an A/D-secocorrin.* Mechanistically, this transformation can be interpreted as the acid-catalyzed reversal of the (acid/base-induced) (A→D) cyclization of 19-acyl-1-methylidene-1,19-secocorrins, and, as such, it requires an angular acyl group at C-19 (or C-1).

The results communicated here demonstrate the existence of kinetically readily accessible transitions[8] between the structural types of 1,20-dimethyl-1,20-dihydro-20-corphinol *(1)*, 19-acetyl-1-methylidene-1,19-secocorrin *(2)* and 19-acetyl-1-methylcorrin *(3)*. In this context, the secocorrin structure *(7)* assumes the role of a "transit structure" (cf. Schemes 1 and 2). At the same time, *(7)* corresponds to the primary dissociation product in the fragmentative reaction variant of the ("semibenzoin") rearrangement[1], which provides a direct link between the dihydrocorphinols *(1)* and 19-acetylcorrins *(3)*. It remains experimentally uncertain whether the ring contractions *(1a, b)→(3a, b)* described in [1] are direct rearrangements (either fragmentative or concerted) or whether they proceed *via* secocorrinoid intermediates of type *(2)*.

We find it noteworthy that the species formally derived by deprotonation of the hydroxyl group of *(7)* is of the same structural type as the (still hypothetical) intermediate *(7a)* in the photochemical A/D secocorrin → corrin cycloisomerization described in 1969[4b]. The latter was the starting point for our search for potentially biomimetic versions of the (A→D) cyclization.



Scheme 3. Model investigation in the 20-demethyl-series. The configurational assignments are tentative (see [1]). For experimental details: *A. Fässler*, Dissertation ETH Zürich (in preparation).

The tertiary nature of the hydroxyl group at C-20 or, from the biosynthetic point of view, the presence of a methyl group at this bridging carbon atom, seems to be a prerequisite of the dihydrocorphinol → corrin transformation. If this methyl group is absent from the model system, an alternative reaction occurs under mild conditions (Scheme 3). Thus, triethylammonium acetate in benzene irreversibly tautomerized the 20-demethyl derivative *(8)*[9] at room temperature to give the isomeric ketone *(9)*; under analogous conditions, *(1d)* was stable up to 90 °C. This difference in behavior between the 20-methyl- and 20-demethyl-model series should be viewed in relation to the *raison d'être* of the methylation at C-20 in the biosynthesis of vitamin B$_{12}$.

Received: September 28, 1981 [Z 946 IE]
German version: Angew. Chem. *93*, 1108 (1981)

---

[1] *V. Rasetti, A. Pfaltz, Ch. Kratky, A. Eschenmoser*, Proc. Natl. Acad. Sci. USA *78*, 16 (1981).

[2] For structure and nomenclature of the "corphin" hexahydroporphinoid ligand system cf. *A. P. Johnson, P. Wehrli, R. Fletcher*, Angew. Chem. *80*, 622 (1968); *P. M. Müller, S. Farooq, B. Hardegger, W. S. Salmond, A. Eschenmoser, ibid. 85*, 954 (1973); *12*, 914 (1973).

[3] *A. R. Battersby, G. W. J. Matcham, E. McDonald, R. Neier, M. Thompson, W. D. Woggon, V. Ya. Bykhovskii, H. R. Morris*, J. Chem. Soc. Chem. Commun. *1979*, 185; *N. G. Lewis, R. Neier, G. W. J. Matcham, E. McDonald, A. R. Battersby, ibid. 1979*, 541; *G. Müller, R. D. Gneuss, H. P. Kriemler, A. I. Scott, A. J. Irwin*, J. Am. Chem. Soc. *101*, 3655 (1979).

[4] a) *A. Eschenmoser*, Qu. Rev. Chem. Soc. *24*, 366 (1970); Naturwissenschaften *61*, 513 (1974); Chem. Soc. Rev. *5*, 377 (1976); b) *Y. Yamada, D. Miljkovic, P. Wehrli, B. Golding, P. Löliger, R. Keese, K. Müller, A. Eschenmoser*, Angew. Chem. *81*, 301 (1969); Angew. Chem. Int. Ed. Engl. *8*, 343 (1969); c) *A. Pfaltz, N. Bühler, R. Neier, K. Hirai, A. Eschenmoser*, Helv. Chim. Acta *60*, 2653 (1977).

[5] The cyclization studies in the formyl series were based on the knowledge then current, *i.e.* that C-20 of uroporphyrinogen III is eliminated in the course of the biosynthesis of cobyric acid ("obviously as a C$_1$-fragment").

[6] The reaction type responsible for the ring contraction in the biosynthesis of vitamin B$_{12}$ is still not known. For the present state of knowledge cf. *C. Nussbaumer, M. Imfeld, G. Wörner, G. Müller, D. Arigoni*, Proc. Natl. Acad. Sci. USA *78*, 9 (1981); *L. Mombelli, C. Nussbaumer, H. Weber, G. Müller, D. Arigoni, ibid. 78*, 11 (1981); *A. R. Battersby, M. J. Bushell, C. Jones, N. G. Lewis, A. Pfenninger, ibid. 78*, 13 (1981).

[7] With acetic acid/triethylamine (4:1 to 1:1.5) in nonpolar solvents at 100–125 °C, *(1d)* yielded complex mixtures from which (after complexation with $Ni^{II}$) neither *(3a)* nor *(2a)* could be isolated.

[8] The reaction arrows in Scheme 2, leading from *(6)* to *(3)* and from *(7)* to *(6)* are mechanistically plausible, but the corresponding conversions have not yet been experimentally demonstrated.

[9] Synthesized from the corresponding carbonyl compound (cf. [1]) by (diastereoselective) reduction of the chlorocadmium complex with $ZnBH_4$ in $CH_2Cl_2$ at 0 °C, and subsequent (careful) decomplexation with $CF_3COOH/CH_3CN$ (1:50) at room temperature.

## Stabilization of Diphosphorus Tetrabromide as the Bis(pentacarbonylchromium) Complex

By *Axel Hinke, Wilhelm Kuchen,* and *Jürgen Kutter*[*]

In solutions of *(1)* there exists the equilibrium

$$n\,RP(X){-}P(X)R \rightleftharpoons (RP)_n + n\,RPX_2$$

*(1)*

R = alkyl, aryl; X = Br, I

whose position at a given temperature is a function of, R, X and solvent[1]. Disproportionation of *(1)* can be prevented by coordination to metal(0) centers, *e.g.* as in complexes of type *(2)*[2,3].

$$(CO)_5CrRP(X){-}P(X)RCr(CO)_5$$ *(2)*

$R = C_6H_5$, 4-$CH_3OC_6H_4$,

Analogous disproportionations also occur with the diphosphorus tetrahalides $P_2Cl_4$ and $P_2I_4$[4,5], and presumably particularly fast, with the as yet unknown $P_2Br_4$.

We have now succeeded in stabilizing diphosphorus tetrabromide as a ligand in complex *(4)*, which we have obtained *via* three routes:

1) from the products of the reaction of $(CO)_5Cr\cdot THF$ with $PBr_3$, whereby $(CO)_5CrPBr_3$ is principally formed,
2) by the partial reduction of $(CO)_5CrPBr_3$ with magnesium,
3) from the tetraaminodiphosphane complex *(3)*[6] thus

$$(CO)_5Cr{-}(Et_2N)_2PP(NEt_2)_2{-}Cr(CO)_5 \xrightarrow[-\,Et_2NH\cdot HBr]{+\,HBr}$$

*(3)*

$$(CO)_5Cr{-}Br_2PPBr_2{-}Cr(CO)_5$$

*(4)*

*(4)* forms orange-yellow crystals that are relatively air-stable, and readily soluble in chlorohydrocarbons, benzene, and toluene, but however, only sparingly soluble in pentane. The structure of *(4)* was derived from the elemental analysis and spectroscopic data. The IR spectrum, therefore, shows the characteristic pattern of bands for the $(CO)_5CrL$ groups in the $\nu$(CO) - (2081 m, 2001 s, 1995 vs, 1964 vw $cm^{-1}$ (*n*-pentane)), $\delta$(CrCO)- and $\nu$(CrC)-regions. The $^{31}P$-NMR spectrum shows a singlet at $\delta = 178.0$ (0.03 M in toluene, standard: 85% $H_3PO_4$). Apart from the intense signal for the molecular ion *m/z* 762 (47%), fragments, corresponding to a successive loss of all the CO ligands, occur in the EI mass spectrum; only the $M^+$ ion occurs in the FD mass spectrum. The molecular weight (754±3%) was determined cryoscopically in benzene.

Evidence for the formation of free diphosphorus tetrabromide was obtained from the reduction of $PBr_3$ with magnesium in tetrahydrofuran (THF) or with $(C_6H_5P)_5$ in $CS_2$, as well as from the reaction of white phosphorus with $PBr_3$, and of $(Et_2N)_4P_2$ with HBr. In all cases the coupled $^{31}P$-NMR spectrum of the reaction solution temporarily shows a singlet at $\delta \approx 145$ (for comparison: $P_2Cl_4$: $\delta = 155$[7]; $P_2I_4$: $\delta = 106$[5]). A transient signal observed at $\delta = 150$ (in $PBr_3$) in the system $C_2H_4/PBr_3/AlBr_3$ had previously been assigned to $P_2Br_4$[8]. The appearance of the signal in the above mentioned reactions strongly supports the assignment to $P_2Br_4$. Moreover, the low-field shift upon coordination has the expected order of magnitude[3,9].

### *Procedure*

All operations were performed under conditions of rigorous oxygen- and moisture-exclusion.

*(4)*: $Cr(CO)_6$ (5.50 g, 25 mmol) in 370 mL of THF is irradiated in a quartz photoreactor (Fa. Normag, Lampe TQ 150 Original Hanau) for 5.5 h. After dropwise addition of $PBr_3$ (6.77 g, 25 mmol) in 10 mL of benzene over 30 min and being stirred for 2 h, solvent and excess $Cr(CO)_6$ are removed *in vacuo* at room temperature. Toluene (20 mL) is added to the residue, the mixture is cooled to −30 °C for some hours before being filtered at −35 °C. The crystals are washed with a little toluene, and dried *in vacuo* at room temperature; yield 1.3 g, decomp. above *ca.* 130 °C, black coloration at *ca.* 150 °C.

*(4)*: Using liquid-nitrogen cooling, hydrogen bromide (*ca.* 250 mL) is condensed into a solution of *(3)* (804 mg) in 300 mL of toluene. The reaction mixture is stirred constantly and gradually warmed up to room temperature, filtered, concentrated to *ca.* 40 mL, and refiltered. Pentane is added until the solution becomes turbid. Then the mixture is cooled to −35 °C and the crystals are filtered off after 24 h. Total yield (after concentration and recooling of the filtrate) 762 mg (90%).

Received: April 21, 1981 [Z 944 IE]
German version: Angew. Chem. *93*, 1112 (1981)

---

[1] *A. Hinke*, Diplomarbeit, Universität Düsseldorf 1978.
[2] *W. Kuchen, A. Hinke*, unpublished results.
[3] *A. Bohne*, Diplomarbeit, Universität Düsseldorf 1981.
[4] *A. Besson, L. Fournier*, C. R. Acad. Sci. *150*, 102 (1910).
[5] *M. Baudler, P. Junkes, G. Sadri*, Z. Naturforsch. *B 266*, 759 (1971).
[6] *W. Kuchen, J. Kutter*, unpublished results.
[7] *A. A. Sandoval, H. C. Moser*, Inorg. Chem. *2*, 27 (1963).
[8] *R. I. Pyrkin, Ya. A. Levin, E. I. Gol'dfarb*, Zh. Obshch. Khim. *43*, 1705 (1973).
[9] *E. Vincent, L. Verdonck, G. P. van der Kelen*, J. Mol. Struct. *65*, 239 (1980).

---

[*] Prof. Dr. W. Kuchen, Dipl.-Chem. A. Hinke, Dipl.-Chem. J. Kutter
Institut für Anorganische Chemie und Strukturchemie der Universität
Universitätsstrasse 1, D-4000 Düsseldorf (Germany)

## $(Ph_4P)_2[CuCN(MoS_4)]$ and $(Me_4N)_2(CuCN)_2MoS_4$: Thiomolybdate Ligands on the Cu Atoms of a CuCN Molecule and a *zigzag*-CuCN Chain

By *Achim Müller, Mechtild Dartmann, Christian Römer, William Clegg,* and *George M. Sheldrick*[*]

The antagonistic interaction, important in veterinary medicine, between $Cu^{n+}$ and TM ($=MoS_4^{2-}$)—*e.g. via* formation of a "[Cu]TM protein complex"[1] after reab-

---

[*] Prof. Dr. A. Müller, M. Dartmann, C. Römer
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld 1 (Germany)
Prof. G. M. Sheldrick, Dr. W. Clegg
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

sorption—was demonstrated by *Mills* by determining the tissue levels of Cu and Mo in rats which had been given various amounts of $^{64}CuCl_2$ and $(NH_4)_2{}^{99}MoS_4$ in their diet[1].

Our previous investigations showed that a variety of structurally interesting polynuclear Cu complexes are formed[2-4] from $MoS_4^{2-}$ and $Cu^{n+}$ in the presence of triphenylphosphane (and also with $MoOS_3^{2-}$, $WS_4^{2-}$, $WOS_3^{2-}$ and $Ag^+$[2,3]). We have now found that $MoS_4^{2-}$ may also coordinate directly to neutral Cu compounds such as the "CuCN molecule" or an infinite CuCN chain, resulting in the binuclear complex $(Ph_4P)_2[(CuCN)MoS_4]$ *(1)* (Fig. 1) and the *catena*-complex $(Me_4N)_2(CuCN)_2MoS_4$ *(2)* (Fig. 2) with a novel solid-state structure. *(1)* and *(2)* were characterized by full crystal structure determinations[5,6]. The new reactions show that the triphenylphosphane ligand is not essential for the formation of thiomolybdato complexes of copper, which we consider to be models for the $Cu^{n+}$-TM interaction[2,3].

The molecular structure of the binuclear complex anion of *(1)* is shown in Figure 1. It contains a linear Mo···Cu···CN arrangement with almost trigonal-planar coordination of Cu and tetrahedral coordination of Mo.

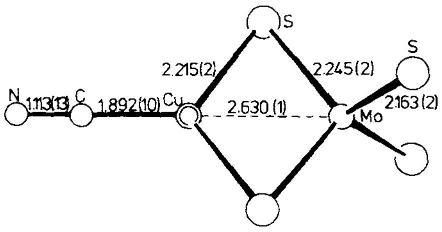


Fig. 1. Structure of the complex anion in crystals of *(1)* (distances in Å).

Infinite chains of complex anions are aligned parallel to the x-axis in the novel solid-state structure of *(2)*. A bidentate $MoS_4^{2-}$ ligand is coordinated to each Cu atom of a zigzag ...CuCNCuCN... chain (angle of fold 107.2(5)°). A further "CuCN molecule" is attached to the free *S*-coordination sites of the thiomolybdate ligand. This results in distorted tetrahedral or trigonal-planar environment for the non-equivalent Cu atoms. The Cu···Mo···CuCN fragment is linear and lies along a crystallographic $C_2$-axis parallel to the z-axis. The complex anion in *(2)* may also be described as a CuCN chain with the binuclear anionic complexes of *(1)* as ligands. The geometrical parameters of the corresponding parts of *(1)* and *(2)* are thus very similar, and have not been given in Figure 2.

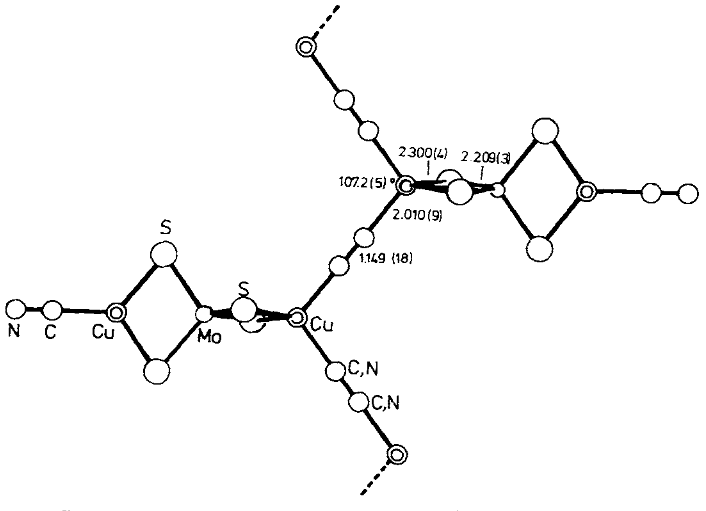


Fig. 2. Partial structure of the complex *catena*-anion in crystals of *(2)*.

The structure may prove illuminating for Cu-Mo-antagonism, because it has been indicated that this arises from the formation of a [Cu]TM-protein complex[1] (blocking of Cu for metabolism by coordination of $MoS_4^{2-}$ to a Cu-carrying protein).

### *Experimental*

*(1)*: $(Ph_4P)_2MoS_4$ (1.6 g) is added to a suspension of CuCN (0.18 g) in 50 mL of $CH_3CN/CH_2Cl_2$ (1 : 1). The reaction mixture is stirred for *ca.* 10 min (until an almost clear solution results). The solution is filtered and *ca.* 28 mL of $Et_2O$ is added (until a slight cloudiness appears). *(1)* precipitates slowly on cooling to *ca.* 5 °C. The red crystals are filtered off, washed with 5 mL of ice-cold $CH_2Cl_2$ and 10 mL of $Et_2O$, and dried in air; yield 1.0 g[7].

*(2)*: $(Me_4N)_2MoS_4$ (0.28 g) and CuCN (0.135 g) in 50 mL of $CH_3CN/CH_2Cl_2$ (1 : 1) are stirred for 60 min in a sealed Erlenmeyer flask. After addition of 5 mL of $Et_2O$, the filtrate is allowed to stand for 2 d in a sealed vessel. The dark brown crystals which precipitate are filtered off, washed with 5 mL of ice-cold acetonitrile and 10 mL of dimethyl ether, and dried in air; yield 0.22 g.

Received: February 11,
in revised form: June 9, 1981 [Z 895a IE]
German version: Angew. Chem. *93*, 1118 (1981)

---

[1] *C. F. Mills*, Chem. Br. *15*, 512 (1979); Philos. Trans. R. Soc. London *B 288*, 51 (1979).

[2] *A. Müller, E. Diemann* in *A. Müller, E. Diemann*: Transition Metal Chemistry: Current Problems of General, Biological and Catalytical Relevance, Verlag Chemie, Weinheim 1981, p. 221.

[3] Cf. *A. Müller, E. Diemann, R. Jostes, H. Bögge*, Angew. Chem. *93*, 957 (1981); Angew. Chem. Int. Ed. Engl. *20*, 934 (1981).

[4] *A. Müller, H. Bögge, H. G. Tölle, R. Jostes, U. Schimanski, M. Dartmann*, Angew. Chem. *92*, 665 (1980); Angew. Chem. Int. Ed. Engl. *19*, 654 (1980); *A. Müller, H. Bögge, U. Schimanski*, J. Chem. Soc. Chem. Commun. *1980*, 91; Inorg. Chim. Acta *45*, L249 (1980).

[5] *(1)* (structure determination in Bielefeld): Space group C2/c, $a=1119.3(1)$, $b=2013.0(4)$, $c=2023.7(3)$ pm, $\beta=91.66(1)°$, $Z=4$; 3959 reflections with $I \geq 1.9\sigma(I)$, $R=0.071$.

[6] *(2)* (structure determination in Göttingen): Space group $I2_12_12_1$, $a=815.7(2)$, $b=1201.9(2)$, $c=2139.6(4)$ pm, $Z=4$; 1094 reflections with $I \geq 1.5\sigma(I)$, $R=0.061$. The C and N atoms in the *zigzag* chain are disordered (refined as $C_{1/2}N_{1/2}$).

[7] The complex anion of *(1)* was also obtained by another method (*A. G. Wedd*, personal communication; see also *S. F. Gheller et al.* Inorg. Chim. Acta *54*, L 131 (1981). We could prepare the corresponding Ag compounds of *(1)* with $MoS_4^{2-}$ and $WS_4^{2-}$ ligands having the same molecular but different crystal structures (space group $P2_1/C$), too.

---

## Determination of the Structure of New Tetrathiomolybdato Complexes of $Fe^{II}$, $Cu^I$ and $Ag^I$ by the Resonance Raman Effect: Textbook Examples for its Application in Coordination Chemistry

By *Achim Müller, Anne-Marie Dommröse,*
*Wolfram Jaegermann, Erich Krickemeyer,*
and *Sabyasachi Sarkar*[*]

The relevance of $MoS_4^{2-}$ to the MoFe cofactor[1,2] of nitrogenase (or its model compounds) and to Cu-Mo antag-

---

[*] Prof. Dr. A. Müller, A. M. Dommröse, Dipl.-Chem. W. Jaegermann, E. Krickemeyer, Dr. S. Sarkar
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld 1 (Germany)

onism[3] has frequently been pointed out. We report here the syntheses of new tetrathiomolybdato (TM) complexes of iron and silver and the structural characterization of these and related complexes by the Resonance Raman Effect (RRE). Using this method the ***influence of the nearest and next nearest neighbors on the vibrations of the ligand chromophore*** is investigated. For this purpose, TM complexes can be regarded as particular textbook examples (high symmetry of the free ligand, which has a very intense electronic transition in the VIS range and unique electronic properties[1,2]).

Apart from $MoS_4^{2-}$, species with $FeS_2MoS_2$ groups are probably also formed upon hydrolysis of the MoFe protein of nitrogenase[1a]. For the synthesis of the cofactor[1a], precursors with high Fe content, *e.g.* $[Fe(DMSO)_6][(Cl_2Fe)MoS_4]$ *(1)* are probably particularly suitable. In the $M^+$ ($M^+ = Cu$, Ag)/$PPh_3$(=L)/TM system, various multinuclear complexes are formed[1b,2], but only with $Ag^+$ the "symmetrical" trinuclear complex[2] $L_2AgMoS_4AgL_2$ *(2)* (with a doubly bridging TM ligand), the synthesis of which is described here for the first time.

Figure 1 shows the resonance Raman spectra (cf. [4]) of *(1)* and *(2)* as well as those of $L_2CuMoS_4CuL$ *(3)*[2] and $(Me_4N)_2(CuCN)_2MoS_4$ *(4)*[5]. The spectra of the compound $L_2AgMoS_4AgL$ *(5)*[2], which is analogous to *(3)*, as well as those of $(Ph_4P)_2[(CuCN)MoS_4]$ *(6)*[5] were recorded. The intensities of bands due to the totally symmetric vibrations of the TM ligands[8] were strongly enhanced (solid samples, rotating cell technique) using the 488 nm line of an Ar ion laser which lies within the absorption bands of the ligand internal charge-transfer transitions of the $MoS_4^{2-}$ chromophores[2,6] (for all the complexes and for $MoS_4^{2-}$ [7] at *ca.* 470 nm[6]). Using the same excitation line, resonance Raman spectra can also be obtained for $MoOS_3^{2-}$ and $ReS_4^-$ [2,7] and their complexes.

The intensity enhancement as well as the number of overtone bands is especially remarkable for complexes with high local ligand symmetry (especially for *(2)*, but also for *(3)*, *(4)*, and *(5)*) (Fig. 1). In *(5)* one finds $\nu_1 = 442$, $2\nu_1 = 882$, $3\nu_1 = 1320$, $4\nu_1 = 1760$, $5\nu_1 = 2200$, $\nu^* = 460$, $\nu_1 + \nu^* = 900$, $2\nu_1 + \nu^* = 1340\,cm^{-1}$ (see below). The structures or structural fragments in Figure 1 result from the analysis of the spectra.

*Influence of the nearest neighbors:* The spectra of species with only one coordinated metal atom (local $C_{2v}$ symmetry of the $MS_2MoS_2$ fragment), as in *(1)* or *(6)*, show characteristic bands due to the totally symmetric vibrations of the terminal *and* bridging $MoS_2$ groups[9] (stretching ($\nu$), as well as bending vibrations ($\delta$)), and also of the corresponding combination and overtone bands. The complexes with two coordinated metal atoms, *i.e.* with equivalent (as in *(2)*) or almost equivalent Mo—S bonds (as in *(3)* to *(5)*), *i.e.* with local $D_{2d}$ symmetry of the $MS_2MoS_2M$ fragment, show (as expected) strong symmetrical stretching vibration bands ($\nu$) as well as bands of the corresponding overtones (cf. Fig. 1).

*Influence of the next nearest neighbors:* The deviation from "$D_{2d}$ symmetry" (nearly $C_{2v}$ for the extended fragment $P_2MS_2MoS_2MP$) can clearly be recognized in the compounds *(3)* and *(4)*, which are unsymmetrically substituted at Cu and Ag, respectively, (therefore *and* because of the stoichiometry *(4)* should crystallize in a novel solid-state structure with unsymmetrically coordinated Cu atoms[5]), and especially in *(5)* (cf. hatched overtones in Fig. 1) but not in *(2)*, since on the high energy side of the bands of the different overtones weak features appear that can approximately be assigned to combination bands of the type $n\nu_1(A_1) + \nu^*(A_1)$ (assuming $C_{2v}$ symmetry for the

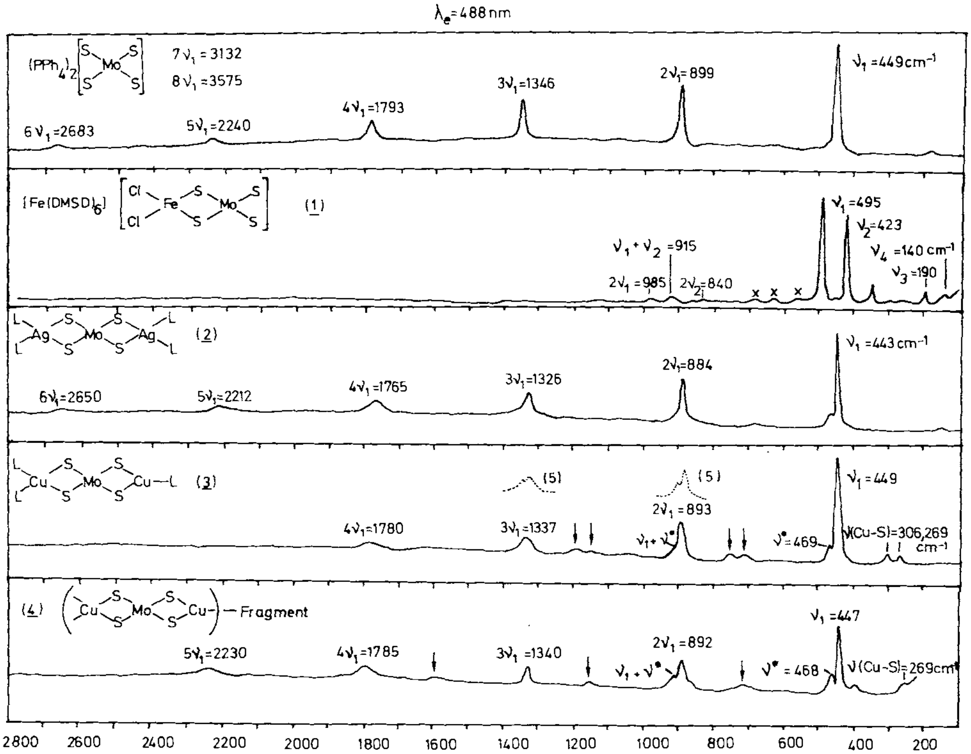


Fig. 1. Resonance Raman spectra of $MoS_4^{2-}$ (without overtones and combination bands [2, 7]), *(2)*, *(3)*, and *(4)* with symmetrically and unsymmetrically coordinated $MS_2MoS_2M$ moieties (local $D_{2d}$ symmetry; $\Gamma_{sym}(\nu) = 1A_1$; $\nu_1 = \nu_s(MoS)$) as well as of *(1)* [9] with an $MS_2MoS_2$ moiety (local $C_{2v}$ symmetry; $\Gamma_{sym}(\nu,\delta) = 4A_1$; $\nu_1 = \nu_s(MoS^t)$, $\nu_2 = \nu_s(MoS^b)$, $\nu_3 = \delta(MoS_2^t)$, $\nu_4 = \delta(MoS_2^b)$. ×: combination bands of $\nu$ and $\delta$, ↓: combination bands of $\nu_s(CuS)$ with $n_i\nu_1(MoS)$ [10].

extended fragments; for the transition $D_{2d} \rightarrow C_{2v}$ the correlation $B_2 \rightarrow A_1$ holds). Unnambiguous proof of the structure of the symmetrically coordinated trinuclear complex *(2)* (Fig. 1), for which suitable single crystals for a crystal structure determination could not be obtained, was therefore acheived[10].

### *Experimental*

*(1):* $FeCl_2 \cdot 4H_2O$ (1.2 g) is added to a stirred solution of $(NH_4)_2MoS_4$ (0.52 g) in 50 mL of dimethyl sulfoxide (DMSO). The solution is heated to 40°C for 5 min, then cooled to room temperature. After addition of 5 mL of $CH_2Cl_2$, the solution is filtered and the filtrate kept in the refrigerator for 12 h, whereby deep red crystals separate out; these were filtered, washed with $CH_2Cl_2$, and dried over $P_4O_{10}$. Yield 1.2 g [Space group $P\bar{1}$, $a = 855.8(2)$, $b = 999.5(2)$, $c = 1035.0(2)$ pm, $\alpha = 86.89(2)$, $\beta = 89.78(2)$, $\gamma = 89.62(2)°$, $Z = 2$; 3500 observed reflections, $R = 0.069$; Fe—Mo 277.5 pm; statistical disorder[2] of $X_2M'S_2MX'_2$ ($X'/X = Cl, S$; $M'/M = Fe, Mo$): Fe(Mo)—$S_{br}$ 226.8 pm].

*(2):* A solution of $(NH_4)_2MoS_4$ (0.22 g) in 100 mL of $H_2O$ is extracted with a solution of 0.21 g $AgNO_3$ and 0.73 g $PPh_3$ in 25 mL of $CH_2Cl_2$ for 3 min. The organic phase is filtered off and $PPh_3$ (6 g) added. A mixture of acetone/*n*-pentane (10 mL/50 mL) is slowly added to the $CH_2Cl_2$ so that two layers result. After 2 d, red needles of *(2)* separate out. Yield 0.25 g.

Received: February 11,
in revised form: June 9, 1981 [Z 895b IE]
German version: Angew. Chem. *93*, 1119 (1981)

---

[1] *E. I. Stiefel*, in *M. P. Coughlan:* Molybdenum and Molybdenum Containing Enzymes, Pergamon Press, New York 1980; b) *A. Müller, E. Diemann:* Transition Metal Chemistry: Current Problems of General, Biological and Catalytical Relevance, Verlag Chemie, Weinheim 1981 (contributions from *D. Coucouvanis*, as well as *A. Müller, E. Diemann*).

[2] Cf. *A. Müller, E. Diemann, R. Jostes, H. Bögge*, Angew. Chem. *93*, 957 (1981); Angew. Chem. Int. Ed. Engl. *20*, 934 (1981).

[3] a) *C. F. Mills*, Chem. Br. *15*, 512 (1979); b) Philos. Trans. R. Soc. London *B 288*, 51 (1979).

[4] *R. J. H. Clark* in *F. J. Comes, A. Müller, W. J. Orville-Thomas:* Spectroscopy in Chemistry and Physics: Modern Trends, Elsevier, Amsterdam 1980.

[5] *A. Müller, M. Dartmann, C. Römer, W. Clegg, G. M. Sheldrick*, Angew. Chem. *93*, 1118 (1981); Angew. Chem. Int. Ed. Engl. 1060 (1981).

[6] *A. Müller, E. Diemann, C. K. Jørgensen*, Struct. Bonding *14*, 23 (1973).

[7] The spectrum of $MoS_4^{2-}$ shows more details than those previously published by us and other authors [2], since an optimal RRE can be observed with $PPh_4^+$ salts or salts of this type with bulky cations (*e.g.* for $Ph_4P(ReS_4)$ overtones up to $10\nu_1(A_1)$ [2] and for $(Ph_4P)_2MoS_4$ also several combination band progressions with $\lambda_e = 488$ nm excitation which was also used for all other spectra of Fig. 6 in [2]).

[8] *K. H. Schmidt, A. Müller*, Coord. Chem. Rev. *14*, 115 (1974).

[9] The spectrum of *(6)* ($\nu_1 = 482$, $\nu_2 = 418$, $\nu_3 = 205$, $\nu_4 = 151$, $\nu(CuS) = 288$ $cm^{-1}$) corresponds to that of *(1)* with regard to the sequence of the main bands. The presence of $(Ph_4P)_2MoS_4$ (in a probably distorted crystal lattice), for which the RRE is considerably stronger (see text), leads to a band at 447 $cm^{-1}$.

[10] The interpretation of other features (combination bands of the $MoS_4^{2-}$ chromophore, weak bands of other vibrations *e.g.* of $\nu(CuS)$, and especially of combination bands of the type $\nu(CuS) + n_i\nu_1(MoS)$) for the investigation of the electronic structure of these multi-metal complexes is also interesting. The appearance of the combination bands of the latter type proves impressively the strong electronic interaction of $Cu^+$ and $MoS_4^{2-}$ in *(3)*, *(4)*, and *(6)*, which also follows from EH-SCCC-MO-calculations.

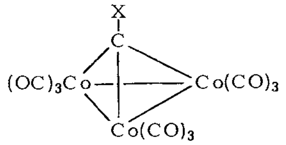
---

## Hydroformylation of Alkylidyne(nonacarbonyl)tricobalt Clusters: Model Reaction for the Direct Conversion of Synthesis Gas into $C_1$- and $C_2$-Oxygenated Compounds[**]

By *Giuseppe Fachinetti, Raffaello Lazzaroni,* and *Sergio Pucci*[*]

The spectroscopic and structural properties[1] of $(CO)_9Co_3C—OH$ *(1)* define this compound as a member of the well known family of alkylidyne(nonacarbonyl)tricobalt clusters[3], which have previously been photochemically hydrogenated[2]. *Bergman* and *Stuhl*[4] have shown that the complex $(CO)_9Co_3CR$ is thermally converted by hydrogen into alkanes, alkenes, $Co_4(CO)_{12}$ and traces of cobalt metal. These observations and the fact that *(1)* exists in equilibrium with $HCo(CO)_4$ and $Co_2(CO)_8$[5] persuaded us to assume *(1)* as being a possible intermediate in the hydrogenation of CO in the homogeneous phase, in the presence of carbonylcobalt compounds, carried out by *Rathke* and *Feder*[6].

In an attempt to gain support for this hypothesis, we investigated the reactions of the alkylidene complexes *(2)*—*(4)*[7] with synthesis gas at high temperatures and pressures in the presence of $Co_2(CO)_8$: like *(1)*, compounds *(2)*, do not react with $CO/H_2$ to give alkenes and, hence, have been considered by us to be model compounds for the labile *(1)*.



*(1)*, X = OH
*(2)*, X = $OCH_3$
*(3)*, X = H
*(4)*, X = D
*(5)*, X = $CH_3$
*(6)*, X = *n*-$C_4H_9$

The methoxy derivative *(2)*, whose IR spectrum in the CO stretching region is superimposable on that of *(1)*, reacted completely with $CO/H_2$ (xylene, $Co_2(CO)_8$, *ca.* 115 bar, 10 h, 120°C). No precipitate was observed, the only carbonyl compounds detected at the end of the reaction being $HCo(CO)_4$ and $Co_2(CO)_8$. The organic products were identified as dimethyl ether and 2-methoxyethanol (1:10)—apart from varying amounts of 2-methoxyethyl formate—corresponding to methanol and ethylene glycol, respectively, two of the products of the catalytic CO-hydrogenation[6].

$$(2) \xrightarrow[Co_2(CO)_8]{CO/H_2} H_3COCH_3 + H_3COCH_2CH_2OH + H_3COCH_2CH_2OCHO$$

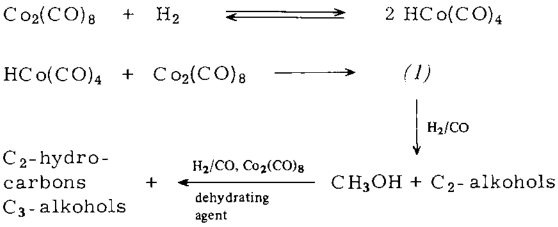
These results indicate that the intermediary occurrence of the hydroxymethylidyne cluster *(1)* in the CO hydrogenation could not only explain the formation of methanol

---

[*] Dr. G. Fachinetti [+]
Istituto di Chimica Generale, Università di Pisa
Via Risorgimento 35, I-56100 Pisa (Italy)
Dr. R. Lazzaroni, Dr. S. Pucci
Centro di studio del C.N.R. per le Macromolecole
Stereordinate ed Otticamente Attive
Via Risorgimento 35, I-56100 Pisa (Italy)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the National Research Council (C.N.R., Roma). The authors wish to thank Dr. *L. Kaplan* for helpful discussions.

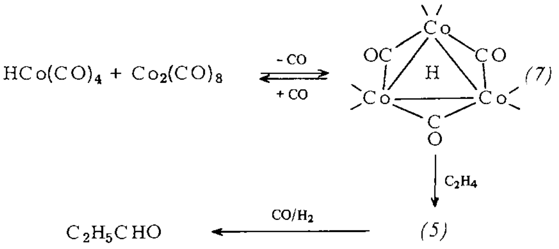
but also that of $C_2$-alcohols; higher homologues could form in the presence of a dehydrating agent and under oxo-synthesis conditions (Scheme 1).



Scheme 1. Possible mechanism for the Fischer-Tropsch reaction: a sequence of hydroformylation steps.

A sample withdrawn after 4 h contained methoxyacetaldehyde, presumably the precursor of 2-methoxyethanol. In addition, the reaction of *(3)* and *(4)* with syngas, which proceeds under milder conditions, affords $CH_3CHO$ and $CH_2DCHO$ in quantitative yields, thus confirming that aldehydes and, under more drastic conditions, alcohols and alkanes are generated from alkylidine complexes without the intermediacy of alkenes. The previously reported formation of propionaldehyde[8] from $Co_3CH_3C(CO)_9$ and syngas could be considered as a special case of the general reaction.

The unsaturated 46e trinuclear cluster $HCo_3(CO)_9$ *(7)* reacts with acetylene[9] and—presumably with $H_2$ evolution — with ethylene to give $(CO)_9Co_3CCH_3$ *(5)*; with terminal alkynes and alkenes[10], *(7)* reacts to give the corresponding alkylidine complexes. *(7)* can also be obtained from $HCo(CO)_4/Co_2(CO)_8$ solutions[5]. On these grounds the following multi-step hydroformylation of alkenes is plausible.



Scheme 2. Possible mechanism for the hydroformylation of alkenes (oxo synthesis).

The reaction of the pentylidene clusters *(6)*[12] with syngas yield, apart from 5% *n*-pentane, 76% of oxygenated $C_6$-products, whereby the ratio normal : branched is 3.4—a value similar to that found for the hydroformylation of 1-pentene by carbonylcobalt compounds[11]. This result can be interpreted in several ways: 1) Alkenes and the corresponding alkylidynes generate, under oxo synthesis conditions, the same reactive intermediate. 2) The hydroformylation of alkylmethylidynes proceeds *via* alkenes. 3) Alkylidyne complexes occur as intermediates in the oxo synthesis. Further investigations are necessary to verify these hypotheses.

## *Procedure*

All investigations were carried out in a 50 mL steel autoclave equipped with a siphon to withdraw liquid samples: the vessel was charged with 15 mL of a *p*-xylene (toluene for *(6)*) solution containing 3 mmol of the alkylidyne complex $Co_2(CO)_8$ (1.5 mmol), and syngas. The disappearance of the alkylidyne complex was followed by thin layer chromatography (silica gel, *n*-hexane). The carbonyl complexes were identificated by IR spectroscopy and the organic products by mass spectroscopy (GC-MS). Yields of organic products were obtained by GC-comparison with standard solutions. *(2)—(4)* were prepared and purified as described in [7]. *(6)*, prepared as described in [12] was purified by chromatography (silica gel/*n*-hexane) and then sublimed.

## *Reaction of (2)—(4) and (6) with syngas:*

*(2):* The reaction was complete after 15 h at 120 °C and *ca.* 115 bar syngas. A sample withdrawn after 4 h contained — apart from traces of $CH_3OCH_2CH_2OH$ — $CH_3OCH_2CHO$, $CH_3OH$, and $CH_3OCH_3$ (10 : 1 : 1). The final composition of the solution was $CH_3OCH_2CH_2OH$ (60% yield), $CH_3OCH_3$ (6%), $CH_3OCH_2CH_2CHO$ (10%). The products must be analyzed immediately after sampling, since the concentration of alcohols rapidly decreases upon exposure to air. The possible presence of small amounts of $CH_4$ was not checked.

*(3):* The reaction was complete after 45 min at 100 °C and *ca.* 95 bar syngas. $CH_3CHO$ was produced as final product in quantitative yield.

*(4):* Conditions similar to *(3)*. On the basis of the mass spectra the maximum amount of non-deuterated aldehyde is 30%; $CH_3CDO$ was not formed.

*(6):* The reaction was complete after 15 h at 120 °C and 120 bar syngas. A sample withdrawn after 3 h contained 1-hexanal and 2-methylpentanal (3.4 : 1). At the end of the reaction the product composition was thus: 1-hexanol (58% yield), 2-methylpentanol (17%), *n*-pentane (5%), 1-hexanal (1%), and 2-methylpentanal (trace).

Received: May 4, 1981 [Z 932 IE]
German version: Angew. Chem. *93*, 1097 (1981)

CAS Registry numbers:
*(1)*, 71032-29-6; *(2)*, 41751-68-2; *(3)*, 15664-75-2; *(4)*, 31886-81-4; *(5)*, 13682-04-7; *(6)*, 13682-06-9; *(7)*, 71204-90-5; $H_2$, 1333-74-0; CO, 630-08-0

---

[1] *H. N. Adams, G. Fachinetti, J. Strähle*, Angew. Chem. *93*, 94 (1981); Angew. Chem. Int. Ed. Engl. *20*, 125 (1981).
[2] *G. L. Geoffroy, R. A. Epstein*, Inorg. Chem. *16*, 2795 (1977).
[3] *D. Seyferth*, Adv. Organomet. Chem. *14*, 97 (1976).
[4] *R. Bergman, L. S. Stuhl*, personal communication to *E. L. Muetterties* cited in *E. L. Muetterties, J. Stein*, Chem. Rev. *79*, 479 (1979).
[5] *G. Fachinetti, L. Balocchi, F. Secco, M. Venturini*, Angew. Chem. *93*, 215 (1981); Angew. Chem. Int. Ed. Engl. *20*, 204 (1981).
[6] a) *J. W. Rathke, H. M. Feder*, J. Am. Chem. Soc. *100*, 3623 (1978); b) *H. M. Feder, J. W. Rathke*, Ann. N. Y. Acad. Sci. *333*, 45 (1980).
[7] *D. Seyferth, J. E. Hallgren, P. L. K. Hung*, J. Organomet. Chem. *50*, 265 (1973).
[8] *K. Tominaga, N. Yamagami, H. Wakamatsu*, Tetrahedron Lett. *25*, 2217 (1970).
[9] *G. Fachinetti, S. Pucci, P. F. Zanazzi, U. Methong*, Angew. Chem. *92*, 657 (1979); Angew. Chem. Int. Ed. Engl. *18*, 619 (1979).
[10] *G. Fachinetti*, unpublished results. – This observation was made when propylene and 3-methylpentyne were used.
[11] For a recent review on the oxo synthesis: *P. Pino, F. Piacenti, M. Bianchi* in *I. Wender, P. Pino:* Syntheses *via* Metal Carbonyls. Vol. 2. New York 1977, pp. 43—231; see also *R. C. Ryan, C. U. Pittmann Jr., J. P. O'Connor*, J. Am. Chem. Soc. *99*, 1986 (1977).
[12] *R. Markby, I. Wender, R. A. Friedel, F. A. Cotton, H. W. Sternberg*, J. Am. Chem. Soc. *80*, 6529 (1958).

**Molecular Shapes—Theoretical Models of Inorganic Stereochemistry.** By *J. K. Burdett*. J. Wiley & Sons, Chichester 1980. x, 287 pp., bound, £ 15.75.

Qualitative comprehensive concepts for the theoretical understanding and systematization of the structure and stereochemistry of molecules are certainly as important as the further development of "exact" quantum-chemical methods of calculation. A clearcut example are the Woodward-Hoffmann rules and all their consequences for development and cross-fertilization of organic and theoretical chemistry.

*Burdett*'s interesting little book, written in response to the explosively growing number of structure determinations and structural types, attempts a review of the most important qualitative and semiquantitative theoretical concepts for describing the bonding relationships and stereochemistry of inorganic and organometallic molecules. The author does not address himself so much to specialists, *i.e.* theoreticians or structural chemists (for whom, however, the book can serve as a useful synopsis) as to experimental chemists, teachers, and advanced students. Mindful of the need for "simple" theories on the basis of qualitative MO concepts and relying on arguments of perturbation theory and symmetry considerations as method-independent as possible, *Burdett* gives a review that is successful in its total impression without succumbing to the danger of losing sight of the limits of application and the often limited informative value of the various simple theoretical approaches. The reader is assumed to have little general basic theoretical knowledge, and the material is presented with the help of numerous examples.

After a brief introduction into the fundamentals of perturbation theory and MO theory (description of simple approximate MO methods) and the angular overlap model (which the author considers particularly useful), the first main part of the book (Chapters 3—7) deals with model ideas of structure theory for main-group molecules $AY_n$. Following a description of the VSEPR (valence shell electron pair repulsion) model and the well-known VB description of molecular geometries with directed hybrid orbitals, stereochemical statements are developed on the basis of qualitative one-electron MO's and Walsh diagrams. This chapter has been kept relatively short, and probably deliberately so, as a really exhaustive treatment of the subject can be found in a recent book by *Gimarc*. After a quite detailed and clear description of the Jahn-Teller effect of first and second order on molecular geometry, there is a chapter explaining simple semiquantitative derivations of molecular structures from the angular overlap model. Critical evaluations of bonding concepts in structural isomerisms, comments on σ-bonding effects and steric influences, and also a glimpse at some results of quantitative MO calculations complete the main-group part of the book. The author then turns to the stereochemistry of transition-metal systems (Chapters 8—13), presents the principles of crystal field theory, and uses for describing transition-metal-ligand interactions and their stereochemical consequences the methods already used for main-group molecules. The geometry of excited states, σ- and π-bonding effects in transition-metal complexes, and thermodynamic properties are interpreted on the basis of MO theory. Particularly worth reading is Chapter 13, in which with readily understandable PMO analyses based on the results of quantitative calculations, a substantially more detailed picture of the molecular orbitals of transition-metal complexes or of common metal-ligand fragments is developed than would be possible with the angular overlap model. Statements on electronic structure and stereochemistry are then derived from shape (hybridization) and energy of the valence orbitals.

The last two chapters of the book deal with the structure of rings, cage compounds, clusters, and solids; the author's results cited here form a connection with the ideas of MO theory developed on and applied to simple molecules.

Apart from the often somewhat small figures, *Burdett*'s book is very readable and free from ballast. The construction is clear. Each chapter is preceded by a short summary and statement of its aims. The book can certainly fulfil its purpose stated in the preface, which in itself is well worth reading, namely to contribute to the qualitative understanding of molecular structures with the aid of simple theoretical models. It would be desirable to give the book a firm place in chemical education.

*Peter Hofmann* [NB 546 IE]

**Recent Books**

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

**Polymer Chemistry.** An Introduction. By *R. B. Seymour* and *C. E. Carraher, Jr.* Marcel Dekker, Basel 1981. xvi, 564 pp., bound, SFr. 80.00.—ISBN 0-8247-6979-1

**Synthetic Reagents. Vol. 4.** Mercuric Acetate, Periodic Acid and Periodates, Sulfuryl Chloride. Edited by *J. S. Pizey*. John Wiley & Sons, Chichester 1981. 426 pp., bound, £ 32.50.—ISBN 0-470-27133-7

**Progress in Pesticide Biochemistry. Vol. 1.** Edited by *D. H. Hutson* and *T. R. Roberts*. John Wiley & Sons, Chichester 1981. xi, 346 pp., bound, £ 24.00.—ISBN 0-471-27290-X

**Handbuch der Präparativen Anorganischen Chemie, Vol. 3.** Edited by *G. Brauer*. Enke Verlag, Stuttgart 1981. 3rd Edit. xiv, pp. 1407—2113, bound, DM 288.00 (all three volumes must be orded).—ISBN 3-432-87823-0

**Oxygen and Life. Second BOC Priestley Conference.** Issued by The Royal Society of Chemistry, London 1981. Special Publication No. 39. xii, 224 pp., bound, £ 11.00.—ISBN 0-85186-825-8

**Aliphatic and Related Natural Product Chemistry. Vol. 2.** Senior Reporter: *F. D. Gunstone*. The Royal Society of Chemistry, London 1981. xiii, 265 pp., bound, £ 40.00.—ISBN 0-85186-652-2.—A volume of the series "Specialist Periodical Reports"

**Inorganic Biochemistry. Vol. 2.** Senior Reporter: *H. A. O. Hill.* The Royal Society of Chemistry, London 1981. xiv, 347 pp., bound, £ 40.00.—ISBN 0-85186-555-0.—A volume of the series "Specialist Periodical Reports"

**Messen, Steuern und Regeln in der Chemischen Technik.** Edited by *J. Hengstenberg, B. Sturm,* and *O. Winkler.* Springer-Verlag, Berlin 1981. 3rd revised edit. xii, 500 pp., bound, DM 210.00.—ISBN 3-540-10092-X

**Methoden der Organischen Chemie.** In 16 volumes. Vol. IV/1d: Reduktion, Teil II. Edited by *H. Kropf.* Thieme Verlag, Stuttgart 1981. 4th completely new edit. *Ca.* 1000 pages, bound, *ca.* DM 780.00.—ISBN 3-13-201104-5

**Elektrochemie II.** Elektrodenprozesse, Angewandte Elektrochemie. Taschentext 42. By *C. H. Hamann* and *W. Vielstich.* Verlag Chemie, Weinheim 1981. xv, 428 pp., bound, DM 52.00.—ISBN 3-527-21081-4

**Lexikon alchemistisch-pharmazeutischer Symbole.** By *W. Schneider.* Verlag Chemie, Weinheim 1981. 2nd edit. 140 pp., bound, DM 38.00.—ISBN 3-527-25898-1

**Polarographische Analyse.** By *M. Geissler.* Verlag Chemie, Weinheim 1981. 1st edit. 194 pp., bound, DM 73.00.—ISBN 3-527-25887-6

**Hazards in the Chemical Laboratory.** Edited by *L. Bretherick.* The Royal Society of Chemistry, London 1981. 3rd edit. xxi, 567 pp., bound, £ 15.00.—ISBN 0-85186-419-8

**Reactivity of Metal-Metal Bonds.** ACS Symposium Series No. 155. Edited by *M. H. Chisholm.* American Chemical Society, Washington 1981. 327 pp., bound, $ 39.00.—ISBN 0-8412-0624-4

**Handbook of Automated Analysis.** Continuous Flow Techniques. By *W. A. Coakley.* Marcel Dekker, Basel 1981. xii, 144 pp., loose-leaf SFr. 55.00.—ISBN 0-8247-1392-3

**Dielectric Properties of Binary Solutions.** A Data Handbook. By *Y. Y. Akhadov.* Pergamon Press, New York 1981. 475 pp., bound, $ 112.50.—ISBN 0-08-023600-6

**Analytical Chemistry of Polycyclic Aromatic Compounds.** By *M. L. Lee, M. V. Novotny,* and *K. D. Bartle.* Academic Press, New York 1981. xi, 462 pp., bound, $ 60.00.—ISBN 0-12-440840-0

**A Guidebook to Mechanism in Organic Chemistry.** By *P. Sykes.* Longman, London 1981. 5th edit. 397 pp., bound, £ 6.95.—ISBN 0-582-44121-8

**Im Schatten der Sensation—Leben und Wirken von Fritz Strassmann.** Portrayed by *F. Krafft* after documents and records. Verlag Chemie, Weinheim 1981. xvii, 541 pp., bound, DM 150.00.—ISBN 3-527-25818-3

**Natural Products as Medicinal Agents.** Edited by *J. L. Beal* and *E. Reinhard.* Hippokrates Verlag, Stuttgart 1981. 528 pp., bound, DM 98.00.—ISBN 3-7773-0540-5

**Structure and Bonding, Vol. 45: Breakdown of the One-Electron Pictures in Photoelectron Spectra.** By *G. Wendin.* Springer-Verlag, Berlin 1981. vii, 130 pp., bound, DM 66.00.—ISBN 3-540-10584-0

**Air Pollution Control Equipment.** By *H. Brauer* and *Y. B. G. Varma.* Springer-Verlag, Berlin 1981. vii, 388 pp., bound, DM 196.00.—ISBN 3-540-10463-1

**Analytiker-Taschenbuch Band 2.** Edited by *R. Bock, W. Fresenius, H. Günzler, W. Huber,* and *G. Tölg.* Springer-Verlag, Berlin 1981. viii, 351 pp., bound, DM 78.00.—ISBN 3-540-10338-4

**Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden. Anleitungen für die chemische Laboratoriumspraxis, Band 15.** By *E. Pretsch, T. Clerc, J. Seibl,* and *W. Simon.* Springer-Verlag, Berlin 1981. 2nd edit. ix, 316 pp., bound, DM 39.80.—ISBN 3-540-10556-5

**Bioorganic Chemistry.** A Chemical Approach to Enzyme Action. By *H. Dugas* and *C. Penney.* Springer-Verlag, Berlin 1981. xii, 508 pp., bound, DM 59.00.—ISBN 3-540-90491-3

**Annual Reports on NMR Spectroscopy. Vol. 11A.** Edited by *G. A. Webb.* Academic Press, London 1981. x, 282 pp., bound, £ 35.00.—ISBN 0-12-505311-8

**Lectins—Biology, Biochemistry, Clinical Biochemistry. Vol. 1.** Proceedings of the Third Lectin Meeting. Edited by *T. C. Bog-Hansen.* W. de Gruyter, Berlin 1981. xii, 418 pp., bound, DM 120.00.—ISBN 3-11-008483-X

**Der historische Weg der Chemie, Band I und II.** By *W. Strube.* VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1981. Band I: 3rd edit. 192 pp., bound, DM 21.00; Band II: *Ca.* 224 pp., bound, *ca.* DM 23.50.

---

**Editorial office:** Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany, Telephone (06201) 602-1, Telex 465516 vchwh d.

**Editor:** *O. Smrekar,* **Translation Editors:** *I. G. Neil* and *A. Stimson.*

**Publishers:** Verlag Chemie GmbH. (Managing Director *Dr. Helmut Grünewald*) Pappelallee 3, D-6940 Weinheim, Federal Republic of Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Federal Republic of Germany, Telephone Weinheim (06201) 602-1, Telex 465516 vchwh d.

# AUTHOR INDEX

G.E. = Reference to Volume *93* (1981) of the German Edition of Angewandte Chemie. References are given for Review Articles and Short Communications only.—No "G.E." reference is given for a Book Review.

# SUBJECT INDEX

FP = Full paper (review article) SC = Short communication
G.E. = Reference to Volume *93* (1981) of the German Edition of Angewandte Chemie
References are given for Review Articles and Short Communications only.